This article summarizes the top 20 research studies of 2021 identified as POEMs (patient-oriented evidence that matters) that did not address the COVID-19 pandemic. Sodium-glucose cotransporter 2 inhibitors and glucose-like peptide 1 receptor agonists prevent adverse cardiovascular and renal outcomes in patients with type 2 diabetes mellitus and also reduce all-cause and cardiovascular mortality. Most older adults (mean age, 75 years) with prediabetes do not progress to diabetes. Among patients in this age group with type 2 diabetes treated with medication, an A1C level of less than 7% is associated with increased risk of hospitalization for hypoglycemia, especially when using a sulfonylurea or insulin. For patients with chronic low back pain, exercise, nonsteroidal anti-inflammatory drugs, duloxetine, and opioids were shown to be more effective than control in achieving a 30% reduction in pain, but self-discontinuation of duloxetine and opioids was common. There is no clinically important difference between muscle relaxants and placebo in the treatment of nonspecific low back pain. In patients with chronic pain, low- to moderate-quality evidence supports exercise, yoga, massage, and mindfulness-based stress reduction. For acute musculoskeletal pain, acetaminophen, 1,000 mg, plus ibuprofen, 400 mg, without an opioid is a good option. Regarding screening for colorectal cancer, trial evidence supports performing fecal immunochemical testing every other year. For chronic constipation, evidence supports polyethylene glycol, senna, fiber supplements, magnesium-based products, and fruit-based products. The following abdominal symptoms carry a greater than 3% risk of cancer or inflammatory bowel disease: dysphagia or change in bowel habits in men; rectal bleeding in women; and abdominal pain, change in bowel habits, or dyspepsia in men and women older than 60 years. For secondary prevention in those with established arteriosclerotic cardiovascular disease, 81 mg of aspirin daily appears to be effective. The Framingham Risk Score and the Pooled Cohort Equations both overestimate the risk of cardiovascular events. Over 12 years, no association between egg consumption and cardiovascular events was demonstrated. Gabapentin, pregabalin, duloxetine, and venlafaxine provide clinically meaningful improvements in chronic neuropathic pain. In patients with moderate to severe depression, initial titration above the minimum starting dose of antidepressants in the first eight weeks of treatment is not more likely to increase response. In adults with iron deficiency anemia, adding vitamin C to oral iron has no effect. In children with pharyngitis, rhinosinusitis, acute bronchitis, or acute otitis media, providing education combined with a take-and-hold antibiotic prescription results in 1 in 4 of those children eventually taking an antibiotic. (Am Fam Physician. 2022;online. Copyright © 2022 American Academy of Family Physicians.)
called the Information Assessment Method (https://can rate it using a validated questionnaire. This process is unlikely to occur.

In older patients with type 2 diabetes, a consistent A1C level of less than 7% is associated with at least one hospitalization for the treatment of hypoglycemia. Treatment with a sulfonylurea or insulin magnifies the risk.

3. Do SGLT-2 inhibitors or GLP-1 receptor agonists improve patient-oriented outcomes in patients with type 2 diabetes?6

Both SGLT-2 inhibitors and GLP-1 receptor agonists reduce all-cause mortality, cardiovascular mortality, nonfatal myocardial infarction, and kidney failure in patients with diabetes. SGLT-2 inhibitors, the diabetes medications ending in -flozin (e.g., dapagliflozin [Farxiga]), and GLP-1 receptor agonists, the medications ending in -tide (e.g., dulaglutide [Trulicity]), decrease cardiovascular and renal outcomes to a greater extent than placebo or other treatments. They should be considered in addition to metformin and perhaps another glucose-lowering therapy for most patients with type 2 diabetes.

4. What effect do SGLT-2 inhibitors have on mortality, cardiovascular outcomes, and renal outcomes in patients with and without type 2 diabetes, heart failure, or kidney disease?3


TABLE 1

Type 2 Diabetes Mellitus

Clinical question

Bottom-line answer

1. What is the likelihood that older adults with prediabetes will develop diabetes mellitus over an average of 6.5 years?7

More than 90% of older adults with prediabetes will not develop diabetes. Prediabetes is a risk factor for a risk factor. Or not. Older patients generally will not progress to diabetes over 6.5 years. They will stay at prediabetic A1C levels or revert to normal levels. In other words, if a patient makes it to their mid-70s without a diagnosis of diabetes, it is unlikely to occur.

2. What are the risks of overtreatment in patients 70 years or older with type 2 diabetes?8

Tight control of diabetes leads to unnecessary hospitalizations in older patients. Sulfonylureas should be used with caution.

In older patients with type 2 diabetes, a consistent A1C level of less than 7% is associated with at least one hospitalization for the treatment of hypoglycemia. Treatment with a sulfonylurea or insulin magnifies the risk.

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4. What effect do SGLT-2 inhibitors have on mortality, cardiovascular outcomes, and renal outcomes in patients with and without type 2 diabetes, heart failure, or kidney disease?3

Exercise is the main intervention that produces sustained improvement in chronic low back pain. The interventions that are more effective than control in achieving at least a 30% reduction in pain are exercise, oral nonsteroidal anti-inflammatory drugs, duloxetine (Cymbalta), and opioids, but discontinuation of duloxetine and opioids was common in the study. Exercise is the only intervention resulting in sustained relief. Lower-quality data suggest that manipulation and topical capsaicin are also effective. It is possible the inclusion criteria for this systematic review missed important studies.

Muscle relaxants are not reliably effective for treating low back pain. Despite benzodiazepine or nonbenzodiazepine muscle relaxants being used for almost 50 years to treat low back pain, the evidence supporting their use is of low certainty. None of the treatments produce a clinically important difference over placebo treatment. Nonsteroidal anti-inflammatory drugs should be used for the treatment of low back pain.

Patients with low back pain do better when told that their MRI results are unrecommenced, compared with seeing the actual report without context. Information given to patients without context can be harmful. Patients with low back pain who were given the results of their MRI without interpretation by a clinician had greater pain, less self-efficacy, and lower function, even after six weeks of conservative treatment, than patients who were reassured that their MRI results were normal with age-related findings.

Acute muscle pain, oral acetaminophen plus ibuprofen is safer than combinations that include opioids, with equal effectiveness. A single dose of an opioid analgesic provides acute pain relief similar to a single dose of an acetaminophen and ibuprofen combination in patients with acute musculoskeletal pain in the emergency department. Opioids increase the likelihood of nausea or vomiting. There is no added benefit from 800 mg of ibuprofen compared with 450 mg. These results are similar to those of previous studies of opioids and varying doses of ibuprofen.

There is low-quality and, in some cases, moderate-quality evidence for a range of noninvasive, nondrug therapies for chronic pain. Exercise, oral nonsteroidal anti-inflammatory drugs, duloxetine (Cymbalta), and opioids, but discontinuation of duloxetine and opioids was common in the study. Exercise is the only intervention resulting in sustained relief. Lower-quality data suggest that manipulation and topical capsaicin are also effective. It is possible the inclusion criteria for this systematic review missed important studies.

Multiple nondrug therapies are effective for chronic musculoskeletal pain. There is low-quality and, in some cases, moderate-quality evidence for a range of noninvasive, nondrug therapies for chronic pain. Exercise, yoga, massage, and mindfulness-based stress reduction have health benefits, are relatively inexpensive, and do not require interaction with the health system.

Regular FIT is an effective screening method for colorectal cancer. Screening with FIT every other year for at least six years identified fewer cancers or advanced adenomas initially but surpassed a single sigmoidoscopy after three rounds of testing. The increased detection might be in part due to greater participation in FIT than sigmoidoscopy.

Polyethylene glycol (Miralax) and senna are the best initial treatments for chronic constipation. In this limited systematic review without formal data synthesis, the authors concluded there is good evidence to recommend polyethylene glycol or senna as first-line therapy and moderate evidence to support fiber supplements, other stimulant laxatives, magnesium-based products, and fruit-based products.

Dysphagia, changes in bowel habits, and rectal bleeding are the most worrisome abdominal symptoms for cancer or IBD. Using a cutoff of 3% risk (from the National Institute for Health and Care Excellence), dysphagia or changes in bowel habits in men and rectal bleeding in women should prompt referral for further workup to exclude cancer or IBD. In addition, abdominal pain, changes in bowel habits, or dyspepsia in patients older than 60 years should be investigated because they predict cancer or IBD in more than 3% of men and women.
tended to be larger in younger patients. This is important for shared decision-making. For example, an estimated risk of 10% based on the Pooled Cohort Equations might lead to prophylactic treatment before moving to another medication. Depression. Unfortunately, this means waiting six to eight weeks to judge the response to treatment before moving to another medication.

For new-generation antidepressants, including selective serotonin reuptake inhibitors, venlafaxine, and mirtazapine (Remeron) with iron deficiency anemia?27 Given the balance of benefits and harms, there is moderate-quality evidence for anticonvulsants (gabapentin and pregabalin were similarly effective and well tolerated) and SSRIs (duloxetine and venlafaxine were similarly effective and well tolerated). Rubeftacets (usually salicylates) appear to be effective but are not as well studied and have low-quality evidence. Acupuncture, opioids, and tricyclic antidepressants cannot be recommended based on current evidence. The next POEM identified 436 children with pharyngitis, rhinosinusitis, acute bronchitis, or acute otitis media whose treating physician had reasonable doubts about the need for antibiotics. Patients were randomized to no antibiotics; an immediate antibiotic; or an antibiotic prescription to be filled only if the child had fever, felt much worse after 24 hours, or was not improving after a longer period (varied by type of infection). Only 25% of children in the delayed antibiotic group and 12% in the no antibiotic group ultimately filled a prescription, and there was no difference between these groups and the immediate antibiotic group in the duration of symptoms (eight days) or complications. Gastrointestinal symptoms and cost were higher in those receiving an antibiotic.

Table 4

<table>
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<td>13. What dose of aspirin is best for secondary prevention in people with established ASCVD?20</td>
<td>The best daily dosage of aspirin to use for secondary prevention of ASCVD is 81 mg. There is no advantage to using a 325-mg dose of aspirin for patients with established ASCVD, and people taking the higher dose often switch to the lower dose (although the reason is unclear).</td>
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<td>14. How well do the Framingham Risk Score and Pooled Cohort Equations estimate the risk of cardiovascular events in the general population?23</td>
<td>These two commonly used cardiovascular risk scores overestimate the risk of cardiovascular events by about double. The Framingham Risk Score and Pooled Cohort Equations both significantly overpredicted the five-year risk of a composite cardiovascular event outcome. This is consistent with other research and should give us pause as we use these risk scores to guide therapeutic decision-making. For example, a person with a 10-year risk of 10% probably has a true risk closer to 5%, leading to very different guideline recommendations for a statin.</td>
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<td>15. How do routine clinical measurements of systolic blood pressure compare with ideal blood pressure measurement?24</td>
<td>Office measurements tend to overestimate “true” blood pressure. Compared with blood pressure measurements that follow the strict protocols used in research, measurement in typical physician offices will be an average of 4.6 to 7.5 mm Hg higher for systolic readings. This study also found wide variations in clinical blood pressure readings compared with the reference standard. SPRINT demonstrated that reducing a systolic blood pressure to less than 120 mm Hg is associated with decreased mortality. However, most guidelines suggest higher goals, given that the SPRINT method of blood pressure measurement was more accurate than the method used in usual clinical practice, which overestimates true blood pressure.</td>
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<td>Eggs do not increase the risk of cardiovascular disease. Over an average of 12 years, egg consumption is not associated with increased cardiovascular events. This meta-analysis showed that eating more than one egg per day, on average, was associated with an approximately 11% decreased likelihood of coronary artery disease. However, this decrease may be due to a healthy user bias (i.e., eating eggs might be associated with healthier habits).</td>
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<td>Low doses of selected antidepressants work just as well as higher doses. For new-generation antidepressants, including selective serotonin reuptake inhibitors, venlafaxine, and mirtazapine (Remeron), initial titration over the first eight weeks of treatment provides no benefit over starting with the minimum dose in patients with moderate to severe depression. Unfortunately, this means waiting six to eight weeks to judge the response to treatment before moving to another medication.</td>
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<td>“Take-and-hold” prescriptions for upper respiratory tract infections reduce antibiotic use and adverse effects. A strategy of providing education about the natural history of respiratory symptoms in children combined with giving a take-and-hold prescription (to be filled only if symptoms persist) resulted in only 1 in 4 children eventually taking an antibiotic. However, it increased the number of children who used other medications to control symptoms, which indicates the parents’ need to do something. Symptom severity and time to resolution, complications, and follow-up visits were similar whether children received immediate, delayed, or no antibiotic treatment. Immediate treatment resulted in more gastrointestinal symptoms. Similar results have been shown in adults.</td>
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<td>Vitamin C should not be added to iron replacement therapy. This study found no difference in hemoglobin or serum ferritin level after three months in adults with iron deficiency anemia who were treated with oral iron plus vitamin C vs. oral iron alone.</td>
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ASCVD = athrombotic cardiovascular disease; SPRINT = Systolic Blood Pressure Intervention Trial.

Information from references 19-22.

The next identified therapies. Opioid studies were of low quality and also showed more harms (number needed to harm = 12). Only a few trials with low-certainty evidence studied acupuncture and tricyclic antidepressants. A systematic review identified RCTs that compared treatment of moderate to severe depression using the minimum licensed dose of a selective serotonin reuptake inhibitor, venlafaxine, or mirtazapine (Remeron) with a dosing regimen that allowed titration to higher doses.23 There was no improvement in the balance of effectiveness and harms between taking the minimum dose and titrating to higher doses, although patients taking venlafaxine may respond to a higher dose if they show no response to the minimum dose.

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Finally, clinicians have long recommended that people taking iron supplements also take vitamin C because it theoretically improves absorption. A study tested the theory by randomizing 440 adults with iron deficiency anemia to ferrous succinate, 100 mg, plus vitamin C, 200 mg, or to placebo, and found that absorption was significantly higher in the supplemented group, though these results have not been replicated in all studies.

22. What therapies are recommended for acute pain from non–low back musculoskeletal injuries?

Topical NSAIDs are first-line therapy for non–low back musculoskeletal injuries. Oral NSAIDs, acetaminophen, acupressure, or TENS may also be used. The American College of Physicians and American Academy of Family Physicians collaborated to create guidelines on the management of non–low back musculoskeletal injuries. Based on a large systematic review and network meta-analysis, they give a strong recommendation for topical diclofenac as first-line therapy and a conditional recommendation for oral NSAIDs, acetaminophen, acupressure, or TENS. Opioids are not recommended because of greater adverse effects and risk of prolonged use.


23. What is the optimal duration of antibiotics for common infections?

Physicians should screen for tobacco use in all adults and provide behavioral interventions and pharmacotherapy to aid in smoking cessation. Physicians should screen for tobacco use in all adults and provide behavioral interventions and pharmacotherapy to aid in smoking cessation. Physicians should screen for tobacco use in all adults and provide behavioral interventions and pharmacotherapy to aid in smoking cessation. Physicians should screen for tobacco use in all adults and provide behavioral interventions and pharmacotherapy to aid in smoking cessation. Physicians should screen for tobacco use in all adults and provide behavioral interventions and pharmacotherapy to aid in smoking cessation. Physicians should screen for tobacco use in all adults and provide behavioral interventions and pharmacotherapy to aid in smoking cessation.

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<td>21. Are short antibiotic courses as effective as longer courses for non–low back musculoskeletal injuries?</td>
<td>Short antibiotic courses should be used for community-acquired pneumonia, COPD exacerbation, uncomplicated pyelonephritis, and nonpurulent cellulitis. American College of Physicians guidelines recommend five days of antibiotics for community-acquired pneumonia, five days for COPD exacerbation, five to seven days for uncomplicated cellulitis, and five to six days for nonpurulent cellulitis. Longer courses may be necessary. Guidance is needed on whether there is any clinical improvement.</td>
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