Acute treatment of migraine in adults

SUMMARY AND RECOMMENDATIONS

- There is high-quality evidence from placebo-controlled randomized trials that the following drugs are effective for the treatment of acute migraine attacks:
  - Nonsteroidal anti-inflammatory drugs (NSAIDs): Aspirin, ibuprofen, naproxen, and diclofenac (see 'Nonsteroidal anti-inflammatory drugs' above)
  - Triptans: Sumatriptan, rizatriptan, eletriptan, almotriptan, zolmitriptan, naratriptan, and frovatriptan (see 'Triptans' above)
  - The combination of sumatriptan and naproxen (see 'Triptans with NSAIDs' above)
  - Antiemetic/dopamine receptor antagonists: Chlorpromazine, prochlorperazine, and metoclopramide (see 'Antiemetics' above)
- For adults with mild to moderate migraine attacks not associated with vomiting or severe nausea, we suggest initial treatment with simple analgesics, including NSAIDs or acetaminophen, rather than other migraine-

specific agents (**Grade 2C**). (See 'Mild to moderate attacks' above and 'Simple analgesics' above.)

- For adult outpatients with moderate to severe migraine attacks, we suggest treatment with a triptan or the combination of sumatriptan-naproxen, rather than other migraine-specific agents (**Grade 2C**). There are no efficacy data that definitively support use of one triptan versus another; different pharmacologic properties and delivery routes may help guide the choice. Patients who do not respond well to one triptan may respond to a different triptan. (See 'Moderate to severe attacks' above and 'Triptans' above and 'Triptans with NSAIDs' above.)

- Abortive treatments for migraine are usually more effective if they are given early in the course of the headache; a large single dose tends to work better than repetitive small doses. Triptan treatment, in particular, should be given at the first sign of pain in patients susceptible to cutaneous allodynia. (See 'Factors predicting response' above.)

- Many oral agents are ineffective in migraine because of poor absorption secondary to migraine-induced gastric stasis. Therefore, a non-oral route of administration should be selected for patients whose migraines present early with significant nausea or vomiting. (See 'Approach to treatment' above.)

- For patients who present to the hospital emergency department with moderate to severe migraine, particularly if the migraine is accompanied by vomiting or significant nausea, we suggest initial treatment with either subcutaneous sumatriptan 6 mg or a parenteral antiemetic agent rather than other migraine-specific drugs (**Grade 2C**); reasonable antiemetic choices are intravenous (IV) metoclopramide (10 mg) or prochlorperazine (10 mg). When giving IV metoclopramide or prochlorperazine for migraine, we suggest adjunct use of diphenhydramine (12.5 to 20 mg IV every hour up to two doses) to prevent akathisia and other dystonic reactions (**Grade 2C**). (See 'Emergency settings' above and 'Antiemetics' above.)

  - A more aggressive alternative option, based upon the results of one clinical trial, is high-dose metoclopramide (20 mg IV every 30 minutes

up to four doses) given with diphenhydramine. (See 'Metoclopramide' above.)

- IV dihydroergotamine (DHE 45) 1 mg combined with intravenous (IV) metoclopramide 10 mg is also a reasonable alternative for treatment of intractable severe migraine in the emergency department, and it can be used if metoclopramide monotherapy is ineffective. Parenteral DHE 45 should not be used as monotherapy. DHE 45 is contraindicated in patients with ischemic vascular disease involving cardiac, cerebrovascular, or peripheral circulations. (See 'Dihydroergotamine' above.)

● For patients who are treated in the emergency department or clinic for migraine headache with one of the standard abortive therapies discussed above, we recommend adjunctive treatment with IV or intramuscular dexamethasone (10 to 25 mg) to reduce the risk of early headache recurrence (**Grade 1B**). (See 'Abortive therapy plus parenteral dexamethasone' above.)

● Sublingual, oral, or rectal ergotamine is the drug of choice in relatively few patients with migraine because of uncertain efficacy and risk of serious side effects. Suitable candidates may be those with prolonged duration of attacks (eg, greater than 48 hours) and possibly frequent headache recurrence. (See 'Ergotamine' above.)

● Prophylactic headache treatment is indicated if the headaches are frequent, long lasting, or account for a significant amount of total disability. This topic is discussed separately. (See "Preventive treatment of migraine in adults".)

An overview of asthma management

SUMMARY AND RECOMMENDATIONS

- The four essential components of asthma management are: routine monitoring of symptoms and lung function, patient education, control of trigger factors and amelioration of comorbid conditions, and pharmacologic therapy. (See 'Components of asthma management' above.)

- The goals of asthma treatment are to reduce impairment from symptoms, minimize risk of the various adverse outcomes associated with asthma (eg, hospitalizations, loss of lung function), and minimize adverse effects from asthma medications. (See 'Goals of asthma treatment' above.)

- Effective asthma management requires a preventative approach, with regularly scheduled visits during which symptoms are assessed, pulmonary function is monitored, medications are adjusted, and ongoing education is provided. (See 'Monitoring patients with asthma' above.)

- Patients should learn to monitor asthma control at home (eg, frequency and severity of dyspnea, cough, chest tightness, and short-acting beta agonist [SABA] use). Patients with moderate to severe asthma and those with poor perception of increasing asthma symptoms may also benefit from assessment of their peak expiratory flow rate at home. A personalized asthma action plan should be provided with detailed instructions on how to adjust asthma medications based upon changes in symptoms and/or lung function (form 2). (See 'Patient education' above.)

- Environmental triggers and co-existing conditions that interfere with asthma management should be identified

and addressed for each patient. (See 'Controlling triggers and contributing conditions' above.)

- Pharmacologic therapy varies according to asthma severity and asthma control. Asthma control can be judged, irrespective of medication use, based on the current level of symptoms, FEV_1 or PEFR values, and number of exacerbations requiring oral glucocorticoids per year (table 11 and table 12 and table 13). (See 'Categories of asthma severity' above and "Asthma in children younger than 12 years: Treatment of persistent asthma with controller medications".)

- A stepwise approach to therapy is recommended, in which the dose of medication, the number of medications, and/or the frequency of administration are increased as necessary and decreased when possible (figure 2 and figure 3 and figure 4). (See 'Initiating therapy in previously untreated patients' above.)

- At each return visit, the patient's asthma control is evaluated (table 14). If the asthma is not well-controlled, therapy should be "stepped-up." If the asthma is well-controlled, therapy can be continued or possibly "stepped-down" to minimize medication side effects. (See 'Adjusting medication in patients already on controller therapy' above and "Asthma in children younger than 12

years: Treatment of persistent asthma with controller medications".)

- Guidelines for when to refer a patient to a pulmonologist or an allergist/immunologist are provided. (See 'When to refer' above.)

Approach to the child with acute diarrhea in resource–limited

SUMMARY

- Diarrhea is the passage of loose or watery stools at least three times in a 24 hour period. Diarrheal illness is the second leading cause of child mortality; among children younger than five years it causes 1.5 to 2 million deaths annually. Diarrheal illness may consist of acute watery diarrhea, invasive (bloody) diarrhea, or chronic diarrhea (persistent ≥14 days) (table 1). (See 'Introduction' above.)

- The approach to the child with diarrhea includes classification of the type of diarrheal illness, assessing and correcting fluid and electrolyte losses, administering appropriate nutrition, and managing associated co-morbid conditions. (See 'Clinical assessment' above.)

- The degree of dehydration should be assessed at presentation based on physical signs and symptoms (table 3). Fluid management consists of two phases: replacement and maintenance (table 5 and table 6 and table 4). The goal of replacement therapy is to replenish deficits in water and electrolytes lost. This phase is

continued until all signs and symptoms of diarrhea are absent and the patient has urinated. Maintenance therapy counters ongoing losses of water and electrolytes; this phase is continued until all symptoms resolve. (See 'Hydration status' above and 'Fluid and electrolytes' above.)

- In general, the approach to rehydration in patients with severe malnutrition should be conservative because of the risk of fluid overload; intravenous fluids should be used only in patients with overt shock. All patients with severe malnutrition and diarrhea should be started on empiric broad spectrum antibiotics immediately, as well as appropriate nutritional therapy. (See 'Malnourished children' above and "Management of complicated severe acute malnutrition in children in resource-limited countries".)

- The goal of nutrition management for patients without malnutrition is to encourage sufficient feeding both during and after the diarrheal illness episode to prevent development of malnutrition and chronic enteropathy. (See 'Nutrition' above.)

- Antibiotics are not indicated for most children with acute watery diarrhea; suspected cholera is an important

exception in which antibiotic therapy is warranted (table 7). (See 'Antibiotics' above.)

- Treatment of invasive diarrhea includes the same approach to fluids, electrolytes, and nutrition as in acute watery diarrhea. In addition, empiric antibiotic therapy with activity against *Shigella* species should be initiated. (See 'Invasive diarrhea' above and "Shigella infection: Treatment and prevention in children".)

- Preventive measures for acute diarrhea among children in resource-limited settings include breastfeeding, consumption of safe food and water, adherence to hygienic practices, and vaccination against rotavirus infection. (See 'Prevention' above.)

Approach to the patient with dyspnea

SUMMARY AND RECOMMENDATIONS

- Dyspnea is a term used to characterize a subjective experience of breathing discomfort that comprises qualitatively distinct sensations that vary in intensity. Dyspnea is considered acute when it develops over hours to days and chronic when it has been present for more than four to eight weeks. (See 'Definition of dyspnea' above.)

- Dyspnea can be the first manifestation of a variety of cardiopulmonary disorders. It is not uncommon for a patient to have more than one problem contributing to breathing discomfort. (See 'Pathophysiology' above.)

- The history and physical examination lead to accurate diagnoses in patients with dyspnea in approximately two-thirds of cases. Important components of the history include the characteristics of dyspnea (ie, timing, severity, and triggers), exposures that may contribute to the lung disease (eg, allergens, cold air, occupational agents, cigarette smoke), and interventions or

medications that reduce dyspnea. (See 'Clinical assessment' above.)

- The patient's description of breathing discomfort can help narrow down diagnostic possibilities. In addition, the presence of more than one type of breathing discomfort can lead to recognition that more than one disease process is contributing to dyspnea. (See 'Descriptors of breathing discomfort' above.)

- Breathing discomfort arising over the course of minutes to hours (acute dyspnea) generally requires prompt evaluation and treatment. The evaluation of acute dyspnea is described separately. (See 'Evaluation of acute dyspnea' above and "Evaluation of the adult with dyspnea in the emergency department".)

- Among the many causes of chronic dyspnea (table 6), the most common are asthma, chronic obstructive pulmonary disease (COPD), interstitial lung disease, cardiomyopathy, and obesity/deconditioning. In addition, deconditioning is often a contributing factor in patients with chronic lung disease. (See 'Initial testing in chronic dyspnea' above.)

- When evaluating chronic dyspnea, we follow a step-wise diagnostic approach of initial testing (table 7), follow-up testing (table 8A-C), and advanced testing (table 9), starting with the tests that are the least invasive and most

likely to yield a diagnosis. Within each tier, the individual tests are selected based on the patient's clinical features, results of prior tests, and response to therapy. (See 'Initial testing in chronic dyspnea' above.)

- The initial tests are selected based on a review of the clinical findings for patterns suggestive of one or two of the above five most common causes of dyspnea (table 7). When asthma or COPD is suspected, the initial testing might be limited to spirometry pre and post bronchodilator, while an older patient with coronary artery disease and peripheral edema should be evaluated for heart failure before considering spirometry. (See 'Initial testing in chronic dyspnea' above.)

- Follow-up testing in the evaluation of dyspnea should clarify abnormalities that were noted on initial testing, but were not diagnostic (table 8A and table 8B and table 8C). In addition, some patients with normal results on initial testing, but persistent symptoms, require further evaluation. Thoracic computed tomography (CT) is generally reserved for patients in whom there is a suspicion of interstitial lung disease, occult emphysema, or chronic thromboembolic disease. Echocardiography is useful for evaluating suspected left ventricular dysfunction, pulmonary hypertension, and diastolic

dysfunction. (See 'Follow-up testing in chronic dyspnea' above.)

- Advanced testing includes procedures such as right heart catheterization, stress echocardiography, cardiopulmonary exercise testing (CPET), and invasive CPET (table 9). Cardiopulmonary exercise testing is a useful study in patients in whom the cause of their breathing discomfort remains elusive after standard testing, in patients in whom deconditioning is a serious consideration, and in patients who appear to have breathing discomfort out of proportion to their physiologic derangements. (See 'Unclear cause of dyspnea on exertion' above.)

Community-acquired pneumonia in children: Outpatient treatment

SUMMARY AND RECOMMENDATIONS

- Community-acquired pneumonia (CAP) is defined as an acute infection of the pulmonary parenchyma in a patient who has acquired the infection in the community. The clinical manifestations and diagnosis of CAP are discussed separately. (See "Community-acquired pneumonia in children: Clinical features and diagnosis".)

- The decision to hospitalize a child with pneumonia must be individualized and is based upon age, underlying medical problems, and severity of illness (table 1). (See 'Indications for hospitalization' above.)

- Children with CAP who are treated in the outpatient setting are treated empirically. It is not necessary to identify a microbiologic etiology in children who are well enough to be treated as outpatients. Decisions regarding empiric antimicrobial therapy for CAP in children are

usually based upon age unless there are other overriding epidemiologic or clinical factors to suggest a specific etiologic agent. (See 'Overview' above.)

- Infants younger than three to six months of age with suspected bacterial CAP or who are hypoxemic should be admitted to the hospital for management. Afebrile infants one to four months of age who are thought to have afebrile pneumonia of infancy (eg, *Chlamydia trachomatis*) can be treated in the outpatient setting if they are not hypoxemic and remain afebrile. (See "Pneumonia in children: Inpatient treatment" and "Chlamydia trachomatis infections in the newborn".)

- We recommend that empiric antibiotic therapy for CAP in children six months to five years of age who are thought to have bacterial pneumonia (eg, abrupt onset, moderate to severe respiratory distress, and supportive laboratory data if obtained (table 3)) include coverage for *Streptococcus pneumoniae* (table 2) (**Grade 1B**). (See 'Children <5 years' above.)

- We initiate macrolide antibiotics for initial empiric therapy for suspected atypical CAP (table 3) in children ≥5 years who are treated as outpatients. For children ≥5 years with clinical features strongly suggestive of typical bacterial or *S. pneumoniae* pneumonia (table 3),

amoxicillin remains the drug of choice (table 2). (See 'Children ≥5 years' above.)

- In infants and children six months and older, the usual duration of antimicrobial therapy is five days for azithromycin and 7 to 10 days for other agents. (See 'Duration' above.)

- Children who are treated for CAP as outpatients should have follow-up within 24 to 48 hours. Those whose condition has worsened at follow-up should be evaluated for potential complications and hospitalized. (See 'Monitoring response' above and "Pneumonia in children: Inpatient treatment".)

- Children recovering from CAP may continue to cough for several weeks to four months, depending upon the etiology. Those recovering from typical or atypical bacterial pneumonia may have moderate dyspnea on exertion for two to three months. (See 'Clinical course' above.)

- Follow-up radiographs in children with uncomplicated CAP who remain asymptomatic are not needed. Follow-up radiographs two to three weeks after completion of therapy may be helpful in children with recurrent pneumonia, persistent symptoms, severe atelectasis,

unusually located infiltrates, or round pneumonia. (See 'Radiographs' above.)

- Most otherwise healthy children who develop pneumonia recover without any long-term sequelae. (See 'Prognosis' above.)

Evaluation of headache in adults

SUMMARY AND RECOMMENDATIONS

- While episodic tension-type headache is the most frequent headache type in population-based studies, migraine is the most common diagnosis in patients presenting to primary care physicians with headache. Clinicians can easily

become familiar with the most common primary headache disorders and how to distinguish them (table 1). (See 'Epidemiology and classification' above.)

- Using the patient history as the primary diagnostic tool, the initial headache evaluation (algorithm 1) should determine whether there is a potentially dangerous secondary cause of headache or whether the headache is due to one of the common types of primary headache. (See 'Evaluation' above.)

- The mnemonic **SNOOP** is a reminder of the danger signs ("red flags") for the presence of serious underlying disorders that can cause acute or subacute headache:

  - **S**ystemic symptoms, illness, or condition (eg, fever, weight loss, cancer, pregnancy, immunocompromised state including HIV)
  - **N**eurologic symptoms or abnormal signs (eg, confusion, impaired alertness or consciousness, papilledema, focal neurologic symptoms or signs, meningismus, or seizures)
  - **O**nset is new (particularly for age >40 years) or sudden (eg, "thunderclap")
  - **O**ther associated conditions or features (eg, head trauma, illicit drug use, or toxic exposure; headache awakens from sleep, is worse with Valsalva maneuvers, or is precipitated by cough, exertion, or sexual activity)
  - **P**revious headache history with headache progression or change in attack frequency, severity, or clinical features

  Any of these findings should prompt further investigation (algorithm 1), including brain imaging with MRI or CT. (See 'Danger signs' above and 'Indications for imaging studies' above.)

- Differences in patient demographics, comorbidities, and headache features can guide the evaluation to help ensure appropriate diagnosis and management. (See 'Patient settings' above.)

  - Thunderclap headache may be the harbinger of subarachnoid hemorrhage and other potentially ominous etiologies (table 4) (see

'Sudden onset' above)

- The absence of similar headaches in the past is another finding that suggests a possible serious disorder (see 'New or recent onset headache' above)
- Chronic daily headache is a syndrome that encompasses a number of primary and secondary headaches (see 'Chronic headache' above)
- Older patients are at increased risk for secondary types of headache (eg, giant cell arteritis, trigeminal neuralgia, subdural hematoma, acute herpes zoster and postherpetic neuralgia, and brain tumors) and some types of primary headache (hypnic headache, cough headache, and migraine accompaniments) (see 'Older patients' above)
- Pre-eclampsia must be ruled in or out in every pregnant woman over 20 weeks of gestation with headache (see 'Pregnancy' above)
- Fever associated with headache may be caused by intracranial, systemic, or local infection, as well as other etiologies (table 5) (see 'Fever' above)
- Headache is a frequent sequelae of mild traumatic brain injury (see 'Traumatic brain injury' above)

Iron deficiency in infants and children <12 years: Treatment

SUMMARY AND RECOMMENDATIONS

Initial approach

— For children with presumed iron deficiency anemia (IDA) (on the basis of history and initial laboratory testing), we suggest an empiric trial of oral iron therapy AND dietary changes rather than either intervention alone (**Grade 2C**):

- To initiate oral iron therapy, we suggest a dose of 3 mg/kg of elemental iron once daily, rather than higher doses (**Grade 2C**). A 3 mg/kg dose of ferrous sulfate is generally effective and is tolerated by most children. For maximum absorption, the iron should be given 30 to 45 minutes before meals or two hours after meals, and only with juice or water. Administration with food or milk should be avoided. (See 'Dose and scheduling' above.)

- Meanwhile, the following dietary goals should be implemented to prevent recurrence (table 2) (see 'Dietary changes' above):

  - Infants younger than 12 months of age should be fed with breast milk or iron-fortified formula. A cow's milk-based formula is acceptable if there is no

evidence of cow's milk protein-induced colitis. Infants should not be given low-iron formula or unmodified cow's milk.

- For patients six months and older, especially breastfed infants, ensure adequate consumption of iron in complementary foods. These include infant cereals, which are fortified with iron, foods rich in vitamin C, and pureed meats.
- For children older than 12 months of age, intake of cow's milk should be limited to less than 20 oz per day and bottle feeding should be discontinued to limit milk intake. Excessive intake of cow's milk is the primary reason for the development of IDA in this age group and can be associated with occult intestinal blood loss.

- After beginning therapeutic iron, perform follow-up testing to determine the response, consisting of a complete blood count (CBC) or hemoglobin (Hgb). The testing should be performed when the child is healthy, about four weeks after beginning iron therapy for children with mild anemia, or one to two weeks after beginning iron therapy in those with moderate to severe anemia. Follow-up is essential to confirm that the anemia was due to iron deficiency and to ensure that it is adequately treated. This is particularly important because

of the effects of iron deficiency on neurodevelopment. (See 'Follow-up assessment for response' above.)

If the Hgb has increased by 1 g/dL, therapy is continued, and the CBC is retested at three months to ensure that the Hgb and other parameters reach the age-adjusted normal range. Oral iron therapy should be continued for at least one month after the Hgb reaches the normal range for age, to ensure that iron stores are replenished. A serum ferritin concentration can also be measured to check iron stores prior to discontinuation of iron therapy. (See 'Responders' above.)

Further evaluation

— Patients who do not demonstrate an adequate response within four weeks of initiating iron therapy should be reevaluated. Potential causes of recurrent or refractory IDA include ineffective treatment (nonadherence or incorrect dosing), an incorrect diagnosis, or ongoing blood loss or malabsorption (table 3). Our approach is as follows:

- Interview the parent to determine whether the iron therapy has been given at the appropriate dose and timing, whether the appropriate diet modifications have been made, and if there has been any significant intercurrent illness (which might cause a transient decrease in Hgb). The most common reason for failure is

that the treatment plan was not correctly followed. (See 'Nonresponders' above.)

- If the patient has indeed been taking an appropriate dose of iron and has not had an intercurrent illness, perform additional laboratory tests to rule out conditions that might simulate or complicate IDA such as thalassemia trait or anemia of chronic disease (table 4). In addition, several stool samples should be tested for occult blood. If the results are positive, additional screening should be performed for common causes of gastrointestinal blood loss, including cow's milk protein-induced colitis in infants, and celiac disease and inflammatory bowel disease (IBD) in older children. (See 'Nonresponders' above.)

Refractory iron deficiency anemia

- Intravenous iron therapy may be warranted for patients with severe or persistent anemia who have proven oral iron intolerance, malabsorption, or nonadherence despite family education and support to optimize oral therapy. Several forms of intravenous (IV) iron therapy with good safety profiles are available. Selection among these options may depend on relative costs and availability, time required for administration, and maximum

permissible dose per infusion. (See 'Intravenous iron therapy' above.)

- Encouraging a diet with ample servings of vegetables and fruits
- Limiting eating at restaurants, particularly fast-food restaurants
- Limiting portion size (which for young children often is less than a "serving size" as listed on a food label)

Activity goals (see "Physical activity and strength training in children and adolescents: An overview", section on 'Physical activity'):

- Encouraging moderate to vigorous physical activity for one or more hours daily [4].
- Limiting television and other screen time – Minimal screen time for children under two years of age; maximum of about one hour daily after age two years [2,6].

Management of childhood obesity in the primary care setting

SUMMARY AND RECOMMENDATIONS

— Obesity during childhood is associated with long-term health consequences and is influenced by genetic, epigenetic, behavioral, and environmental factors. Among these, only behavioral and environmental factors are modifiable during childhood, so these are the focus of clinical interventions.

We suggest the following practices among providers of primary care to children. These suggestions are based primarily on expert opinion; some are supported by clinical studies, usually with short-term outcomes.

- Universal measurement of body mass index (BMI) and plotting of results on a BMI chart to track changes over time. (See 'Body mass index' above.)
- Routine assessment of all children for obesity-related risk factors, to allow for early intervention. This includes recording the obesity status (BMI) of the biological parents and assessing key nutritional and physical activity habits (table 6 and table 7). (See 'Nutritional assessment' above and 'Activity assessment' above.)
- For children with obesity, weight-related comorbidities should be assessed through a focused review of systems (table 4), physical examination (table 2), and laboratory screening (table 3). (See 'Assessment of comorbidities' above.)

- For all children and their families, routine health care should include obesity-focused education. The key goals are to address the common diet-related problems encountered in children (table 8), set firm limits on television and other media early in the child's life, and establish habits of frequent physical activity. (See 'Diet' above and 'Sedentary activity' above and 'Physical activity' above.)

- For children who are overweight or obese, we suggest a series of clinical counseling interventions in the primary care setting (**Grade 2C**). Each session can be brief (3 to 15 minutes); this brief format is most practical for the primary care setting and is supported by limited clinical evidence. Additional contact time is valuable if time permits or if an allied health care provider (eg, dietitian or registered nurse) is available to provide counseling. (See 'Brief clinical intervention' above and 'Intensity of intervention' above.)

- Educational materials are available from a variety of sources to facilitate the counseling. These materials have much in common and have not been directly compared; it is reasonable for providers to select materials with messaging that is best suited to their community. Options include a Healthcare toolkit and an outline for a brief clinical intervention, which is based on the principles of motivational interviewing. (See 'Example and materials' above.)

- For patients who do not respond to a brief clinical intervention or for those with severe obesity, higher-intensity approaches are needed. These interventions are implemented in stages (table 1) and usually require referral to specialized weight management programs or tertiary care centers. (See 'Staged approach to weight management' above.)

- To establish a therapeutic relationship and enhance effectiveness, the communication and interventions should be supportive rather than

blaming, and focused on the entire family, rather than on the child alone. Long-term changes in behaviors that are related to obesity risk should be emphasized, rather than diets and exercise prescriptions, which tend to set short-term goals. When implemented in a supportive fashion, with a focus on healthy eating behaviors rather than rigid or highly restrictive dieting, interventions to support weight loss do not predispose to eating disorders. (See 'Theoretical background' above.)

- To be effective in managing populations with obesity, primary care offices should develop an efficient office system for calculating and tracking BMI at each visit and have a wide range of blood pressure cuffs (including a "large adult" size) and high-capacity scales (ideally up to 500 or 1000 lbs). It is also helpful to have office furniture that is appropriate for large patients and their families, including sturdy armless chairs and low examination tables. (See 'Office systems' above.)

- The American Association of Clinical Endocrinologists and American College of Endocrinology 2017 guideline for the management of dyslipidemia and prevention of CVD makes the following recommendations [48]:
  - For extreme-risk patients, such as those with progressive disease after achieving an LDL-C <70 mg/dL (1.8 mmol/L), those with CVD and diabetes, CKD, or heterozygous familial hypercholesterolemia (HeFH), or those with history of premature atherosclerotic CVD (<55 years in a man or <65 years in a woman), the LDL-C goal should be <55 mg/dL (1.4 mmol/L).
  - For very high-risk patients, such as those with an acute coronary syndrome or those with carotid or peripheral artery disease or those with diabetes or CKD with one or more risk factors, or HeFH, the goal is <70 mg/dL (1.8 mmol/L).

Management of elevated low density lipoprotein-cholesterol (LDL-C) in primary prevention of cardiovascular disease

SUMMARY AND RECOMMENDATIONS

- Patients with cardiovascular disease (CVD) (table 1), should be recommended lifestyle (modification) interventions associated with improved clinical outcomes and recommended a lifelong statin. (See "Prevention of cardiovascular disease events in those with established disease or at high risk", section on 'Lifestyle modification'.)

- For most patients with CVD, independent of baseline low density lipoprotein cholesterol (LDL-C), we recommend lifelong high-intensity statin therapy (atorvastatin 40 to 80 mg or rosuvastatin 20 to 40 mg) rather than moderate intensity statin or no LDL-C lowering therapy (**Grade 1A**). For patients who do not tolerate these doses, the maximally tolerated dose of a statin should be used.

- After the patient's highest tolerated statin dose has been settled upon, the LDL-C should be reevaluated and statin adherence/tolerance should be explored if the degree of LDL-C reduction is less than expected. (See 'Our approach' above.)

  - In patients at **very high risk** (see 'Definitions' above) for CVD events and whose LDL-C remains above 70 mg/dL, we recommend the addition of ezetimibe or a

PCSK9 antibody (**Grade 1B**). In most cases this second drug will be ezetimibe for cost reasons.

- In patients at **high risk** (see 'Definitions' above) for CVD events and whose LDL-C remains above 70 mg/dL after treatment with statin, we suggest the addition of ezetimibe or a PCSK9 antibody (**Grade 2B**).

- We discuss the benefits and risks of additional therapy with the patient. Some patients may reasonably choose to not have a second agent added to the statin. In most cases, ezetimibe is preferred to PCSK9 antibody for reasons of cost.

- In high-risk patients who do not tolerate any statin regimen and are not already receiving PCSK9 antibody therapy, we suggest treatment with a PCSK9 antibody rather than no therapy or ezetimibe alone (**Grade 2B**).

Overview of the management of osteoporosis in postmenopausal women

SUMMARY AND RECOMMENDATIONS

- Lifestyle measures should be adopted universally to reduce bone loss in postmenopausal women. Lifestyle measures include adequate calcium and vitamin D, exercise, smoking cessation, counseling on fall prevention, and avoidance of heavy alcohol use. In general, 1200 mg of elemental calcium daily, total diet

plus supplement, and 800 international units of vitamin D daily are advised. Postmenopausal women who are getting adequate calcium from dietary intake alone do not need to take calcium supplements (table 1). If dietary intake is inadequate, we suggest calcium supplementation (**Grade 2B**). (See 'Lifestyle measures' above.)

Many patients require vitamin D supplementation as it is difficult to achieve goals with diet alone (table 3). (See "Calcium and vitamin D supplementation in osteoporosis".)

- In addition to nonpharmacologic therapy, we recommend that postmenopausal women with established osteoporosis (T-score ≤-2.5) or fragility fracture be treated with a pharmacologic agent (**Grade 1A**). (See 'Candidates for therapy' above.)

- For the treatment of high-risk postmenopausal women with T-scores between -1.0 and -2.5, we also suggest pharmacologic therapy (**Grade 2B**). A reasonable cutpoint that may be cost effective in some settings is a 10-year probability of hip fracture or combined major osteoporotic fracture of ≥3.0 or ≥20 percent, respectively. (See 'Candidates for therapy' above.)

- For the treatment of osteoporosis in postmenopausal women, we suggest oral bisphosphonates as first-line

therapy (**Grade 2B**). We prefer oral bisphosphonates as initial therapy because of their efficacy, favorable cost, and the availability of long-term safety data. (See 'Initial therapy' above and "The use of bisphosphonates in postmenopausal women with osteoporosis".)

- For most postmenopausal women with osteoporosis, we suggest either alendronate or risedronate as the initial choice of bisphosphonate (**Grade 2B**). Oral ibandronate may be more convenient for patients, but a reduction in hip fracture risk has not been established in randomized trials. (See 'Choice of drug' above and "The use of bisphosphonates in postmenopausal women with osteoporosis".)

- Patients who have esophageal disorders (achalasia, scleroderma involving the esophagus, esophageal strictures, varices), gastrointestinal intolerance to oral bisphosphonates, history of Roux-en-Y gastric bypass, or an inability to follow the dosing requirements of oral bisphosphonates, including an inability to sit upright for 30 to 60 minutes and/or to swallow a pill, should not be treated with oral bisphosphonates and can be treated instead with intravenous (IV) bisphosphonate therapy. Zoledronic acid is the only IV bisphosphonate that has demonstrated efficacy for fracture prevention and is, therefore, our agent of choice. (See

'Contraindications/intolerance to oral bisphosphonates' above.)

- Patients who are allergic to bisphosphonates or who develop severe bone pain with them require an alternative treatment. In such patients who have severe osteoporosis (T-score of -3.5 or below even in the absence of fractures, or T-score of -2.5 or below plus a fragility fracture), we suggest treatment with teriparatide rather than denosumab (**Grade 2B**). In such patients who require therapy but who do not meet criteria for severe osteoporosis but have had fragility fractures, we suggest treatment with denosumab rather than teriparatide (**Grade 2B**). For patients with no history of fragility fractures, raloxifene is a reasonable alternative, particularly in women at high risk for breast cancer. (See 'Contraindications/intolerance to any bisphosphonates' above.)

Denosumab is an option for patients with osteoporosis at high risk for fracture and in those with impaired renal function. For some patients with severe osteoporosis, however, it may be beneficial to treat with teriparatide first (maximum of two years), followed by denosumab, to preserve the gains in bone mineral density (BMD) achieved with teriparatide. Because of emerging concerns about an increased risk of vertebral fracture after

discontinuation of denosumab, the need for indefinite administration of denosumab should be discussed with patients prior to its initiation. (See "Denosumab for osteoporosis", section on 'Duration of therapy' and "Parathyroid hormone/parathyroid hormone-related protein analogs for osteoporosis", section on 'After teriparatide'.)

- For patients starting on therapy, we obtain a follow-up dual-energy x-ray absorptiometry (DXA) of the hip and spine after two years, and if BMD is stable or improved, less frequent monitoring thereafter. (See 'Our approach' above.)

- The finding of a clinically significant BMD decrease or a new fracture in a treated patient should trigger additional evaluation for contributing factors, which may include poor adherence to therapy, inadequate gastrointestinal absorption, inadequate intake of calcium and vitamin D, or the development of a disease or disorder with adverse skeletal effects. (See 'Bone mineral density decreased or fracture during therapy' above.)

- For patients who have a decrease in BMD (<5 percent) while correctly taking bisphosphonates orally and who have no discernible contributing factors, we suggest continuing the same therapy (**Grade 2C**). We repeat the

BMD two years later. An alternative option is to switch therapies at the time of the initial decrease in BMD. (See 'Bone mineral density decreased or fracture during therapy' above.)

- For patients who have a decrease in BMD (≥5 percent) while correctly taking bisphosphonates orally, we suggest switching from an oral to an IV bisphosphonate (**Grade 2C**). If the lack of response is related to poor absorption, switching to an IV preparation should result in a more favorable response. Other alternatives include switching to a different oral bisphosphonate, recombinant human PTH (teriparatide), or denosumab. (See 'Bone mineral density decreased or fracture during therapy' above.)

- For postmenopausal women with severe osteoporosis (T-score of -2.5 or below plus a fragility fracture) who continue to fracture after one year of bisphosphonate therapy, we suggest discontinuing the bisphosphonate and switching to teriparatide (**Grade 2B**). (See 'Bone mineral density decreased or fracture during therapy' above and "Parathyroid hormone/parathyroid hormone-related protein analogs for osteoporosis", section on 'After teriparatide'.)

Denosumab is an alternative option for patients who are unresponsive to other therapies and in those with

impaired renal function. However, in the absence of contraindications, it may be beneficial to treat with teriparatide first (maximum of two years), followed by denosumab, to preserve the gains in BMD achieved with teriparatide. Because of emerging concerns about an increased risk of vertebral fracture after discontinuation of denosumab, the need for indefinite administration of denosumab should be discussed with patients prior to its initiation. (See "Denosumab for osteoporosis", section on 'Duration of therapy'.)

Peptic ulcer disease: Management

SUMMARY AND RECOMMENDATIONS

- Patients with peptic ulcer disease should be tested for *H. pylori*. Patients with *H. pylori* should be treated with a goal of eradication of *H. pylori* infection. In patients treated for *H. pylori,* eradication of infection should be confirmed four or more weeks after the completion of eradication therapy. (See "Indications and diagnostic tests for Helicobacter pylori infection".)

- Patients with peptic ulcers should be advised to avoid nonsteroidal anti-inflammatory drugs (NSAIDs). Contributing factors should be addressed and treated (eg, treating medical comorbidities, poor nutritional status, ischemia). (See "Peptic ulcer disease: Genetic, environmental, and

psychological risk factors and pathogenesis" and "Unusual causes of peptic ulcer disease".)

- All patients with peptic ulcer disease should receive antisecretory therapy to facilitate ulcer healing. The choice and duration of therapy varies based on the etiology, ulcer location (eg, gastric or duodenal), and the presence of ulcer complications (eg, bleeding, gastric outlet obstruction, ulcer penetration, perforation). (See 'Antisecretory therapy' above.)

- Patients with duodenal ulcers who have been treated do not need further endoscopy unless symptoms persist or recur. (See 'Duodenal ulcers' above.)

- The decision to perform surveillance endoscopy in patients with a gastric ulcer should be individualized. We suggest surveillance endoscopy (with biopsies of the ulcer if still present) be performed after 12 weeks of antisecretory therapy in patients with gastric ulcers and any one of the following (see 'Endoscopy after initial therapy' above):

  - Symptoms despite medical therapy.
  - Unclear etiology.
  - Giant gastric ulcer (>2 cm).
  - Biopsies not performed or inadequate sampling on the index upper endoscopy.
  - Ulcer appears suspicious for malignancy on index upper endoscopy (mass lesion, elevated irregular ulcer borders, or abnormal adjacent mucosal folds).
  - Initial endoscopy was performed for bleeding.
  - Risks factors for gastric cancer.

- Maintenance antisecretory therapy should be limited to high-risk subgroups of patients with peptic ulcer disease. These include individuals with any one of the following. (See 'Maintenance therapy' above.):

  - Refractory peptic ulcer
  - *H. pylori*-negative, NSAID-negative ulcer disease
  - Giant (>2 cm) ulcer and age >50 years or multiple comorbidities
  - Failure of *H. pylori* eradication

- Frequently recurrent peptic ulcers (>2 documented recurrences a year)
- Continued NSAID use

- Approximately 60 percent of peptic ulcers heal spontaneously but with eradication of *H. pylori* infection, ulcer healing rates are >90 percent. Even with continued proton pump inhibitor (PPI) use, approximately 5 to 30 percent of peptic ulcers recur within the first year based on whether *H. pylori* has been successfully eradicated. Approximately 5 to 10 percent of ulcers are refractory to antisecretory therapy with a PPI. The risk of complications in patients with chronic peptic ulcer disease is 2 to 3 percent per year. (See 'Disease course' above and "Approach to refractory or recurrent peptic ulcer disease" and "Overview of the complications of peptic ulcer disease".)

Poor weight gain in children younger than two years: Management

SUMMARY AND RECOMMENDATIONS

- Poor weight gain refers to abrupt weight loss following a period of normal growth along a well-established pattern, or weight gain that tracks along a growth channel either

well below the fifth percentile of the growth curves (figure 1A-B) or a growth curve proportionate to, but lower than, the child's expected height trajectory (figure 2A-B). (See 'Definition' above.)

- The primary cause of poor weight gain in preschool and school-age children and adolescents is inadequate dietary intake relative to typical metabolic and growth needs, which may be related to underlying medical, environmental, or social problems, alone or in combination. (See 'Etiology' above.)

- The diagnostic approach typically involves performing a complete history and physical examination to identify the major symptoms (table 1) and etiologic categories (table 2), screening for possible disease entities, initiating an empiric treatment regimen, and monitoring the clinical response. The pace of the evaluation is tailored to the severity of the problem. (See 'Diagnostic approach' above.)

- The most important aspects of the physical examination are the growth measurements and the growth pattern. The pattern of growth helps to narrow the differential diagnosis. (See 'Growth parameters' above.)

- Nutritional counseling and dietary intervention are the first steps to therapy and should begin during the

evaluation. If the child increases his or her dietary intake sufficiently, catch-up weight gain should be accomplished in a three- to six-month time frame. (See 'Management' above.)

Preventive care in adults: Recommendations

SUMMARY AND RECOMMENDATIONS

- Recommendations for preventive services are summarized for adults <65 years (table 2) and adults ≥65 years (table 3). (See 'Prioritizing preventive services' above.)

- Preventive services for a given patient should be prioritized according to his or her age, risk factors and preferences. This is discussed separately. (See "Preventive care in adults: Strategies for prioritization and delivery".)

Screening and prevention, adults younger than 65 years

Priority health problem	Population	Preventive intervention(s)*
Cardiovascular disease		
Risk assessment	Patients ≥20 years	CVD risk assessment every three to five years
Hypertension	All patients	Blood pressure screening/control
Hyperlipidemia	Patients between 17 and 21 years	One-time screening for dyslipidemia
	Risk factors: Women ≥35 years, men ≥25 years Without risk factors: Women ≥45 years, men ≥35 years	Dyslipidemia screening/control

Obesity	All patients	Screen with BMI Select patients for treatment based on risk factors
Physical activity	All patients	Counseling to exercise
Diabetes mellitus	Adults with hypertension or hyperlipidemia	Screen for diabetes mellitus
	Adults aged 40 to 70 years with BMI ≥ 25 kg/m^2	Screen for diabetes mellitus as part of cardiovascular risk assessment
Cancer		
Breast cancer	Concerning family history	Refer for genetic counseling/testing
	Hereditary breast and ovarian syndrome	Screen per recommendations
	Women >40	Discuss screening, individual decision; if screening desired, screen with mammography every two years

Cervical cancer	Women 21 to 29 years	Pap smear every three years
	Women ≥30 years	Pap smear every three years Or Pap smear + HPV testing every five years
Colorectal cancer	Patients with risk factors	Screen per recommendations
	Patients ≥50 years without risk factors	Screening (decide among colonoscopy, flexible sigmoidoscopy, fecal occult blood test)
Lung cancer	Patients 55 to 74 years, ≥30 pack-year smoking history and either currently smoking or quit in the past 15 years	Consider screening with low-dose helical CT scan
Prostate cancer	High-risk men 40 to 45 years	Discuss screening, individual decision

	Men ≥50 years without risk factors	Discuss screening, individual decision
Melanoma	High-risk patients	Periodic skin exam
	Average-risk patients	Remain vigilant for suspicious lesions
Immunizations		
Influenza	All patients	Annual influenza vaccination
Tdap/Td	All patients	Tdap at least once Td every 10 years
Varicella	Patients without evidence of immunity	Varicella vaccine
HPV	Women until 26 years Men until 21 years MSM until 26 years	HPV vaccine
Zoster	Patients ≥50 years	Zoster vaccine
Pneumococcal disease	Patients with risk factors	Pneumococcal vaccine*

Meningococcal disease	Patients with risk factors	Meningococcal vaccine
Hepatitis B	Patients with risk factors Patients with diabetes <60 years and consider if ≥60 years if risk factors	Hepatitis B vaccine
Sexually transmitted infections/blood-borne infections		
Chlamydia	Women <25 years Women ≥25 at increased risk Men at increased risk	Screening for chlamydia
Gonorrhea	Women at increased risk (including sexually-active women <25 years) Men at increased risk	Screening for gonorrhea
Hepatitis B	Patients with risk factors	Screening for hepatitis B

Hepatitis C	Patients born in the United States between 1945 and 1965	One-time screening for hepatitis C
	Patients with risk factors	Screening for hepatitis C
HIV	All patients	One-time screening
Syphilis	Patients with risk factors	Screening for syphilis
Psychosocial health concerns		
Depression	All patients	Brief screening
Alcohol	All patients	Screen for alcohol misuse
Tobacco	Smokers and tobacco users	Smoking/tobacco cessation
Other drug use	All patients	Assess for unhealthy drug use
Intimate partner violence	All patients	Screen for intimate partner violence on initial visit
	Concerning history or physical exam findings	Screening for intimate partner violence
Osteoporosis	Postmenopausal women <65	BMD screening

	years with risk factors Men with clinical manifestations of low bone mass	

Refer to individual UpToDate topics for more detailed discussions of screening and preventive counseling.

CVD: cardiovascular disease; BMI: body mass index; HPV: human papillomavirus; CT: computed tomography; Tdap: tetanus, diphtheria, and acellular pertussis vaccination; Td: tetanus, diphtheria vaccine; MSM: men who have sex with men; HIV: human immunodeficiency virus; BMD: bone mineral density.

* The pneumococcal vaccine (23-valent polysaccharide vaccine or 13-valent conjugate vaccine) and schedule varies depending upon the risk factor. Refer to UpToDate topic on pneumococcal vaccination in adults for details.

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Summary of screening, prevention, and counseling recommendations for adults age ≥65 years

Priority problem	Brief recommendation
Historical information and counseling	
Exercise	Moderate-to-vigorous aerobic activity three to five times per week Weight training or resistance exercises to maintain strength Flexibility activities to maintain range of motion Balance training to improve stability and prevent falls
Alcohol use	CAGE questionnaire Counseling to stop drinking
Tobacco use	Ongoing regular counseling to stop smoking Consideration of pharmacotherapy
Medication use	Regular review of medication list for:
	Completeness, accuracy, adherence, and affordability
	Drug-drug, drug-disease interactions
	Careful attention to use of specific drug types/classes including warfarin, digoxin, antidiabetic, analgesic,

	antihypertensive, psychotropic, and anticholinergic drugs
Urinary incontinence (UI)	Inquire about presence and severity biannually Presence of UI should trigger medication review, GU exam, appropriate blood and urine tests
Driving	Consideration of driving problems in those with problems with vision, mobility, or cognition For demented patients, recommend stop driving or refer for detailed driving assessment
Social support	Regular screening for financial and social support
Elder mistreatment	Routine direct questioning about problems with abuse or neglect
Advance directives	Discussion and documentation of preferences with living will and designation of healthcare power-of-attorney
Physical examination and testing	
Blood pressure	Measure annually If treatment initiated, monitor orthostatic blood pressure, renal function, and electrolytes
Weight	Weight loss of 10% or more per year triggers assessment of undernutrition, possible medical or medication-related causes, dental status, food security, food-related functional status, appetite and intake, swallow ability, and previous dietary restrictions
Hearing and	Annual screening for hearing loss with patient

vision	inquiry and exam (Whisper test or handheld audiometry) Vision assessment as part of the routine workup for older adults with cognitive decline, functional impairment, or falls
Cognition	Targeted screening in patients with memory complaints or new functional impairment with MMSE, Mini-Cog, Clock Drawing Test, Memory Impairment Screen, SLUMS, or MoCA
Mood	Screen all older adults for depression with two questions: During the last month:
	1) Have you been bothered by feeling down, depressed, or hopeless?
	2) Have you often been bothered by having little interest or pleasure in doing things?
Gait and balance	Get Up and Go Test
Lipids	Screen and treat older adults with CAD risk exceeding 10% over 10 years
Bone density	Screening densitometry for osteoporosis for women at age 65
Abdominal aortic aneurysm (AAA)	One-time screening ultrasound in men aged 65 to 75 with any history of smoking or family history of AAA requiring repair
Diabetes	Screen adults (to age 70) with BMI ≥25 kg/m^2, hypertension or hyperlipidemia
Cancer screening	

Cancer screening	Key considerations in older adults:
	Life expectancy: Will this patient live long enough to benefit?
	Potential harms: Procedural complications, anxiety, cost, and overdiagnosis
	Individual patient preference
Breast cancer	Shared decision-making; if woman opts to be screened, biennial mammography if life expectancy is at least 10 years
Colorectal cancer	Annual FOBT versus Screening colonoscopy every 10 years versus Flexible sigmoidoscopy every five years as long as life expectancy is at least five years
Cervical cancer	May safely discontinue Pap smears at or after age 65 after three consecutive normals within a 10-year period May discontinue after hysterectomy for benign indication
Lung cancer	Annual low-dose chest CT scan for high-risk individuals to age 80 years; discontinue if person has not smoked for 15 years or if life expectancy is limited
Immunization	
Tetanus-diptheria vaccine	Booster every 10 years in patients who have received primary series (alternative: booster once after age 50); Tdap once
Influenza vaccine	Annual vaccination
Pneumococcal	Give PCV13 followed by PPSV23 6 to 12

vaccine (PCV13 and PPSV23)	months later, once after age 65 Revaccinate PPSV23 once after age 65 if an initial vaccination was given before age 65 and five years have elapsed since the first dose
Herpes zoster vaccine	One-time vaccination after age 50
Other	
Aspirin	Consider daily aspirin in patients with five-year CAD risk of 3% or greater Weigh risks of gastrointestinal bleeding
Calcium and Vitamin D	1200 mg of elemental calcium (diet and/or supplement) and at least 800 international units of Vitamin D

CAGE: Cut down, Annoyed, Guilty, Eye-opener; GU: genitourinary; MMSE: Mini Mental State Examination; SLUMS: St. Louis University Mental Status Test; MoCA: Montreal Cognitive Assessment; BMI: body mass index; FOBT: fecal occult blood test; CT: computed tomography; CAD: coronary artery disease.

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four to six weeks. If the value is normal, the dose can be reduced further or stopped. Most patients with hypothyroidism have symptoms and a high serum TSH concentration within one month after discontinuing therapy.

Many of these patients are reluctant to discontinue their thyroid hormone, especially if they have taken it for many years. In this case, the goal should be to provide an appropriate dose of T4 (adjusted to maintain a normal serum TSH concentration) to avoid the potential adverse cardiac and skeletal effects of overtreatment.

Treatment of primary hypothyroidism in adults

SUMMARY AND RECOMMENDATIONS

- Overt primary hypothyroidism is characterized biochemically by a high serum thyroid-stimulating hormone (TSH) concentration and a low serum free thyroxine (T4) concentration. All patients with overt primary hypothyroidism require treatment (regardless of symptoms), unless the hypothyroidism is transient (as

after painless thyroiditis or subacute thyroiditis) or reversible (due to a drug that can be discontinued). (See 'Defining hypothyroidism' above and "Disorders that cause hypothyroidism", section on 'Transient hypothyroidism'.)

- The goals of therapy are amelioration of symptoms, normalization of TSH secretion, reduction in size of goiter (if present), and avoidance of overtreatment (iatrogenic thyrotoxicosis). (See 'Goals of therapy' above.)

- The treatment of choice for correction of hypothyroidism is synthetic thyroxine (T4, levothyroxine). For the vast majority of patients with hypothyroidism, we suggest **not** using combination T4-triiodothyronine (T3) therapy (**Grade 2B**). However, T4-T3 therapy may improve symptoms in selected patients (eg, after thyroidectomy or ablative therapy with radioiodine). We discourage the use of combined therapy in older patients, patients with underlying cardiovascular disease in whom excessive T3 levels might precipitate an arrhythmia, and in pregnant women. (See 'Standard replacement therapy' above and 'Candidates for combined T4 and T3 therapy' above.)

  When T4-T3 therapy is used, the T4-to-T3 ratio should be approximately 13:1 to 16:1 (table 4). (See 'Dosing and available preparations' above.)

- We suggest that patients remain on the same formulation of T4 (**Grade 2C**). Either a generic or a brand-name formulation is acceptable. If a switch from one manufacturer to another is made by the pharmacy and there is concern regarding equivalent efficacy of the preparations, we measure a serum TSH six weeks after changing preparations to document that the serum TSH is still within the therapeutic target. (See 'T4 formulations' above.)

- The initial dose can be the full anticipated dose (1.6 mcg/kg/day) in young, healthy patients, but older patients and those with coronary heart disease should be started on a lower dose (25 to 50 mcg daily). T4 should be taken on an empty stomach, ideally an hour before breakfast. (See 'Initial dose' above and 'Timing of dose' above.)

- After initiation of T4 therapy, the patient should be reevaluated and serum TSH should be measured in six weeks and the dose adjusted accordingly. Symptoms may begin to resolve after two to three weeks, but steady-state TSH concentrations are not achieved for at least six weeks. (See 'Initial monitoring and dose adjustments' above.)

- We aim to keep TSH within the normal reference range (approximately 0.5 to 5.0 mU/L). For patients who have possible hypothyroid symptoms and a serum TSH that is confirmed by repeat measurement to be at the upper limits or above the reference range, we suggest increasing the dose of T4 with the aim of lowering the serum TSH value into the lower half of the reference range (**Grade 2C**). However, it is important to note that there is an age-related shift towards higher TSH concentrations in older patients, with an upper limit of normal of approximately 7.5 mU/L in 80 year olds. (See 'Persistent symptoms' above.)

Management of low density lipoprotein cholesterol (LDL-C) in the secondary prevention of cardiovascular disease Jun 04, 2018

SUMMARY AND RECOMMENDATIONS

- Patients with cardiovascular disease (CVD) (table 1), should be recommended lifestyle (modification) interventions associated with improved clinical outcomes and recommended a lifelong statin. (See "Prevention of cardiovascular disease events in those with established disease or at high risk", section on 'Lifestyle modification'.)

- For most patients with CVD, independent of baseline low density lipoprotein cholesterol (LDL-C), we recommend lifelong high-intensity statin therapy (atorvastatin 40 to 80 mg or rosuvastatin 20 to 40 mg) rather than moderate intensity statin or no LDL-C lowering therapy (**Grade 1A**). For patients who do not tolerate these doses, the maximally tolerated dose of a statin should be used.

- After the patient's highest tolerated statin dose has been settled upon, the LDL-C should be reevaluated and statin adherence/tolerance should be explored if the degree of LDL-C reduction is less than expected. (See 'Our approach' above.)

  - In patients at **very high risk** (see 'Definitions' above) for CVD events and whose LDL-C remains above 70 mg/dL, we recommend the addition of ezetimibe or a

PCSK9 antibody (**Grade 1B**). In most cases this second drug will be ezetimibe for cost reasons.

- In patients at **high risk** (see 'Definitions' above) for CVD events and whose LDL-C remains above 70 mg/dL after treatment with statin, we suggest the addition of ezetimibe or a PCSK9 antibody (**Grade 2B**).

- We discuss the benefits and risks of additional therapy with the patient. Some patients may reasonably choose to not have a second agent added to the statin. In most cases, ezetimibe is preferred to PCSK9 antibody for reasons of cost.

- In high-risk patients who do not tolerate any statin regimen and are not already receiving PCSK9 antibody therapy, we suggest treatment with a PCSK9 antibody rather than no therapy or ezetimibe alone (**Grade 2B**).