IN DEPTH

Are IUDs an effective and safe form of birth control for teen patients?

Evidence-based answer

Yes. Contraceptive failure rates are similar among those who use intrauterine devices (IUDs), implants, or depot medroxyprogesterone acetate (DMPA) injections, while pill, patch, or ring (PPR) methods have higher failure rates (SOR: B, cohort study). When compared with oral contraceptives, IUDs in adolescents have similar or better continuation rates (SOR: B, systematic review of cohort studies). Adolescents receiving IUDs have similar risk of infection but higher expulsion rates than women receiving IUDs who are 18 to 21 years old (SOR: B, retrospective cohort study).

Evidence summary

A 2009 systematic review of 6 cohort studies (N=1,489 in the 4 studies outlined) and 7 case series (N=464 in the 3 cases outlined) examined the appropriateness of IUDs in women younger than 22 years.  

IUD continuation rates ranged from 48% to 88% at 1 year and were similar to continuation rates for combined oral contraceptives. Continuation rates in adolescents were similar or better than the rates in nonadolescents. IUD expulsion rates ranged from 5% to 22% at 6 to 48 months. Cumulative pregnancy rates increased from 2% at 6 months to 11% at 48 months. One small cohort study reported a 3% pregnancy rate at 2 years for IUDs and 0% for combined oral contraceptives in adolescents (no statistical analysis reported).  

A 2012 prospective cohort study of 7,486 eligible patients, 14 to 45 years of age at risk for unintended pregnancy, compared the effectiveness of long-acting reversible contraception (LARC; ie, IUDs and implants) (n=5,781) versus DMPA (n=176) versus PPR (n=1,527).  

Patients were followed for 3 years (first 5,090 patients) or 2 years (remainder of cohort). The primary outcome
was contraceptive failure. Evaluation of pregnancy rates by age groups was a secondary outcome.

The contraceptive failure rate among patients using DMPA injections was similar to those of patients using IUDs or implants. The failure rate among all patients using PPR was 4.55 per 100 patient-years compared with 0.27 per 100 patient-years among patients using LARC (HR 21.8; 95% CI, 13.7–34.9). Patients younger than 21 years who were using PPR had nearly twice the risk of unintended pregnancy compared with older women (HR 1.9; 95% CI, 1.2–2.8). No difference was noted based on age in the effectiveness between DMPA and IUDs.

A 2012 retrospective cohort assessed IUD use among 233 adolescents and young women. It compared the IUD retention probability between the under 18-year-old and 18- to 21-year-old age groups. The follow-up period was 8 years.

The risk of removal/expulsion was significantly greater in the under 18-year-old group compared with the 18- to 21-year-old group (HR 2.85; \( P < .001 \)). No significant difference was noted between groups regarding risk of infection (RR 1.56; \( P > .05 \)). The continuation rate with IUDs at 5 years was 50% in adolescents <18 years and 71.5% in the 18- to 21-year-old group (\( P < .001 \)), which are higher than the reported continuation rates for other hormonal contraceptives. The study concluded that IUDs appear to be a safe option in young adolescents.

### Recommendations from others

A 2012 committee opinion from the American College of Obstetricians and Gynecologists states that LARCs (including IUDs) are safe and appropriate contraceptive methods for adolescents, with higher rates of satisfaction and continuation than other reversible contraceptives.

### REFERENCES

Funny numbers

Political satirist Stephen Colbert coined the term “truthiness” to mean those things that feel so right to us they just have to be true. He was lampooning a culture where people use their opinions to guide finding their own facts.

One way people can find (or create) their own facts is to manipulate statistical methods to get “better” results. In his cautionary book, Proofiness: The Dark Arts of Mathematical Deception, Charles Seife explores the many ways one can generate truthiness with numbers, walking readers through entertaining examples of the distortions that bedevil statistical presentations of all kinds.¹

We all know that relative risk reduction makes an effect seem larger than absolute risk reduction. Yet, we generally seem to be blind to a similar phony fact that Seife calls “over-precision,” where something becomes more believable to us when an author presents the numbers using more decimals. If $P<.05$, we yawn, but if $P=0.0451$, it looks like the researchers nailed it. Another example of over-precision is attempting to quantify the unquantifiable. I’ve always considered my life a bit more nuanced than a 2-digit, quality-adjusted life-year. According to Seife, people can also rig the data by comparing apples to oranges in various subtle ways. Researchers often try to compare the apples of today with the oranges of yesterday in case-control studies. Apple and orange problems also arise when diagnostic criteria change or when we extrapolate outcomes in adults to outcomes in children (or men to women, or Americans to Laplanders).

A third set of problems Seife calls “Rorschach’s Demon,” the tendency to project associations into randomness. We doctors do a reasonable job distinguishing associations from causation. But I’ll bet we’re regularly taken in by “regression to the moon,” because anyone can draw a line through a random scattershot of data points and generate a regression coefficient (although that person may have to ignore the underlying assumptions of the method).

We consumers of evidence will probably not be able to tell if such common numerical distortions are deliberate proofiness or just plain ignorance. Either way, evidence-based medicine should have no tolerance for them. The truth is hard enough to comprehend as it is.

4 Things to know about motivational interviewing for managing diabetes in primary care

1. **Type 2 diabetes mellitus (T2DM) is a common and burdensome disease in the United States.**
   The estimated overall prevalence of diabetes among adults in the United States ranges from 5.8% to 12.9%, and diabetes and its complications made up 14% of healthcare expenditures in 2009. T2DM is a growing problem, with the current number of patients with T2DM at around 25.8 million and the number of patients is estimated to reach 300 million by 2025.

2. **Health behaviors greatly affect T2DM.**
   Lifestyle changes can have important effects on T2DM. A systematic meta-analysis of 10 RCTs (N=960) looking at text messaging to reinforce lifestyle changes demonstrated an effect on glycemic control; glycosylated hemoglobin (HbA1C) was reduced significantly in experimental groups compared with control groups (–1.1% vs –0.42%; \( P < .001 \)).

   Weight loss has particularly important salubrious effects on T2DM, reversing the core pathophysiology associated with the disease. A study of 30 subjects on a very-low-calorie diet demonstrated that caloric restriction both decreased insulin resistance and increased insulin secretion. Additionally, the American Diabetes Association recommends lifestyle intervention as first-line therapy for T2DM.

3. **Motivational interviewing provides improved adherence to participation in lifestyle changes for T2DM.**
   An RCT looked at motivational interviewing in African American patients with diabetes as a means to promote physical activity, decrease glucose levels, and decrease body mass index (BMI). Sixty-two patients were assigned to usual care (basic information on DM symptoms and referral to a DM educator) or motivational interviewing, with outcomes obtained at baseline and 3-month follow-up. Participants in the motivational interviewing group received a maximum of 6 sessions in 3 months, lasting 45 minutes to 1 hour. Endpoints were physical activity (measured by accelerometer print outs), glucose levels, and BMI.

   The motivational interviewing group had better odds of adhering to the recommended time for physical activity of 150 minutes per week (66.7% vs 38.8%; OR 2.92; 95% CI, 1.6–14.3). In addition, BMI decreased in the motivational interviewing group by an average of 2 kg/m², compared with an increase of 0.5 kg/m² in the intervention group (\( P = .046 \)). Glucose averages dropped by 24.3 mg/dL in the motivational interviewing group compared with an increase of 2.9 mg/dL in the usual-care group (\( P = .043 \)). No significant change was noted in HbA1C.

4. **Motivational interviewing is an effective tool for improving outcomes in metabolic syndrome.**
   A 2008 RCT assessed the effect of motivational interviewing on weight loss and physical activity as modifiable risk factors in patients with prediabetes. Patients (N=140) were randomized to receive informational leaflets or individual behavioral counseling using motivational interviewing. The patients in the intervention group received up to 11 sessions over 6 months with average contact time being 34 minutes per encounter. The primary outcomes were weight loss of 5% and moderate physical activity (150 minutes per week) after 6 months.

   More patients in the intervention group reached the weight loss target of 5% of body weight (24% vs 7%; OR 3.96; 95% CI, 4–21; NNT=6). The proportion achieving the physical activity target of 150 minutes per week did not increase significantly (38% vs 28% for controls; OR 1.6; 95% CI, 0.7–3.8). Although this study only looked at a 6-month endpoint, a sustained weight loss of this magnitude could meaningfully reduce diabetes risk.

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**REFERENCES**

Does adjuvant treatment with coenzyme Q10 improve statin tolerance?

Evidence-Based Answer
No, use of coenzyme Q10 supplementation does not affect rates of statin-induced myopathy (SOR: B, meta-analysis of RCTs). Coenzyme Q10 is not associated with any change in the number of patients remaining on statin therapy (SOR: B, RCT). In the event of statin-induced myopathy, current guidelines recommend discontinuation of original statin therapy, establishment of a causal relationship, and initiation of a different statin with gradual dose titration as tolerated (SOR: B, evidence-based guideline).

A 2015 meta-analysis of 6 RCTs examined the effect of coenzyme Q10 supplementation on myopathy in 302 patients taking various statin medications. No statistically significant difference was found with coenzyme Q10 supplementation compared to placebo with respect to either muscle pain (5 trials, n=253; standard mean difference [SMD] –0.53; 95% CI, –1.3 to 0.28) or plasma CK levels (5 trials, n=226; mean difference [MD] 12 units/L; 95% CI, –14 to 38). Of note, the individual trials were small (n<60), the dose of coenzyme Q10 and duration of therapy varied widely, and different myopathy-associated subjective scales were used in the trials.

A 2007 RCT discussed in the meta-analysis above is reviewed separately here as it additionally evaluated the number of patients who remained on statin therapy when treated with coenzyme Q10 compared with placebo. The trial included 44 patients with self-reported myalgia, who had been unable to continue taking adequate doses of statin therapy. The patients were randomized to receive placebo or 200 mg coenzyme Q10 daily for 12 weeks, and both groups underwent an upward dose titration of simvastatin starting at 10 mg daily and doubling every 4 weeks to a maximum dose of 40 mg/d.

No difference was noted in the number of patients tolerating 40 mg simvastatin (73% with coenzyme Q10 vs 59% with placebo, \(P=.34\)) or in the number of patients remaining on any dose of statin therapy (73% with coenzyme Q10 vs 82% with placebo, \(P=.47\)).

A 2013 evidence-based clinical practice guideline by the American College of Cardiology/American Heart Association (ACA/AHA) on treatment of blood cholesterol recommended discontinuation of statin therapy if muscle symptoms developed. The ACA/AHA also recommended clinicians do an evaluation to establish a causal relationship between the muscle symptoms and statin therapy and to rule out other conditions. If muscle symptoms resolved and no contraindication existed, the ACA/AHA recommended initiating a low dose of a different statin and gradually increasing the dose as tolerated (strength of recommendation IIa, defined as reasonable to consider, and level of evidence B, defined as data from single RCT or nonrandomized studies).

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Is warfarin safe and effective for prevention of noncardioembolic ischemic stroke?

Evidence-Based Answer
No, do not use warfarin to prevent thrombotic stroke. Warfarin is no better than aspirin for secondary prevention after a noncardioembolic ischemic stroke, and it carries an increased risk of bleeding and death (SOR: A, systematic reviews of RCTs).

A systematic review of 11 randomized and quasirandomized controlled trials with 2,487 patients examined the benefit of any anticoagulation after a first stroke or transient ischemic attack (TIA) in patients without a cardioembolic explanation for their stroke or TIA. The primary outcome measure was death or dependency at the end of a mean of 1.9 years of follow-up. Trials that compared an anticoagulant with an antiplatelet drug were excluded, but trials in which both comparison groups used antiplatelet agents were included.

The reviewers found no significant difference in the primary outcome between the anticoagulation and control groups (2 trials, n=326; OR 0.83; 95% CI, 0.52–1.3). Treatment with warfarin also provided no significant reduction in nonfatal stroke, myocardial
infarction, or vascular death (4 trials, n=575; OR 0.96; 95% CI, 0.68–1.4). The risk of fatal and nonfatal intracranial hemorrhage was increased in patients treated with warfarin (9 trials, n=1,214; OR 2.5; 95% CI, 1.2–5.6). Nine included trials predated both the routine use of CT to evaluate stroke and TIA and the use of international normalized ratio to monitor anticoagulation. Of the 2 remaining studies, 1 evaluated heparin (n=1,095) and the other (n=178) compared warfarin versus aspirin versus aspirin plus warfarin.1

Another systematic review of 5 RCTs with 4,076 patients investigated the benefit of oral anticoagulation versus oral antipatelet therapy for the secondary prevention of a recurrent stroke or TIA after cerebral ischemia of noncardioembolic origin.2 There was a statistically significant increase in death in the anticoagulated group versus the antiplatelet group (5 trials; N=4,015; RR 2.4; 95% CI, 1.3–4.3) without a significant reduction in recurrent ischemic stroke (3 trials, n=1,692; RR 1.0; 95% CI, 0.6–1.8). The authors recommended against the use of oral anticoagulation for the secondary prevention of noncardioembolic stroke.

**Evidence-Based Answer**

Probiotics improve global irritable bowel syndrome (IBS) symptoms; however, which individual species or combination is most effective remains unclear (SOR: B, meta-analyses of RCTs).

A 2014 systematic review and meta-analysis of 35 RCTs (N=3,452) evaluated the effect of probiotics on IBS symptoms.1 IBS diagnosis was based on clinician’s opinion or diagnostic criteria (Manning; Kruis score; Rome I, II, or III) with a minimum therapy (intervention) duration of 7 days. A single probiotic was used in 16 trials (8 Lactobacillus, 3 Bifidobacterium, 2 Escherichia coli, 1 Streptococcus, 1 Saccharomyces, and 1 study with either Lactobacillus or Bifidobacterium) while 19 trials used a combination of probiotics.

Fewer patients in the probiotic group had persistent or unimproved IBS symptoms compared with placebo (23 trials, n=2,575; 56% vs 73%; RR 0.79; 95% CI, 0.70–0.89) resulting in an NNT of 7 (95% CI, 4–13). Adverse events were increased in the probiotics group compared with placebo (24 trials, n=2,407; 17% vs 14%; RR 1.2; 95% CI, 1.0–1.4; NNH=35). Specific details of adverse effects were not reported. Statistically significant heterogeneity was detected among studies.

Another systematic review and meta-analysis (10 RCTs, 9 of which were included in above meta-analysis, N=862 patients) evaluated the efficacy of specific probiotic species versus placebo in alleviating individual IBS symptoms such as abdominal pain, distension, flatulence, stool frequency, stool consistency, straining, and urgency.3 Treatment in most trials lasted 4 to 8 weeks. All results were reported as standard mean difference (SMD, where a change of 0.2 is considered small, 0.6 moderate, and 1.2 large).

Pain scores improved if probiotic treatment included *Bifidobacterium breve* (3 trials, n=154; SMD –0.34; 95% CI, –0.66 to –0.02), *Bifidobacterium longum* (4 trials, n=202; SMD –0.48; 95% CI, –0.91 to –0.06), or *Lactobacillus acidophilus* (6 trials, n=328; SMD –0.31; 95% CI, –0.61 to –0.01). Distension scores were improved in probiotics containing *B breve* (3 trials, n=154; SMD –0.45; 95% CI, –0.77 to –0.13) or the combination of *Bifidobacterium infantis*, *Lactobacillus casei*, and *Lactobacillus plantarum*.
Compared with placebo at 12 weeks, tegaserod 12 mg increased the number of patients with clinical response (RR 1.5; 95% CI, 1.4–1.8; NNT=7). One study demonstrated clinical response to the 4-mg dose compared with placebo at 12 weeks (40.3% vs 26.9%, respectively; \( P < .0001; \) NNT=8).²

A 2012 RCT of 102 pediatric patients (average age 5.2 years) studied the effects of oral metoclopramide (0.15 mg/kg per day) with oral PEG (0.6 g/kg per day) versus placebo with PEG on chronic functional constipation as diagnosed by the Rome III criteria.² After fecal disimpaction, patients received PEG for 12 weeks combined with either metoclopramide or placebo for the initial 4 weeks. Treatment response was defined as 1 to 2 soft and easy bowel movements per day with no symptom relapse 6 months after initiation of treatment. Groups showed no significant difference in response rate with 85% response in metoclompramide plus PEG and 84% response in placebo plus PEG (\( P = .39 \)).²

A 2010 randomized, double-blinded trial of 1,798 women (average age 43.3 years, 78% white) with constipation-predominant IBS (based on Rome II criteria) compared oral renzapride 4 mg daily, 2 mg twice daily, and placebo for 12 weeks. The primary outcome was the number of months each patient had a response in overall IBS symptoms on a 7-point categorical scale (from significantly worse to significantly relieved) compared with baseline. A monthly response was defined subjectively as at least moderate relief for 3 of 4 weeks or significant relief for 2 of 4 weeks. Renzapride showed a statistically significant improvement in average number of months of symptomatic relief compared with placebo at both 4 mg daily (0.55 vs 0.44; \( P = .027 \)) and 2 mg twice daily (0.6 vs 0.44; \( P = .004 \)). Renzapride 4 mg daily was also associated with a higher number of bowel movements per day compared with placebo (0.22 vs 0.13; \( P = .003 \)).³

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What is the role of prokinetic agents in patients with constipation?

Evidence-Based Answer

The role for prokinetic agents in the treatment of chronic constipation or constipation-predominant irritable bowel syndrome (IBS) in adults and children is unclear. Tegaserod increases the frequency of spontaneous bowel movements (SBM) in patients with chronic constipation (SOR: A, meta-analysis of RCTs). The addition of metoclopramide to polyethylene glycol (PEG) does not improve constipation in children more than the use of PEG alone (SOR: B, single RCT). Renzapride modestly improves subjective assessment of symptoms and increases daily bowel movements in adults with constipation-predominant IBS (SOR: B, single RCT).

A 2007 meta-analysis included 13 RCTs assessing use of tegaserod for the treatment of IBS and chronic constipation in predominantly female patients (N=11,287) older than 12 years.¹ Two studies specifically assessed chronic constipation by comparing oral tegaserod dosed daily at 4 and 12 mg with placebo over a 12-week period. Patients (n=1,745) reported SBMs at 4 and 12 weeks. Clinical response was defined as an increase of 1 or more SBM per week.


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Evidence-Based Answer

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What is the best treatment for superior oblique myokymia?

Evidence-Based Answer
There is no single best treatment for superior oblique myokymia (SOM), but all of the following therapies were reported to be at least somewhat effective: carbamazepine, phenytoin, propranolol, topical timolol, memantine, gabapentin, prism lenses, and microvascular decompression of the trochlear nerve (SOR: C, case series and case reports). Mirtazapine, onabotulinumtoxinA, and baclofen were ineffective long-term; mild symptoms may self-resolve (SOR: C, case studies).

A retrospective case series of 20 patients with SOM, defined as a unilateral episodic oscillopsia and/or diplopia caused by superior oblique muscle contractions, reported on various medical therapies. The primary outcome was patient-reported relief of oscillopsia, but the scale was not defined. Patients were 70% females, and 65% had diplopia and oscillopsia. Mean onset was 37 years of age, mean time to presentation was 3.1 years, and follow-up was 1 to 12.5 years (mean 6.5 years) from symptom onset to most recent visit.

Overall, 18 patients were prescribed carbamazepine (see TABLE): 6 patients reported significant improvement for 9 months to 5 years follow-up with no adverse events, 4 patients had transient improvement, 5 patients had initial improvement, but discontinued therapy because of undescribed adverse events, and 3 patients had no relief. Seven patients tried baclofen without relief. Five patients tried extended-release propranolol: 3 improved, 1 with partial relief that nearly resolved when valproic acid was added, while 2 remained symptomatic. One patient on phenytoin showed symptom relief for 6 years; another remained symptomatic. No length of follow-up information was given for baclofen or propranolol.

A case report presented a 47-year-old man with a 6-year history of SOM (diplopia and pulsating feeling in right eye) who failed carbamazepine, gabapentin, baclofen, and timolol eye drops and declined onabotulinumtoxinA. Trochlear nerve microvascular decompression provided sustained relief at 18 months follow-up. The patient experienced some postoperative transient dizziness, nausea, and vomiting.

In a case report of a 40-year-old woman with SOM for 2 years, gabapentin controlled symptoms for 12 months; however, the patient suffered tiredness, weight gain, and loss of libido and eventual

<table>
<thead>
<tr>
<th>Reference</th>
<th>Medication regimen evaluated</th>
<th># Patients</th>
<th>Outcomes</th>
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<tr>
<td>Retrospective case series¹ (N=20)</td>
<td>Carbamazepine 200 mg BID titrated to QID PRN and as tolerated 18</td>
<td>Transient partial relief to long-term significant relief</td>
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<td></td>
<td>Baclofen 5 mg TID titrating to maximum 20 mg QID 7</td>
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<td>Propranolol ER 80 mg daily 5</td>
<td>Relief with monotherapy</td>
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<td>Valproic acid unknown dose added to propranolol ER 1</td>
<td>Improvement in patients with initial partial relief</td>
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<td></td>
<td>Phenytoin 100 mg TID 1</td>
<td>Inconsistent relief</td>
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<tr>
<td>Case report² (N=1)</td>
<td>Carbamazepine, gabapentin, baclofen, and timolol eye drops 1</td>
<td>Almost no relief</td>
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<td></td>
<td>Microvascular decompression of trochlear nerve 1</td>
<td>Relief</td>
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<td>Case report³ (N=1)</td>
<td>Gabapentin, dose increased by 300 mg every week until 2,400 mg/d 1</td>
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<td>Memantine 5 mg daily, titrating by 5 mg every 3 days max of 20 mg daily in 2 divided doses 1</td>
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<td>Prism lenses (prescription unspecified) 1</td>
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<td>Eye exercises 1</td>
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<td>Carbamazepine (dose unspecified) 1</td>
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<td>Timolol 0.5% ophthalmic solution BID in the affected eye then decreased to once daily after significant symptom relief 1</td>
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<tr>
<td>Case report⁵ (N=1)</td>
<td>G-15 lens glasses: right eye plano = 2 base down; left eye plano 1</td>
<td>Relief</td>
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TABLE
Outcomes of treatments for superior oblique myokymia
Evidence-Based Answer

Perhaps. Among patients who already have a diagnosis of obstructive sleep apnea (OSA), the presence of edema may indicate greater OSA severity, even after adjusting for confounders such as body mass index (BMI). The finding of edema appears to be independent of measurable pulmonary hypertension (SOR: C, small cohort and cross-sectional trials).

A 2008 retrospective, cross-sectional study of 378 patients with OSA (defined by an apnea-hypopnea index [AHI] >15) examined the proportion of these individuals who had leg edema, and the relevant characteristics of each group.\(^1\) The patients had no history of heart failure, liver failure, proteinuria, or chronic obstructive pulmonary disease, and patients taking calcium-channel blockers were excluded. Patients were evaluated with polysomnography to determine severity of sleep apnea and with a physical exam to identify presence and severity (from 1+ to 4+) of leg edema.

Pretibial edema was noted in 133 subjects (35%), a percentage that the authors stated is consistent with previous studies investigating edema in patients with OSA. The mean AHI was 41 in the edema group versus 28 in the nonedema group ($P=.04$), even after adjustment for other factors that correlate with edema such as BMI, age, obesity, hypertension, or diabetes.\(^1\)

A small 2009 prospective cohort trial of 70 male patients with newly diagnosed OSA investigated the relationship among sleep apnea, pretibial edema, and pulmonary hypertension.\(^2\) Overall, 29 of the subjects had both OSA and pretibial edema (vs 41 patients without edema). Most (28 of 29) edematous patients completed right heart catheterization. Investigators found that most patients had evidence of elevated pulmonary artery systolic pressure (PAS >30 mmHg in 82% of patients).

A weakness of this study was the lack of catheterization data in the nonedematous patients, but most nonedematous subjects did complete a first-pass ventriculogram. Many patients had some degree of right or left ventricular dysfunction, but there was no significant difference in ventricular function between edematous and nonedematous patients who had an interpretable first-pass ventriculogram. Right
ventricular dysfunction (defined as RVEF <40%) was present in 77% edematous versus 61% nonedematous subjects (P=.27), while left ventricular dysfunction (defined as LVEF<55%) was present in 41% edematous versus 30% nonedematous subjects (P=.64). Another small cross-sectional study from 2002 sought to clarify the relationship among OSA, edema, and pulmonary hypertension by determining whether subjects with leg edema and pulmonary hypertension had a higher frequency of OSA than edematous subjects with no pulmonary hypertension. The study examined 28 patients in a primary care setting with bilateral lower extremity edema, 16 of whom had pulmonary hypertension on echocardiogram (PAS >30 mmHg) and 12 of whom did not. Echocardiograms of all patients were free of valvular disease, systolic dysfunction, and diastolic dysfunction. All patients had normal lung function (defined as absence of obstructive or restrictive lung disease on pulmonary function test). Patients were excluded if they used edema-causing medications. All patients underwent polysomnography, and OSA was diagnosed as AHI >20 events/h.

Overall, a large proportion (68%) of the total study population met the definition of OSA, with no significant difference in percentage of OSA between the 2 groups (63% with OSA in pulmonary hypertension group vs 75% with OSA in comparison group; P=.48). The authors concluded that the presence of leg edema without other apparent cause may be a better marker for undiagnosed sleep apnea than the presence of pulmonary hypertension on echo, although they acknowledged that their small sample size made the results prone to type II error.

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Can you treat a patient with suspected urinary tract infection (UTI) over the phone?

Evidence-Based Answer

Phone management of UTI symptoms results in no difference in short-term symptom control compared with office management (SOR: C, small RCT). Symptoms such as dysuria, frequency, hematuria, and back pain each slightly increase the likelihood of a positive UTI while vaginal discharge and vaginal irritation moderately decrease the likelihood (SOR: A, meta-analysis of RCTs). Immediate use of antibiotics without testing may result in faster resolution of symptoms compared with management based on urinalysis (SOR: C, extrapolated from RCT of clinic patients).

An RCT of 72 nonpregnant women ≥18 years of age who called their usual provider with symptoms associated with uncomplicated UTI were randomly assigned to receive care over the phone (n=36) or usual office care (n=36). Symptom scores were collected at baseline and at days 3 and 10 of antibiotic therapy.

At days 3 and 10, the authors found that symptom scores for dysuria, frequency, and urgency were not significantly different between treatment groups.

A systematic review of 9 RCTs (N=2,331) investigated the accuracy and precision of history taking and physical examination for the diagnosis of UTI. Patients were women 18 to 65 years old living in the United States, United Kingdom, and New Zealand without risk factors (functional or anatomic abnormality of the urinary tract) for complicated UTI. A random-effects model was used to generate likelihood ratios and confidence intervals.

A urine dipstick test was used as the gold standard for diagnosis. Four symptoms and 1 sign significantly increased the probability of UTI when presenting at the office: dysuria (LR+ 1.5; 95% CI, 1.2–2.0), urinary frequency (LR+ 1.8; 95% CI, 1.1–3.0), hematuria (LR+ 2.0; 95% CI, 1.3–2.9), back pain (LR+ 1.6; 95% CI, 1.2–2.1), and costovertebral angle tenderness (LR+ 1.7; 95% CI, 1.1–2.5). Conversely, a history of vaginal discharge (LR+ 0.3; 95% CI, 0.1–0.9) and a history of vaginal irritation (LR+ 0.2; 95% CI, 0.1–0.9) were found to slightly decrease the likelihood of UTI.

An RCT examined 309 nonpregnant women, 18 to 70 years old, who presented at a primary care clinic with symptoms consistent with an uncomplicated
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(immunocompetent, not pregnant, no comorbidities, no known urologic abnormalities, premenopausal) UTI. Patients were randomly assigned to 5 treatment approaches: empirical antibiotics without testing (n=66); empirical delayed (by 48 hours) antibiotics without testing (n=62); or targeted antibiotics based on a symptom score (n=69), a dipstick result (n=58), or a positive result on midstream urine analysis (n=54). Outcome measures included symptom severity at days 2 and 4, symptom duration, and use of antibiotics. Patients who delayed antibiotics by 48 hours had symptoms for an average of 37% longer than patients who began taking antibiotics immediately without testing (incident rate ratio [IRR] 1.4; 95% CI, 1.1–1.7). In the midstream urine group, symptoms lasted 73% longer than patients who began taking empiric antibiotics immediately (IRR 1.7; 95% CI, 1.2–2.4). Ambar M. Zulfiqar, MD Yu Wah, MD University of Texas Health Science Center at Houston Houston, TX


Is capsule endoscopy more effective than esophagogastroduodenoscopy (EGD) in diagnosing varices in patients with liver cirrhosis?

Evidence-Based Answer
No. Esophageal capsule endoscopy (ECE) has lower sensitivity and specificity than EGD for detection of medium and large esophageal varices and is not recommended as the initial screening method for patients with liver cirrhosis (SOR: A, meta-analysis of cross-sectional cohort studies). Nevertheless, ECE may be cost effective in certain healthcare delivery models compared with EGD (SOR: B, Markov cost models).

A 2014 meta-analysis identified 15 cross-sectional cohort studies (N=936) to compare ECE and EGD for detection of varices in adult patients with cirrhosis or portal vein thrombosis. Studies were included if they reported measurements of diagnostic accuracy of ECE and used EGD as the reference standard. Studies were excluded if participants had prior therapies for varices or if data were not available per participant.

The meta-analysis identified a pooled sensitivity of ECE for detection of varices of 84.8% (95% CI, 77.3%–90.2%) and a specificity of 84.3% (95% CI, 73.1%–91.4%). In 9 of 10 studies, participants preferred ECE over EGD. The authors did not recommend ECE to replace EGD given the lower sensitivity and specificity of EGD. Caveats included study heterogeneity, lack of reporting of adverse effects (swallowing difficulty, capsule retention), limitation of blinding, mixing of surveillance and screening populations, and variation in categorization of severity of varices.

A 2009 decision analysis screening used a Markov model of 50-year-old adults to compare the cost effectiveness of ECE and EGD as screening strategies for esophageal varices. In the 15-year modeling process, each yearly interval brought a distinct possible outcome (nondetection of any varices, detection of small varices, detection of large varices with subsequent treatment, death) that continued or ended the screening process.

Calculated life-years saved and cost/life-year favored the ECE screening strategy (ECE: 12.81 life-years saved; $22,589 cost/life-year vs EGD 12.67 life-years saved, $23,083 cost/life-year). ECE remained slightly superior when variceal detection sensitivity held above 50%. The authors concluded that ECE and EGD are both acceptable options. Limitations included reliance on published estimates, lack of prospective data, and a low assumed ECE complication rate (0%).

A 2007 budget impact analysis of patients with compensated cirrhosis in a hypothetical managed care setting compared per-member per-month costs (PMPM) when enrolled in ECE- or EGD-based screening strategies to detect esophageal varices. A 10-year Markov model tested 5 strategies: empiric beta-blocker (BB) therapy; BB therapy after detection of varices with EGD; endoscopic band ligation (EBL) of varices detected with EGD; BB therapy if ECE confirmed varices; and EBL of varices detected by ECE.

The analysis found that empiric BB therapy without screening was the least costly strategy with the lowest PMPM (PMPM=$1.59; avg. 10-year cost of care per patient $38,241). ECE with resulting BB therapy for indicated patients was the next preferred strategy (PMPM=$1.79; avg. 10-year cost of care per patient: $43,043). The most expensive approach involved using...
EGD after ECE (PMPM=$1.92; avg. 10-year cost of care per patient: $46,046). The use of ECE added only $0.20 PMPM more than empiric BB blocker use alone. Sensitivity analysis indicated that local costs of both ECE and EGD and prevalence of cirrhosis would dramatically affect the budget impact of each screening strategy. The authors concluded that ECE was on par with costs for other interventions introduced into healthcare systems.

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What is the best treatment strategy to heal and prevent recurrence of acute esophagitis in the elderly?

Evidence-Based Answer
Proton pump inhibitors (PPIs) are significantly more effective than H₂-receptor antagonists (H₂RA) for healing esophagitis in the elderly within the first 8 weeks (SOR: A, meta-analysis of 2 RCTs). Treatment with a low-dose PPI for 6 more months after initial treatment of 6 months is better than placebo for prevention of recurrence of esophagitis (SOR: B, RCT).

A retrospective analysis of 2 multicenter, double-blind RCTs (N=550) compared omeprazole with H₂RAs for healing of esophagitis and improving GERD symptoms in a subgroup of 154 patients ≥65 years of age. Patients had endoscopically confirmed esophagitis and received omeprazole 20 mg daily or either cimetidine 400 mg daily or ranitidine 150 mg BID for 4 weeks, and if esophagitis was unhealed by endoscopy or the patient was still symptomatic, patients received another 4 weeks of the same treatment. Duration of symptoms at enrollment was 3 years in the omeprazole group and 1.9 years in the H₂RA group (P<.05).

After 4 weeks, 53% (42 of 79) of the omeprazole group were healed compared with 27% (20 of 75) in the H₂RA group (P<.001; NNT=4). At the end of the 8 weeks, 70% (55 of 79) of the omeprazole-treated group and 29% (22 of 75) of the H₂RA group were healed (P<.001, NNT=3). Adverse events leading to withdrawal from the trial were similar between the groups (6% in omeprazole group and 8% in H₂RA group). Two major adverse events unrelated to drug treatment occurred in the omeprazole group: myocardial infarction and respiratory failure.

A 2003, double-blind, placebo-controlled RCT (N=164) evaluated the efficacy of pantoprazole for preventing the recurrence of esophagitis in the elderly during a 1-year follow-up. All patients, aged 65 to 93 years old, with acute esophagitis defined endoscopically by the Savary-Miller criteria grades I–III, were treated initially with pantoprazole 40 mg daily for 8 weeks. Thereafter, the 113 patients with endoscopically documented healing of esophagitis were treated for an additional 6 months with pantoprazole 20 mg daily. The 105 patients who remained healed by endoscopy at 6 months were then randomized to receive pantoprazole 20 mg daily or placebo for the next 6 months.

After 12 months, the intention-to-treat and per-protocol rates of esophagitis remaining healed were significantly higher in the pantoprazole group compared with placebo (see TABLE). Compared with placebo-treated patients, patients treated with pantoprazole 20 mg daily had a significantly lower incidence of reflux

### TABLE

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Number of patients</th>
<th>Dose (daily)</th>
<th>Treatment duration</th>
<th>Percent healed or remaining healed (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pantoprazole</td>
<td>164</td>
<td>40 mg</td>
<td>0-8 weeks</td>
<td>Intention-to-treat: 81% (75–87)</td>
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<td></td>
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<td></td>
<td>Per protocol: 94% (90–98)</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>133</td>
<td>20 mg</td>
<td>8 weeks to 6 months</td>
<td>Intention-to-treat: 82% (75–89)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Per protocol: 92% (88–97)</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>49</td>
<td>20 mg</td>
<td>6-12 months</td>
<td>Intention-to-treat: 80% (68–91)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Per protocol: 95% (89–100)</td>
</tr>
<tr>
<td>Placebo</td>
<td>56</td>
<td>n/a</td>
<td>6-12 months</td>
<td>Intention-to-treat: 30% (18–42)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Per protocol: 33% (20–45)</td>
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</tbody>
</table>
symptoms (22.4% vs 67.7%; \( P < .0001 \)). The NNT with pantoprazole after the initial 6 months to reduce one relapse of esophagitis was 2. At 12 months, 9 of the 12 who dropped out refused to undergo a final endoscopy.\(^1\)

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**Does calcium supplementation in adults increase the risk of kidney stones?**

**Evidence-Based Answer**  
Calcium supplementation does lead to a very small increase in the risk of kidney stone formation in adult women. This increased risk equates to 1 additional patient developing symptomatic nephrolithiasis in 274 women taking a calcium supplement for 7 years (SOR: B, RCT and cohort study).

As part of a large RCT, 36,282 postmenopausal women between 50 and 79 years old were randomly assigned to either a daily dose of 1,000 mg elemental calcium (as calcium carbonate) plus 400 IU vitamin D3 or placebo.\(^1\) Exclusion criteria included hypercalcemia, renal calculi, steroid use, or calcitriol use. The primary endpoint of the study was the effect of calcium plus vitamin D supplementation on fracture risk, but the authors also monitored the incidence of renal calculi. The patients were instructed to take the supplements with meals to maximize absorption and patient compliance was determined by weighing returned pill bottles during clinic visits.

During the mean follow-up of 7 years, kidney stones were reported by 449 women (2.5%) in the calcium/vitamin D group, as compared with 381 women (2.1%) in the placebo group (HR 1.2; 95% CI, 1.0–1.3). This ratio translates to an NNH of 274 patients over a 7-year period.\(^1\)

Similarly, a large cohort study also followed the incidence of kidney stones as a secondary endpoint.\(^2\) This prospective cohort study began in 1976 with an initial questionnaire completed by more than 100,000 female registered nurses in 11 US states. Follow-up questionnaires were completed by the women in 1980, 1984, 1986, 1990, and 1992. In 1984, the questionnaire began including questions about supplemental calcium intake. The 1992 questionnaire inquired about the date and incidence of any history of kidney stone diagnoses. For those who did report a history, a supplementary questionnaire was sent out to help clarify the diagnoses. The response rate on the supplementary questionnaire was 95%. Functionally, this was a 12-year prospective cohort, because any kidney stone occurring between 1980 and 1992 was included. There were 91,731 women with no prior history of renal stones included in the study, all between the 34 and 59 years old.

From 1980 to 1992, there were 864 cases of new symptomatic kidney stones. After adjustment for potential confounders, the relative risk among subjects who took any amount of calcium supplementation compared with women who took none was 1.2 (HR 1.2; 95% CI, 1.0–1.4). The authors commented that higher doses of calcium did not add additional risk compared to lower doses (no data shown).\(^2\)

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**Is adding clopidogrel to aspirin more effective than aspirin alone for reducing the risk of recurrent strokes?**

**Evidence-Based Answer**  
Clopidogrel plus aspirin is more effective than aspirin alone for reducing recurrent strokes in patients who have had an ischemic stroke or transient ischemic attack (TIA). There are no significant differences in risk of bleeding (SOR: A, meta-analysis of RCTs and single RCT). However, it is unclear if the combination is more effective than clopidogrel alone.

A 2013 meta-analysis of 13 RCTs (N=90,433) evaluated the effects of adding clopidogrel to aspirin (dual therapy) versus aspirin alone on stroke reduction and major hemorrhage.\(^1\) Included patients had a mean age of 63 years, with a history of stroke or other vascular event or cardiovascular risk factors,
In patients with atrial fibrillation and a drug-eluting stent, what is the safest method of anticoagulation management?

**Bottom line**
In populations in which most, but not all patients, had atrial fibrillation (AFib) or received a drug-eluting stent (DES), dual antithrombotic therapy (DAT) with warfarin and clopidogrel appeared to be safer—with less major bleeding and fewer composite endpoints of death and clotting events—than triple antithrombotic therapy (TAT) with an oral anticoagulant (OAC), clopidogrel, and aspirin (SOR: B, RCT). Dual antiplatelet therapy (DAPT) with aspirin and clopidogrel was also associated with less bleeding than TAT but more cardiovascular events and mortality (SOR: B, meta-analysis of cohort studies).

**Evidence summary**
A 2013 RCT evaluated the safety of DAT and TAT after percutaneous coronary intervention (PCI) in 573 patients (average age 70 years) previously taking unspecified OAC (target INR as indicated for underlying condition). DAT consisted of OAC and clopidogrel 75 mg/d while TAT added aspirin 80 to 100 mg/d. The most common indication for OAC was AFib (69%); 63% of patients received a DES while 31% received a bare metal stent.

After 1 year, the incidence of the primary endpoint of any bleeding episode was higher for TAT versus DAT, but no difference was noted in major bleeding (see **TABLE**). The incidence of composite of death and clotting events (stroke, myocardial infarction [MI], stent thrombosis, target vessel revascularization) was lower for DAT than TAT.

A meta-analysis of 9 cohort studies (N=1,996) compared TAT with DAPT after stenting for the outcomes of major adverse cardiovascular events (MACE), all-cause mortality, and major bleeding. DAPT was with aspirin and clopidogrel (doses unspecified). The percent of patients receiving DES varied by trial but averaged around 50%. Five trials included only patients previously receiving long-term OAC (most for AFib with INR goal 2–3) who were assigned to TAT or DAPT at the physician’s discretion based on unspecified assessment of thrombotic versus bleeding risk. The remaining 4 trials (n=694) compared TAT in patients previously receiving OAC to an age- and sex-matched control cohort receiving DAPT without an OAC indication. One of these 4 trials was included in all

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Efficacy</th>
<th>Safety=risk of bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality and clotting events: DAT vs TAT(^1)</td>
<td>Favors DAT: HR 0.60; 95% CI, 0.38–0.94; DAT NNT(^n=14)</td>
<td>Favors DAT for any bleed: HR 0.36; 95% CI, 0.26–0.50; TAT NNH(^n=4)</td>
</tr>
<tr>
<td>MACE: TAT vs DAPT(^2)</td>
<td>Favors TAT: 7 trials, n=1,588; OR 0.60; 95% CI, 0.42–0.86; TAT NNT(^n=20)</td>
<td>DAPT for major bleed 6 months post-PCI: OR 2.12; 95% CI, 1.05–4.29; TAT NNH(^n=43) (5 trials, n=1,267)</td>
</tr>
<tr>
<td>All-cause mortality at 1 year: TAT vs DAPT(^2)</td>
<td>Favors TAT: 6 trials, n=1,448; OR 0.59; 95% CI, 0.39–0.90; DAPT NNT(^n=32)</td>
<td></td>
</tr>
<tr>
<td>Ischemic stroke: TAT vs DAPT(^2)</td>
<td>No difference: 4 trials, n=976</td>
<td></td>
</tr>
<tr>
<td>Ischemic stroke: TAT vs DAPT/DAT(^3)</td>
<td>Favors TAT: 6 trials, n=1,972; OR 0.29; 95% CI, 0.15–0.58</td>
<td>Favors DAPT/DAT for major bleed: OR 2.00; 95% CI, 1.41–2.83; TAT NNH(^n=15) (7 trials, n=3,930)</td>
</tr>
<tr>
<td>Post-PCI all-cause mortality: TAT vs DAPT/DAT(^2)</td>
<td>No difference: 6 trials, n=4,569</td>
<td></td>
</tr>
<tr>
<td>Post-PCI MI: TAT vs DAPT/DAT(^2)</td>
<td>No difference: 7 trials, n=4,709</td>
<td></td>
</tr>
</tbody>
</table>

\(^n\)NNT or NNH for dual therapy versus triple therapy.
\(^b\)Major bleed=hematocrit drop >15%, transfusion of >2 units blood, need for corrective surgery, intracranial or retroperitoneal bleed, or any combination of these.
\(^d\)DAPT in this meta-analysis consisted of warfarin + an antiplatelet (1 trial, n=500).

CI=confidence interval; DAPT=dual antiplatelet therapy with aspirin and clopidogrel; DAT=dual antithrombotic therapy with warfarin and clopidogrel; HR=hazard ratio; MACE=major adverse cardiovascular events; MI=myocardial infarction; NNH=number needed to harm; NNT=number needed to treat; OAC=oral anticoagulant; OR=odds ratio; PCI=percutaneous coronary intervention; TAT=triple antithrombotic therapy with OAC, clopidogrel, and aspirin.
outcomes analysis and 1 other was included in the MACE and mortality outcomes only.

TAT was associated with fewer MACE (cardiac death, acute MI, stent thrombosis, or target lesion revascularization) and lower all-cause mortality compared with DAPT, but with no difference in ischemic stroke and an increased risk of major bleed during the first 6 months after PCI (see TABLE). Funnel plots revealed no evidence of publication bias. A meta-analysis of 9 cohort studies compared TAT (n=1,446) with DAT or DAPT (n=3,671) after stenting (unspecified type). The most common indication for OAC was for AFib. Four of these trials were also included in the meta-analysis above. The additional studies analyzed in this meta-analysis were of shorter follow-up and 1 included OAC in the DAT group. However, much of the difference in included studies is unexplainable due to incomplete reporting of reasons for trial exclusion. Four of the trials compared TAT with a DAPT control cohort without an OAC indication and were included in all pooled results.

TAT was associated with a reduction in ischemic stroke, but also an increase in major bleeding (definition not clearly reported) compared with DAPT/DAT (see TABLE). There was no difference in all-cause mortality or MI after PCI.

and were followed for a mean of 1 year. Four trials included only patients (n=1,930) with recent ischemic stroke (≤30 days).

Dual therapy reduced the odds of subsequent strokes by 33% compared with placebo (OR 0.67; 95% CI, 0.46–0.97; NNT=39) and major hemorrhage was not increased (OR 0.91; 95% CI, 0.43–2.1). The limitation of the meta-analysis is that it did not explore the effects of other variables that may have affected the outcome such as blood pressure control, time to treatment, and stroke etiology. Additionally, specific dosing was not reported and the study did not include the comparison of aspirin versus clopidogrel.

A subsequent RCT conducted in 114 centers in China (N=5,170) also evaluated any effect of dual therapy versus aspirin alone initiated within 24 hours of a stroke for prevention of recurrent stroke in 90 days. Patients had a median age of 62 years and were treated a median of 13 hours from onset of TIA or minor stroke. On day 1, both groups received aspirin 75 to 300 mg (dosed at clinician’s discretion). Patients assigned to aspirin subsequently received 75 mg/d. Patients assigned to dual therapy received a loading clopidogrel dose of 300 mg on day 1, followed by 75 mg/d (days 2–90) plus aspirin 75 mg/d (days 2–21) followed by placebo (days 22–90).

In 90 days, 8.2% of the dual therapy group suffered a recurrent stroke compared with 11.7% of the aspirin group (HR 0.68; 95% CI 0.57–0.81). No significant difference was noted in the risk of moderate or severe hemorrhage (fatal hemorrhage, intracranial hemorrhage, hemodynamic compromise, or transfusion), which occurred at rate of 0.3% in both groups. Also, there was no significant difference in rate of any bleed (2.3% with dual therapy vs 1.6% with aspirin; HR 1.41; 95% CI, 0.95–2.1). A limitation of this study was the uncertainty whether the result can be extrapolated to USA-based populations. Also, the study design essentially pitted aspirin alone versus clopidogrel alone for days 22 to 90.
FPIN will be presenting at STFM in Minneapolis, MN, this year! Come join us for our session titled, “The Winning Trifecta for Successful Faculty Development Projects: Time, Effort, and Reward.”

**When:** Monday, May 2, 2016  
**Time:** 1:45 p.m.–2:45 p.m.  
**Where:** Hilton Minneapolis Hotel  
1001 S. Marquette Ave., Minneapolis, MN 55403

We will also be present throughout the conference from April 28 through May 2. Schedule your membership meetings with us today by visiting www.fpin.org/conference. Someone from our team will contact you for scheduling.
Does health coaching lead to weight loss in obese individuals?

Evidence-Based Answer
Yes, health coaches appear to assist with weight loss in obese adults (SOR: C, small observational and case studies).

A nonblinded randomized pilot trial of 44 adult patients with body mass indexes (BMIs) of 30 to 40 kg/m² examined the effectiveness of 3 distinct types of health coaches.¹ Patients were assigned to a professional health coach (a health professional who provides health information and support), a peer coach (a patient who had the same health condition), or a mentor (a patient who had faced a similar health condition and was successfully coping). All patients were given a calorie goal of 1,200 to 1,500 kcal/d and 12 separate 1-hour behavioral weight loss group meetings over 6 months. From weeks 6 to 24, patients followed goal contracts with their coaches on weight loss, activity, and diet.

Over 6 months, the patients in the professional group lost 9.1%, the peer group lost 9.6%, and the mentor group lost 5.7% of initial body weight, but these effects were not statistically significant (P=.26 ANOVA). In analyses of patients who completed the trial (N not reported), a significant difference in weight loss was noted between the professional and mentor groups (11% vs 5.7%; P=.04). More patients in the professional group lost 10% of their initial body weight compared with the mentor group (57% vs 17%; P=.03).¹

A single group pre-post observational study evaluated the effectiveness of weight loss with weekly health coaching over the phone during a 12-week period in 14 adults.² Mean weight loss from baseline was 3.8 kg (P=.002) and BMI decreased by 1.2 kg/m² (P=.003). Overall, 92% of the planned phone sessions were completed. Eight of the patients completed all 12 sessions and lost more weight than patients who did not participate in all 12 sessions (5.4 vs 3.8 kg; P=.05).

A case report described a health coaching structure across 4 family medicine clinics.³ Health coaches provided face to face, email, or phone support to patients every 2 to 4 weeks over 6 months. The primary intervention involved a “My Healthy Habit Journal”;

the health coaches assisted patients in developing action plans to address dietary habits or increase exercise. Overall, 48% of patients in the program enacted behavior change; however, no data were collected on the success of this behavior change.

One case report described a 55-year-old man weighing 450 lb who entered into health coaching as a prerequisite to bariatric surgery.⁴ The health coaches assisted him with developing a “wellness vision” and a lifestyle plan that aligned with that vision.

After 3 months, the patient lost >30 lb and no longer required a cane to ambulate. The patient continued to meet with his health coach monthly and averaged a 10-lb weight loss per month. Overall, the patient lost 240 lb, 53% of his body weight (time frame not specified), and maintained this weight loss for 3 years with continued guidance from a wellness coach.⁴

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Do low sodium diets reduce the morbidity and mortality in patients with congestive heart failure?

Evidence-Based Answer
In patients with systolic congestive heart failure (CHF) on high doses of furosemide (at least 125 mg twice daily) and fluid restriction, outpatient sodium restriction of 1.8 g daily leads to increased admissions compared with ad lib sodium intake of 2.8 g daily (SOR: B, inconsistent RCTs). Evidence is insufficient to make a recommendation for diastolic failure, and lower doses of furosemide might require different dietary advice.

A 2008 RCT compared a normal sodium diet (120 mmol or 2.8 g daily) with a low sodium diet (80 mmol or 1.8 g daily) in 232 patients (average age 72 years) 30 days after discharge from hospitalization for decompensated systolic CHF.¹ At randomization, patients had NYHA
class II CHF, were adherent to discharge dietary recommendations, were taking furosemide (250–500 mg orally twice daily) and were restricted to 1,000 mL fluid daily. Patients were contacted weekly to assess dietary compliance.

After 180 days, the normal sodium diet group had a significant reduction in readmission rate (primary outcome) compared with the low sodium diet group (7.6% vs 26.3%; \( P < .005; \) NNH=6) and a reduction in the secondary outcome of combined mortality and readmission rate (12.7% vs 39.5%; \( P < 0.001; \) NNH=4).1

A 2009 RCT compared 8 different combinations of sodium intake (120 vs 80 mmol/d), fluid intake (1,000 vs 2,000 mL/d), and furosemide doses (125 vs 250 mg orally twice daily) in 410 patients (aged 53–86 years) 30 days after discharge from hospitalization for decompensated systolic CHF.2 Prior to randomization, all patients were treated with furosemide 250 mg orally twice daily, 1,000 mL of fluid restriction, and 120 mmol sodium daily. At randomization, patients had NYHA class II CHF.

The group treated with 1,000 mL/d of fluid restriction, high-dose furosemide (250 mg twice daily), and sodium 120 mmol/d had the lowest readmission rate (7.7%), significantly different from the 7 other groups (\( P < .0001\)). In multivariate analysis, sodium restriction (80 vs 120 mmol/d) increased readmission (OR 2.46; 95% CI, 1.84–3.29).2

A 2013 RCT compared individualized counseling on salt and fluid restriction with generic counseling in 97 patients (average age 75 years) with compensated CHF with or without reduced ejection fraction and history of objective fluid retention.3 All patients were on angiotensin-converting enzyme inhibitors, beta-blockers, and 40 to 80 mg oral furosemide daily. Individualized twice-monthly counseling incorporated patients’ culture and lifestyle to maximize likelihood of adherence to 2 to 3 g sodium and restriction to 1.5 liters of fluid per day. Generic counseling consisted of a one-time recommendation to “avoid salt and not drink too much.” Patients were assessed at 12 weeks (90% follow-up). Researchers used a composite endpoint of NYHA change, hospitalization, weight, edema, quality of life, and diuretic reduction. “Improvement” was defined as no deterioration and at least 1 of the 6 endpoints improved.

Improvement was greater in the intervention group (51% vs 16%; \( P < .001; \) NNT=3), primarily due to improved NYHA classification and edema. Dietary compliance assessment by phone interview was limited to 38 patients.3

Is hemochromatosis associated with an increased risk of cardiovascular disease?

Evidence-Based Answer

In patients with genetic hemochromatosis, there is no increased risk of coronary heart disease or acute myocardial infarction (SOR: B, meta-analysis of case-control and prospective observational studies and a large cohort study).

Hemochromatosis is an autosomal recessive iron overload disease most commonly due to HFE mutations C282Y, H63D, and S65C with variable disease expression and penetrance.

A meta-analysis reviewed individual patient data of 53,880 patients with HFE mutations from 1 prospective observational and 10 case-control studies, to identify an association between hemochromatosis and coronary heart disease.1 In total, 10,541 patients with coronary events (unstable angina, acute myocardial infarction, acute or chronic ischemia) were documented, of whom 5,724 had an acute myocardial infarction.

After adjustment for traditional cardiovascular risk factors, a logistic regression analysis found no association between HFE mutations and coronary heart disease or acute myocardial infarctions (see TABLE).1

A prospective cohort study examined the occurrence of myocardial infarction, angina pectoris, chronic ischemia, cardiomyopathy, and arrhythmias in 3,531 patients with hemochromatosis compared with 37,369 randomly selected matched controls.2 A total of 259 patients with hemochromatosis (7%) were diagnosed with ischemic heart disease, compared with 3,077 controls (8%). After adjusting for diabetes, there was no increased risk of ischemic heart disease (HR 1.07; 95% CI, 0.94–1.21).
A cohort study in Denmark selected 667 patients with NYHA class III–IV systolic heart failure enrolled in a prospective, randomized, placebo-controlled multicenter echocardiogram trial, studying the effect of a selective agonist on DA2-dopaminergic and α2-adrenergic receptors. The heart failure etiology was classified as ischemic, hypertensive, dilated cardiomyopathy, valve disease, arrhythmia, or unknown. The patients were genotyped for the HFE variants C282Y, H63D, and S65C and followed for 5 years.

A total of 231 (35%) of the patients with heart failure were found to carry at least 1 of the 3 HFE polymorphisms, which is not significantly different from the prevalence in the Danish population (54%, P=.922).

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What pillow types are best for neck pain?

Evidence-Based Answer

In side-sleeping patients without chronic neck pain, standard shaped rubber pillows reduce the incidence of morning neck pain while feather pillows increase pain, compared with patients’ usual pillows. For patients with chronic neck pain without nerve impingement, water-based pillows are superior to roll-shaped pillows and standard (down or foam) pillows in diminishing pain severity upon waking (SOR: B, small RCTs).

A 2009 RCT looking at the relationship between pillow type and the incidence of neck pain enrolled 106 patients without chronic neck pain who considered themselves side sleepers and were not undergoing treatment for neck pain. Primary outcomes included reported neck pain before sleep and morning neck pain.

Patients were randomly assigned to 1 of 5 treatment groups, which was determined by the order they received the pillow types. Patients used personal pillows as a control for the initial 7 days of the study then used each of the 5 different pillow types for 7 days: feather filled, polyester fiber filled, standard shape memory foam, contoured memory foam, or standard shaped rubber. Attempts to blind patients to pillow types were made by removing all identifying tags or labels, and placing pillows in uniform white pillow cases. After each 7-day trial period, patients returned to their baseline control pillow for a 1-week “washout” period. This continued for 10 weeks, until all patients had experienced each of the 5 experimental pillows.

About 75% of patients reported no pain when using their own pillow. Data from all patients showed decreased odds of morning neck pain with rubber pillows compared with baseline control pillow (OR 0.6; 95% CI, 0.4–0.9). Additionally, feather pillows showed a significant increase in the odds of morning neck pain (OR 1.9; 95% CI, 1.3–2.7). No significant changes in waking or evening neck pain were seen between the other tested pillow types and baseline control pillows.

A 1997 RCT evaluating the possible benefits of pillow types for preexisting neck pain enrolled 41 patients with benign cervicalgia (neck pain without neurological symptoms) at baseline. After 1 week of using their own pillow, all patients slept 2 weeks on
each of 2 experimental pillows: a polyester tubular roll-shaped pillow and a water-based pillow. The order in which the pillows were used was randomly assigned. The patients’ personal pillows were considered controls and were typically a “standard” down or foam pillow. Patients recorded pain characteristics in daily journals. Pain scores were evaluated on a 5-point Likert scale rated 1 (no pain) to 5 (severe pain).

The water-based pillow resulted in a lower mean morning pain score of 3.75 after the 2 weeks of use compared with the standard pillow mean score of 4.83 ($P < .025$) and the roll pillow mean score of 4.67 ($P < .005$). No significant difference was noted between the roll pillow and standard pillow. Data for evening neck pain intensity did not show a significant difference between pillow types.  

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