Top 2020 studies relevant to primary care

From the PEER team

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Abstract

Objective To summarize high-quality studies for 10 topics from 2020 that have strong relevance to primary care practice.

Selecting the evidence Study selection involved routine literature surveillance by a group of primary health care professionals. This included screening abstracts of high-impact journals and EvidenceAlerts, as well as searching the American College of Physicians Journal Club.

Main message Topics of the 2020 articles most likely to affect primary care practice included whether antibiotic prophylaxis reduces maternal infections following operative vaginal birth; which second-line agent after metformin reduces cardiovascular outcomes for patients with diabetes; whether gabapentin is effective for alcohol use disorder; whether compression stockings prevent recurrent cellulitis; guideline recommendations for management of dyslipidemia to reduce cardiovascular risk; whether intermittent fasting is superior to consistent mealtimes for weight loss; whether vitamin C added to iron supplementation increases hemoglobin more than iron alone; whether antacid-lidocaine combinations are superior to antacid alone for epigastric pain; whether dapagliflozin improves renal and cardiovascular outcomes in chronic kidney disease; and whether empagliflozin improves cardiovascular outcomes in patients with heart failure. Five "runner-up" studies are also briefly reviewed.

Conclusion Research from 2020 produced several high-quality studies in diabetes and cardiovascular disease, but also included a variety of other conditions relevant to primary care such as vaginal operative births, alcohol use disorder, weight loss, and chronic leg edema.

An overwhelming number of studies relevant to primary care are published every year, making it challenging for family physicians to keep up to date with the literature. We have summarized our top 10 articles from 2020, along with 5 "runners-up" that we thought would offer value for physicians within a comprehensive family medicine practice.

Selecting the evidence

The PEER (Patients, Experience, Evidence, Research) team identified studies by routine literature surveillance of the table of contents from high-impact medical journals (eg, *New England Journal of Medicine* and *Lancet*). We also regularly reviewed EvidenceAlerts[1] and the American College of Physicians Journal Club, both of which identify highly rated articles relevant to primary care. The studies were then ranked by our team. All results are statistically significant unless otherwise noted.

Editor's key points

- Staying apprised of 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 topics (and 5 runners-up) of 2020 that could have meaningful effects on comprehensive family medicine practice.
- Topics include antibiotic prophylaxis following operative vaginal birth; second-line agents for patients with diabetes; gabapentin for alcohol use disorder; compression stockings for recurrent cellulitis; guideline recommendations for management of dyslipidemia; intermittent fasting compared with consistent mealtimes for weight loss; vitamin C added to iron supplementation; antacid-lidocaine combinations versus antacid alone for epigastric pain; dapagliflozin in chronic kidney disease; and empagliflozin in patients with heart failure.
- Runners-up include alcohol abstinence in atrial fibrillation; turmeric for osteoarthritis pain; vitamin D for children and for other indications; physical therapy versus steroid injections for knee osteoarthritis; and colchicine for coronary artery disease.

Main message

Does antibiotic prophylaxis reduce maternal infection following operative vaginal birth?

Bottom line: A single dose of intravenous amoxicillin and clavulanic acid given within 6 hours after operative (vacuum- or forceps-assisted) birth reduces maternal infections, perineal problems, health care visits, and costs.[2]

Methods: A publicly funded, multicentre, blinded randomized controlled trial (RCT) included 3427 women (mean age of 30 years) who delivered at 36 weeks or later via forceps or vacuum delivery. Women were randomized to a single dose of intravenous (IV) amoxicillin–clavulanic acid (1 g and 200 mg) or IV saline within 6 hours of delivery. The primary outcome was confirmed or suspected maternal infection 6 weeks after delivery.

Results: Administration of IV antibiotic prophylaxis within 6 hours of delivery significantly reduced the rate of maternal infection to 11% versus 19% in the placebo group at 6 weeks' follow-up (risk ratio of 0.58; 95% CI 0.49 to 0.69; number needed to treat [NNT] of 13). Fewer women treated with antibiotics experienced perineal pain (46% vs 55%), had wound breakdown (11% vs 21%), or had primary care visits relating to perineal issues (28% vs 38%). There was a cost saving of £53 (approximately $93) per patient in the antibiotic treatment group.

Which second-line agent after metformin reduces cardiovascular outcomes in patients with diabetes?

Bottom line: After metformin, glucagonlike peptide 1 (GLP1) agonists or sodium-glucose cotransporter-2 (SGLT2) inhibitors should be considered as second-line agents for the reduction of cardiovascular risk. Both classes decrease cardiovascular outcomes, particularly in higher-risk patients.

Methods: Two new reviews examined the effect of diabetes medications on cardiovascular outcomes: an umbrella review of 36 systematic reviews and 31 new RCTs,[3] and a systematic review of 453 RCTs of 21 drugs in 9 classes with network meta-analysis.[4]

Results: In patients with low cardiovascular risk, GLP1 agonists and SGLT2 inhibitors reduced myocardial infarction, and GLP1 agonists also reduced death.[4] The confidence in these findings, however, was rated as low. Sulfonylureas worsened diabetic retinopathy.[4]

In patients with high cardiovascular risk, GLP1 agonists and SGLT2 inhibitors reduced mortality and cardiovascular death; GLP1 agonists also reduced stroke, and SGLT2 inhibitors decreased hospitalization for heart failure.[4]

Compared with placebo, dipeptidyl peptidase 4 (DDP4) inhibitors, sulfonylureas, acarbose, and insulin had no effect on cardiovascular outcomes.[3] Pioglitazone reduced combined cardiovascular outcomes, myocardial infarction, and stroke but increased risk of heart failure.[3] Metformin likely decreases risk of major adverse cardiovascular events.[3] For patients taking metformin, increased risk of severe hypoglycemia was seen with insulin and sulfonylureas.[4]

Is gabapentin an effective treatment for patients with alcohol use disorder?

Bottom line: Gabapentin can prevent return to drinking for patients with alcohol use disorder, particularly among those who experience more severe withdrawal symptoms.[5]

Methods: A 16-week double-blind RCT (N = 90) compared gabapentin (up to 1200 mg/d) and placebo on heavy drinking days (>5 standard drinks/d) and the relationship of alcohol withdrawal symptoms with medication response. Participants were adults (mean age of 50 years, 77% male, average 11 drinks/d) with alcohol use disorder, who reported current or historical alcohol withdrawal symptoms.

Results: At 16 weeks, 27% of the participants taking gabapentin experienced no heavy drinking days versus 9% in the placebo group (NNT = 5). Total abstinence was also greater in the gabapentin group (18% vs 4%, NNT = 7). Patients reporting more severe withdrawal symptoms had greater benefit (less relapse to heavy drinking, NNT = 3; and more total abstinence, NNT = 3) than those with less severe withdrawal symptoms. Mild to moderate dizziness was more common with gabapentin than with placebo (57% vs 33%, number needed to harm of 5).

Do compression stockings prevent cellulitis?

Bottom line: In patients with a history of recurrent cellulitis and chronic leg edema, compression stockings reduce episodes of recurrent cellulitis (15% vs 40% after 6 months).[6]

Methods: A randomized, non-blinded trial (N = 84) compared compression stockings plus cellulitis prevention education (eg, skin care, exercise) with education alone. Participants had chronic leg edema, with an average of 2 episodes of cellulitis in the previous 2 years (mean age of 64 years, mean body mass index of 41 kg/m^2). Stockings were mostly knee height and seemed to be class 2 (23 to 32 mm Hg) or higher.

Results: The trial was stopped early owing to the efficacy of the intervention. After 6 months, 15% of participants in the intervention group developed the primary outcome of recurrent cellulitis versus 40% in the control group (NNT = 4). Stocking wearers reported an 8-point (out of 100) better quality of life, likely a clinically meaningful difference. Leg volumes were reduced with stockings but not with education alone (-4.3% vs +1.3%). Of participants randomized to wear compression stockings, 88% reported wearing them 4 or more days per week. No adverse effects were reported.

What are the latest recommendations on dyslipidemia management for cardiovascular disease (CVD) risk reduction from the US Department of Veterans Affairs and Department of Defense?

Bottom line: A CVD risk-based, non–low-density lipoprotein (LDL) target approach to dyslipidemia management using shared decision making is advocated. Diet, regular physical activity, and, if deemed appropriate, moderate-dose statins are considered the foundational strategies of care.[7]

Methods: The authors conducted a systematic search of peer-reviewed literature from December 2013 to May 2019 for evidence relevant to 12 key questions, focusing on RCTs, systematic reviews, and meta-analyses. Recommendations were rated using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) method, with CVD mortality as the primary consideration.

Results: Key recommendations included the following. For patients not taking statins, if measuring lipid levels, nonfasting levels should be ordered. Levels should be measured no more frequently than every 10 years. Repeat CVD risk assessment every 5 years or sooner, depending on risk. Offer moderate-dose statins (eg, 10 to 20 mg of atorvastatin) to patients with a 10-year CVD risk (nonfatal myocardial infarction, stroke, or coronary artery disease death) greater than 12%, an LDL level of 4.9 mmol/L or greater, or the presence of diabetes. Offer moderate-dose statins to patients with 10-year CVD risk of 6% to 12% after discussion of risks, benefits, and preferences.

For secondary prevention, use moderate-dose statins. If a patient is at high risk (eg, recurrent events or peripheral artery disease and smoking or diabetes) and willing, offer high-dose statins and consider additional medications such as ezetimibe or icosapent (if triglyceride levels are high).

Do not routinely monitor lipid levels or target LDL levels in patients receiving statins.

Encourage a dietitian-led Mediterranean diet and regular aerobic physical activity of any intensity and duration.

Does intermittent fasting result in greater weight loss than consistent mealtimes with no calorie restriction?

Bottom line: Intermittent fasting and consistent meal timing (CMT) resulted in similar and minimal weight loss at 12 weeks (0.9 kg vs 0.7 kg, respectively).[8]

Methods: An RCT (116 participants analyzed) compared time-restricted eating (TRE; a form of intermittent fasting that involves eating without restriction between 12:00 PM and 8:00 PM with no other caloric consumption for the remainder of the day) and CMT (3 meals/d at structured time windows with snacking permitted). Participants (mean age of 47 years, 40% female, mean weight of approximately 100 kg) were sent prompts via a mobile app, reminding them when they could eat (TRE) or with reminders such as "fruits and vegetables are healthy snacks" (CMT). Other than these prompts, no recommendations regarding caloric amount or content were made to either group. No recommendations were made regarding physical activity to either group.

Results: Adherence was 92% for CMT and 84% for TRE. At 12 weeks, the TRE group had lost a mean of 0.9 kg and the CMT group had lost a mean of 0.7 kg, with no significant difference between the groups. Individual participant weight change varied substantially (from roughly 7 to 8 kg of weight loss to approximately 3 kg weight gain in both groups).

Does adding vitamin C to iron supplements improve hemoglobin more than iron alone for iron deficiency anemia?

Bottom line: For patients with iron deficiency anemia, iron supplementation plus vitamin C has no advantage over iron alone in terms of hemoglobin levels.[9]

Methods: In a non-blinded RCT (N = 440), adult patients with iron deficiency anemia (mean age of 38 years, 97% female, mean hemoglobin level of 88 g/L) were randomized to receive oral iron supplements plus vitamin C (100 mg ferrous succinate plus 200 mg vitamin C, 3 times/d) or iron alone.

Results: At 2 weeks, mean hemoglobin increased by 20.0 g/L with iron plus vitamin C and 18.4 g/L with iron alone, which was not statistically different (difference of 1.6 g/L; 95% CI -0.3 to 3.5 g/L). No differences in hemoglobin levels were found at any other time points or with serum ferritin levels at 8 weeks. No differences in adverse events were observed between groups.

How does antacid alone compare with a gastrointestinal cocktail for epigastric pain in patients presenting to the emergency department?

Bottom line: For patients presenting to the emergency department with epigastric pain or dyspepsia, antacid alone provided similar pain relief compared with antacid and lidocaine combinations, and it was more palatable. In these patients, it is important to rule out underlying cardiovascular causes.[10]

Methods: A double-blind RCT (N = 89) compared the effect of antacid alone with an antacid-lidocaine 2% solution and an antacid-lidocaine 2% viscous gel on epigastric pain symptoms in patients presenting to the emergency department (mean age of 41 years, 64% female, 21% with previous gastroesophageal reflux disease or peptic ulcer disease; mean baseline pain score on a 100-mm visual analogue scale [VAS] was 66). A minimum clinically important difference was set at a 13-mm decrease on the VAS.

Results: At 30 minutes, antacid alone decreased pain by 20 mm on the combination solution by 17 mm, and the combination viscous gel by 9 mm. At 60 minutes, all groups reached the minimum clinically important difference (32 mm for antacid alone, 26 mm for solution, 21 mm for viscous gel). At both 30 and 60 minutes, no statistical difference was found between groups. Patients found antacid alone more palatable, with better scores for taste, bitterness, and overall acceptability. Fourteen percent of enrolled patients had a discharge diagnosis of cardiovascular pathology.

Does dapagliflozin improve renal and cardiovascular outcomes in patients with chronic kidney disease?

Bottom line: In patients with a history of chronic kidney disease, with or without diabetes, 1 in 19 patients who take dapagliflozin will avoid 1 primary outcome event in 2.4 years.[11]

Methods: A double-blind RCT (N = 4304) compared dapagliflozin (10 mg/d) and placebo in patients with an estimated glomerular filtration rate (eGFR) between 25 and 75 mL/min/1.73 m^2 and a urinary albumin-to-creatinine ratio of 23 to 565 mg/mmol, with or without diabetes (mean age of 62 years, 33% female; 75% had an eGFR of 30 to <60 mL/min/1.73 m^2; 68% had diabetes).

Results: The primary outcome was a composite of a sustained 50% decline in eGFR, end-stage renal disease (dialysis for ≥28 d, kidney transplantation, sustained eGFR <15 mL/min/1.73 m^2), or death from renal or cardiovascular causes. The primary outcome occurred in 9.2% of those taking dapagliflozin and 14.5% of those taking placebo over 2.4 years (NNT = 19). The benefit was similar in patients with or without diabetes. Additional outcomes favouring dapagliflozin were reduced end-stage renal disease (5.1% vs 7.5% for placebo; NNT = 42), all-cause death (4.7% vs 6.8%; NNT = 48), and the composite outcome of heart failure, hospitalization, and cardiovascular death (4.6% vs 6.4%; NNT = 56).

Does empagliflozin reduce cardiovascular outcomes in patients with heart failure?

Bottom line: In patients with chronic heart failure and reduced ejection fraction, the addition of empagliflozin to standard therapy reduces the risk of hospitalization regardless of the presence of diabetes.[12]

Methods: A double-blind RCT (N = 3730) compared empagliflozin (10 mg) with placebo in patients with heart failure (mean age of 67 years, 76% male; 50% of patients had diabetes; 75% were class II according to New York Heart Association criteria; 73% had an ejection fraction ≤30%; and the mean eGFR was 62 mL/min/1.73 m^2) already receiving standard heart failure therapy.

Results: At 16 months, the primary composite end point (cardiovascular death or hospitalization for heart failure) occurred less frequently with empagliflozin (19.4%) compared with placebo (24.7%; hazard ratio of 0.75; 95% CI 0.65 to 0.86; NNT=19), driven primarily by the reduction in hospitalizations. Benefit was seen regardless of the presence of diabetes. Genital infections were more frequent with empagliflozin (1.7% vs 0.6%; number needed to harm of 91).

Runners-up (all were RCTs)

Alcohol abstinence in atrial fibrillation: In 140 adults with a history of atrial fibrillation who regularly consumed alcohol (≥10 drinks/wk), abstaining from alcohol significantly reduced recurrence of atrial fibrillation to 53% versus 73% in the control group (NNT = 5) over 6 months. Atrial fibrillation–related hospital visits were also reduced by 1 visit for every 9 people who abstained compared with those who continued to drink.[13]

Turmeric for osteoarthritis pain: In 70 adults with knee osteoarthritis, 63% randomized to receive 1000 mg of *Curcuma longa* (turmeric) daily were classified as responders (based on improvement in pain, function, and global assessment), compared with 38% taking placebo (NNT = 4). Adverse events were not different between groups.[14]

Vitamin D for children and for other indications: Vitamin D was not effective when taken as a prenatal supplement to prevent asthma in children.[15] Vitamin D was also not effective in preventing asthma exacerbation in children with low vitamin D levels,[16] tuberculosis in children,[16] or depression in older adults.[17] Vitamin D (with calcium) might prevent recurrence of benign paroxysmal positional vertigo, but methodologic issues prevent definitive conclusions.[18]

Physical therapy versus steroid injections for knee osteoarthritis: In 156 patients with knee osteoarthritis, physiotherapy (approximately 12 sessions) improved pain and function more than corticosteroids (approximately 3 injections) over 1 year.[19]

Colchicine for coronary artery disease: In 5522 adults with stable coronary artery disease, 0.5 mg of colchicine daily reduced a composite end point of cardiovascular events (cardiovascular death, myocardial infarction, ischemic stroke, or coronary revascularization) to 6.8% versus 9.6% in the placebo group at 29 months. Despite this benefit, a trend (but not statistically different) to higher overall mortality was observed with colchicine (2.6% vs 2.2% with placebo).[20]

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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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