Should preparticipation physicals for school-age athletes include routine EKGs?

Evidence-based answer
Probably not. It is unclear whether screening reduces the risk of sudden cardiac death (SCD); US experts do not recommend it routinely for school-aged athletes (strength of recommendation [SOR]: C, observational studies and expert opinion). However, further cardiac work-up, including EKG, is indicated if concern exists about increased cardiovascular risk (SOR: C, expert opinion).

Evidence summary
SCD in athletes is a rare event; researchers estimate the annual incidence at 0.5 to 2 per 100,000 athletes per year.¹² The rarity of SCD, lack of registries recording cases, multiple causes, and varying demographics limit accurate estimation of its incidence.³

An Italian study suggests lower SCD mortality with EKG screening
An Italian observational study of 33,735 athletes reported results of a 25-year program of mandated SCD screening (1979 to 2004).⁴ Researchers found that the incidence of sudden death was 89% lower at the end of the screening program (0.4/100,000 athletes/year) compared with the baseline at the beginning (3.6/100,000 athletes/year).

The program used highly trained sports medicine physicians and supplemented the history and physical examination with universal EKG screening. Screening began at 12 to 14 years of age and was repeated regularly as long as the athlete was engaging in competition. The incidence of SCD in nonathletes (0.79/100,000 nonathletes/year) did not change over the 25 years of the study.

Limitations of this study include lack of a control group of unscreened athletes and time-dependent bias (athletes who died suddenly during the prescreening period would never have made it to the first screening, so that group of athletes already represented a selected lower-risk population). In addition, the study used a short measurement time (approximately 3 years) to establish a baseline SCD incidence, resulting in a higher incidence than the average in other studies.


continued
An Israeli study suggests otherwise

An uncontrolled observational study in Israel compared the number of SCDs before and after implementation of a mandatory nationwide screening program for athletes. The screening included a medical questionnaire, physical examination, resting EKG, and exercise stress test. Researchers estimated the SCD incidence by scrutinizing newspaper reports of sudden deaths in athletes for two time periods: 12 years before and 12 years after the intervention.

They identified 24 presumed cardiac deaths, all in male athletes 12 to 44 years of age (mean 23.9 years). The incidence of SCD in the athletes before and after this protocol was 2.54 and 2.66/100,000 athletes/year, respectively (P not significant).

An advantage of this study is the longer period used to estimate SCD incidence (12 years compared with approximately 3 years). A disadvantage is that the researchers calculated the SCD incidence by relying only on media reports rather than a death registry.

A US comparison study supports the Israeli findings

Researchers compared SCD rates in high school and college athletes in Minnesota with the rates reported in the Italian study. They collected mortality data from several sources, including a national death registry over 23 years, during which time routine EKG screening of Minnesota athletes was not mandated or recommended. SCD mortality rates remained stable at 0.97/100,000 athletes/year (range 0.5–1.3). This was not significantly different from the death rate seen with screening in the Italian study.

Recommendations

The European Society of Cardiology Study Group of Sport Cardiology and the International Olympic Committee advocate routine screening.

The American Heart Association (AHA) and the American College of Sports Medicine don’t recommend routine EKGs as part of the preparticipation evaluation of school-aged athletes. The AHA recommends that a qualified examiner perform a full history and physical exam, which includes 12 key risk factor assessments (TABLE), and advocates cardiovascular referral for patients who show concerning positive findings.

<table>
<thead>
<tr>
<th>Personal history</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Exertional chest pain or discomfort</td>
</tr>
<tr>
<td>2. Unexplained syncope or near syncope (exertional syncope is of particular concern)</td>
</tr>
<tr>
<td>3. Excessive exertional and unexplained dyspnea or fatigue associated with exercise</td>
</tr>
<tr>
<td>4. Previous recognition of a heart murmur</td>
</tr>
<tr>
<td>5. Elevated systemic blood pressure</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Family history</th>
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</thead>
<tbody>
<tr>
<td>6. Premature death (sudden and unexpected or otherwise) in one or more relatives &lt;50 years old because of heart disease</td>
</tr>
<tr>
<td>7. Disability from heart disease in a close relative &lt;50 years</td>
</tr>
<tr>
<td>8. Relatives with: hypertrophic or dilated cardiomyopathy, long QT syndrome or other ion channelopathies, Marfan syndrome, or clinically important arrhythmias</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physical examination</th>
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<tbody>
<tr>
<td>9. Heart murmur—perform auscultation in both supine and standing positions (or with Valsalva maneuver), specifically to identify murmurs of dynamic left ventricular outflow tract obstructions</td>
</tr>
<tr>
<td>10. Femoral pulses to exclude aortic coarctation</td>
</tr>
<tr>
<td>11. Physical stigmata of Marfan syndrome</td>
</tr>
<tr>
<td>12. Brachial artery blood pressure (sitting position), preferably in both arms</td>
</tr>
</tbody>
</table>

Alan Remde, MD
Robert Wood Johnson Medical School, FMR at Capital Health, Trenton, NJ

Nancy Calabretta, MS, MEd
Cooper University Hospital, Camden, NJ

Assistant Editor: Justin Bailey, MD
FMR of Idaho, Boise

REFERENCES
From the Editor

Good tables

Dear EBP Readers,

I have an Amish-made cherrywood kitchen table that I really like. It’s small enough to foster intimacy, but big enough to hold the snacks and drinks that fuel a conversation. It expands to accommodate family, and is solid enough to support kids’ elbows and platters of holiday favorites. It has no metal parts; rather, it was built with mortise and tenon, an intimate understanding of the materials, and a whole lot of loving care. It is elegant in its functional simplicity.

As an editor, I also appreciate good, solid tables in medical publishing. Data tables are a great way to condense a lot of information into a small space, and they also approach elegance when they allow the reader to see patterns and associations that would not otherwise be evident in a text presentation. A really fine table, in fact, is often separated from the paper it first adorned and goes on to lead an independent existence on the Internet or elsewhere. All authors should aspire to this outcome for their tables.

Let me share with you a few of the features that I think make for a solid (data) table:

1. The title should be complete enough to allow the table to be understood independent of the rest of the paper.
2. The table should be referenced, so everyone knows where the data came from.
3. Column and row headings should be clear and complete.
4. Column (or row) headings should contain the units of measure.
   - Repeating units in the cells is distracting.
   - Changing units within a column (or row) is confusing.
5. Variables to be compared should be placed side by side.
6. Cells should contain only 1 or 2 data points.
7. The table should use primarily positive numbers.
   - Lots of negative signs can be distracting, too.

These 7 steps will at least get you started building a table that is strong and functional. But as with fine woodworking, achieving elegance will take a bit more effort: an intimate understanding of your data, diligent effort, and a whole lot of loving care.

Regards,

Jon O. Neher, MD
Diving for PURLs

**PURLs Criteria**

Relevant: Is the topic relevant to family medicine?
Valid: Are the findings scientifically valid?
Change in practice: Would this change practice?
Medical care setting: Is this implementable in clinic, etc?
Implementable: Can we implement this immediately?
Clinically meaningful: Are results clinically meaningful?

**Meta-analysis questions the benefit of general health checks**


This meta-analysis of 14 RCTs (3 from the United States and 11 from Europe) evaluated the effect of general health checks in more than 180,000 people 18 to 65 years old on total, cardiovascular, and cancer mortality compared with no check-ups. A general check-up was defined as “contact between a person and a health care professional to identify signs, symptoms, or risk factors for disease that were previously unrecognized.”

The content of this check-up varied. Most included measurement of blood pressure, cholesterol, and body mass index. Some check-ups also included biochemistry panel, an electrocardiogram, history, urine analysis, clinical examination, vision and hearing screening, and cancer screening. The check-ups occurred in screening clinics, primary care clinics, or the workplace.

In the check-up group there was no decrease in total mortality (RR 0.99; 95% CI, 0.95–1.03), cardiovascular mortality (RR 1.03; 95% CI, 0.91–1.17), or cancer mortality (RR 1.01; 95% CI, 0.92–1.12) compared with the control group.

<table>
<thead>
<tr>
<th>Relevant</th>
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<th>Yes</th>
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<tbody>
<tr>
<td>Valid</td>
<td>No</td>
<td>Implementable</td>
<td>Yes</td>
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<tr>
<td>Change in practice</td>
<td>No</td>
<td>Clinically meaningful</td>
<td>Yes</td>
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**Bottom line:** The validity of the outcome is weakened by the large heterogeneity among the studies, particularly in the area of what constitutes a check-up. We need studies to determine which specific items in health check-ups are effective at decreasing morbidity and mortality so providers focus their efforts on these interventions.

Review Author and Summary Author: Anne Mounsey, MD, University of North Carolina, Department of Family Medicine

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**Block the beta-blockers?**


This cohort study enrolled more than 44,000 patients aged 45 or older to determine whether beta-blockers versus no beta-blockers reduced the primary composite outcome of cardiovascular mortality, new-onset myocardial infarction (MI), or nonfatal stroke. Patients were enrolled from 7 sites around the world and were followed for an average of 44 months.

Patients were analyzed in 1 of 3 groups: history of MI, known coronary artery disease (CAD) without MI, and no CAD but with at least 3 known risk factors for CAD (eg, current smoking, hypertension, or diabetes). Propensity score matching, a statistical technique that matches people from each group based on demographic and medical history, was used. Between 40% and 60% of the original cohorts were retained.

For patients with previous MI, the HR for cardiovascular mortality among those taking beta-blockers compared with no beta-blockers was 0.90 (95% CI, 0.79–1.03); for those with CAD without previous MI the HR was 0.92 (95% CI, 0.79–1.08); for those with ≥3 CAD risk factors the HR was 1.18 (95% CI, 1.02–1.36).

<table>
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<tr>
<th>Relevance</th>
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**Bottom line:** The current recommendation to use beta-blockers long term after MI is based on small cohort trials and expert opinion, and much of the evidence comes from trials conducted before modern revascularization techniques and current medical therapy, such as statins and antiplatelet agents. By contrast, this recent and large cohort study did not find long-term beta-blockers beneficial.

Review Author and Summary Author: Kate Rowland, MD, The University of Chicago, Department of Family Medicine

Additional information can be found at: [www.fpin.org/purlsoverview](http://www.fpin.org/purlsoverview)
**Use NSAIDs for biliary colic**


This meta-analysis of 11 RCTs comprising 1,076 subjects between 18 and 86 years old with biliary colic compared NSAIDs with placebo or other drugs in controlling pain and cholelithiasis-related complications (eg, cholecystitis, acute pancreatitis, or cholangitis).

For complete pain relief at 2 hours, NSAIDs were equivalent to opioids (RR 1.05; 95% CI, 0.82–1.33), better than spasmolytics (RR 1.47; 95% CI, 1.03–2.10), and far better than placebo (RR 3.77; 95% CI, 1.65–8.61). There were fewer complications with NSAIDs compared with all other drugs and placebo (RR 0.53; 95% CI, 0.31–0.89).

**Bottom line:** Start with NSAIDs for biliary colic pain relief.

Review Author and Summary Author: Kohar Jones, MD, The University of Chicago, Department of Family Medicine, Chicago, IL

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**Cognitive behavioral therapy effective in pharmacotherapy-resistant depression**


This multisite RCT compared antidepressant treatment augmented with cognitive behavioral therapy (CBT) to antidepressants (usual care) alone. It included 469 patients (18–75 years of age) recruited from 73 UK general practices who had been taking antidepressants for ≥6 weeks, scored ≥14 on the Beck Depression Inventory (BDI), and met the International Classification of Diseases-10 criteria for depression. CBT treatment involved 12 to 18 50- to 60-minute sessions. The primary outcome was “response,” defined as 50% reduction in BDI score from baseline to 6-month follow-up.

Forty-six percent of the intervention group and 22% of the usual-care group met criteria for response (odds ratio 3.26; 95% CI, 2.10–506; P<.001). Relative to the usual-care group, participants in the CBT group demonstrated reduced symptoms of depression and anxiety on multiple secondary outcome measures at 6- and 12-month follow-up assessments.

**Bottom line:** For patients with treatment-resistant depression, the addition of CBT to their current pharmacotherapy is more effective than pharmacotherapy alone.

Review Author and Summary Author: Irene Skowronek, PhD, University of North Carolina, Department of Family Medicine

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**Should people with CKD take statins?**


This meta-analysis, including both primary and secondary prevention studies, summarized the benefits and harms of statin therapy for adults with chronic kidney disease (CKD). Eighty-six trials with more than 51,000 participants compared statin therapy with placebo or no treatment. Principal outcomes analyzed included all-cause and cardiovascular mortality.

Statin treatment reduced all-cause mortality in people not receiving dialysis (RR 0.81; 95% CI, 0.74–0.88), but did not alter all-cause mortality in people receiving dialysis (RR 0.96; 95% CI, 0.88–1.04) or recipients of kidney transplants (RR 1.05; 95% CI, 0.84–1.31). Statins reduced cardiovascular mortality in people not receiving dialysis (RR 0.78; 95% CI, 0.68–0.89), but had no significant effect on people receiving dialysis (RR 0.94; 95% CI 0.82–1.1) or recipients of kidney transplants (RR 0.68; 95% CI, 0.45–1.02).

**Bottom line:** Statin therapy reduces all-cause and cardiovascular mortality in people with CKD not on dialysis. The benefits for patients on dialysis or patients who have received kidney transplants are uncertain.
Does urinating after intercourse reduce the risk of urinary tract infections among women?

Evidence-Based Answer

Overall, urinating after intercourse does not reduce the risk of symptomatic urinary tract infections (UTIs) among sexually active young healthy women (SOR: B, cohort and case-control studies). However, there may be some protection in voiding within 15 minutes for women without any history of past UTIs (SOR: C, heterogeneous cohort and case-control studies).

A prospective cohort study conducted at the University of Washington Student Health Center and the Group Health Cooperative of Puget Sound examined 819 healthy women, 18 to 40 years old, for risk factors of symptomatic UTIs. Women were given diaries to record sexual intercourse, use of contraception and method, voiding within 1 hour after intercourse, and vaginal and urinary symptoms. Analysis of the 154 women who developed a symptomatic UTI revealed that voiding within 1 hour after intercourse did not significantly reduce the risk of UTI compared with women who did not void within 1 hour.

A case-control study examined the risk factors for recurrent UTIs in 482 healthy women, 18 to 30 years old, at the same location as above. Case patients were women with a UTI during the preceding month and either more than 3 symptomatic UTIs within the past year or 2 symptomatic UTIs within the past 6 months. Age-similar women without a history of more than 1 UTI in any 12-month period and no UTI within the preceding 12 months were used as the control patients.

Compared with the control group, there was no difference among patients with recurrent UTIs in either voiding before intercourse (62% vs 53% at the university; 57% vs 51% at the HMO) or voiding after (33% vs 33% at the university; 28% vs 26% at the HMO). These results were not statistically significant.

Another cohort study followed 285 healthy women, 18 to 39 years old, for 6 months after their first UTI. A self-administered questionnaire was completed at enrollment, 2, 4, and 6 months after enrollment, and/or at the time of recurrence. When comparing the voiding habits of women who developed a second UTI (n=54) with those who did not, there was no statistically significant association with urinating before intercourse (OR 0.60; 95% CI, 0.14–2.6; P=.5), urinating after intercourse (OR 0.60; 95% CI, 0.20–1.8; P=.36), or urinating neither before nor after intercourse (OR 1.3; 95% CI, 0.34–4.6; P=.74). The timing of postcoital urination was not specified.

The University of Michigan Health Service conducted a case-control study (N=1,641) utilizing 2 different control groups to identify behaviors that may minimize the risk of UTIs in healthy women. Each participant completed a self-administered questionnaire addressing behaviors and medical history. In women without prior history of UTIs, always urinating within 15 minutes after intercourse compared with never was protective (OR 0.10; 95% CI, 0.02–0.64). In women with any history of past UTI(s), urinating 15 minutes after intercourse did not alter the risk of getting a UTI (OR 2.4; 95% CI, 0.39–15) compared with women who did not void after intercourse.

The most recent American College of Obstetricians and Gynecologist Practice Bulletin reports insufficient evidence for postcoital voiding and UTI prevention.

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Fort Bragg, NC

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


What are the most common causes of acute urinary retention in women?

Evidence-Based Answer

Acute urinary retention (AUR) is associated with a wide variety of medical conditions that can be classified as postpartum, postoperative, gynecological, urological, neurological, rectal, or psychiatric. Common etiologies outside the postoperative and postpartum periods include detrusor failure without other abnormalities, psychogenic urinary retention, and neurogenic urinary retention (SOR: C, case series).

The etiology of AUR in women is not well understood. Much of the evidence is limited to case studies and
small case series that do not state inclusion criteria or describe a standard diagnostic evaluation. The results from 3 case series studies are included in the TABLE.

A prospective analysis of a consecutive series of 18 women (median age 68 years) treated for AUR in 6 hospitals in Copenhagen was published in 1987. Underactive detrusor function without other organic abnormality was found in half the patients. Three patients had underactive detrusor function and obstruction (cystocele in 2 and urethral stricture in 1). Obstruction (urethral calculus, total uterine prolapse) with normal detrusor function was found in 2 patients.

In a study of 27 consecutive cases of AUR in girls and women in North Carolina and Virginia published in 1983, all patients had a complete history, physical exam, volume of catheterized urine at initial presentation, urinalysis, urine culture, excretory urography, cystometrography and, in some cases, cystoscopy. The age range of patients was 14 to 82 years.

A retrospective then prospective survey of 103 women with AUR in the Bristol Clinical Area of the United Kingdom was reported in 1976. Patients were included if the retention was painful and acute in onset, and if less than 1 L of urine was obtained on catheterization. The most common causes were postpartum and postoperative. The remaining women were admitted to the hospital and had diagnoses grouped as gynecological, urological, neurological, psychiatric, and rectal. The gynecological causes were most often fibroids and retroverted uterus. The urological causes included patients with inflammation, and bladder neck and urethral obstruction.

Can metformin be safely used in elderly patients?

Evidence-Based Answer
Yes. There does not appear to be an increased risk of lactic acidosis in elderly patients with diabetes taking metformin when doses are adjusted for creatinine clearance (SOR: C, disease-oriented outcomes).

A 2011 subgroup analysis of a larger retrospective cohort study reported outcomes in 180 diabetic Japanese adults older than age 65 (average age 70) who were treated with metformin for glucose control. The patients received metformin 250, 500, or 750 mg daily depending on creatinine clearance, although the exact creatinine cutoff levels were not described. Outcomes measured were HbA1c and lactic acid levels.

There was no difference between the reduction of HbA1c from baseline between the elderly and nonelderly groups (data presented graphically). For the 34 patients aged >75 years, HbA1c decreased from 7.9% to 7.2% after 12 months of metformin use (P<.001). There were no cases of lactic acidosis during the study period.

A 1990 prospective cohort study enrolled 24 patients between 70 and 80 years of age to see if metformin was efficacious and safe in elderly patients with diabetes. Prior to participating, some patients were on metformin alone (n=2), metformin combined with another hyperglycemic drug (sulfonylurea; n=15), a sulfonylurea alone (n=3), insulin alone (n=1), or controlled with diet only (n=1). The investigators had the patients take metformin alone when possible.

<table>
<thead>
<tr>
<th>Cause</th>
<th>Klarskov (N=18)</th>
<th>Preminger (N=27)</th>
<th>Doran (N=103)</th>
</tr>
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<tbody>
<tr>
<td>Unknown</td>
<td>4 (22)</td>
<td>4 (15)</td>
<td></td>
</tr>
<tr>
<td>Neurological</td>
<td>8 (30)</td>
<td>7 (7)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>3 (11)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detrusor failure without other abnormality</td>
<td>9 (50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychogenic</td>
<td>8 (30)</td>
<td>3 (3)</td>
<td></td>
</tr>
<tr>
<td>Postoperative</td>
<td>4 (15)</td>
<td>25 (24)</td>
<td></td>
</tr>
<tr>
<td>Gynecological</td>
<td>3 (17)</td>
<td>17 (17)</td>
<td></td>
</tr>
<tr>
<td>Urinary obstruction</td>
<td>2 (11)</td>
<td>7 (7)</td>
<td></td>
</tr>
<tr>
<td>Urinary Inflammation</td>
<td></td>
<td>7 (7)</td>
<td></td>
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<tr>
<td>Urinary iatrogenic</td>
<td></td>
<td>1 (1)</td>
<td></td>
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<tr>
<td>Postpartum</td>
<td>33 (32)</td>
<td></td>
<td></td>
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<tr>
<td>Rectal</td>
<td>3 (3)</td>
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</table>

Values are n (%).
(sulfonylureas were discontinued in 9 cases). The metformin dose used was either 850 or 1,700 mg daily, depending on creatinine clearance (30–60 mL/min or >60 mL/min, respectively).

No significant changes in glycemic control from baseline were found at 1 and 2 months of the therapy (HbA1c 10.5% vs 9.7% at 2 months). Lactic acid levels were unchanged in the higher dose group from baseline to 1 month to 2 months (1.7 to 1.7 to 1.5 mmol/L) and decreased in the lower dose group (2.2 to 1.6 to 1.2 mmol/L; \( P < .05 \)).

A 2010 cross-sectional study enrolled 66 patients with diabetes who were older than 80 years (range 80–90 years of age, mean 83.6 years) receiving metformin at 3 different doses (1,000, 1001–2,000, or >2,000 mg daily). A group of 79 younger patients (range 37–79 years of age, mean 59.9 years) was enrolled as a control group. There was no significant difference in lactate levels between the elderly and control groups (13.2 and 13.5 mg/dL, respectively) and no cases of lactic acidosis were identified. The older group did receive lower doses of metformin and had lower estimated creatinine clearances than the younger group.

**Evidence-Based Answer**

**Should you biopsy pigmented lesions on the palms or soles?**

**Evidence-Based Answer**

Pigmented lesions of the palms and soles are common in some ethnic groups. Biopsy should be considered if the lesion is 9 mm or more in diameter (SOR: B, Japanese cohort studies).

A retrospective observational study was conducted to evaluate the prevalence and dermatoscopic characteristics of plantar melanocytic nevi and the relationship between acral nevi and acral lentiginous melanoma on the soles of Japanese patients. A total of 1,697 patients were included in the control group.

The melanoma group consisted of 104 patients with malignant melanoma of various types on the soles of the feet. Photographs and dermatoscopic images of the nevi on the soles and toes were obtained and independently examined by 2 dermatologists.

Compared with the control group, the melanoma group did not have a significant difference in the prevalence of benign melanocytic nevi (13% vs 10%; \( P > .05 \)) or the mean size (4.8 vs 3.8 mm; \( P > .05 \)) of melanocytic nevi on the soles of the feet.

An observational study was conducted to determine the number, size, and distribution of acquired melanocytic nevi in a Japanese population and to evaluate the relationship between number of acquired nevi and development of acral or nonacral malignant melanoma. Eighty-two patients with malignant melanoma were compared with 600 patients with cutaneous disorders other than malignant melanoma or melanocytic nevus as the control group. Experienced dermatologists counted the number of acquired melanocytic nevi 2 mm or larger in diameter on the whole body except the scalp and genital areas. For statistical analyses, the subjects were divided into 5 age categories (0–19, 20–39, 40–59, 60–79, and >80 years old).

Significantly more acquired nevi were found on the whole body in patients with nonacral melanoma compared with the control group in the 40–59 and 60–79 age groups, but no significant difference was noted in the number among individuals who had acquired nevi on soles, palms, and nail apparatus between acral melanoma group and the control group in the 40–59 and 60–79 age groups.

In a retrospective observational study, clinical and histopathologic features of 144 pigmented lesions excised from the soles of Japanese patients were investigated, to propose clinical guidelines for early detection of plantar malignant melanoma. Ages, clinical diagnosis, maximum diameter, and color photographs of the lesions of the patients were reviewed.

Of the 144 pigmented lesions excised from plantar surface of 137 Japanese subjects, 140 were melanocytic nevi. All acquired melanocytic nevi and dysplastic nevi were <9 mm in diameter. In contrast, all lesions of plantar malignant melanomas were \( \geq 9 \) mm in diameter. Mean maximum diameter of plantar malignant melanomas was significantly larger than that of acquired melanocytic plantar nevi including dysplastic nevi (32 vs 4 mm; \( P < .001 \)).
What are effective nonhormonal treatments for vasomotor symptoms in menopause?

Evidence-Based Answer

Escitalopram and gabapentin are more effective for reducing hot flashes than placebo (SOR: B, individual RCTs). Participation in a mindfulness training program is associated with reduced bother from hot flashes, but has not been shown to be better than placebo (SOR: B, single RCT). Evidence is insufficient to determine the effect of exercise on vasomotor symptoms in menopause.

In 2011, an 8-week RCT was performed to determine the efficacy of escitalopram (10–20 mg/d) compared with placebo in the treatment of menopausal hot flashes in 205 peri- and postmenopausal women.1 Hot flash frequency and severity (rated mild, moderate, or severe) were recorded twice daily in a diary.

Women receiving escitalopram reported a statistically greater mean reduction hot flashes per day (4.6 vs 3.2 for placebo; P<.001). Also, significantly more women in the escitalopram group than the placebo group had a decrease in hot flash severity from “moderate to severe” to “mild to moderate” (24% vs 14%; P<.001).1

A 2008 RCT of 200 postmenopausal women compared gabapentin with placebo for the treatment of menopausal hot flashes.2 Women received either gabapentin 300 mg or placebo 3 times a day for 4 weeks. The primary outcome measure was percent change from baseline in hot flash score as calculated from participant diaries recording number and severity of hot flashes.

The gabapentin group reported a greater decrease in hot flash score compared with the placebo group (51% vs 26%, respectively; P<.001). Common adverse effects in the gabapentin group included dizziness (18%), unsteadiness (14%), and drowsiness (12%); however, these symptoms returned to baseline rates by week 4.2

A 2011 RCT examined the effect of participation in a mindfulness training program on the degree of bother from night sweats and hot flashes in 110 peri- and postmenopausal women with moderate or severe hot flashes who were randomized to either the intervention or waitlist control.3 The primary outcome measure was overall degree of bother from hot flashes as recorded in patient diaries based on a 4-point bother scale (“not at all” to “extremely bothered”). At 20 weeks, bother from hot flashes was significantly reduced from baseline in both groups; moreover, the magnitude of change was similar (22% for mindfulness training and 11% for control; P=.07).

A Cochrane review of 9 RCTs (N=276 patient) examined the effectiveness of exercise for the treatment of vasomotor symptoms of menopause.4 Comparing exercise with no treatment, hormone replacement therapy, or yoga, the authors concluded that the evidence was insufficient to determine the effectiveness of exercise as a treatment for menopausal vasomotor symptoms.

How effective is electroconvulsive therapy for chronic pain?

Evidence-Based Answer

Electroconvulsive therapy (ECT) has analgesic properties independent of its improvement of depression in some patients with chronic pain. Patients receiving ECT have reported a decrease in pain by as much as 60%, compared with a decrease of 16% in a control group. Some subgroups of pain patients are more likely to benefit from ECT, such as patients with fibromyalgia, reflex sympathetic dystrophy, or phantom limb pain (SOR: B, case-control studies).

The effect of ECT on fibromyalgia was studied prospectively in a case series of 15 patients.1 Recruited from a rheumatology department, patients were evaluated to ensure that they did not have any mental
disorders. They received 4 to 6 sessions of ECT (time frame not specified). Assessments were made before ECT and 3 days after the last ECT session.

The number of tender points decreased significantly with ECT from 16 to 6.7 points ($P=.0006$) at 3 days. Scores on a 0–10 visual analog pain scale decreased significantly with ECT from 7.5 to 3.2 at 3 days ($P=.0006$) and remained low at 3 months ($4; P=.0013$). The Beck’s depression inventory (maximal score is 63) did not change significantly at 3 days (from 13 to 12; $P=.29$).

A case-matching study was done comparing outcomes of chronic pain and major depression in 25 inpatients on a Chronic Pain Treatment Service treated with ECT and medications and 22 controls treated with medications only. Both groups received the same behavioral and pharmacological treatments for depression and chronic pain. Patients usually received ECT 3 times a week for a total of 10 to 12 treatments. Patients were matched on sex, age, admission date, psychiatric diagnoses, and, as much as possible, on race and pain syndrome diagnosis. The most common pain diagnosis, in 12 of the cases, was low-back pain. Outcome measures included 0–10 pain rating scales and the Montgomery-Åsberg Depression Inventory (scoring range 0–60). Measurements were made on the first 2 days of admission and the last 3 days of admission.

The percent change in the depression score did not differ significantly between the ECT and control groups (56% vs 41%; $P=.166$). The ECT group’s pain score decreased from 8.1 to 3.4, while the control group’s score decreased from 6.9 to 5.5 (improvement of 60% vs 16%; $P<.0001$). Limitations of the study included the lack of blinding and no follow-up data on the duration of the analgesic effects.

A review of the medical literature through 2000 (that did not describe the search methodology) discussed 17 case series involving more than 156 patients who received ECT for a variety of pain syndromes. Despite the heterogeneity of the clinical cases and no attempt to combine data in a meta-analysis, the reviewers drew several conclusions: (1) a pain syndrome clearly secondary to depression is likely to respond to ECT; (2) a chronic atypical pain syndrome without an associated depression has a much smaller chance of receiving any benefit from ECT; and (3) there may be pain syndromes that do respond to ECT even in the absence of depression, such as reflex sympathetic dystrophy and phantom limb pain. Conversely, the authors concluded that patients with poststroke thalamic pain did not appear to benefit from ECT.

Evidence-Based Answer

Diet counseling, exercise, and the combination of diet and exercise counseling are more effective than limited diet advice in reducing the risk of progression to diabetes in patients at risk (SOR: B, meta-analysis of RCTs with an inconsistent RCT).

A meta-analysis of 21 RCTs involving 8,084 patients with impaired glucose tolerance reviewed different aspects of prevention of type 2 diabetes, such as lifestyle interventions or pharmacological interventions. The lifestyle interventions included diet modification and exercise programs to encourage weight loss in participants. The pharmacological interventions included acarbose, flumamine, glipizide, metformin, phenformin, or orlistat.

There was a significant reduction of progression to diabetes with lifestyle interventions (7 trials; N=1,978) including targeted dietary education (HR 0.67; 95% CI, 0.49–0.92; NNT=6), exercise recommendations for 3x/week to daily (HR 0.49; 95% CI, 0.32–0.74), and diet/exercise combinations (HR 0.49; 95% CI, 0.40–0.59) compared with limited advice and support on diet and exercise. Pharmacological interventions were pooled as oral diabetes medications or weight-loss medications. Oral diabetes medication (9 trials; N=6,714; HR 0.70; 95% CI, 0.62–0.79; NNT=10) and orlistat (2 trials; N=3,952; HR 0.44; 95% CI, 0.28–0.69; NNT=5) showed a statistically significant risk reduction compared with a placebo.

Another RCT, published after the meta-analysis, evaluated the prevention of type 2 diabetes in...
102 patients who were older than 40 years and overweight (body mass index >25 kg/m²), and had impaired glucose tolerance. The overall cumulative incidence of progression to diabetes was not significantly reduced in the intervention group, which included individual motivational interviewing that focused on weight reduction, increased physical activity, increased fiber and carbohydrate intake, and decreased fat intake, compared with the control group (RR 0.45; 95% CI, 0.2–1.2).

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What is the long-term prognosis for patients with coronary artery disease and von Willebrand’s disease?

Evidence-Based Answer
The long-term prognosis is unknown. No clinical studies have evaluated long-term outcomes in patients with von Willebrand’s disease (vWD) and comorbid coronary artery disease (CAD). It is also unknown if there is an association between coronary heart disease (CHD) risk and decreased von Willebrand’s factor (vWF) levels in the general population (no SOR, conflicting cohort studies and meta-analysis).

vWD is an inherited defect in vWF protein whose function is to promote formation of the platelet plug in hemostasis.

A prospective cohort study of 625 men with major coronary events and 1,266 men without known CAD (mean age 52 years) compared baseline vWF levels to evaluate whether vWF concentrations are prospectively related to CHD risk in the general population. Over a 16-year period, men in the top third of vWF levels (>126 IU/dL) were significantly more likely to have had a coronary event compared with those in the lowest third (<90 IU/dL) (OR 1.8; 95% CI, 1.4–2.4; P <.0001), with little change after adjustment for smoking and other risk factors (OR 1.8; 95% CI, 1.4–2.4; P <.001).

These authors also performed a meta-analysis (including their own study) of 6 prospective cohort studies (N=21,354, mean age 56 years) comparing 1,524 patients with CAD with 19,830 control patients to evaluate whether serum vWF concentration was related to CHD in the general population. There was a significantly increased risk of myocardial infarction (MI) for patients with vWF levels in the highest third (>126 IU/dL) compared with those in the lowest third (<90 IU/dL) (OR 1.5; 95% CI, 1.1–2.0).

A subsequent prospective cohort study of 9,758 men (aged 50–59 years) with no known CAD who were followed more than 5 years examined the association between plasma vWF levels and fatal or nonfatal MI and stable or unstable angina pectoris. A total of 158 MIs and 142 angina pectoris events were observed. Baseline levels of vWF were higher for individuals who subsequently developed an MI, but not angina pectoris. After adjustment for conventional cardiovascular risk factors (hypertension, hyperlipidemia, smoking, and/or diabetes), the risk of MI was higher in individuals with plasma vWF in the highest quartile than in those in the lowest quartile (RR 3.0; 95% CI, 1.6–5.8; P <.01).

Finally, in a more recent large prospective study evaluating the predictive value of serum markers of CHD (N=18,569 patients without known CAD at recruitment) followed for more than 17 years, there were 2,549 major coronary events (72% men, mean age 55 years, 1,073 CHD deaths and 701 nonfatal MI; 28% women, mean age 55 years, 385 CHD deaths and 300 nonfatal MI). There was no difference in the incidence of CHD for individuals with vWF levels in the top third (>124 IU/dL) versus the lowest third (≤88 IU/dL) adjusted for age, sex, smoking, lipids, and other risk factors (OR 1.1; 95% CI, 0.97–1.7).

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We invite your questions and feedback. Email us at EBP@fpin.org.
What dietary factors impact PT/INR with warfarin utilization?

Evidence-Based Answer

Foods containing vitamin K affect prothrombin time/international normalized ratio (PT/INR) levels in patients taking warfarin. A higher baseline intake of dietary vitamin K is associated with less PT/INR fluctuation (SOR: C, disease-oriented evidence). The effect of specific dietary items like alcohol, cranberry, mango, avocado, grapefruit, soymilk, and cranberry juice is mixed (SOR: B, systematic review of low-quality trials).

Vitamin K (TABLE 1) is essential to activating factors II, VII, IX, and X and proteins C and S to allow coagulation. Coumadin inhibits metabolism of vitamin K, thereby impairing clotting. Nearly 50 years ago, it became clear that dietary vitamin K was the source of instability in PT/INR values.¹

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Vitamin K content of selected foods⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium</td>
<td>High</td>
</tr>
<tr>
<td>25–100 mcg/100-g serving</td>
<td>100–500 mcg/100-g serving</td>
</tr>
<tr>
<td>Lettuce</td>
<td>Beet greens</td>
</tr>
<tr>
<td>Asparagus</td>
<td>Turnip greens</td>
</tr>
<tr>
<td>Okra</td>
<td>Mustard greens</td>
</tr>
<tr>
<td>Peas</td>
<td>Brussel sprouts</td>
</tr>
<tr>
<td>Celery</td>
<td>Broccoli</td>
</tr>
<tr>
<td>Canned tuna</td>
<td>Green onions</td>
</tr>
<tr>
<td>Kiwi fruit</td>
<td>Cabbage</td>
</tr>
<tr>
<td>Soybean oil</td>
<td></td>
</tr>
<tr>
<td>Canola oil</td>
<td></td>
</tr>
<tr>
<td>Shortening (cottonseed oil)</td>
<td></td>
</tr>
<tr>
<td>Olive oil</td>
<td></td>
</tr>
</tbody>
</table>

In 2004 an observational study evaluated the relationship between dietary vitamin K and PT/INR levels in 39 patients taking warfarin for a variety of reasons, most often metallic heart valve and chronic atrial fibrillation.² These researchers demonstrated that a vitamin K-depleted diet (26 mcg/d, or 20% of baseline) led to an increase in INR from 2.6 to 3.3 by day 7 (P=.005), and a vitamin K-rich diet (591 mcg/d or 5 times baseline) led to a decrease in INR from 3.1 to 2.8 by day 4 (P=.04).

A 2005 cohort study reviewed food diaries for 26 patients taking warfarin with unstable INR values (defined as those with standard deviation [SD] >0.5 of INR values and at least 3 dose changes in the last 6 months) and compared these with data from 26 patients with stable INR values.³ Patients with instability due to poor compliance, medications, illness, or excessive alcohol use were excluded. Patients with unstable values had considerably lower baseline dietary vitamin K levels (29 vs 76 mcg/d; P<.001). Interestingly, variability in intake was higher in the stable group than the unstable group (SD of 4.2 vs 3.4 mcg; P<.001).

A systematic review of 181 studies examined interactions of various specific foods with warfarin.⁴ Patient numbers were small and no study was rated “excellent quality.” Stringent criteria were used to look at study quality and probability of causation based on the evidence presented. Results are shown in TABLE 2.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Effect of certain foods on INR in patients receiving warfarin⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degree of causation</td>
<td>Increased INR</td>
</tr>
<tr>
<td>Highly probable</td>
<td>Alcohol (if liver disease)</td>
</tr>
<tr>
<td>Mango</td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td>Grapefruit juice</td>
</tr>
<tr>
<td>Ginseng</td>
<td></td>
</tr>
<tr>
<td>Possible</td>
<td>Cranberry juice</td>
</tr>
</tbody>
</table>

INR=international normalized ratio.


Which maneuver is most effective for treatment of shoulder dystocia?

**Bottom line**

No RCTs have evaluated which maneuver is most effective or safest for resolving a shoulder dystocia. Both the American College of Obstetricians and Gynecologists (ACOG) and the Royal College of Obstetricians and Gynaecologists (RCOG) state that McRoberts maneuver followed by (or in conjunction with) suprapubic pressure are the first interventions that should be used. A 2011 study found delivery of the posterior shoulder to be the next most effective method. If additional maneuvers are needed, they should be chosen based on provider experience and maternal factors.

**Evidence summary**

Shoulder dystocia is an infrequent but potentially catastrophic obstetric emergency, occurring in 0.6% to 1.4% of all vaginal deliveries. It is defined as a delivery that requires additional obstetric maneuvers after failure of gentle downward traction on the fetal head to effect delivery of the shoulders. While there are risk factors associated with shoulder dystocia, it remains essentially unpredictable and unpreventable. Because of its unpredictability and potentially deleterious effects on mother and baby, conducting a well-structured RCT would be difficult. Data collection is further hampered by inconsistent documentation with respect to when shoulder dystocia actually occurs, accurately listing maneuvers to resolve the dystocia in the order they occurred, and the amount of time elapsed between delivery of the head and body.

Both ACOG and RCOG recommend McRoberts and suprapubic pressure as the first maneuvers due to their success rates, relative technical ease, and lower rates of neonatal injury. ACOG calls this a “reasonable” first approach, while RCOG says it is a more successful approach. It should be noted, however, that neonatal injury increases proportionately with the total number of maneuvers used, regardless of which ones are attempted first.

A 2011 retrospective chart review of 132,098 term cephalic liveborn deliveries with 2,018 (1.5%) shoulder dystocias found that when delivery of the posterior shoulder was attempted, regardless of its order in the sequence, 84.4% of the dystocias resolved. Additionally, when used as the third maneuver, it appeared to result in less neonatal injury compared with other internal techniques.

Notably, the Gaskin maneuver (turning a woman onto hands and knees) was not included in the 2011 study due to its infrequent occurrence (22 of 2,018 shoulder dystocias with 1 documented neonatal injury). In the midwifery community and in other parts of the world, use of the Gaskin maneuver is more common. While ACOG does not specifically mention it in its 2002 bulletin, RCOG does in its 2005 and its 2012 updated guideline. RCOG states that if both McRoberts and suprapubic pressure fail, then either internal maneuvers or the Gaskin maneuver are reasonable next steps.

**REFERENCES**


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Are opioids effective for treatment of chronic nonspecific low-back pain in adults?

**Bottom line**

Tramadol and other opioids are more effective than placebo for pain relief in chronic nonspecific low-back pain (SOR: A, systematic reviews of RCTs). However, even sustained-release morphine plus oxycodone for breakthrough is no more effective than naproxen in reducing pain and disability in this population (SOR: B, lower quality RCT).

**Evidence summary**

**Tramadol**

In a 2010 Cochrane systematic review, 3 double-blinded RCTs (N=908) compared opioids with an inactive placebo for management of chronic (>12 weeks) lower back pain. Subjects with compression fractures, arthritis, cancer, and infections were excluded. All of the trials used tramadol (average daily dose of 150 mg) as the active opioid agent, while 2 of these trials used a combination product consisting of tramadol and acetaminophen. The primary outcome measure was pain intensity.

A meta-analysis performed on the 3 trials showed subjects receiving tramadol had better pain relief than those receiving placebo (standardized mean difference [SMD] –0.71; 95% CI, –0.84 to –0.57). Another meta-analysis of a smaller subset (n=878) of subjects in these 3 trials demonstrated improvement in function (evaluated by the Roland Disability Questionnaire) with tramadol versus placebo (SMD –0.17; 95% CI, –0.31 to –0.04). These trials had a dropout rate of more than 28% in the treatment arms and 52% in the placebo arms, which could limit the generalizability of the studies.

**Naproxen**

One additional RCT comparing naproxen (250 mg up to 4 times daily) versus a titrated dose of sustained-release morphine (with the option for additional oxycodone up to a maximum morphine equivalent of 200 mg daily) was described in the systematic review. Neither pain (SMD –0.58; 95% CI, –1.42 to 0.26) nor disability (SMD –0.06; 95% CI, –0.88 to 0.76) outcomes were significantly different between sustained-release morphine (n=11) and naproxen (n=12), perhaps due to small sample size.

**Medications vs placebo**

In a 2011 systematic review, 17 RCTs (N=3,766) were evaluated to assess the efficacy of medications in treating chronic nonspecific lower back pain versus placebo. Of these 17 studies, 7 trials examined opioid treatment, 4 included tramadol (including the 3 RCTs in the previously mentioned Cochrane review), 2 assessed oxymorphone extended-release, and the final study tested oxytrex (oxycodone plus very-low-dose naltrexone).

There was greater pain relief in subjects receiving opioids compared with those receiving placebo (7 trials; N=2,350; SMD –0.54; 95% CI, –0.72 to –0.36). Tramadol was not significantly more efficacious than placebo for improving function using the Roland Disability Questionnaire (4 trials; N=1,258; SMD –0.19; 95% CI, –0.31 to 0.08).

In most of the studies, patients who had previously responded well to opioids were able to be included in the trials if back pain worsened, which may limit the generalizability of the results.

**REFERENCES**


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**GLOSSARY**

| ARR=absolute risk reduction | LOE=level of evidence |
| CDC=Centers for Disease Control and Prevention | MRI=magnetic resonance imaging |
| CI=confidence interval | NNH=number needed to harm |
| CT=computed tomography | NNT=number needed to treat |
| FDA=US Food and Drug Administration | NSAI=nonsteroidal anti-inflammatory drug |
| HR=hazard ratio | OR=odds ratio |
| RCT=randomized controlled trial | RR=relative risk |
| SOR=strength of recommendation | SSRI=selective serotonin reuptake inhibitor |

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