**What is the best way to determine if a patient has type 1 or type 2 diabetes mellitus?**

**Evidence-based answer**

The only way to differentiate various types of diabetes is by assessing a patient’s history, physical, and laboratory workup. There is no single test or finding that differentiates the 2 types (SOR: B, cross-sectional studies).

**Evidence summary**

A multicenter, cross-sectional study of 2,435 newly diagnosed youth with diabetes (age ≤20 years) classified incidence of diabetes based on race/ethnicity and diabetes type. In the 0–9 year-old group, type 1 diabetes (based on healthcare provider assessment) was present in 99% of children and type 2 was present in 1%. However, the incidence of type 2 diabetes increased in the 10–19 year-old group to 23%.

Further analysis of this age group revealed that GAD65 autoantibody was present in 21% of patients with type 2 diabetes and 66% of patients with type 1 diabetes. This result suggested that GAD65 antibody positivity was not unique to either type of diabetes.

A cross-sectional analysis of data from a multicenter RCT with 1,206 patients aged 10–17 years with type 2 diabetes, previously diagnosed by an endocrinologist based on their phenotypic presentation, evaluated the frequency of islet autoantibodies (ie, GAD65 and IA2) and described associated clinical and laboratory findings. Autoantibody positivity for either GAD65 or IA2, or both, was noted in 9.8% of children who (based on comprehensive clinical evaluation) had type 2 diabetes.

When various other clinical parameters were compared (BMI, blood pressure, acanthosis nigricans, insulin use, HbA1C, c-peptide, lipid panels), the authors found that regardless of antibody status, clinical findings overlapped in antibody-positive and antibody-negative individuals. As an example, acanthosis nigricans, a typical sign of insulin resistance, was present at a somewhat higher rate...
in antibody-negative than antibody-positive individuals (84% vs 68%, respectively; \(P<.01\)). The median BMI in antibody-negative individuals was higher than in antibody-positive individuals (34.9 vs 21.9 kg/m\(^2\); \(P<.01\)).

**Recommendations**

The American Association of Clinical Endocrinologists recommends a combination of clinical presentation, family history, and laboratory workup (including insulin level, c-peptide, islet autoantibodies) to help distinguish type of diabetes, particularly in younger people.

**REFERENCES**

The $1,000 pill

My parents were born during the Great Depression and internalized the values of thrift and frugality required during those desolate times. As young parents, they passed those values along to me. Now I am always looking for deals and silently bemoaning the price of milk, gasoline, and other staples the prices of which fluctuate daily.

But price shock at the gas pump and grocery store are nothing like price shocks in the medical world. In medicine, for example, we have drugs that cost crazy amounts—like $1,000 a pill.

That pill is sofosbuvir, which, like simprevir, is used to cure hepatitis C. A 12-week course of sofosbuvir costs $84,000. Simprevir is cheaper, but still costs more than $66,000 for 12 weeks. The numbers are staggering, especially when you consider that 12 weeks of sofosbuvir only costs between $70 and $140 to manufacture. A course of simprevir costs between $130 and $270 to manufacture, making simprevir’s price tag a slightly less egregious form of grand larceny.¹

Let’s do some math. There are about 3.2 million people in the United States with hepatitis C. If all were treated with sofosbuvir, the makers would gross $269 billion (with a “b”). Subtracting manufacturing costs and $2.4 billion in development still leaves $266 billion in profit. Also consider that there are about 140 million people in the world with chronic hepatitis C. If someone managed to sell sofosbuvir to all of them at the US price, the makers would reap over $11 trillion. (Note: I had to do this math long hand because my calculator does not have that many zeros.)

How much money is this? Well, according to the US Treasury, the national debt expanded by $28 billion during the depression and Roosevelt’s New Deal (1933–1941). Currently, 30 brand-new US Virginia-class nuclear attack submarines ($2.7 billion each) will set you back $81 billion. This means the makers of sofosbuvir could theoretically afford curing hepatitis C in the United States—both finance a national stimulus package and become a major nuclear power...and still have $157 billion dollars left over!

At $1,000 a pill, this new deal is a bad deal indeed.

Not so sweet: Honey for acute cough in children

This Cochrane review compared the efficacy of honey with diphenhydramine or dextromethorphan, as well as no treatment or placebo in children with acute cough from viral or bacterial sources. It included 3 trials with 568 children, ages 1–18 years, and evaluated cough and related symptoms using a 7-point Likert scale with caregiver responses ranging from “extremely” (6 points, worst) to “not at all” (0 points, best). Secondary outcomes included improvement in quality of sleep in children and caregivers (also evaluated on a 7-point Likert scale, with higher scores indicating better sleep), quality of life, and adverse effects.

Pre- and postintervention Likert scale comparison found honey was better at reducing cough frequency than no treatment (mean difference [MD] −1.1; 95% CI, −1.5 to −0.6) and placebo (MD −1.9; 95% CI, −3.4 to −0.3). Honey was also likely better at reducing cough frequency compared with diphenhydramine (MD −0.57; 95% CI, −0.9 to −0.24), but was no better than dextromethorphan (MD −0.14; 95% CI, −0.33 to 0.06).

Honey was inferior to dextromethorphan in reducing cough severity (MD 0.61; 95% CI, 0.27–0.94), but superior to diphenhydramine (MD −0.6; 95% CI, −0.94 to −0.26), no treatment (MD −0.97; 95% CI, −1.47 to −0.46), and placebo (MD −1.83; 95% CI, −3.3 to −0.34).

Similarly, there was no difference between honey and dextromethorphan with regard to the children’s sleep (MD 0.03; 95% CI, −1.1 to 1.2) or parents’ sleep (MD −0.16; 95% CI, −0.84 to 0.53), but honey improved sleep for both the children and parents compared with diphenhydramine, no treatment, or placebo.

There was no difference in adverse events among any of the treatment groups. Cough duration, cost, changes in quality of life, and appetite were not studied.

Bottom line: Honey may be better than no treatment, placebo, or diphenhydramine for acute cough in children aged 1–18 years, but is no better than dextromethorphan.

Review and Summary Authors: Jennie Broders Jarrett, PharmD, BCPS, and Jason Corbo, PharmD, BCPS, UPMC St. Margaret FMRP, Pittsburgh, PA

Brief intervention reduces medication overuse headaches

This cluster-randomized controlled study compared a brief education-based intervention for 30 patients with usual care for 45 patients diagnosed with medication overuse headache. All patients were adults, 18 to 50 years old. Per design, the intervention was allocated by practice not individual patient.

The intervention group received a presentation on the topic, feedback on medication overuse headache, and a plan for medication reduction. The usual-care group received standard treatment that could include a reduction plan, prophylactic medications, and other abortive medications. The primary outcomes of the study were number of headaches and medication days per month.

Patients in the brief intervention group had 7.3 fewer headache days per month (95% CI, −11.3 to −3.2) and 7.9 fewer days of medication use (95% CI, −12.5 to −3.2), with chronic headache resolution in 50% of the intervention group compared with 3% in the usual-care group (P<.001; NNT=3).

Bottom line: Although this brief intervention for medication overuse headache demonstrates reduction in headache and medication overuse days, it is not implementable without more details about and access to the training provided to the physicians in the study.

Review and Summary Author: Maryellen Schroeder, MD, UPMC St. Margaret FMRP, Pittsburgh, PA

| Relevant | Yes | Medical care setting | Yes |
| Valid | Yes | Implementable | Yes |
| Change in practice | No | Clinically meaningful | Yes |

Additional information regarding the PURLs and Diving for PURLs series can be found at: http://www.fpin.org/purls-faqs/
This RCT compared 2 diagnostic methods for finding new-onset atrial fibrillation among patients with recent (within 6 months) ischemic stroke or transient ischemic attack.

A 30-day event-triggered ECG (intervention group, 280 patients) was compared with a “usual” workup, including a 24-hour ECG (control group, 277 patients). The primary outcome was detection of atrial fibrillation or flutter lasting ≥30 seconds within 90 days; secondary outcome was atrial fibrillation lasting ≥2.5 minutes.

Atrial fibrillation was detected in 45 of 280 patients (16.1%) in the intervention group compared with 9 of 277 (3.2%) in the control group, resulting in an absolute difference of 12.9% (95% CI, 8.0–17.6; number needed to screen [NNS]=8 to detect 1 additional case of atrial fibrillation or flutter ≥30 seconds). Twenty-eight patients in the intervention group (9.9%) had episodes of atrial fibrillation lasting ≥2.5 minutes compared with 7 patients in the control group (2.5%), with an absolute difference of 7.4% (95% CI, 3.4–11.3; NNS=14 to detect 1 additional case of atrial fibrillation or flutter ≥2.5 minutes).

**Bottom line:** In patients who have had a cryptogenic stroke, extended 30-day monitoring is superior to 24-hour ECG monitoring for detecting previously undiagnosed atrial fibrillation. However, the precise relationship (cause and effect) between atrial fibrillation and cryptogenic stroke is unknown.

Review and Summary Author: Elizabeth Mohan, MD, UPMC St. Margaret FMRP, Pittsburgh, PA

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This randomized trial compared shoe advice with podiatry care in 205 adults aged ≥50 years with nontraumatic musculoskeletal forefoot pain of ≥6 months’ duration. Patients with diabetes and rheumatoid arthritis were excluded.

The shoe advice group received verbal guidance and a standardized handout about appropriate shoe fit at a primary care office. The podiatric care group received usual podiatric care including, but not limited to, recommended or custom footwear or orthotics at a podiatry office.

Primary outcomes were foot pain and foot function; secondary outcomes were general health, social participation, and adherence. Data collection relied on patient questionnaires every 3 months for 1 year.

Intention-to-treat analysis revealed no differences in foot-related pain and dysfunction scores between the 2 study groups at all follow-up intervals. Foot-related pain and dysfunction scores decreased significantly from baseline in both study groups at 3 months and 12 months. General health and social participation did not change.

**Bottom line:** Shoe advice with a standardized handout from a primary care office may be as effective as podiatric care for improvement in nontraumatic forefoot pain and disability. However, adequate advice may require a highly knowledgeable provider.

Review and Summary Author: Pooja Saigal, MD, NorthShore University Health System/University of Chicago, Chicago, IL
Do office-based literacy interventions promote language development in children?

**Bottom line**
Reach Out and Read programs are associated with an improvement in receptive language development in preschool children (SOR: B, heterogeneous RCTs), although they probably have less effect on expressive language development (SOR: C, heterogeneous RCTs).

**Evidence summary**
Reach Out and Read (ROR) is a literacy intervention program adopted by many primary care offices in which reading advice is given to parents and an age-appropriate book is given to patients during well-child checks.\(^1\-^5\)

In 2003, a case series reported language outcomes of 64 children at their 3-year well-child check in an urban pediatric clinic that had implemented ROR.\(^1\) A Peabody Picture Vocabulary Test III and The Expressive One Word Vocabulary Test measured receptive and expressive language, respectively.

A multivariate analysis revealed higher receptive language scores when increased anticipatory guidance and more books purchased by parents were combined (r^2=0.025, \(P=.0006\)). The same analysis also revealed higher expressive language scores when increased number of visits and increased number of books purchased were combined (r^2=0.18; \(P<.001\)).\(^1\)

A cross-sectional survey in 2002 compared 2 clinics in South Bronx, New York.\(^2\) Expressive and Receptive One Word Picture Vocabulary Tests were compared for 200 children ages 2–6 years in clinic A with an established ROR program and clinic B with no exposure to ROR. Children exposed to ROR scored higher on receptive language testing (81.5 vs 74.3; \(P=.005\)) but lower on expressive language testing (81.6 vs 84.3; \(P=.26\)).

A similarly constructed 2001 cross-sectional survey of 122 children aged 2–6 years compared Expressive and Receptive One Word Picture Vocabulary Tests in 2 inner-city clinics.\(^3\) Again, 1 clinic had an established ROR program and the other did not. Receptive vocabulary was improved in the intervention group (94.5 vs 84.8; \(P<.001\)), but expressive vocabulary was not (84.3 vs 81.6; \(P=.23\)).

In 2000, an RCT with 205 infants aged 5–11 months placed patients in an ROR program or general care during their well-child visits.\(^4\) After 3 well-child checks or after the child reached 22 months, a Modified MacArthur Communication Development Inventory was performed for expressive and receptive language.

Higher receptive language (51.0 vs 39.3; \(P=.004\)) and expressive (22.1 vs 15.9; \(P=.01\)) language was noted in children tested at 18–25 months. However, in children 13–25 months, no statistical differences were observed.\(^4\)

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**REFERENCES**
How do the safety, efficacy, and patient satisfaction of uterine aspiration for miscarriage management compare between the office and the operating room?

**Bottom line**

Uterine aspiration in an office setting has similar low rates of complications and high rates of efficacy compared with the operating room (OR). Patient preferences and appropriate pain expectations are key for patient satisfaction.

**Evidence summary**

**Safety**

Uterine aspiration in the office has low rates of complications. An RCT directly compared uterine evacuation in the OR under general anesthesia with a treatment room setting in the hospital using intravenous sedation. In this study, 73 women received care in the treatment room and 68 women were treated in the OR. All women had a diagnosis of incomplete abortion at <14 weeks, defined by a dilated cervical canal at presentation and estimated uterine size on exam. Severely anemic (Hgb <8) women and those with signs of infection were excluded. Uterine evacuation was completed with sharp curettage in both groups.

No uterine perforation or major complication leading to hysterectomy occurred in either group. Blood transfusion was significantly more common for those treated in the OR under general anesthesia (35% vs 18%; \(P < .03\)), including 2 cases of blood loss >500 mL.

A 2006, prospective, observational study enrolled women who had already chosen surgical management for first-trimester pregnancy loss. Clinicians gave women a choice between having the procedure in the office (n=115) using manual vacuum aspiration (MVA) or in the OR (n=50).

Hemorrhage-related complications occurred more commonly in the OR than in the office setting (mean blood loss 311 vs 70 mL; \(P < .001\)). No major complications were noted in either group.

A 2007 nonrandomized study compared 157 women undergoing uterine aspiration in the operative setting with electric vacuum aspiration under anesthesia (n=68) or outpatient setting using MVA with local anesthetic (n=89) for first-trimester pregnancy loss. No significant differences were noted in objective blood loss or fever between the 2 groups.

**Efficacy**

Efficacy of MVA in the office is high. A retrospective study of 1,677 medical charts of women who had an office MVA found that 99.5% had complete evacuation. Only 8 patients (0.5%) required a second procedure because of retained products.

A similar study from 2009 in the United Kingdom reviewed the charts of 245 women with early pregnancy loss who were treated with MVA in a hospital unit (not in the OR) and found a 95% success rate. Of the 12 patients with retained products of conception, 8 underwent standard curettage and 4 were managed expectantly with good result.

**Satisfaction**

Satisfaction is similar for MVA in the office and in the OR. In the 2006 prospective study of 165 women, 89% of those who underwent aspiration in the office would choose the same procedure again, while 93% of those who underwent aspiration in the OR would choose the procedure again (\(P = .11\)). Interestingly, the study found that a disparity between expected and experienced pain was negatively associated with patient satisfaction, highlighting the importance of conferring realistic expectations in patient education.

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**REFERENCES**


What is the best nonsurgical therapy for carpal tunnel syndrome (CTS)?

Evidence-Based Answer
Local corticosteroids injections, splinting, and therapeutic ultrasound all appear to be effective in the short-term treatment of CTS compared with placebo or no treatment. Ergonomic keyboards do not appear to be effective. Among effective treatments, none were clearly superior and no head-to-head trials were evaluated (SOR: B, systematic reviews).

A 2009 Cochrane review of 12 randomized and quasirandomized trials (N=671) assessed the effectiveness of local corticosteroid injection compared with placebo or other nonsurgical interventions for treatment of CTS. Compared with injection of placebo (saline or lignocaine), corticosteroid injections improved subjective reporting of clinical severity on a 5-point ordinal scale (2 trials, N=141; risk ratio [RR] 2.6; 95% CI, 1.7–3.9).

Two trials compared local corticosteroid injection with systemic corticosteroid. The first (N=60) showed no improvement in symptoms (on a 50-point scale) at 2 weeks with local injection versus oral corticosteroid (mean difference [MD] –4.2; 95% CI, –8.7 to 0.26), but did show a difference at both 8 weeks (MD –7.2; 95% CI, –11 to –2.9) and 12 weeks (MD –7.1; CI, –12 to –2.5). The second trial (N=37) found improvement in symptoms (by subjective report of clinical severity at 1 month, no further description) with local corticosteroid injection compared with single systemic corticosteroid injection (RR 3.2; 95% CI, 1.0–9.9). Other single trials found no improvement with local corticosteroid injection compared with other nonsurgical treatments including splinting, high-dose corticosteroid injection, or multiple corticosteroid injections.

A 2012 Cochrane review of 19 RCTs with 1,190 patients compared wrist splinting for CTS. Only 2 trials directly compared splinting with no treatment. Wrist splinting demonstrated significant improvement using the Levine Questionnaire (1–5 scale) compared with no treatment at 4 weeks (1 trial, N=80; MD –1.1; 95% CI, –1.3 to –0.85), 3 months (1 trial, N=48; MD –0.90; 95% CI, –1.1 to –0.69), and 6 months (1 trial, N=34; MD –0.9; 95% CI, –1.1 to –0.69).

A 2012 systematic review combined 2 RCTs comparing therapeutic ultrasound versus placebo in 68 patients with CTS. A significant improvement, defined as more patient ratings of overall symptoms as “good or excellent,” was seen in ≤3 months in the ultrasound group (RR 2.4; 95% CI, 1.4–4.0).

Another Cochrane review examined 2 RCTs of CTS symptom relief with ergonomic versus standard keyboards. In the first trial (N=25), CTS symptoms were not statistically different at 6 weeks on a 10-point symptom scale (MD –0.20; 95% CI, –1.5 to 1.1). At 12 weeks, patients using ergonomic boards had significantly lower symptom scores (MD –2.4; 95% CI, –4.5 to –0.35). The second trial (N=80) evaluated patients at 6 months and found no significant difference on a 10-point symptom scale (MD 0.70; 95% CI, –0.97 to 2.4).

In a patient with panic disorder, is a combination of medication and psychotherapy superior to either alone for long-term treatment and prevention of symptoms?

Evidence-Based Answer
In patients with panic disorder, antidepressant medication combined with psychotherapy is slightly superior to either alone during active treatment. After therapy is discontinued, psychotherapy and combination treatment are equally effective at preventing future symptoms, and superior to antidepressants alone (SOR: A, systematic review of RCTs). Benzodiazepines do not appear to add benefit to psychotherapy alone (SOR: C, meta-analysis of heterogeneous RCTs).

A systematic review of 21 RCTs with 1,709 patients with panic disorder compared treatment using antidepressant medication or psychotherapy with the combination of both strategies. Selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants (TCAs) were used in 22 of 23 comparisons and the monoamine oxidase
inhibitor phenelzine was used in 1 comparison. Psychotherapy included behavioral therapy or cognitive-behavioral therapy (CBT) in 22 comparisons and psychodynamic therapy in 1 comparison. The primary outcome was significant improvement (“very much or much improved”) from baseline on the Clinical Global Impression Scale (CGIS), 40% or greater improvement in the Panic Disorder Severity Scale (PDSS), or a 50% or greater reduction in panic frequency on the Fear Questionnaire—Agoraphobia subscale.

During the treatment phase (up to 36 weeks), combination therapy had a better response rate than medication alone (11 trials, N=669; RR 1.6; 95% CI, 1.2–2.2) and psychotherapy alone (19 trials, N=1,257; RR 1.2; 95% CI, 1.0–1.5). After discontinuation of therapy (measured 6–24 months later), patients who underwent combination therapy had fewer symptoms than patients in the antidepressant-alone group (5 trials, N=376; RR 1.6; 95% CI, 1.2–2.1), but no difference in response compared with patients in the psychotherapy-alone group (9 trials, N=658; RR 0.96; 95% CI, 0.79–1.2). The review was limited by the lack of validated rating scales for panic disorder at the time of the RCTs, and the lack of control over additional therapies after discontinuation.

Another systematic review of 3 RCTs involving 243 patients with panic disorder compared the efficacy of benzodiazepines, psychotherapy, or both. Alprazolam was used in 2 studies and diazepam in the third. Psychotherapy consisted of behavioral therapy in 2 trials and CBT in 1 trial. Response was defined as “much improved” or “very much improved” on the CGIS or a score of 7 or below on the PDSS.

Two trials involving 166 patients showed no difference between combination therapy compared with psychotherapy alone at 8 weeks (RR 0.78; 95% CI, 0.45–1.4) and after treatment had ended up to 7 months later (RR 0.62; 95% CI, 0.36–1.1). In 1 RCT, combination therapy was superior to benzodiazepine at the end of 8 weeks of treatment (N=77; RR 3.4; 95% CI, 1–11). However, this finding barely met the level of statistical significance (P=.05). After discontinuation of treatment (7–12 months of naturalistic follow-up), no significant difference was found (RR 2.3; 95% CI, 0.79–6.7). The review authors noted that the small number of studies and patients involved was a significant obstacle to determining the superiority of one treatment over another.

The American Psychiatric Association recommends SSRIs, serotonin-norepinephrine reuptake inhibitors (SNRIs), TCAs, benzodiazepines, and CBT for panic disorder with no preference given to any specific therapy or combination.1

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How well does serum blood urea nitrogen-to-creatinine ratio correlate with prerenal etiology of acute kidney injury (acute renal failure)?

The blood urea nitrogen-to-creatinine ratio (BCR) does not reliably correlate to a prerenal etiology of acute kidney injury (AKI) (SOR: B, cohort studies).

Evidence-Based Answer

A 2012, retrospective cohort trial compared 20,126 patients older than 14 years admitted to an Australian medical center from 2000 through 2002 to assess if BCR is a useful predictor of prerenal azotemia (PRA), traditionally believed to be associated with a BCR >20, or acute tubular necrosis (ATN), traditionally believed to be associated with a BCR ≤20.1 AKI was defined according to the Risk, Injury, Failure, Loss and End-Stage (RIFLE) kidney disease classification system using glomerular filtration rate criteria, which is a validated tool.

A total of 3,641 patients met criteria for AKI by RIFLE criteria who were further divided into those with high BCR (>20) or low BCR (≤20). The authors did not find a bimodal distribution of BCR, suggesting that there was no useful diagnostic threshold for predicting PRA versus ATN.1

In a 2002 prospective cohort trial of 102 hospitalized patients with AKI at Nassau County Medical Center, NY, the BCR was compared with various indices including fractional excretion of urea nitrogen (FEun) and fractional excretion of sodium (Fena) for discerning PRA versus ATN.2 Three groups
were established: prerenal failure (50 patients; average age 49 years), prerenal failure on diuretics (27 patients; average age 51 years), and ATN (25 patients; average age 47 years). The diagnosis was established by an attending nephrologist based on expert guidelines (rapidly increasing BUN [>30 mg/dL] and Cr [>1.5 mg/dL], serum Cr increase >0.5 mg/dL in the preceding 2 days) and thorough analysis of patient history, physical exam findings, rate, and extent of azotemia, urinalysis, and urinary and serum indices, including sodium, urea, and creatinine. FEUN was found to have 85% sensitivity and 92% specificity. The findings support that a FEUN ≤35% and a FENa <1% are better markers for PRA than a BCR >15 (TABLE).

A retrospective outcomes trial of 191 patients (57% women, mean age 42 years) hospitalized in Pakistan for cholera examined the usefulness of the admission BCR as a predictor of AKI. Patients had BCR levels measured at admission and discharge (average stay 3.8 days). The mean BCR remained consistent at 12 (95% CI, 11–12) at admission and 12 (95% CI, 10.6–12.8) at discharge despite the fact that the average amount of fluid resuscitation was 25 liters. Additionally, of the 31% (60) patients who developed AKI, the average BCR upon initial presentation was lower than that of those who did not develop AKI (no data provided; P=.04).

### TABLE: Utility of laboratory findings for determining prerenal azotemia as the etiology for acute kidney injury²

<table>
<thead>
<tr>
<th>Laboratory finding</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>+LR</th>
<th>-LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCR &gt;15</td>
<td>87%</td>
<td>80%</td>
<td>4.4</td>
<td>0.16</td>
</tr>
<tr>
<td>FEUN ≤35%</td>
<td>90%</td>
<td>96%</td>
<td>22</td>
<td>0.11</td>
</tr>
<tr>
<td>FENa &lt;1%</td>
<td>77%</td>
<td>96%</td>
<td>19</td>
<td>0.24</td>
</tr>
</tbody>
</table>

BCR=blood urea nitrogen-to-creatinine ratio = [BUN (mg/dL)/Cr (mg/dL)].
FEUN=fractional excretion of urea nitrogen = [(UUN/BUN)/(UCr/PCr)] × 100.
FENa=fractional excretion of sodium = [(UNa/PNa)/(UCr/PCr)] × 100.

In a 2007 RCT, a total of 90 patients with myofascial pain (66 women, 24 men; age range 25–40 years) were randomly assigned to 1 of 5 study groups: Group 1 received botulinum toxin-A 10 U, group 2 received lidocaine 5% 1 mL, and groups 3, 4, and 5 were treated by other conservative measures without a trigger point injection. A 10-cm visual analog scale (VAS) measured pain intensity.

At week 1 posttreatment, all groups showed statistically significant improvement compared with baseline, with group 1 showing a VAS percent change of −39% (P<.05), group 2, −40% (P<.05), group 3, −31% (P<.05), group 4, −39% (P<.05), and group 5, −29% (P<.05). However, none of the treatment methods proved to be superior when intergroup comparisons were made. At 1 month, statistically significant improvements were detected in both the botulinum toxin-A and lidocaine groups from baseline (group 1, −71%; P<.05; group 2, −74%; P<.05). These 2 groups were found to be equally effective.

In 2001, a systematic review of 23 RCTs evaluated whether needling therapies have specific efficacy in the management of myofascial pain (ie, efficacy beyond placebo). The 23 trials were divided into 4 categories: (1) direct wet needling, (2) direct dry needling, (3) indirect wet needling, and (4) indirect dry needling. Fourteen trials (N=563) investigated direct wet needling with different substances including bupivacaine, lidocaine plus steroid, botulinum toxin-A, and isotonic saline. Eight of the 10 studies compared wet needling using different substances and found the effects were independent of the substance used. Five trials (N=532) directly compared dry with wet needling and found no difference between the 2 groups. Data were not pooled because the studies were of differing quality and design; many different parts of the body were represented, and were performed in 6 different countries. The authors concluded that that no difference exists between trigger
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Evidence-Based Answer

Both probiotics and soluble fiber improve global symptoms scores for IBS that are of unclear clinical significance (SOR: B, meta-analyses of heterogeneous RCTs). Exercise and mindfulness training appear to produce clinically important improvement in IBS symptoms (SOR: B, single RCTs).

A 2008 meta-analysis of 20 RCTs involving 1,404 patients with IBS compared treatment effects of probiotics versus placebo. Probiotic therapy led to a higher proportion of global symptom score responders than placebo therapy (risk ratio [RR] 0.77; 95% CI, 0.62–0.94), although the definition of a responder versus nonresponder had little uniformity across studies. A similar magnitude of improvement was seen with the secondary outcome of improved abdominal pain (RR 0.78; 95% CI, 0.69–0.88). Again, definitions of improvement in abdominal pain were not consistent across studies. Not enough data were available to assess any difference in other secondary outcomes such as bloating or flatulence.

A 2004 systematic review of 17 RCTs including 1,363 patients with IBS assessed the treatment effect of added fiber intake on global IBS symptom scores. This review found a general increase in dietary fiber led to improvement in IBS symptom scores (not defined) (RR 1.3; 95% CI, 1.2–1.5) compared with placebo. Soluble fiber (eg, psyllium, ispaghula, calcium polycarbophil) also showed improvement in global IBS symptom scores (RR 1.6; 95% CI, 1.4–1.8) when compared with placebo. Insoluble fiber (eg, wheat bran, corn) did not lead to significant clinical improvement (RR 0.89; 95% CI, 0.72–1.1).

A 2011 RCT of 102 patients with IBS compared the effect of increased physical activity with no change in activity on IBS symptoms. The intervention group received telephone advice from a physical therapist once or twice a month aiming for a moderate level of activity. After 12 weeks, the 500-point IBS severity score (IBS-SS) improved significantly from baseline when comparing the physical activity group and the control group (–51 vs –5; P=.003). A change of 50 points was noted to be clinically significant.

A 2011 RCT of 75 female patients with IBS compared the efficacy of mindfulness training, a cognitive-behavioral technique, to support group involvement in reducing IBS symptom severity. The mindfulness group had greater reductions in IBS-SS (26% vs 6.2%; P=.006) immediately and 3 months after intervention (38% vs 12%; P=.001) compared with the group receiving IBS support group participation only. The overall decrease in the IBS-SS for the mindfulness group was well above the clinically significant mark of 50 points (75 points immediately and 108 points after 3 months).

What are the most effective nonpharmacologic therapies for irritable bowel syndrome (IBS)?

A 2010 RCT of 80 patients with myofascial pain syndrome (52 women, 28 men; age range 19–58 years) compared the efficacy of local anesthetic injection and dry needling methods on pain. Patients were randomly assigned to receive either local anesthetic injection with 2 mL 1% lidocaine (group 1, n=40) or dry needling (group 2, n=40). Both groups were also given stretching exercises.

VAS scores (0–10) showed a statistically significant decrease from baseline in both group 1 (from 5.8 to 2.3; P<.001) and group 2 (from 5.6 to 3.8; P<.001) at 4 weeks, but no difference between groups (P=.053). The authors concluded that exercise associated with local anesthetic and dry needling injections were equally effective for myofascial pain.

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**Is fennel tea an effective treatment for colic in infants?**

**Evidence-Based Answer**

Maybe. Fennel seed oil reduces crying time in infants with colic (SOR: B, small RCTs). The optimal amount or formulation of fennel is unclear.

Fennel seed oil has been suggested as a treatment for colic in infants. In all studies listed here, colic was diagnosed by Wessel’s criteria: agitation and crying lasting longer than 3 hours per day for at least 3 days per week for longer than 3 weeks.

A 2003, double-blinded RCT evaluated the effect of fennel seed oil on colic in 125 infants 2 to 12 weeks old who were either breastfed or formula-fed. Infants were excluded if they were preterm, struggling with weight gain, on medications, or ill. Parents administered 5 to 20 mL 0.1% fennel seed oil in polysorbate solution or matched placebo at their discretion up to 4 times a day for a total of 7 days, with a daily maximum dose of 12 mg/kg. Infants were followed after the intervention for 7 days. The treatment was considered effective, or colic eliminated, if cumulative crying was reduced to less than 9 hours per week.

Colic was eliminated in 40 of 62 (65%) infants in the treatment group and 14 of 59 (24%) infants in the control group, for an absolute risk reduction (ARR) of 41% (95% CI, 25–57) and an NNT of 2 (95% CI, 2–4). No significant difference was noted in efficacy of treatment between the breastfed and formula-fed infants.

A 2005, double-blinded RCT studied the effect of 0.1% fennel seed oil with German chamomile and lemon balm on colic in 93 term, breastfed infants 21 to 60 days old. Infants had literate mothers and were without current infections, gastrointestinal disorders, metabolic disease, or failure to thrive. They received 1 ml/kg of treatment or matched placebo twice daily at 5 pm and 8 pm for 7 days and followed for 14 days after the intervention. Effect was measured by reduction of crying time by 50%. Thirty-five of 41 (85%) infants responded in the treatment group and 23 of 47 (49%) infants responded in the control group (ARR 36%; NNT=3).

A nonblinded RCT in 2008 examined the effect of massage, sucrose, fennel tea, hydrolyzed formula, or breastfeeding alone on crying time in 175 infants 4 to 12 weeks old. Infants had normal development, were breastfed, and were without gastrointestinal disorders or previous treatment for colic. Thirty-five infants were given 35 mL of an undefined concentration of fennel tea 3 times a day for 7 days. The primary outcome was mean reduction in crying time after the treatment period.

The fennel tea group had a baseline average crying time of 5.1 h/d, which decreased to 3.2 h/d after 7 days (P<.001). No significant reduction was noted in crying time in breastfed-only infants, from a baseline of 4.6 h/d to 4.5 h/d after 7 days (P>.05). Major limitations of the study included an undefined concentration of fennel in the tea and the lack of a between-group comparison.

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**FMR of Idaho**

**Boise, ID**


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**What is the most effective treatment for alopecia areata?**

**Evidence-Based Answer**

Intralesional and topical corticosteroids are moderately effective in the short term (12 weeks) for patchy hair loss in alopecia areata. There do not appear to be effective long-term treatment options; however, spontaneous remission is common (SOR: B, RCTs and evidence-based guideline).

A 2011 RCT compared the efficacy of 0.1% topical betamethasone valerate foam twice daily, intralesional triamcinolone acetonide 10 mg/mL every 3 weeks, and 0.1% tacrolimus ointment twice daily for the treatment of alopecia areata in 78 patients aged 11 to 50 years over 12 weeks. Response to treatment was measured using a quantitative hair regrowth grade.

Compared with baseline after 12 weeks, 60% of patients treated with intralesional triamcinolone reported >75% hair regrowth (P<.05) and 43% of patients treated with topical betamethasone reported...
>75% hair regrowth ($P<.05$). No participants in the tacrolimus group demonstrated >75% hair regrowth after 12 weeks. There was no comparison between groups.1

A 2011 randomized placebo-controlled trial examined the effectiveness of twice-daily pimecrolimus 1% cream and clobetasol propionate 0.05% compared with placebo for the treatment of alopecia areata in 100 patients (age range 3–65 years) referred to a university dermatology department.2 Patients were examined at 4, 8, and 12 weeks.

At week 12, the average area of alopecia regrowth was 54% in the pimecrolimus group, 47% in the clobetasol group, and 36% in the placebo group. No statistically significant difference was noted among the groups.3

A 2008 Cochrane review of 17 RCTs involving 540 adult and pediatric patients examined the long-term benefit of multiple treatments for patients with alopecia areata.3 The primary endpoint examined was >50% hair regrowth. The 17 trials compared a wide variety of topical and oral treatments with placebo including topical and systemic steroids, topical and systemic immunomodulators, antidepressants, and ultraviolet light therapy.

The review authors concluded that there was no significant long-term treatment benefit specific to hair growth compared with placebo for any intervention. Due to heterogeneity of the 17 chosen trials, data were not pooled. The authors noted that due to the possibility of spontaneous remission of alopecia areata, patients may consider not being treated or using a wig.3

The 2012 evidence-based guidelines for the treatment of alopecia areata from the British Association of Dermatologists summarized current research and updated the 2003 guidelines from the same group.4 The updated guidelines noted that few treatments have been subjected to randomized controlled trials and spontaneous remission is common (up to 80%).

For limited patchy hair loss, they recommended potent topical steroids (based on “good quality case control and cohort studies”) and intralesional corticosteroids (based on “short-term evidence”).

For extensive patchy hair loss or alopecia totalis/universalis, they recommended contact immunotherapy (based on “systematic review of case control or cohort studies”) and a wig or hairpiece (based on “expert opinion and consensus”). They recommended contact immunotherapy, but noted the response rate is low and the treatment is not easily available.4

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ionized magnesium was lower during menses (1.14 mEq/L), during menstrual-related attacks (1.12 mEq/L), and during nonmenstrual-related attacks (1.16 mEq/L) relative to control (1.2 mEq/L). However, the only value that achieved statistical significance was during menstrual-related attacks (P<.01).

Serum magnesium concentration related to migraine status and headache frequency
A case-control study compared serum magnesium levels between 140 migraineurs and 140 matched controls without migraines. The average serum magnesium concentration was significantly lower among migraine sufferers (2.2 vs 2.6 mEq/L; P<.000). Sex, age, and the presence of aura were not independently associated with a significant difference in serum magnesium concentrations. However, a linear relationship between mean magnesium level and headache frequency was noted (r=0.21; P=.016).

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REFERENCES

Ironized magnesium concentration related to menses and migraine status
A prospective cohort trial compared both ionized and total serum magnesium concentrations of 61 patients diagnosed with menstrual migraine with those of 66 controls. Mean total serum magnesium concentration was normal among all patients tested regardless of menses or migraine status. However, ionized magnesium was lower during menses (1.14 mEq/L), during menstrual-related attacks (1.12 mEq/L), and during nonmenstrual-related attacks (1.16 mEq/L) relative to control (1.2 mEq/L). However, the only value that achieved statistical significance was during menstrual-related attacks (P<.01).

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REFERENCES

Evidence-Based Practice learning objectives
1. To become knowledgeable about evidence-based solutions to commonly encountered clinical problems.
2. To understand how ground-breaking research is changing the practice of family medicine.
3. To become conversant with balanced appraisals of drugs that are marketed to physicians and consumers.
1. Which of the following statements is true regarding differentiation between type 1 and type 2 diabetes mellitus in adolescents or young adults?  
   - a. Differentiation can be established based on islet antibodies alone  
   - b. Islet autoantibodies and acanthosis nigricans cannot coexist in the same individual  
   - c. Differentiation depends in part on family history  
   - d. Patients with a high body mass index will likely have an elevated level of islet antibodies

2. Which of the following interventions has the least solid evidence of consistently helping alleviate symptoms of carpal tunnel syndrome?  
   - a. Corticosteroid injection  
   - b. Therapeutic ultrasound  
   - c. Ergonomic keyboard use  
   - d. Wrist splinting

3. A 55-year-old woman with fibromyalgia presents with significant trigger point pain. She is interested in injections for 3 trigger points that are particularly bothersome. In counseling about injections, you can reliably state:  
   - a. Botulinum toxin-A injections are more effective than lidocaine and steroid injections  
   - b. Lidocaine and steroid injections are more effective than saline injections  
   - c. Dry needling will likely work as well as injecting any available fluid  
   - d. Bupivacaine injections are not effective

4. With regard to determining prerenal etiology in acute kidney injury, which of the following statements is true?  
   - a. The BCR (blood urea nitrogen-to-creatinine ratio) >15 is the gold standard  
   - b. FENa (fractional excretion of sodium) <1% has a lower positive likelihood ratio (+LR) for the diagnosis of prerenal azotemia than BCR  
   - c. FEUN (fractional excretion of urea nitrogen) ≤35% has a higher +LR for the diagnosis of prerenal azotemia than BCR  
   - d. FEUN <35% has a lower specificity for the diagnosis of prerenal azotemia than BCR

5. All of the following interventions have been shown to be helpful in reducing symptom severity in irritable bowel syndrome except  
   - a. Soluble fiber  
   - b. Probiotics  
   - c. Mindfulness training  
   - d. Insoluble fiber

6. A mother brings in her 6-week-old infant for persistent crying. She has heard that fennel is good for colic. You can tell her:  
   - a. Fennel cannot be safely used in infants because only the whole seed is effective  
   - b. Fennel might be effective, but not much data are available on the best compound or dose  
   - c. Fennel teas have been proven effective in multiple well-designed trials  
   - d. Fennel oil is not effective and has significant toxicity

7. Which of the following statements is true regarding treatment for alopecia areata?  
   - a. Intralesional corticosteroids are effective in the short term  
   - b. All cases should be treated aggressively, as spontaneous resolution is rare  
   - c. Pimecrolimus 1% is more effective than placebo  
   - d. Topical corticosteroids have shown good long-term results

8. Which of the following statements is true about the treatment of panic disorder?  
   - a. Selective serotonin reuptake inhibitors (SSRIs) are superior to the combination of cognitive-behavioral therapy (CBT) and SSRIs for the long-term treatment of panic disorder  
   - b. After the treatment phase is complete, benzodiazepines are more effective in preventing symptoms than psychotherapy  
   - c. Current American Psychiatric Association guidelines suggest using serotonin-norepinephrine reuptake inhibitors before other medication classes  
   - d. Combining antidepressants with CBT may provide a small benefit over either alone, during the active treatment phase
The Family Physicians Inquiries Network is thrilled to announce that select HelpDesk Answers articles will now be featured in *The Journal of Family Practice*!

Be sure to check out this new addition in the May print issue of JFP or view online at [http://www.jfponline.com/articles/helpdesk-answers.html](http://www.jfponline.com/articles/helpdesk-answers.html).
Does screening patients with hypertension for microalbuminuria improve outcomes?

**Evidence-Based Answer**

The presence of microalbuminuria is associated with an increased risk of cardiovascular and cerebrovascular disease (SOR: B, prospective cohort trials). However, it is not clear if screening for microalbuminuria in hypertensive patients will improve outcomes.

A 2000 prospective cohort trial observed 204 untreated hypertensive patients for 9.5 years to evaluate if the presence of microalbuminuria adds to the increased risk of ischemic heart disease in this patient population. Microalbuminuria was found to be the strongest predictor of developing ischemic heart disease regardless of subsequent hypertension treatment (risk ratio [RR] 4.2; 95% CI, 1.5–12). When adjusted for the effects of other risk factors of ischemic heart disease, the risk increased (RR 5.6; 95% CI, 1.9–17).

A 2003 prospective cohort trial of 144 elderly hypertensive patients, without previous cardiovascular complications, evaluated if baseline values of urinary albumin excretion and other cardiovascular risk factors are predictive of cardiovascular complications. Patients with microalbuminuria at baseline had a higher incidence of cardiovascular events (myocardial infarction, angina pectoris, cerebral infarction or hemorrhage, aortic dissection) during the 8-year follow-up than patients who had normoalbuminuria at baseline (18% vs 7.2%; \(P=0.05\)).

A longitudinal cohort trial examined depressive symptoms and risk factors for depression in 439 adult patients with asthma. Data were collected via telephone interview at baseline, 2 years, and 4 years. The 20-item Center for Epidemiological Studies for Depression Scale (CESD) was administered during each interview.

The prevalence of depression among the participants was 17% at the first interview, 14% at the second interview, and 15% at the time of the third interview. By comparison, the estimated prevalence of depression in the general adult population is approximately 7%. The study dropout rate was 28% by the time of the third interview. Individuals who scored positive for depression at baseline were more likely to drop out (OR 1.8; 95% CI, 1.1–3.0).

A meta-analysis and meta-regression compared the prevalence of anxiety and depression among adolescents with asthma with the prevalence of anxiety...
and depression among adolescents without asthma.\textsuperscript{2}

Eligible studies included case-control, observational cohort, or cross-sectional studies, with a minimum of 50 subjects, aged 13 to 18 years.

Analysis of the 8 eligible trials revealed a higher prevalence of depression among adolescents with asthma (n=3,564), compared with control adolescents without asthma (n=24,884) (27\% vs 13\%; OR 2.1; 95\% CI, 1.7–2.6).\textsuperscript{2}

A retrospective cohort identified 1,812 adults with moderate to severe persistent asthma (asthma diagnosis for ≥12 months, and either 2 courses of oral corticosteroids in the past 12 months or a short-acting beta-agonist and at least 2 additional long-term controllers) from the Greenfield Online Panel, a web-based cohort of nearly 4 million individuals weighted to match US Census demographics.\textsuperscript{3} The individuals completed the 5-item Asthma Control Test (an observational, cross-sectional questionnaire) and self-reported additional information, including comorbidities, healthcare use, and attitudes and behaviors toward asthma. Each respondent also completed a 14-question survey about type and degree of activity limitations.

Twenty-five percent of the participants reported depression. Among the survey participants, depression was associated with outdoor activity limitation (OR 1.6; 95\% CI, 1.1–2.2); physical activity limitation (OR 1.8; 95\% CI, 1.3–2.5); and daily activity limitation (OR 1.6; 95\% CI, 1.0–2.4) when compared with study patients who did not report depression.\textsuperscript{3}

\textbf{Evidence-Based Answer}

Are cannabinoids safe and effective for treatment of patients with rheumatoid arthritis?

Sativex, an oromucosal cannabinoid spray unavailable in the United States, improves pain on movement, pain at rest, and quality of sleep in patients with rheumatoid arthritis; however, the improvements are small and may not be clinically meaningful. Adverse effects including dizziness, lightheadedness, dry mouth, nausea, and falls are significantly more common with Sativex than with placebo (SOR: \textit{C}, small, low-quality RCT).

A Cochrane review identified 1 multicenter, randomized, double-blind, parallel group trial that examined the efficacy and safety of a cannabis-based medicine, Sativex (containing 2.7 mg tetrahydrocannabinol and 2.5 mg cannabidiol per activation), for 58 patients with rheumatoid arthritis over 5 weeks of treatment.\textsuperscript{1} Patients were on a stable regimen of prednisolone and NSAIDs for 1 month and disease-modifying antirheumatic drugs for 3 months. The average age of the patients was 63 years, and 79\% (n=46) were female.

The daily dose in the last week of treatment was 5.4 sprays for the treatment group and 5.3 sprays for the placebo group. Clinical assessments, conducted in the morning, included pain on movement, pain at rest, morning stiffness, and sleep quality assessed by a 0–10 numerical rating scale; the Short-Form McGill Pain Questionnaire (SF-MPQ), which is 15 items on a 0–3 scale; and the 28-joint disease activity score (DAS28), a calculated score based on sedimentation rate and number of tender points. On all of these scales, a lower score indicates fewer symptoms. The baseline score, the average of the last 4 days of the 14-day baseline period prior to treatment, was compared with the endpoint score, the average of the last 14 days of the 5-week treatment period.\textsuperscript{1}

Statistically significant improvements were noted for Sativex versus the placebo group in pain on movement (median difference [MD] –0.95; 95\% CI, –1.8 to –0.02), pain at rest (MD –1.0; 95\% CI, –1.9 to –0.18), quality of sleep (MD –1.2; 95\% CI, –2.2 to –0.14), DAS28 (MD –0.76; 95\% CI, –1.2 to –0.28), and SF-MPQ verbal pain at present (mean –0.72; 95\% CI, –1.3 to –0.14).\textsuperscript{2} No statistically significant improvement
was noted in morning stiffness, SF-MPQ total intensity of pain, or SF-MPQ intensity of pain at present.

Adverse effects were more likely in the treatment group (risk ratio [RR] 1.8; 95% CI, 1.1–3.0). The most common adverse effects in the treatment group were dizziness (26%, NNH=5), light headedness (10%, NNH=17), dry mouth (13%, NNH=8), nausea (6%, NNH=36), and falls (6%, NNH=16). There were no withdrawals due to adverse effects in the treatment group and 3 withdrawals in the placebo group (11%). No serious adverse events were noted in the treatment group. The type of placebo and blinding of placebo was not described, contributing to the low quality of the study. One of the authors was employed by the pharmaceutical company that makes Sativex.

The NICE Clinical Guidelines, which is an evidence-based guideline for the management of rheumatoid arthritis, does not mention cannabinoids.

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Is patient-controlled analgesia effective for patients with sickle cell pain crisis?

Evidence-Based Answer
Patient-controlled analgesia (PCA) is no better than continuous infusion or intermittent dosing of opioids for pain control in patients with sickle cell disease (SCD) experiencing vaso-occlusive crisis. PCA may lead to lower cumulative doses of opioids than continuous infusion (SOR: B, RCTs).

Two trials met inclusion criteria for a 2011 systematic review of PCA versus intermittent dosing in the treatment of SCD vaso-occlusive crisis, I looking at meperidine and the other morphine.1

In one RCT (N=20 adults aged 17–39 years), meperidine via PCA (25–30 mg/h) was compared with intramuscular meperidine (75–100 mg) as needed every 3 to 4 hours. No significant difference in pain was noted.1

In the other RCT (N=45 adults aged 18–65 years), 2 different dosing regimens (low and high dose) were used for 2 separate PCA versus intermittent intravenous treatment groups. No significant difference was noted in a 100-mm pain scale between either the low- or high-dose PCA groups compared with intermittent dosing (WMD –0.10 mm; 95% CI, –27 to 27 mm and WMD 9 mm; 95% CI, –18 to 36 mm, respectively). Additionally, no significant difference was noted in the amount of meperidine or morphine used between the PCA and control groups in each of the studies.1

A 2007 RCT of 25 episodes of vaso-occlusive crisis in 19 patients with SCD between 20 and 42 years old compared intravenous morphine administration via PCA versus continuous infusion.2 A significantly lower mean and total cumulative morphine consumption was noted in the PCA group (0.5 vs 2.4 mg/h; \( P<.001 \); and 33 vs 260 mg; \( P=.018 \)). Based on a verbal response scale (0=no pain, 10=worst pain), mean daily pain scores were comparable (4.9 vs 5.3; \( P=.09 \)).

Great Britain’s 2012 National Institute for Health and Clinical Excellence (NICE) guideline included the 2007 trial above as well as one from 1991.3 NICE guidelines are systematically developed based on the best available evidence and expert consensus opinion and undergo surveillance for updating every 2 years.

The guideline concluded that PCA should be considered in patients who require repeat dosing of opioids. PCA was also noted to have small additional health improvements of between 0.002 and 0.003 quality-adjusted life-years per person as well as lower hospital costs (between £170 and £1,329 [$110 and $863 in US dollars, based on IRS average conversion rates in 2011]), which seem correlated to shorter hospital stays (between 0.39 and 2.8 days).3

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The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the US Department of Navy, Department of Defense, or the US Government.

Does routine testing for tuberculosis (TB) in low-risk areas help to reduce the incidence of TB?

Evidence-Based Answer

Probably not. Routine screening of the general population (including low-risk areas) to reduce the incidence of TB has a number needed to screen (NNS) to prevent 1 case of active TB of 8,000 to 25,000 patients (SOR: C, population models). Current guidelines recommend targeted testing in elevated-risk populations in whom the NNS is lower (SOR: B, national evidenced-based guidelines).

A 2009 study created a population model to estimate the benefits of screening for latent tuberculosis infection (LTBI) with the tuberculin skin test (TST). The model used data from the National Health and Nutrition Examination Survey (NHANES) to determine the prevalence of LTBI and reactivation rate to active TB within the United States. The model used data from other published reports to determine inputs for TST sensitivity and specificity along with isoniazid therapy effectiveness, adverse effects, and compliance. In US-born residents, the NNS to prevent 1 case of active TB was 8,333 to 25,000, whereas in foreign-born residents the NNS was 319 to 1,216.

A 2011 study updated the population model discussed above with data from the Centers for Disease Control and Prevention (CDC) TB surveillance reports, NHANES III, and the US Census in order to estimate the benefits of screening US residents with risk factors for LTBI. The new model also evaluated screening with interferon-gamma release assays (IGRA) and accounted for the financial costs of screening and treatment. LTBI prevalence, reactivation rate, and NNS for TST and IGRA are shown in the Table.

A 2005 joint publication from the CDC, American Thoracic Society, and the Infectious Diseases Society of America recommends targeted testing for LTBI as shown in the Table (Grade AI–strong recommendation based on moderate-quality evidence). In their expert opinion, generalized screening in low-risk areas allocates limited resources away from areas of higher need.

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The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the US Air Force Medical Department, the US Air Force at large, or the Department of Defense.


<table>
<thead>
<tr>
<th>TABLE</th>
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<tr>
<td>Number needed to screen to prevent 1 case of active TB1–4</td>
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</table>

<table>
<thead>
<tr>
<th>Risk group</th>
<th>LTBI prevalence (%)2</th>
<th>TB reactivation (rate per 100 person-years)2</th>
<th>NNS with TST2</th>
<th>NNS with IGRA2</th>
<th>Targeted screening recommended2–4</th>
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<tbody>
<tr>
<td>Infected with HIV</td>
<td>5.3</td>
<td>2.1</td>
<td>71</td>
<td>67</td>
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<tr>
<td>Close contact adult</td>
<td>44</td>
<td>1.0</td>
<td>73</td>
<td>69</td>
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<tr>
<td>Close contact child</td>
<td>20</td>
<td>1.6</td>
<td>110</td>
<td>104</td>
<td>Yes</td>
</tr>
<tr>
<td>Recent immigrant adult</td>
<td>41</td>
<td>0.079</td>
<td>136</td>
<td>128</td>
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</tr>
<tr>
<td>Foreign born living in the United States &gt;5 years</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>6–14 years old</td>
<td>11</td>
<td>0.079</td>
<td>380</td>
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<td>15–24 years old</td>
<td>12</td>
<td>0.079</td>
<td>450</td>
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<td>25–44 years old</td>
<td>21</td>
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<td>45–64 years old</td>
<td>27</td>
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<td>≥65 years old</td>
<td>11</td>
<td>0.079</td>
<td>1,216</td>
<td>1,147</td>
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<tr>
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<td>29</td>
<td>0.079</td>
<td>436</td>
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<tr>
<td>Injection drug user</td>
<td>23</td>
<td>0.079</td>
<td>557</td>
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<tr>
<td>Recent immigrant child</td>
<td>7</td>
<td>0.079</td>
<td>617</td>
<td>582</td>
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<tr>
<td>Former prisoner</td>
<td>19</td>
<td>0.079</td>
<td>655</td>
<td>618</td>
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<tr>
<td>Immunosuppressive drugs</td>
<td>5.3</td>
<td>0.16</td>
<td>1,128</td>
<td>1,064</td>
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<tr>
<td>Underweight</td>
<td>2.8</td>
<td>0.12</td>
<td>2,062</td>
<td>1,946</td>
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<tr>
<td>Gastrectomy</td>
<td>2.8</td>
<td>0.10</td>
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<tr>
<td>Silicosis</td>
<td>2.8</td>
<td>0.10</td>
<td>2,962</td>
<td>2,795</td>
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<td>Diabetic</td>
<td>2.8</td>
<td>0.13</td>
<td>3,631</td>
<td>3,426</td>
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</tr>
<tr>
<td>End-stage renal disease</td>
<td>2.8</td>
<td>0.19</td>
<td>4,904</td>
<td>4,628</td>
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</tr>
<tr>
<td>US-born resident with no risk factors1</td>
<td>0.2–0.8</td>
<td>0.036</td>
<td>8,333 to 25,000</td>
<td>ND</td>
<td>No</td>
</tr>
</tbody>
</table>

HIV=human immunodeficiency virus; IGRA=interferon-gamma release assay; LTBI=latent tuberculosis infection; ND=no data; NNS=number needed to screen; TB=tuberculosis; TST=tuberculin skin test.

*aForeign born US residents living in the United States for ≤5 years.

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Is biofeedback an effective treatment for essential hypertension?

Evidence-Based Answer
Biofeedback has not been shown to significantly lower systolic blood pressure (SBP) or diastolic blood pressure (DBP) in patients with essential hypertension (SOR: C, disease-oriented outcomes).

A 2007 systematic review and meta-analysis of 17 RCTs examined the effectiveness of stress reduction programs in 960 patients with elevated SBP or DBP. Changes were compared from baseline measurements to ≥8 weeks after each respective stress reduction program began.

No difference was noted in SBP/DBP with simple biofeedback (6 trials, N=300; –0.8/–2.0 mmHg; P=not significant [NS]), relaxation-assisted biofeedback (4 trials, N=98; –1.9/–1.4 mm Hg; P=NS), or stress management training (5 trials, N=207; –2.3/–1.3; P=NS). Transcendental meditation programs demonstrated a significant decrease in SBP, but not DBP (6 trials, N=449; SBP –5 mmHg, 95% CI, –9.4 to –0.8 mmHg; DBP –2.1 mmHg, 95% CI, –5.4 to 1.4).1

A 2010 systematic review of 36 RCTs (N=1,660) examined the effectiveness of biofeedback for the treatment of essential hypertension (SBP >140 mmHg or DBP >90 mmHg) in adults.2 Twenty-one trials used biofeedback with no adjunctive antihypertensive therapy, whereas the other 15 studies used biofeedback with antihypertensive therapy. Patients with biofeedback training were compared with groups undergoing antihypertensive therapy alone, placebo (sham biofeedback), no treatment, or other behavior treatments. These groups were studied for <12 months.

Due to the overall poor quality of the included trials and the heterogeneity of outcomes measured, only a narrative summary using the trial authors’ conclusions was reported. The authors of the review found no results that consistently showed the effectiveness of biofeedback for the treatment of essential hypertension compared with the other therapies.2

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The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the US Army Medical Department, the US Army at large, or the Department of Defense.