Physician’s Weekly Updates

Primary Care Guidelines

Migraine: Preventive Treatments

Diabetic Foot

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A Message From the Editor

At Physician’s Weekly, we are proud to present this monograph featuring several features that are applicable to primary care. Created with the assistance of key opinion leaders and experts in their respective fields, these articles discuss challenges and opportunities in primary care and strategies to positively change current practices. In the upcoming months Physician’s Weekly will continue to feature topics that affect primary care physicians and those practicing in related aspects of medicine. Your feedback and opinions are welcome, email keithd@physweekly.com. Thanks for reading!

Sincerely,

Keith D’Oria
Editorial Director, Physician’s Weekly
The ACR update re-emphasizes the importance of aggressive treatment in early RA. In addition to better outcomes, early intensive treatment can help patients maintain physical function and quality of life. Prevention is critical because joint damage resulting from RA is permanent once it occurs. It should be noted that the updated recommendations focus on common clinical scenarios. They should be used as a guide for clinicians with the clear understanding that the best treatment decisions can only be made by having collaborative dialogue with patients. For each patient, physicians must consider:

- The risks and benefits of treatment.
- Comorbidities and concomitant medications.
- Patient preferences.
- Practical economic considerations.

Rheumatoid Arthritis Treatment Recommendations

The goal of early RA treatment is for remission or at least low disease activity. For patients who have been symptomatic for 6 months or less, the usual approach should be disease-modifying antirheumatic drug (DMARD) monotherapy. If disease activity is moderate or high and patients have poor prognosis, combination DMARD therapy can be tried. If disease activity is high in early RA and the prognosis is poor, an anti-tumor necrosis factor (TNF) biologic agent can be used in combination with methotrexate or alone.

Patients who show no response after 3 months on anti-TNF agents can be switched to another anti-TNF drug or to a non-TNF biologic therapy. Those who have taken a non-TNF biologic for 6 months but have had an inadequate response can be switched to a TNF or non-TNF biologic. Patients with high disease activity who have failed TNF treatment because of serious adverse events should be switched to a non-TNF biologic. However, another anti-TNF agent or a non-TNF biologic can be used if the adverse event was not considered serious.

Importantly, the guideline update has revised treatment recommendations on the use of biologics for patients with RA at higher risk because of comorbid conditions, most notably hepatitis C, solid tumors or non-melanoma skin cancers, and congestive heart failure. It also revised recommendations on screening for latent tuberculosis infection, which should be done for all patients before starting biologic therapy. More detailed recommendations on these aspects of the guidelines—as well as recommendations for early RA treatment—can be found here.

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For more information on this article, including the contributor’s financial disclosure information and reference, click here.
Preventive Treatment for Migraine

Updated guidelines on migraine from the American Academy of Neurology address the safety and efficacy of pharmacologic therapies for migraine prevention, including prescription, OTC drugs, and complementary therapies.

About 38% of people who suffer from migraine could benefit from preventive treatments, but less than one-third currently use them. Some analyses have shown that migraine attacks can be reduced by more than half with preventive therapies.

In 2000, the American Academy of Neurology (AAN) published guidelines for migraine prevention. In the 2012 guidelines, the AAN and the American Headache Society issued updated guidelines to account for new evidence. One set of guidelines was developed specifically for prescription products, while another was created for OTC drugs and complementary therapies. In each guideline, the safety and efficacy of pharmacologic therapies for migraine prevention was addressed. The reviews addressed the strength of evidence backing a given drug’s superiority relative to placebo.

Prescription Drugs for Migraine

Among prescription medications, several β-blockers (metoprolol, propranolol, and timolol) and seizure drugs (divalproex sodium, sodium valproate, and topiramate) established “proven efficacy” for migraine prevention based on clinical research. One selective serotonin receptor agonist (frovatriptan) was also proven effective. It’s recommended that clinicians consider offering these medications to migraineurs to reduce the frequency and severity of attacks.

Topiramate was elevated to a Level A recommendation (indicating “proven efficacy”) on the strength of five randomized trials. Other drugs that had previously been used for migraine prevention were downgraded from higher recommendations in 2000 because the current evidence failed to clearly support their efficacy.

OTCs & Complimentary Therapies for Migraine

Petasites, also known as butterbur, were shown to be effective in preventing migraine. Several NSAIDs were found to be “probably effective,” including fenoprofen, ibuprofen, ketoprofen, naproxen and naproxen sodium, and subcutaneous histamine. Magnesium, MIG-99 (feverfew), and ribothiamin were among the complementary treatments that were deemed “probably effective” for migraine prevention.

Botulinum Toxin-Based Drugs

The 2012 guidelines did not address the use of botulinum toxin-based drugs for migraine because these were covered in a separate AAN review published in 2008. That review indicated that botulinum toxin was “probably ineffective” for preventing episodic migraine. However, botulinum toxin has since been approved for preventing chronic migraine. The AAN is currently developing a guideline update that specifically addresses research and data on this treatment.

Important Considerations in Migraine Therapy

There are no absolutes when determining which patients are the ideal candidates for migraine therapies, but some common identifiers include frequent attacks, acute medication use beyond the recommended limits, or consistent use of acute therapies that fail to provide relief. Regular follow-up with patients is important to discuss changes in the pattern of migraine attacks and the efficacy of therapies being used. Physicians and patients are encouraged to collaborate with each other when deciding on treatment options. The key is to consider efficacy, adverse events, and coexisting or comorbid conditions as well as personal considerations. Patients should be reminded that trial and error with therapies will often be necessary.

Readings & Resources


Hypertriglyceridemia can substantially increase the likelihood of patients developing heart disease when compared with those who have normal triglyceride levels. While treatment strategies for this condition are well established, its causes differ from patient to patient, as do the risks they pose to each individual. Clinical practice guidelines from the Endocrine Society on hypertriglyceridemia were published in the Journal of Clinical Endocrinology and Metabolism (view and print guideline summary here). They recommend that more attention be paid to how personal history, physiology, and lifestyle interact to affect risk.

“In recent years, much of the focus surrounding lipids has concentrated on cholesterol,” explains Lars Berglund, MD, PhD, who chaired the Endocrine Society task force that developed the most recent guidelines. “Although there are evidence-based guidelines from respected medical associations that address lipids, data on the complex role of triglycerides in heart disease continue to accumulate. Considering this recent emergence of data on triglycerides, it was important to focus on a guideline that specifically discusses this component of heart disease care.”

Individualized Approach with Elevated Triglycerides

Dr. Berglund stresses that clinicians should not view elevated fasting triglyceride levels as a standalone factor. “Triglycerides should be looked at in the context of other risk factors for cardiovascular disease (CVD) and metabolic disease,” he says. “Assessment should include the evaluation of secondary causes.
Patients with high triglyceride levels need to be evaluated for secondary causes on an individualized basis.

— Lars Berglund MD, PhD

of hyperlipidemia, including endocrine conditions and medications [Table 1]. Central obesity, hyper- 
tension, abnormalities of glucose metabolism, liver 
dysfunction, and family history of dyslipidemia and 
CVD should be assessed.” For example, patients 
with triglyceride levels in the moderate range—200 
mg/dl to 999 mg/dl—may have changes in HDL 
and LDL cholesterol levels and properties, which 
are associated with cardiovascular risk, but insulin 
resistance and other factors should also be considered 
during patient management. Patients with isolated 
hypertriglyceridemia (eg, familial type) are more likely to have larger particles, which are less likely to 
cause cardiovascular risk.

Fatty foods, smoking, and poor exercise also 
contribute to the risk for high triglyceride levels. “Simple carbohydrates that can be broken down 
and absorbed quickly, such as sugar-sweetened 
beverages, white rice, and white bread, contribute to 
an increase in fat formation and triglyceride levels,” says Dr. Berglund. While alcohol can increase HDL 
cholesterol levels, it can also lead to high triglyceride 
levels. Certain prescription medications (eg, bile 
acid sequestrants for high LDL) can also interact 
to raise blood triglyceride levels. “Understanding 
the importance of specific risk factors requires that 
clinicians ascertain a full profile of each patient,” Dr. 
Berglund adds.

Considering Treatment Options for Hypertriglyceridemia

Defining the level of hypertriglyceridemia for indi- 
vidual patients is crucial to determining the goal 
of treatment and should be based on fasting levels. 
The Endocrine Society guidelines define normal 
triglyceride levels as less than 150 mg/dl (Table 2). 
Mild and moderate hypertriglyceridemia are catego- 
rized by levels below 999 mg/dl, which are primarily 
associated with a risk for CVD. When levels rise 
above 1,000 mg/dl, patients should be categorized as 
having severe and very severe hypertriglyceridemia. 
The risk for these individuals is associated more often 
with pancreatitis.

Because weight, diet, and exercise play particularly 
important roles in triglyceride levels, the Endocrine 
Society guideline recommends that initial treatment 
for mild-to-moderate hypertriglyceridemia be 
lifestyle therapy, consisting of dietary counseling, 
physical activity, and a weight reduction program 
for overweight and obese patients. “Overweight or 
obese patients may feel overwhelmed when asked 
to lose weight,” Dr. Berglund says, “but clinicians 
should reassure them that even modest reductions 
in weight can have highly beneficial effects on their 
triglyceride levels.”

For patients at risk for triglyceride-induced pancre-
atitis and for whom lifestyle changes have been 
effective, the guideline recommends that fibrates 
be used as the first-line of drug treatment. Although 
statins have some triglyceride-lowering effects, they 
are not overly effective in patients with very high 
levels, according to Dr. Berglund. The guideline 
recommends that statins not be used as monotherapy 
for severe or very severe hypertriglyceridemia, but 
may be useful for moderate hypertriglyceridemia when 
indicated to modify cardiovascular risk. Fibrates, 
niacin, and n-3 fatty acids are recommended for use 
alone or in combination with statins in patients with 
moderate-to-severe triglyceride levels.

“The key take-home message for all clinicians 
is that patients with high triglyceride levels 
need to be evaluated for secondary causes on an 
individualized basis,” says Dr. Berglund. “Only then 
can we determine the causes and direct our focus 
of treatment. The Endocrine Society guidelines can 
serve as a helpful aid for physicians as they manage 
patients from diagnosis to treatment.”

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Readings & Resources


Stalenhoef A, de Groot J. Association of fasting and nonfasting serum triglycerides with cardiovascular disease and the role of remnant-like 
Guidelines for Diagnosing & Treating Diabetic Foot Infections

The IDSA has released guidelines emphasizing rapid and appropriate therapy for treating diabetic foot infections. A multidisciplinary team should be utilized to assess and address various aspects of the problem.

As the incidence of diabetes has steadily increased over the last several decades throughout the United States, diabetic foot infections have also become increasingly common. As many as one in four people with diabetes will have a foot ulcer in their lifetime, and these wounds can easily become infected. If left unchecked, they can spread and may ultimately require amputation of the toe, foot, or part of the leg. Nearly 80% of all nontraumatic amputations occur in people with diabetes, 85% of which begin with a foot ulcer.

“Lower extremity amputation severely affects quality of life in people with diabetes because it reduces independence and mobility,” says Warren S. Joseph, DPM, FIDSA. “Furthermore, about 50% of patients who have foot amputations die within 5 years, which ranks as a worse mortality rate than for most cancers.” However, about half of lower extremity amputations that are not caused by trauma can be prevented through proper care of foot infections. Preventing amputations is vital. In most cases, these infections can be prevented or cured when properly managed.

Recommendations for Diabetic Foot Infections

In an issue of Clinical Infectious Diseases, the Infectious Diseases Society of America (IDSA) published a clinical practice guideline for diagnosing and treating diabetic foot infections. The guideline addresses 10 common questions with evidence based answers that experts have determined are most likely to help healthcare providers treating these infections. The guideline is a revision and update of IDSA’s 2004 recommendations for managing diabetic foot infections.

With regard to diagnosis, the guideline recommends that infections in foot wounds be defined clinically by the presence of inflammation or purulence, and then classified by severity (Table 1). “The first step is to determine if the wound is infected,” says Dr. Joseph, who was on the IDSA panel that created the guidelines. “An infection is likely if there are at
At least two of the following signs: redness, warmth, tenderness, pain, or swelling. After classifying the severity of the infection, the guideline then provides evidence-based strategies to optimize treatment.

When foot sores are infected, imaging the foot is usually necessary to determine if the bone is infected. The guidelines recommend performing a culture of the wound to determine the bacteria causing the infection but stress the importance of appropriately obtaining those cultures. This information can be used to guide clinicians on whom antibiotics should be provided for treatment.

**Addressing Antibiotic Use for Infection**

The guideline emphasizes the importance of rapid and appropriate therapy for treating infected wounds on the feet. Therapy can include surgical debridement of dead tissue, appropriate antibiotic therapy, and removing pressure on the wound and improving blood flow to the infected area, when necessary. Importantly, many diabetic foot ulcers are not clinically infected and therefore should not be treated with antibiotics. People with clinical evidence of infection, however, require antibiotic therapy. Those with a severe infection should be hospitalized immediately.

“Many patients with foot infections initially receive only antibiotic therapy,” Dr. Joseph says. “In many cases, providing antibiotics alone will be insufficient in the absence of proper wound care and surgical interventions. Unfortunately, clinicians often over-prescribe or inappropriately prescribe antibiotics for diabetic foot wounds. This approach is ineffective and can lead to antibiotic resistance.” Before considering antibiotic therapy, it is important to balance the clinical evidence of infection and its severity with other risks, such as risk factors for MRSA and Pseudomonas infection (Table 2). When antibiotics are necessary, they should be discontinued when the infection is gone, even if the wound has not completely healed.

**Involve Others in Care**

Since treating diabetic foot infections can be complicated, the guidelines recommend involving a multidisciplinary care team that can assess and address various aspects of the problem. “Data have shown that many foot infections are treated improperly,” says Dr. Joseph. “Getting assistance from other providers—including infectious disease specialists, podiatrists, surgeons, and orthopedists—can best address the complicated care of these infections.” For providers in rural areas, the guidelines note that telemedicine may facilitate consults with appropriate experts.

The IDSA guideline is intended to support decision-making processes based on individual circumstances rather than take the place of a physician’s judgment, Dr. Joseph says. “The guidelines will be revisited as more data emerge. Potential performance measures on outcomes of treatment and processes of management are also being explored. In the meantime, it’s hoped that free access to these recommendations will improve the diagnosis and treatment of diabetic foot infections and perhaps alleviate their burden over time.”

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**Table 1: Diabetic Foot Classifications**

<table>
<thead>
<tr>
<th>Clinical Manifestation of Infection</th>
<th>PFHS Grade</th>
<th>IDSA Infection Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Infection present, no defined by the presence of at least 2 of the following items:</td>
<td>1</td>
<td>Uninfected</td>
</tr>
<tr>
<td>Local swelling or indentation.</td>
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<tr>
<td>Erythema.</td>
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<tr>
<td>Local tenderness or pain.</td>
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<td></td>
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<tr>
<td>Local warmth.</td>
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<tr>
<td>Pusulent discharge (thick, opaque to white or sanguineous secretion).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and with no systemic signs as described below).</td>
<td>2</td>
<td>Mild</td>
</tr>
<tr>
<td>Local infection involving deeper than subcutaneous tissues (e.g., abscess, collections, osteomyelitis, necrotizing fasciitis, fasciitis, venomulosis).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No systemic inflammatory response signs (as described below).</td>
<td>3</td>
<td>Moderate</td>
</tr>
<tr>
<td>Local infection has signs of SIRS, as measured by ≥2 of the following:</td>
<td>4</td>
<td>Severe</td>
</tr>
<tr>
<td>Temperature ≥38°C or ≤36°C.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate ≥90</td>
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<tr>
<td>Respiratory rate ≥20 breaths/min or PaCO2 ≥32 mm Hg.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White blood cell count ≥12,000 or ≤4,000 cells/μL, or ≥10% immature (band) forms.</td>
<td></td>
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</tbody>
</table>

*Note: CRP ACR, C-reactive protein; Hct, hematocrit; Hgb, hemoglobin; INR, international normalized ratio; Platelet, platelet count; SIRS, systemic inflammatory response syndrome.*

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**Readings & Resources**


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**About 50% of patients who have foot amputations die within 5 years, which ranks as a worse mortality rate than for most cancers.** — Warren S. Joseph, DPM, FIDS A
According to recent reports from national and international research teams, approximately one-third of all cancers can be prevented by maintaining a healthy weight, eating a healthy diet, and exercising regularly. Published studies have indicated that obesity plays a major role in cancer development through a number of biological mechanisms. Since the American Cancer Society (ACS) last published guidelines on nutrition and physical activity for cancer prevention in 2006, there has been mounting evidence addressing the role of obesity in the development of cancer. While it is not a new concept that daily exercise is important to helping prevent cancer, what has emerged in the literature is that prolonged sitting time (e.g., watching television or sitting at the computer) also appears to significantly increase risks.

Guidelines from the American Cancer Society are intended to empower patients to prevent cancer with proper nutrition and physical activity. Elisa V. Bandera, MD, PhD, discusses why a supportive social and physical environment is paramount.

Elisa V. Bandera, MD, PhD
Associate Professor of Epidemiology
Cancer Institute of New Jersey

In the CA: A Cancer Journal for Clinicians, the ACS published an update to the 2006 guidelines that focused on reducing cancer risk with healthy food choices and physical activity. “The new recommendations emphasize that any level of positive change in diet or exercise is a step in the right direction to encourage patients to achieve optimum weight and exercise levels,” says Elisa V. Bandera, MD, PhD, who was a coauthor of the guidelines. “The loss of only a few pounds for obese and overweight people is beneficial. Small changes may lead to bigger ones and further encourage people to start changing their lifestyle for the better.”

Dr. Bandera says that clinicians should educate patients about the health risks associated with being overweight.
and obese and provide them with the recommendations outlined in the guidelines (Table 1). She believes the most important message to emphasize to patients is to achieve and maintain a healthy weight throughout life. “The evidence for doing this is compelling,” says Dr. Bandera. “Clinicians need to be proactive about reinforcing recommendations for weight control at every patient visit.”

**Exercise & Diet: A Daily Commitment**

Patients should also be advised to make it a priority to exercise and avoid sitting for prolonged periods every day. “If patients are starting a new exercise, it may be beneficial to have them begin with activities that engage different muscle groups,” Dr. Bandera explains. Finding activities that increase strength, flexibility, balance, and cardiovascular health is important because patients may be less likely to become bored.

The ACS guidelines also note that it is important for both patients and physicians to understand the differences between moderate- and vigorous-intensity exercise (Table 2). “The intensity of the exercise determines how quickly optimal levels are reached,” says Dr. Bandera. She adds that the more patients engage in activities that they enjoy, the more likely it is that their exercise program will be sustainable.

Regarding diet, Dr. Bandera says patients should be advised to choose mostly plant-based foods, including a variety of fruits and vegetables each day, and whole grain products instead of refined grains. “What patients eat is almost as important as how much they eat,” she notes. “Portion sizes in the United States have become too large to help maintain a healthy weight. Patients should be educated about proper portion sizes with concrete examples of just how big or small certain portions should be.” Dr. Bandera adds that men and women should be counseled appropriately on drinking alcohol in moderation.

**Taking the Lead to Prevent Cancer**

The ACS acknowledges that educated patients may wish to make healthy lifestyle choices but still face substantial social, economic, and cultural obstacles that hinder their efforts. “Avoiding weight gain often goes beyond personal responsibility and capability to eat right and be physically active,” says Dr. Bandera. “As such, environmental changes are needed for the ACS guidelines to be widely implemented at the community level. This includes increasing access to healthy foods in communities, worksites, and schools. It also means having safe, enjoyable, and accessible places to engage in physical activity in schools and worksites.”

Healthcare professionals have an opportunity to provide leadership and promote the ACS guideline recommendations, according to Dr. Bandera. “The overriding goal is to help patients achieve and maintain a healthy body weight and become and remain physically active throughout life. Clinicians must seize every opportunity to educate patients on diet and activity facts regardless of whether they have a family history of cancer. Patients must realize that the choices they make can have a significant impact on their chances of developing cancer.”

— Elisa V. Bandera, MD, PhD

**Table 1: Summary of Recommendations**

<table>
<thead>
<tr>
<th>Achieve and maintain a healthy weight throughout life.</th>
<th>Adopt a physically active lifestyle.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Be as lean as possible throughout life without being underweight.</td>
<td>Adults should engage in at least 150 minutes of moderate intensity or 75 minutes of vigorous intensity activity each week, or an equivalent combination, preferably spread throughout the week.</td>
</tr>
<tr>
<td>Avoid excess weight gain at all ages. For those who are currently overweight or obese, losing even a small amount of weight has health benefits and is a good place to start.</td>
<td>Children and adolescents should engage in at least 1 hour of moderate or vigorous intensity activity each day, with vigorous intensity activity occurring at least 3 days each week.</td>
</tr>
<tr>
<td>Engage in regular physical activity and limit consumption of high-calorie foods and beverages as key strategies for maintaining a healthy weight.</td>
<td>Limit sedentary behavior such as sitting, lying down, watching television, or other forms of screen-based entertainment.</td>
</tr>
<tr>
<td>Customize a healthy diet, with an emphasis on plant foods.</td>
<td>Doing some physical activity above usual activities, no matter what one’s level of activity, can have many health benefits.</td>
</tr>
<tr>
<td>Choose foods and beverages in amounts that help achieve and maintain a healthy weight.</td>
<td>If you drink alcoholic beverages, limit consumption.</td>
</tr>
<tr>
<td>Limit consumption of processed meat and red meat.</td>
<td>Drink no more than 1 drink per day for women or 2 per day for men.</td>
</tr>
<tr>
<td>Eat at least 2.5 cups of vegetables and fruits each day.</td>
<td></td>
</tr>
<tr>
<td>Choose whole grains instead of refined grain products.</td>
<td></td>
</tr>
</tbody>
</table>

**For Community Action**

Public, private, and community organizations should work collaboratively at national, state, and local levels to implement policy and environmental changes that:

- Increase access to affordable, healthy foods in communities, worksites, and schools, and increase access to and marketing of foods and beverages of low nutritional value, particularly to youth.
- Provide safe, enjoyable, and accessible environments for physical activity in schools and worksites, and for transportation and recreation in communities.

**Readings & Resources**


