

Top studies relevant to primary care practice

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Abstract

Objective To summarize 10 high-quality studies from 2017 that have strong relevance to primary care practice.

Quality of evidence Study selection involved routine literature surveillance by a group of primary care health professionals. This included screening abstracts of important journals and Evidence Alerts, as well as searching the American College of Physicians Journal Club.

Main message Topics of the 2017 articles include whether treating subclinical hypothyroidism improves outcomes or symptoms; whether evolocumab reduces cardiovascular disease as well as low-density lipoprotein levels; whether lifestyle interventions reduce medication use in patients with diabetes; whether vitamin D prevents cardiovascular disease, cancer, or upper respiratory tract infections; whether canagliflozin reduces clinical events in patients with diabetes; how corticosteroid injections affect knee osteoarthritis; whether drained abscesses benefit from antibiotic treatment; whether patients with diabetes benefit from bariatric surgery; whether exenatide reduces clinical events in patients with diabetes; and whether tympanostomy tubes affect outcomes in recurrent acute otitis media or chronic otitis media. We provide brief summaries, context where needed, and final recommendations for 10 studies with potential effects on primary care. We also briefly review 5 “runner-up” studies.

Conclusion Research from 2017 produced several high-quality studies in diabetes management. These have demonstrated benefit for alternative therapies and offered evidence not previously available. This year’s selection of studies also provided information on a variety of conditions and therapies that are, or might become, more common in primary care settings.

Principales études pertinentes à l’exercice des soins primaires

Résumé

Objectif Résumer 10 études de grande qualité effectuées en 2017 qui sont particulièrement applicables à l’exercice des soins primaires.

Editor’s key points

- ▶ As the first point of contact for most patients’ medical concerns, primary care physicians are faced with a growing body of medical evidence that is time sensitive and difficult to navigate. We hope this collection of articles will be useful for a variety of primary care physicians, practising diverse and comprehensive care nationwide.
- ▶ This selection of studies from 2017 provided information on various conditions and therapies that are, or might become, more common in primary care settings, such as corticosteroid injections and treatment of subclinical hypothyroidism.
- ▶ Of interest, research from 2017 has produced several high-quality studies in diabetes management. These have demonstrated benefit for alternative therapies, such as bariatric surgery, and offered evidence not previously available.

Points de repère du rédacteur

- ▶ Les médecins de soins primaires sont le premier point de contact pour répondre à la plupart des préoccupations médicales des patients et ils se trouvent devant un corpus grandissant de données médicales factuelles, sensibles au facteur temps et difficiles à consulter. Nous espérons que cet ensemble d’articles sera utile à divers médecins de famille qui offrent des soins diversifiés et complets dans toutes les régions du pays.
- ▶ Cette collection d’études publiées en 2017 fournit des renseignements sur divers problèmes et traitements qui sont, ou pourraient devenir, plus courants dans les milieux de soins primaires, comme les injections de corticostéroïdes et la thérapie pour l’hypothyroïdie sous-clinique.
- ▶ Il est intéressant de constater qu’en 2017, la recherche a produit plusieurs études de grande qualité sur la prise en charge du diabète. Elles ont corroboré les bienfaits de thérapies non conventionnelles, comme la chirurgie bariatrique, et produit des données probantes qui n’existaient pas auparavant.

Qualité de l'information Le choix des études s'est fait à la suite d'une surveillance systématique des ouvrages scientifiques par un groupe de professionnels des soins de santé primaires, notamment l'examen des résumés d'importantes revues, d'Evidence Alerts, de même que de la rubrique American College of Physicians Journal Club.

Message principal Au nombre des sujets traités dans les articles de 2017 figurent les suivants: Le traitement de l'hypothyroïdie sous-clinique améliore-t-il les résultats ou les symptômes? L'évolocumab réduit-il les maladies cardiovasculaires et les taux de lipoprotéines de basse densité? Les interventions reliées au mode de vie réduisent-elles le recours aux médicaments par les patients diabétiques? La vitamine D prévient-elle les maladies cardiovasculaires, le cancer ou les infections des voies respiratoires supérieures? La canagliflozine réduit-elle les incidents cliniques chez les patients diabétiques? Quels sont les effets des injections de corticostéroïdes sur l'arthrose du genou? L'antibiothérapie est-elle bénéfique après le drainage d'un abcès? Les patients diabétiques bénéficient-ils de la chirurgie bariatrique? L'exénatide réduit-il les incidents cliniques chez les patients diabétiques? Les drains transtympaniques influencent-ils les résultats dans les cas d'otites moyennes aiguës récurrentes ou d'otites moyennes chroniques? Nous présentons des résumés, le contexte, au besoin, et les recommandations finales des 10 études, de même que leurs effets possibles en soins primaires. Nous faisons aussi une brève revue des 5 plus importantes études.

Conclusion En 2017, la recherche a produit plusieurs études de grande qualité sur la prise en charge du diabète. Ces études ont fait valoir les bienfaits de thérapies non conventionnelles et ont cerné des données probantes qui n'existaient pas auparavant. Cette année, la série d'études a aussi fourni des renseignements sur divers problèmes et traitements qui sont, ou pourraient devenir, plus courants dans les milieux de soins primaires.

Primary care physicians are faced with an overwhelming volume of available evidence and research articles. We have summarized a selection of 10 articles, with an additional 5 "runners-up," that have the potential to inform physicians of emerging therapies, clarify the results of popular published research, or change practice.

Quality of evidence

The following studies are the PEER (Patients, Experience, Evidence, Research) Group's choice of the most important articles for primary care physicians published in 2017. Selection involved routine literature surveillance by a group of primary care health professionals. This included screening abstracts of important journals (like *JAMA* or the *New England Journal of Medicine*) and Evidence

Alerts,¹ as well as searching the American College of Physicians Journal Club.

Main message

Will treatment of subclinical hypothyroidism improve outcomes or symptoms?

Bottom line: No clinical benefit was seen when regularly treating patients with a thyroid-stimulating hormone (TSH) level of 4.6 to 10 mIU/L.²

Methods: A randomized controlled trial (RCT) evaluated the clinical outcomes of older Scottish adults (N=737, mean age 74 years) with persistent subclinical hypothyroidism. Patients with TSH levels between 4.6 and 19.9 mIU/L and normal free thyroxine levels (confirmed on repeat testing) were given thyroid replacement treatment (titrated to normalize the TSH level) or placebo (with mock titrations) and followed for 18 months.

Results: At 18 months, those in the treatment group had normal TSH levels (mean 3.5 mIU/L) compared with 5.3 mIU/L in the placebo group. Clinically, there were no differences in hypothyroidism symptom score, tiredness score, or quality of life. Rates of death or cardiovascular disease (CVD) were also similar between groups (although the study was underpowered to show differences). Patients who experienced 1 or more serious adverse events were more common in the placebo group than in the treatment group (21% vs 28%). An earlier Cochrane review also showed no effect.³

Does evolocumab reduce CVD?

Bottom line: Evolocumab (a proprotein convertase subtilisin-kexin type 9 medication) reduced cardiovascular events over about 2 years (number needed to treat [NNT] of 67) with no effect on death. The attained low-density lipoprotein (LDL) level was not related to patient outcomes. Cost (\$7844 per year) remains a barrier.⁴

Methods: An RCT (N=27564) followed patients with CVD (mean age 63 years, median LDL level 2.4 mmol/L, 100% taking statin therapy [70% high-intensity]) for a median of 2.2 years to determine the benefit of evolocumab (140 mg subcutaneously every 2 weeks or 420 mg subcutaneously every month) versus placebo.

Results: The primary composite end point (cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, and coronary revascularization) occurred in 9.8% of the evolocumab group versus 11.3% of the placebo group (NNT=67). Low-density lipoprotein levels decreased by 59% (mean absolute reduction of 1.45 mmol/L); however, lower LDL levels did not correlate to fewer events. There was no difference in death rates. Injection site reactions increased (number needed to harm [NNH] of 200). Rates of other adverse events were not significant. Although antibodies have developed to another proprotein convertase subtilisin-kexin type 9 drug (bococizumab),⁵ this has not occurred with evolocumab.⁴

Can lifestyle intervention reduce medication use in patients with diabetes?

Bottom line: Intense lifestyle intervention is beneficial in type 2 diabetes mellitus (T2DM) management, as 1 in every 3 people with T2DM can reduce their glucose-lowering medications or stop them completely compared with standard care. One in every 4 patients loses 10% of their weight.⁶

Methods: A Danish RCT of 98 patients with a mean 5-year history of T2DM (mean age 55 years, mean hemoglobin A_{1c} (HbA_{1c}) level 6.7%, 79% taking metformin only) compared intense lifestyle intervention (5 to 6 weekly group aerobic exercise sessions 30 to 60 minutes long with some resistance training, along with an individual diet plan and a “smart watch”) with standard care.

Results: No differences were seen in HbA_{1c} levels, although this is because medications were adjusted based on glucose control. Of importance, glucose-lowering medications were more frequently reduced (64% vs 26%, NNT=3) with lifestyle modifications and more patients stopped all glucose-lowering medications in the lifestyle-modification group (56% vs 15%, NNT=3). Additionally, more people lost at least 10% of their body weight in the lifestyle-modification group (31% vs 3%, NNT=4). Musculoskeletal injury was also more common in the lifestyle-modification group (NNH=5).

Can vitamin D prevent CVD, cancer, or upper respiratory tract infections?

Bottom line: High-dose vitamin D has no effect on CVD prevention in adults⁷ or incidence of upper respiratory tract infection (URTI) in children.⁸ Vitamin D and calcium supplementation did not have a statistically significant effect on cancer incidence in postmenopausal women.⁹

Methods: A New Zealand RCT (N=5108) compared high-dose vitamin D (oral vitamin D3: 200000 IU for first dose, then monthly dose of 100000 IU) versus placebo for CVD prevention for 3.3 years in a general population (mean age 66 years, 58% male).⁷ A 6-month Canadian RCT compared high-dose (2000 IU) to low-dose (400 IU) vitamin D with 6 months of follow-up to examine prevention of wintertime URIs in children aged 1 to 5 years.⁸ Finally, a US RCT investigated the effect of vitamin D plus calcium (2000 IU plus 1500 mg per day) compared with placebo for 4 years on cancer risk in postmenopausal women.⁹

Results: High-dose vitamin D did not affect the rate of CVD (hazard ratio [HR] of 1.02; 95% CI 0.87 to 1.20)⁷ or URTI (incidence rate ratio of 1.01; 95% CI 0.88 to 1.16).⁸ Vitamin D and calcium led to a slight but not statistically significant reduction in cancer incidence (3.9% in treatment group vs 5.6% in placebo group [HR=0.70; 95% CI 0.47 to 1.02]).⁹

Can canagliflozin prevent important clinical events in patients with diabetes?

Bottom line: Patients treated with canagliflozin (a sodium-glucose cotransporter-2 inhibitor) are at a lower risk of experiencing cardiovascular events over a

3.6-year treatment period but the harms can be serious (eg, fracture, amputation).¹⁰ The net benefit might be a little higher with empagliflozin, another sodium-glucose cotransporter-2 inhibitor.¹¹

Methods: Two placebo-controlled RCTs with different enrolment and study lengths (combined N=10412) compared the efficacy and safety of canagliflozin (100 to 300 mg daily) in patients with T2DM and CVD or at high CVD risk (mean age 63 years, mean 14-year history of diabetes).¹⁰

Results: At 3.6 years, cardiovascular events occurred in 6.5% of the treatment group compared with 7.6% of the placebo group (HR=0.86; 95% CI 0.75 to 0.97; NNT=91). Mortality occurred in 4.2% of the treatment group and 4.7% of the placebo group (HR=0.87; 95% CI 0.71 to 1.01; the CIs suggest potential benefit [NNT of about 200]). Adverse events included yeast infection in women (NNH=9), genital infection in men (NNH=18), osmotic diuresis (NNH=20), fracture (NNH=120), and amputation (NNH=144).

How do corticosteroid injections affect knee osteoarthritis?

Bottom line: Steroid injections might marginally (by 0.11 mm) increase erosion of knee cartilage; however, the clinical relevance is unknown. There was no difference in knee pain at 3 months¹² but the timing of the assessment was poor, as past research shows corticosteroid injections are effective but the benefit wanes by 3 months.¹³

Methods: An RCT (N=140) compared the efficacy of triamcinolone (40 mg of intra-articular triamcinolone every 3 months) versus saline on progression of cartilage loss and knee pain in patients with knee osteoarthritis.¹² Patients (mean age 59 years) were followed for 2 years, with a pain score taken every 3 months and yearly magnetic resonance imaging (to evaluate cartilage volume).

Results: Triamcinolone injection resulted in 0.11 mm more cartilage volume loss (-0.21 mm) than saline (-0.10 mm) did. No difference in knee pain was reported at the 3-month intervals.

Do abscesses benefit from antibiotic treatment?

Bottom line: Antibiotics can help recovery for 1 in 8 people with small, drained abscesses.¹⁴

Methods: A 3-armed RCT (N=786) compared the effectiveness of 10 days of antibiotics versus placebo on the treatment of an abscess (≤5 cm in diameter) following incision and drainage. Patients (64% adults) were given clindamycin (300mg orally 3 times daily), trimethoprim-sulfamethoxazole (TMP-SMX) (80 mg and 400 mg orally twice daily) or placebo. Doses were adjusted for pediatric patients.

Results: Infections were 67% *Staphylococcus aureus* and 74% of these were methicillin resistant. At 10 days, 83% of the clindamycin group, 82% of the TMP-SMX group, and 69% of the placebo group were cured (NNT=8). The cure rate in the non-*S aureus* infection subgroup was not improved. Recurrence of infection at 30 days after antibiotic treatment occurred in 7% of the clindamycin

group, 14% of the TMP-SMX group, and 12% of the placebo group (not statistically significant). Adverse events were most common in the clindamycin group (22%) compared with the TMP-SMX (11%) and placebo (13%) groups. Diarrhea was the most common adverse event reported (NNH=9 to 11).

What are the benefits of bariatric surgery in patients with diabetes?

Bottom line: Bariatric surgery in patients with T2DM improves weight, glycemic control, and quality of life. Patients might also be able to discontinue diabetes medications.¹⁵

Methods: A 3-armed RCT (N=134) compared the usefulness of bariatric surgery (sleeve gastrectomy or bypass) plus medical treatment versus medical treatment alone as treatment for diabetes outcomes in patients with obesity and T2DM (mean age 49 years; mean body mass index 37 kg/m²; mean HbA_{1c} level 9.2%; 44% using insulin therapy) over 5 years.

Results: Mean HbA_{1c} level at 5 years was 8.5% for the medical therapy group, 7.3% for the bypass group, and 7.4% for the sleeve gastrectomy group. The primary end point of attaining an HbA_{1c} target of 6% or less was achieved in 5% of the medical treatment group, 29% of the bypass group (NNT=5), and 23% of the sleeve gastrectomy group (NNT=6). The end point of attaining an HbA_{1c} level of 6.5% or less without medication was

achieved in 0% of the medical treatment group, 31% of the bypass group (NNT=4), and 23% of the sleeve gastrectomy group (NNT=5). Mean weight was 99 kg in the medical therapy group, 83 kg in the bypass group, and 82 kg in the sleeve gastrectomy group (mean baseline weight was about 104 kg). There was no difference in blood pressure among the groups. Quality of life was statistically significantly better in the surgical arms.

Can exenatide prevent important clinical events in patients with diabetes?

Bottom line: Although the difference in CVD was not significant, the small benefits might be similar in magnitude to other glucagonlike peptide 1 (GLP1) agonists.¹⁶ However, other GLP1 analogues (eg, liraglutide) produced more consistent effects.¹⁷

Methods: The GLP1 agonist exenatide was compared with placebo in an RCT of 14 752 patients with T2DM (median age 62 years, 73% with CVD, median 12-year history of diabetes, median baseline HbA_{1c} level of 8%).¹⁶

Results: At 1 year, mean HbA_{1c} level was 7.5% for the exenatide group and 8% for the placebo group. At 3.2 years, the composite cardiovascular outcome occurred in 11.4% versus 12.2% in those taking placebo (HR=0.91; 95% CI 0.83 to 1.00), with similar results for mortality (7% vs 8%; HR=0.86; 95% CI 0.77 to 0.97). Other outcomes were not statistically significant, including cardiovascular deaths and adverse events.

Do tympanostomy tubes affect outcomes for children with recurrent acute otitis media or chronic otitis media?

Bottom line: Limited evidence is available but what does exist supports a small reduction in acute otitis media (AOM) episodes and short-term hearing improvement for chronic otitis media.¹⁸

Methods: A systematic review (147 articles) assessed the effectiveness of tympanostomy tubes in children with chronic otitis media with effusion and recurrent AOM.

Results: Children with chronic otitis media with effusion treated with tympanostomy tubes (16 RCTs) had a mean improvement in hearing of 9.1 dB at 1 to 3 months. This benefit was no longer observed at 12 to 24 months. Three RCTs reported that tympanostomy tubes variably reduced recurrent AOM; the benefit ranged from 0.55 to 1.14 fewer occurrences of AOM per year.

Runners-up

Rivaroxaban for CVD: Over 2 years, rivaroxaban plus acetylsalicylic acid will reduce the number of cardiovascular events (cardiovascular death, stroke, or myocardial infarction) by 1 in every 77 patients with stable CVD versus acetylsalicylic acid alone. However, 1 major bleed will occur in every 84 patients.¹⁹

Self-monitoring of blood glucose level: Consistent with previous evidence,²⁰ self-monitoring of blood glucose in patients with non-insulin-dependent T2DM does not lead to significant changes in HbA_{1c} level or quality of life.²¹

Probiotics for prevention of antibiotic-associated diarrhea: *Lactobacillus*, when compared with placebo, has no effect on the incidence of antibiotic-associated diarrhea or loose stools in children being treated with antibiotics.²²

Diet of low-FODMAP foods for irritable bowel syndrome: Consistent with previous evidence,²³ a diet of low-FODMAP (fermentable oligo-di-monosaccharides and polyols) foods might reduce abdominal pain in patients with irritable bowel syndrome with diarrhea compared with a diet based on the modified National Institute for Health and Care Excellence guidelines.²⁴

Pregabalin for sciatica: Pregabalin (150 to 600 mg daily) compared with placebo had no effect on a 10-point pain score for sciatic pain at 8 or 52 weeks. Harms, particularly dizziness, dorsalgia (ironically), and malaise, were more common in the pregabalin group.²⁵

Conclusion

Of interest, research in 2017 has produced several high-quality studies in diabetes management. These have demonstrated benefit for alternative therapies and offered evidence not previously available; therefore, we believed it was important to include several of them in this article.

The selection of studies from 2017 has provided information on a variety of conditions and therapies that are, or might become, more common in primary

care settings. We hope this collection of articles will be useful for a variety of primary care physicians, practising diverse and comprehensive care nationwide. 🌿

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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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