

Top 20 Research Studies of 2024 for Primary Care Physicians

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This article summarizes the top 20 research studies of 2024 identified as POEMs (patient-oriented evidence that matters). Based on a network meta-analysis, the oral antibiotics most likely to be effective for community-acquired pneumonia are telithromycin (not available in the United States), azithromycin, amoxicillin-clavulanate, and the quinolones levofloxacin and nemonoxacin (not available in the United States). The oral antivirals molnupiravir and nirmatrelvir-ritonavir reduce hospitalizations in immunocompromised patients with COVID-19. In average-risk infants, a single dose of nirsevimab reduces hospitalizations due to respiratory syncytial virus. Amoxicillin with or without clavulanate is more effective than placebo for children with symptoms of acute sinusitis. Benzyl benzoate 25% is highly effective for scabies in adolescents and adults. *Lactobacillus*-containing probiotics reduce the incidence of recurrent urinary tract infections (UTIs) in premenopausal women with frequent UTIs. Low-dose amitriptyline is effective as second-line therapy for irritable bowel syndrome. For patients with uncomplicated gallstones, conservative management is a reasonable option. Sodium-glucose cotransporter-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists are better than older drugs at improving patient-oriented outcomes for type 2 diabetes. Continuous or intermittent glucose monitoring is minimally effective for control of type 2 diabetes and can be harmful. Phentermine-topiramate and GLP-1 receptor agonists are the most effective drugs for promoting weight loss. Semaglutide is effective for secondary prevention of cardiovascular disease in people with obesity and no diabetes. SGLT-2 inhibitors and GLP-1 receptor agonists decrease cardiovascular death in older adults with type 2 diabetes and heart failure. Beta blockers do not prevent subsequent events after myocardial infarction in patients with preserved ejection fraction. For patients who do not quit smoking after a trial of varenicline or combined nicotine replacement therapy, a higher dose of either drug can increase quit rates. e-Cigarettes increase abstinence from smoking, but long-term vaping is a consequence for some. Oral naltrexone and acamprosate are safe and effective treatments for alcohol use disorder. Cognitive behavior therapy can reduce fatigue attributed to long COVID. New monoclonal antibodies for Alzheimer disease are harmful, expensive, and minimally effective. Clinicians may choose to deliver bad news in person or by telephone, using their judgment or patient preference to decide which is best for the patient.

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For more than 25 years, a team of six clinicians has reviewed 110 medical journals each month to identify studies that are most likely to improve primary care practice. The team includes experts in family medicine, pharmacology, hospital medicine, and women's health.

The goal of this process is to identify POEMs (patient-oriented evidence that matters). A POEM must report at least one patient-oriented outcome, such as improvement in quality of life, symptoms, morbidity, or mortality. It should also be free of important biases that threaten the validity of the study results to avoid errors in clinical decision-making. Finally, if applied in practice, the results would change what many primary care physicians do by adopting a new practice or discontinuing an old one. Of more than 20,000 research studies published in 2024 in journals reviewed by the POEMs team, 253 met the inclusion criteria. These POEMs are emailed daily to subscribers of Essential Evidence Plus

(Wiley-Blackwell, Inc), and select POEMs appear in *American Family Physician (AFP)*.

From 2012 to 2023, we relied on Canadian physicians to vote on the relevance of each POEM to their practice. Since the

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Canadian Medical Association stopped subscribing to Essential Evidence Plus, we chose the top 20 POEMs of 2024 differently. First, each of the POEM authors identified the most relevant POEMs from those that they wrote, totaling 51 POEMs. The POEMs authors, Dr. Grad, and three *AFP* editors (Drs. Sumi Sexton, Kenny Lin, and Jay Siwek) then ranked each POEM for relevance to primary care. The 20 highest ranked studies are included in this article, the 14th installment of the annual series. The full POEMs from this article are available at <https://www.aafp.org/pubs/afp/content/top-poems/2024.html>. A collection of the annual top 20 research studies articles from 2011 to 2023 is available at <https://www.aafp.org/pubs/afp/content/top-poems.html>. This page also has links to the full text of POEMs for each year.

INFECTIOUS DISEASE

The first POEM is a network meta-analysis that sought to identify the most effective initial oral antibiotic for patients with community-acquired pneumonia¹ (Table 1¹⁻⁶). The authors found 24 randomized controlled trials (RCTs) comparing different antibiotics or antibiotic combinations. None were clearly superior; however, the antibiotics judged most likely to lead to a clinical response and reduce mortality at 2 weeks were telithromycin (not available in the United States), azithromycin, amoxicillin-clavulanate, and the quinolones levofloxacin and nemonoxacin (not available in the United States). Because most CIs overlapped, it is reasonable to consider other factors when choosing an antibiotic, such as cost, illness severity, and tolerability. The second study found a clear association between the use of molnupiravir (Lagevrio) or nirmatrelvir-ritonavir (Paxlovid) and improved outcomes in immunocompromised patients with acute COVID-19.² The number needed to treat (NNT) was 12 to prevent one hospitalization and 22 to prevent one death.

The next two POEMs studied infections in children. The first found that a single dose of nirsevimab (Beyfortus) reduced the likelihood of hospitalization for respiratory syncytial virus infection in average-risk infants who did not meet criteria for receiving palivizumab (Synagis; 0.3% vs 1.5%; $P < .001$; NNT = 83).³ Nirsevimab is easier to administer (a single injection vs monthly injections) and much less expensive than palivizumab.

Although we want to be thoughtful about prescribing antibiotics, a meta-analysis of six studies including 936 children with symptoms of acute sinusitis showed a significant benefit of using amoxicillin or amoxicillin-clavulanate compared with placebo (most patients, including those in a large US trial, used amoxicillin-clavulanate).⁴ The clinical response rate at 2 weeks was significantly higher in the antibiotic group (77% vs 59%; NNT = 6), but with a higher rate of diarrhea (13.4% vs 7.2%; number needed to treat to harm = 16).

The next POEM compared two topical treatments for scabies. In an RCT with 110 patients, those treated with benzyl benzoate 25% were much more likely to be cured at 3 to 4 weeks than those treated with permethrin 5% (87% vs 27%; $P < .001$; NNT = 2).⁵ The final POEM in this section randomized premenopausal women with frequent urinary tract infections

(UTIs) to placebo, an oral probiotic, a vaginal probiotic, or both.⁶ At 4 months, a symptomatic UTI occurred in 70% of the placebo group, 61% of the oral probiotic group, 41% of the vaginal probiotic group, and 32% of the group receiving both probiotics. The oral probiotic contained 112.5 billion live, lyophilized lactic acid bacteria and bifidobacteria; the vaginal probiotic contained 1 billion units of three lactobacilli strains.

GASTROENTEROLOGY

Two of the 2024 POEMs addressed gastrointestinal diseases (Table 2⁷⁻⁸). The first studied adults with irritable bowel syndrome who had not responded to first-line treatments such as diet, lifestyle modification, antispasmodics, laxatives, or anti-diarrheals.⁷ They were randomized to receive low-dose amitriptyline (10 mg titrated to 30 mg as tolerated once daily) or placebo, and those taking the active drug were more likely to have a meaningful improvement in symptoms (61% vs 45%; NNT = 7). The second study randomized 434 adults with uncomplicated, symptomatic gallstones to laparoscopic cholecystectomy or conservative management without surgery.⁸ After 18 months, those receiving conservative management were much less likely to have undergone surgery (25% vs 67%; NNT = 3). When looking at the data from the original randomization, pain scores and quality of life were similar between the two groups.

DIABETES

The American Diabetes Association now recommends the earlier and broader use of glucagon-like peptide-1 (GLP-1) receptor agonists and sodium-glucose cotransporter-2 (SGLT-2) inhibitors.⁹ A recent meta-analysis adds to the evidence for this recommendation¹⁰ (Table 3¹⁰⁻¹²). The network meta-analysis reviewed 84 randomized studies of SGLT-2 inhibitors, GLP-1 receptor agonists, dipeptidyl peptidase-4 (DPP-4) inhibitors, and long-acting insulins as monotherapy or combination therapy in adults with type 2 diabetes. Only SGLT-2 inhibitors and GLP-1 receptor agonists reduced all-cause mortality and major adverse cardiovascular events compared with usual care. SGLT-2 inhibitors reduced the progression of chronic kidney disease and heart failure hospitalizations, and GLP-1 receptor agonists reduced stroke. SGLT-2 inhibitors and GLP-1 receptor agonists outperformed insulin in reducing all-cause mortality.

There were surprising results from a meta-analysis of 26 randomized studies of glucose monitoring in patients with type 2 diabetes. This study compared continuous glucose monitors (CGMs) with intermittently scanned CGMs. On average, A1C decreased by a very modest 0.2% to 0.3% among those using either device, and there was no effect on blood pressure or lipids. Compared with CGMs, intermittent monitoring was associated with improved user satisfaction and less psychological stress.¹¹

The benefits of GLP-1 receptor agonists for achieving weight loss are well documented, but less is known about how they compare with other drugs. In a network meta-analysis, GLP-1 receptor agonists were compared with naltrexone-bupropion (Contrave), phentermine-topiramate (Qsymia), and orlistat.¹²

TABLE 1

Infectious Disease

Clinical question	Bottom-line answer
What is the most effective oral treatment for mild to moderate community-acquired pneumonia? ¹	<p>Levofloxacin and nemonoxacin (not available in the United States) are the most effective oral treatments for community-acquired pneumonia.</p> <p>Using clarithromycin as the standard, telithromycin (not available in the United States), azithromycin, amoxicillin-clavulanate, and the quinolones levofloxacin and nemonoxacin produce similar benefits regarding clinical response and mortality. Amoxicillin and penicillin may not be as effective. Doxycycline is recommended in some guidelines; however, it was not included in this analysis due to a lack of recent studies.</p>
Do oral antivirals reduce the likelihood of hospitalization or death in immunocompromised patients with mild to moderate COVID-19? ²	<p>Oral antivirals are associated with lower hospitalization and mortality in immunocompromised patients with mild to moderate COVID-19.</p> <p>In a mostly vaccinated, immunocompromised population, oral antivirals (ie, molnupiravir [Lagevrio] or nirmatrelvir-ritonavir [Paxlovid]) are associated with lower rates of hospitalization and mortality. Baseline rates of hospitalization were much higher in this population than in contemporary studies of healthy adults, so it makes sense that the absolute benefit of the oral antivirals was also higher.</p>
Does a single intramuscular injection of nirsevimab (Beyfortus) reduce the likelihood of hospitalization due to RSV in infants who do not meet the criteria for receiving palivizumab (Synagis)? ³	<p>Nirsevimab reduces hospitalizations due to RSV in average-risk infants.</p> <p>In average-risk infants, a single intramuscular dose of nirsevimab reduces the likelihood of hospitalization due to RSV. Although it is not inexpensive, nirsevimab is much less expensive than palivizumab and only requires a single dose.</p>
Is antibiotic treatment more effective than placebo for resolving symptoms of acute sinusitis in children? ⁴	<p>Antibiotics are effective for children with acute sinusitis.</p> <p>About one-half of the data from the meta-analysis was largely from a single study. After a few weeks, there was a substantial benefit in using amoxicillin, with or without clavulanate, for the treatment of acute sinusitis symptoms in children.</p>
Is benzyl benzoate 25% or permethrin 5% more effective for the topical treatment of scabies in adolescents and adults? ⁵	<p>Benzyl benzoate 25% is highly effective for scabies.</p> <p>Benzyl benzoate 25% was significantly more effective than permethrin 5% for the treatment of scabies (number needed to treat = 2). It was also associated with more skin irritation, but this adverse event was generally mild to moderate and transient.</p>
Do oral or vaginal probiotics reduce the likelihood of UTI recurrence in premenopausal women with frequent UTIs? ⁶	<p>Probiotics reduce the likelihood of recurrent UTI in women with frequent UTIs.</p> <p>Probiotics (oral, vaginal, or both) that contain <i>Lactobacillus</i> reduce the incidence of UTI and prolong the time to the next UTI in premenopausal women with frequent UTIs. Vaginal probiotics (with or without oral probiotics) outperform oral probiotics alone. Vaginal probiotics alone provide a similar benefit to oral plus vaginal supplementation and seem to be the least invasive and least costly option.</p>

RSV = respiratory syncytial virus; UTI = urinary tract infection.

Information from references 1-6.

Phentermine-topiramate and GLP-1 receptor agonists were the most effective for achieving weight loss in adults with overweight or obesity. All of the drugs lowered weight compared with lifestyle modification alone; however, they were associated with increased adverse events, which led to drug discontinuation. More studies are needed to alleviate concerns about the

adverse effects that may emerge with these drugs in the long term.

CARDIOVASCULAR DISEASE

Three top POEMs of 2024 support conversations with patients interested in cardiovascular disease (CVD) prevention (Table

TABLE 2

Gastroenterology

Clinical question	Bottom-line answer
Does titrated low-dose amitriptyline improve symptoms of IBS in adults for whom first-line therapies have failed? ⁷	Low-dose amitriptyline is effective as a second-line therapy for IBS. This study was composed largely of adults with IBS-D (diarrhea) and IBS-M (mixed diarrhea and constipation) of at least moderate severity despite first-line therapy. Titrated low-dose amitriptyline was more effective than placebo in improving symptoms.
Is it safe to watch patients with symptomatic gallstone disease without complications? ⁸	For patients with uncomplicated gallstones, conservative management is a reasonable option. Uncomplicated gallstones can be managed over time with analgesia and monitoring. Although approximately 25% of patients will eventually undergo cholecystectomy after 18 months, there appears to be no need to rush to surgery without evidence of common bile duct blockage or acute pancreatitis.

IBS = irritable bowel syndrome.

Information from references 7 and 8.

TABLE 3

Diabetes

Clinical question	Bottom-line answer
Which new treatments for patients with type 2 diabetes affect mortality, cardiovascular outcomes, and renal outcomes? ¹⁰	SGLT-2 inhibitors and GLP-1 receptor agonists are best at improving patient-oriented outcomes for type 2 diabetes. Of the new treatments for people with type 2 diabetes, SGLT-2 inhibitors and GLP-1 receptor agonists outperform DPP-4 inhibitors and long-acting insulins as monotherapy or combination therapy in adults with type 2 diabetes, reducing all-cause mortality, major cardiovascular events, chronic kidney disease, and heart failure. SGLT-2 inhibitors and GLP-1 receptor agonists are also less likely to cause severe hypoglycemia.
Does continuous glucose monitoring offer a benefit compared with traditional self-monitoring in patients with type 2 diabetes? ¹¹	Continuous or intermittent glucose monitoring is minimally effective, perhaps harmful. In relatively short-term studies, glucose monitoring devices have only a small effect on A1C and do not affect body composition, lipids, or blood pressure. Real-time (continuous) glucose monitors, such as Dexcom G6 and G5, Medtronic TouchCare Nano, and Medtronic Guardian models, may cause psychological stress in users. Intermittent glucose monitors, such as FreeStyle Libre, are better accepted by patients. Both types of devices increase the risk of adverse effects, such as insertion site symptoms and infection.
Which drugs are the most effective for achieving weight loss in adults with overweight or obesity? ¹²	Phentermine-topiramate (Qsymia) and GLP-1 receptor agonists are the most effective drugs for promoting weight loss. In this analysis, phentermine-topiramate and GLP-1 receptor agonists were the most effective drugs for achieving weight loss in adults with overweight or obesity.

DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1; SGLT-2 = sodium-glucose cotransporter-2.

Information from references 10-12.

⁴¹³⁻¹⁵). Semaglutide (Wegovy) can be effective for weight loss, but can it prevent other chronic conditions associated with obesity? An RCT showed that it can decrease the risk of nonfatal

myocardial infarction (MI) in patients who have obesity and established heart disease without diabetes.¹³ This is the type of evidence we need to add semaglutide to our toolbox of drugs

TABLE 4

Cardiovascular Disease

Clinical question	Bottom-line answer
In patients with obesity and established CVD without diabetes, does semaglutide (Wegovy) improve cardiovascular outcomes? ^{7,13}	<p>Semaglutide works for secondary prevention of CVD in people with obesity and established CVD and no diabetes.</p> <p>For patients with obesity and established CVD who do not have diabetes, important individual end points showed that semaglutide decreases the risk of nonfatal MI (number needed to treat = 100) but not cardiovascular mortality (25% vs 3.0%; $P = .07$) during 40 months of follow-up, despite the composite outcome of reduced death, MI, or stroke. It is interesting that the title of this industry-sponsored study says nothing of the fact that this was a group of patients with established CVD. We should not generalize and assume that this drug will work for primary prevention of CVD in patients with obesity who do not have established CVD.</p>
Do SGLT-2 inhibitors improve outcomes in older adults or those who are frail with type 2 diabetes and heart failure? ¹⁴	<p>SGLT-2 inhibitors decrease cardiovascular deaths in older adults with type 2 diabetes and heart failure.</p> <p>In this analysis that pooled data from disparate study designs, SGLT-2 inhibitors had little overall effect on glycemic control or all-cause mortality, but they decreased cardiovascular deaths in older adults or those who are frail with type 2 diabetes and heart failure.</p>
In patients with preserved ejection fraction following acute MI, does long-term use of a beta blocker reduce the likelihood of death or subsequent acute MI? ¹⁵	<p>Beta blockers do not prevent events in patients with preserved ejection fraction after MI.</p> <p>For patients with acute MI and preserved ejection fraction, the use of a beta blocker for a median of 3.5 years did not reduce the likelihood of death or subsequent acute MI.</p>

CVD = cardiovascular disease; MI = myocardial infarction; SGLT-2 = sodium-glucose cotransporter-2.

Information from references 13-15.

for secondary prevention of CVD. One caveat: the effectiveness of semaglutide in people with obesity who do not have CVD (primary prevention) has not been proven.

Some physicians may be reluctant to initiate SGLT-2 inhibitors in older adults or those who are frail because of concerns about adverse effects (eg, UTI) and small effects on glycemic control. A useful meta-analysis included 20 studies of older adults or those who were frail with heart failure and type 2 diabetes.¹⁴ These patients experienced fewer cardiac deaths and

hospitalizations for heart failure with the use of SGLT-2 inhibitors. The cardiovascular and renal benefits of SGLT-2 inhibitors appear to be so robust that we can confidently prescribe this drug class, even in older and frail patients.

Many of us were taught that beta blockers are beneficial in people with ischemic heart disease. The third POEM in this group describes findings that go against conventional teaching. In a well-conducted, open-label study, patients with acute MI who had a left ventricular ejection fraction of at least 50% were randomly assigned to receive long-term treatment with a beta blocker (metoprolol or bisoprolol) or no beta blocker.¹⁵ Bottom line: in patients with MI and preserved ejection fraction, beta blockers had no effect on the primary outcome (a composite of death from any cause or new MI). This finding could be reassuring for some patients who are unable to use beta blockers due to adverse effects.

ADDICTION AND MENTAL HEALTH

For smoking cessation, good-quality evidence supports initial treatment with varenicline (Chantix) for 12 weeks. But what if your patient cannot stop smoking after initial treatment? Should nicotine replacement therapy or a higher dose of varenicline be recommended? A randomized trial addressed this question in patients aged 18 to 75 years who smoked five or more cigarettes per day¹⁶ (Table 5¹⁶⁻¹⁹). In phase 1, participants were randomly assigned to receive a standard dosage of varenicline (2 mg/day) or combined nicotine replacement therapy (21-mg patch plus at least six 2-mg lozenges per day) during weeks 1 through 6. In phase 2 (weeks 7-12), patients who did not successfully quit in phase 1 were randomly assigned to continue their phase 1

medication, increase the dose of their phase 1 medication, or switch to the alternate phase 1 medication for 6 weeks. The dosage of varenicline increased 1 mg (3 mg/day); the dose of the patch in the combined nicotine replacement therapy increased by 21 mg to 42 mg/day plus the lozenges. In patients who were initially treated with standard-dose varenicline and unable to quit, confirmed abstinence occurred significantly more often in patients who increased their varenicline dosage compared with those switching to combined nicotine replacement therapy

TABLE 5

Addiction and Mental Health

Clinical question	Bottom-line answer
What is the best strategy for smoking cessation in adults following initial treatment failure with varenicline (Chantix) or combined nicotine replacement therapy? ¹⁶	<p>Various interventions help patients who did not attain smoking cessation after varenicline or combined nicotine replacement therapy.</p> <p>For patients who do not attain smoking abstinence at 6 weeks after initial treatment with varenicline, increasing the dosage of varenicline (from 2 to 3 mg/day) resulted in a significantly higher quit rate than continuing to use the same dosage for a longer period. Switching to combined nicotine replacement therapy was not effective. For patients who did not respond to initial treatment with combined nicotine replacement therapy, an increased dosage (from a 21-mg patch to a 42-mg patch plus lozenges) or switching to varenicline resulted in a significantly higher quit rate than continuing to use the same dosage of combined nicotine replacement therapy.</p>
For smokers who want to quit, do electronic nicotine-delivery systems increase the likelihood of abstinence at 6 months? ¹⁷	<p>e-cigarettes increase abstinence from smoking, but long-term vaping is a consequence for some.</p> <p>Adult smokers who were given e-cigarettes were significantly more likely to be abstinent at 6 months (number needed to treat = 6-8). In this study, the cost of e-cigarettes was paid for by the study; the results may be less favorable in the real world where patients have to buy their own e-cigarettes.</p>
What medications are safe and effective for the treatment of alcohol use disorder? ¹⁸	<p>Oral naltrexone and acamprosate are safe and effective for alcohol use disorder.</p> <p>This updated systematic review found that, in conjunction with psychosocial interventions, oral naltrexone (50 mg/day) and acamprosate have the strongest evidence for the effective treatment of alcohol use disorder.</p>
Does CBT improve fatigue in patients with long COVID? ¹⁹	<p>CBT can reduce fatigue attributed to long COVID.</p> <p>For patients with severe fatigue at least 3 months after COVID-19, CBT offers significant improvement in symptoms vs usual care.</p>

CBT = cognitive behavior therapy.

Information from references 16-19.

or continuing their initial varenicline dosage (20% vs 0% and 3%, respectively). In patients who were initially treated with combined nicotine replacement therapy and unable to quit, confirmed abstinence occurred more often in patients who switched to varenicline or increased the combined nicotine replacement therapy dose compared with continuing the initial combined nicotine replacement therapy dose (14% and 14% vs 8%, respectively).

Many people believe that e-cigarettes are effective for smoking cessation and less harmful than smoking. An RCT compared e-cigarettes containing nicotine and smoking cessation counseling with smoking cessation counseling and a \$50 voucher that participants could optionally use to buy a nicotine-replacement product.¹⁷ The e-cigarettes with counseling intervention increased smoking abstinence at 6 months (28.9% vs 16.3%; absolute difference = 12.6%); however, more participants in the e-cigarette group were still using nicotine products (e-cigarettes or nicotine replacement) at 6 months (33.7% vs 20.1%). This information should be shared with

motivated patients when discussing e-cigarettes for smoking cessation.

Medications used for the treatment of alcohol use disorder in outpatients include disulfiram, gabapentin, topiramate, naltrexone, and acamprosate. A systematic review examined 118 RCTs of pharmacotherapies for alcohol use disorder.¹⁸ Of the 118 trials, 87 included different levels of psychosocial interventions. The evidence supported using acamprosate or oral naltrexone for reducing the risk of returning to any drinking (NNT = 11 and 18, respectively). The evidence did not show that disulfiram or gabapentin was beneficial compared with placebo, whereas topiramate was associated with only a reduction in the mean percentage of drinking days and number of drinks per day. Oral naltrexone and acamprosate can be used as first-line therapies for alcohol use disorder even if psychosocial intervention is not available.

Long COVID is characterized by symptoms, such as severe fatigue, that last months after the initial infection. A randomized trial in the Netherlands compared the effect of cognitive

TABLE 6

Miscellaneous

Clinical question	Bottom-line answer
Does treatment with monoclonal antibody therapy that targets amyloid improve outcomes in patients with Alzheimer disease? ²⁰	New monoclonal antibodies for patients with Alzheimer disease are minimally effective, harmful, and expensive. Amyloid-targeting antibodies for the treatment of Alzheimer disease have failed to demonstrate clinically meaningful benefits. They are associated with concerning risks of harm, most notably cerebral swelling and hemorrhage identified on imaging studies (number needed to harm = 13). The balance of risk vs benefit does not justify the use of these costly (> \$20,000 annually) drugs.
Does delivery of bad news via telephone increase psychological stress more than in-person communication? ²¹	Use patient preference and clinical judgment to determine the best way to deliver bad news. Delivering bad news by telephone does not affect levels of anxiety, depression, or satisfaction with care compared with delivering the news in person.

Information from references 20 and 21.

behavior therapy delivered by psychologists with usual care for people with severe fatigue following COVID-19.¹⁹ Participants were self-referred. Due to the nature of the intervention, research assistants, participants, and therapists were not blinded to the allocated treatment. The primary outcome was fatigue severity, as assessed by the fatigue subscale of the 20-item Checklist Individual Strength. Clinical response was evaluated at 19 weeks (end of treatment) and 26 weeks. A clinically and statistically significant difference in fatigue scores was observed (−9.3 points at 19 weeks; 95% CI, −13.2 to −5.3, and −8.4 points at 26 weeks; 95% CI, −13.1 to −3.7). At 26 weeks, the percentage of patients who no longer had severe fatigue was much higher for the cognitive behavior therapy group (63% vs 26%; $P < .001$; NNT = 3).

MISCELLANEOUS

Two POEMs did not fit neatly into one of our categories (Table 6^{20,21}). The first was a meta-analysis of published studies that compared one of the new amyloid-targeting monoclonal antibodies with placebo in patients with mostly mild to moderate Alzheimer disease.²⁰ The focus was on whether symptoms improved over 18 months in a way that patients or caregivers would notice (exceeding the minimal clinically important difference). No drug came close to meeting or exceeding this level of benefit, and there were important harms, including intracranial swelling and hemorrhage. Ineffective, harmful, and expensive are not a good combination for our patients.

The last POEM asked whether delivery of bad news via telephone or in person is best for patients.²¹ The mostly observational studies found no differences between the two in levels of psychological stress, anxiety, depression, or posttraumatic distress. In an increasingly online world, patients will help us choose the best method, and knowing may be preferable to waiting for many patients.

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—Sumi Sexton, MD, Editor-in-Chief

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