Clinical Insights:

Effective Care for Patients with Chronic Conditions

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Clinical Insights:
Effective Care for Patients with Asthma

The goals of asthma management are to reduce impairment by achieving asthma control and to reduce risk by preventing exacerbations and hospitalizations and preventing progressive loss of lung function. The essential elements of care to achieve these goals include:

Medications: The following medications may be recommended for patients with asthma, depending on individual circumstances. A step-wise approach is recommended depending on asthma severity and level of control; medications are increased when asthma symptoms are not well-controlled and decreased when asthma symptoms are absent.

- **Long-acting (controller) medications:** To maintain long-term asthma control in patients who will benefit, including patients with persistent asthma and children and infants who require symptomatic treatment two or more times per week.
  - Inhaled corticosteroids (ICSs) are the most potent and consistently effective long-term controller medications for asthma. In general, inhaled corticosteroids are the treatment of choice.
  - For patients treated with inhaled corticosteroids who need additional control, inhaled long-acting beta$_2$-agonists (LABAs) are more effective than leukotriene antagonists; e.g., montelukast, for patients aged 12 years and older.
  - LABAs are only appropriate when used in combination with inhaled corticosteroids. Pediatric and adolescent patients who require addition of LABA to ICS should use a combination product.
  - Abruptly stopping long-acting controller medications, particularly inhaled beta$_2$-agonists, may result in acute worsening of symptoms (withdrawal).
- **Short-acting (rescue) medications:** As needed to promptly relieve acute symptoms.

Patient education: Successful asthma management requires that the patient and/or caregivers understand and have the skills to become active partners in asthma management. Education can decrease asthma hospitalizations and improve daily function. Key elements include respiratory monitoring (symptom and/or lung function); trigger recognition and avoidance; and proper use of appropriate medications. Demonstrate that patients are using inhalers and/or nebulizers correctly. Use spacers for children or spacer/masks for young children.

Written asthma action plan (either symptom-based or peak-flow-based) are particularly recommended for: 1) patients with moderate or severe persistent asthma; 2) those with a history of severe exacerbations; and 3) patients with poorly controlled asthma. A written action plan should include:

- Explicit, patient-specific recommendations for minimizing environmental triggers.
- How to assess changes in symptoms or lung function (see “Respiratory monitoring” below), and adjust medication, as appropriate.
- Actions to take when medications are ineffective or if an emergency situation arises.
- Contacts for securing urgent care, if needed.

Respiratory monitoring: The nature and intensity of self-monitoring should be individualized, based on such factors as asthma severity, patient’s ability to perceive or report airflow obstruction, availability of peak-flow meters, and patient preferences. Either symptom monitoring or peak-flow measurement can be effective. Components of respiratory monitoring may include the following, depending on individual needs:

- **Symptom monitoring:** Early recognition of symptoms (cold, cough, chest tightness) and step-up in medications. (Symptom-based monitoring may be preferred in children.)
- **Peak-flow measurement:** Peak-flow-based monitoring should be considered for the following: 1) moderate or severe persistent asthma; 2) history of severe exacerbations; 3) patients who poorly perceive airflow obstruction and worsening asthma; and 4) patients who prefer this approach. Peak-flow measurement may be done daily, or for two-to three-week intervals when symptoms change, as part of a symptom-based action plan. May also be helpful during exacerbations to guide treatment decisions.
- **Spirometry:** At diagnosis, on stabilization of symptoms and peak flow, and during progressive loss of asthma control. (Regular spirometry may not be needed in mild-to-moderate persistent asthma.)

Trigger recognition and avoidance: Including inhaled allergens (e.g., pollens, animal, cockroach, and dust-mite allergens); occupational exposures (e.g., chemicals and sprays); respiratory irritants (e.g., tobacco smoke, air pollution, and sprays); comorbid conditions (e.g., GERD and sinusitis); and other factors (medications, sulfites, and viral respiratory infections).

Smoking cessation: All patients and avoidance of secondary smoke.

Depression: The association between asthma and depression is less strong than for other chronic conditions such as cardiovascular disease or diabetes. However, screening is always appropriate for patients with any chronic condition. Screening improves the accurate identification of depression in primary care settings, and treatment of depressed adults identified in primary care settings decreases clinical morbidity. Two simple questions may be used as a screening tool ("Over the past two weeks, have you felt down, depressed, or hopeless?" and "Over the past two weeks, have you felt little interest or pleasure in doing things?"). Patients who screen positive (i.e., those who answer 'yes' to either question) should undergo full diagnostic interview.

Influenza vaccine (seasonal): Annually for all children aged 6 months through 18 years, adults aged 50 and older, and adults aged 19 through 49 years with chronic pulmonary diseases (including asthma and COPD); chronic cardiovascular diseases (including coronary heart disease and heart failure); and chronic metabolic diseases (including diabetes). In addition, household contacts or caregivers of people in these groups. (Children aged <6 months should not receive influenza vaccination.)

Pneumococcal vaccine: All adults aged 65 and older, adults who smoke cigarettes, and adults aged 19 through 64 years who have certain medical conditions, including (not a complete list) chronic pulmonary diseases (including asthma), chronic cardiovascular diseases, and diabetes. A one-time revaccination is recommended five years after the first for some groups, including (not a complete list) patients with chronic kidney disease, those who are immunocompromised, and those vaccinated before age 65.

The material in this condition management program is based on:

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CDC. Recommended Immunization Schedules for Persons Aged 0−18 Years—United States, 2010. *MMWR.* 2010;58(51&52). Available at: http://www.cdc.gov/mmwr/PDF/wk/mm5851-Immunization.pdf

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Clinical Insights: Effective Care for Patients with Permanent (Chronic) Atrial Fibrillation

Note: These insights are intended as a guide to the ongoing medical management of patients with long-standing or permanent atrial fibrillation. Atrial fibrillation is classified as paroxysmal, persistent, or permanent (chronic). These insights are intended to inform the effective care of patients with permanent (chronic) atrial fibrillation; that is, atrial fibrillation that has persisted > 1 year; cardioversion has either not been attempted or has failed. Rhythm control is not superior to rate control, but an individual patient's symptoms may warrant an attempt at rhythm control.

Medications: The following medications may be recommended for patients with permanent (chronic) atrial fibrillation, depending on individual circumstances:

- **Anticoagulant/antithrombotic therapy with aspirin or warfarin to reduce stroke risk:** Choice of regimen (aspirin vs. warfarin) should be based on risk stratification ($CHADS_2$ score—a clinical prediction rule for estimating stroke risk in patients with atrial fibrillation), consideration of the expected net clinical benefit of warfarin (rate of events prevented by warfarin minus intracranial hemorrhages attributable to warfarin), availability of high-quality monitoring services, and patient preference. (Note: Clopidogrel (Plavix) is not superior to aspirin and does not replace warfarin.) In some risk categories, $CHADS_2$ scores of 0 or 1, there may be little/no net clinical benefit. The net clinical benefit of warfarin is clear with $CHADS_2$ scores of 2 or more, and greatest in patients with $CHADS_2$ scores of 4 to 6, those with prior history of stroke, and those aged 85+. Note that the threshold of benefit at which patients will chose warfarin anticoagulation varies, and some people at intermediate risk may reasonably decide against it.

$CHADS_2$ stroke risk classification scheme for patients with atrial fibrillation

Risk Factor	Letter Assigned	Point Value
Congestive heart failure	C	1
Hypertension	H	1
Age ≥ 75	A	1
Diabetes mellitus	D	1
History of ischemic stroke or transient ischemic attack	S	2

A patient's $CHADS_2$ score is the sum of the points assigned for each risk factor. The higher the score, the higher the patient's risk for stroke.

- **Rate control (pharmacological) to maintain hemodynamic stability and/or avoid symptoms, and to prevent long-term cardiomyopathy:** First-line agents are beta blockers or nondihydropyridine calcium channel blockers. A second-line agent is digoxin; it is not effective at controlling rate with exertion, but is a reasonable choice for sedentary patients and those with heart failure. Amiodarone is also effective, but not a primary therapy for rate control.
- **Rate control (nonpharmacologic therapy):** For patients who remain symptomatic despite pharmacological rate control. Options include radiofrequency AV node ablation with permanent pacemaker or AV nodal conduction modification.
- **Written action plan that includes:**
  - *For all patients:* Instructions for how to identify and respond to heart rate changes that are persistently outside the patient's target range.
  - *For patients on warfarin:* Instructions for consistent dosing and education about potential drug interactions, dietary and activity guidelines, International Normalized Ratio (INR) monitoring, and appropriate response to missed warfarin doses and signs of bleeding. Patients should have access to clinical support systems for addressing out-of-range INR results.
- **Monitoring:**
  - *For all patients:* Regular assessment of heart rate, with patient at rest and after exercise.
  - *For patients on warfarin:* Routine INR monitoring is required. Goal INR will vary depending on individual circumstances, but the general INR target is 2-3. Attention to potential drug interactions is important.

Smoking cessation: All patients and avoidance of secondary smoke.

Depression: Screening is always appropriate for patients with any chronic condition. Screening improves the accurate identification of depression in primary care settings, and treatment of adults identified in primary care settings decreases clinical morbidity. Two simple questions may be used as a screening tool ("Over the past two weeks, have you felt down, depressed, or hopeless?" and "Over the past two weeks, have you felt little interest or pleasure in doing things?"). Patients who screen positive (i.e., who answer 'yes' to either question) should undergo full diagnostic interview.

Influenza vaccine (seasonal): Annually for all children aged 6 months through 18 years, adults aged 50 and older, and adults aged 19 through 49 years with chronic pulmonary diseases (including asthma and COPD); chronic cardiovascular diseases (including coronary heart disease and heart failure); and chronic metabolic diseases (including diabetes). In addition, household contacts or caregivers of people in these groups. (Children aged <6 months should not receive influenza vaccination).

Pneumococcal vaccine: All adults aged 65 and older, adults who smoke cigarettes, and adults aged 19 through 64 years who have certain medical conditions, including (not a complete list) chronic pulmonary diseases (including asthma), chronic cardiovascular diseases, and diabetes. A one-time revaccination is recommended five years after the first for some groups, including (not a complete list) patients with chronic kidney disease, those who are immunocompromised, and those vaccinated before age 65.

The material in this condition management program is based on:

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Clinical Insights:
Effective Care for Patients with Chronic Obstructive Pulmonary Disease (COPD)

The goals of COPD management are to relieve symptoms, prevent disease progression, improve exercise tolerance and health status, prevent and treat complications and exacerbations, and reduce mortality. The essential elements of care to achieve these goals include:

Smoking cessation: All patients, to slow disease progression, and avoidance of secondary smoke.

Medications: Monotherapy with a long-acting bronchodilator or inhaled corticosteroid is recommended for symptomatic patients with moderate to severe COPD for reducing exacerbations. Patients with FEV_1 <60 percent predicted may be more likely to derive benefit from treatment than those with higher FEV_1. The following medications, either alone or in combination, may be recommended for patients with COPD, depending on individual patient circumstances, such as response to therapeutic trials:

- **Bronchodilators:** Given as needed or on a regular basis to prevent or reduce symptoms. May also reduce disease progression in patients with FEV_1 <60%.
  - The principal bronchodilators are short-acting and long-acting $beta_2$-agonists and anticholinergics or a combination of these.
  - Although methylxanthines (e.g., theophylline) are not recommended as part of routine care, they may be added or substituted if patients have limited benefit and/or intolerable side effects with bronchodilators and/or inhaled corticosteroids.
  - Abruptly stopping daily-use bronchodilators may result in acute worsening of symptoms (withdrawal).
- **Corticosteroids:** Inhaled corticosteroids (ICS) may reduce frequency of exacerbations and slow declines in health status in severe or very severe COPD with frequent exacerbations (three or more in past three years). However, several recent trials have shown an increased risk of pneumonia associated with ICS use in patients with severe COPD. Try to limit oral corticosteroid therapy to short-course treatment of exacerbations.

Written symptom response plan for dealing with new, different, or worsening symptoms.

Long-term oxygen therapy can help improve survival in patients with:

- **$PaO_2 \leq$ 55 mm Hg,**
- **$SaO_2 \leq$ 88 percent,** or
- **PaO_2 55-60 mm Hg with signs of pulmonary hypertension, peripheral edema suggesting heart failure, or polycythemia (hematocrit > 55 percent).**

NIPPV: Non-invasive positive pressure ventilation (NIPPV) is particularly beneficial for COPD exacerbations associated with hypercapnia or respiratory failure.

Pulmonary rehabilitation or exercise should be considered for those with symptoms and FEV_1<50 percent. In patients with severe airway obstruction, pulmonary rehabilitation can reduce hospitalizations and improve health status and exercise capacity. However, the evidence for benefit is less clear for patients with FEV_1>50 percent predicted. The specific components vary: patient education; self-management strategies; nutritional support; respiratory muscle training and exercise prescription. Benefits of programs lasting at least six weeks can include improved exercise tolerance, decreased dyspnea, and decreased fatigue.

Respiratory monitoring: The primary purposes of spirometry are for diagnosis and determining when to initiate treatment (i.e., when FEV_1 is <60 percent predicted). Patients with FEV_1<60 percent predicted may be more likely to benefit from regular treatment than those with higher FEV_1. There is less evidence that spirometry is helpful when there is significant change in symptoms or a complication; or that periodic testing is useful to monitor changes over time.

Trigger avoidance: Including tobacco smoke, occupational dusts/chemicals, and indoor/outdoor air pollutants.

Surgical treatments: For carefully selected patients, consideration of bullectomy, lung volume reduction surgery, or lung transplant may be appropriate.

Depression: Chronic disease is a risk factor for depression. Screening improves the accurate identification of depression in primary care settings, and treatment of depressed adults identified in primary care settings decreases clinical morbidity. Two simple questions may be used as a screening tool ("Over the past two weeks, have you felt down, depressed, or hopeless?" and "Over the past two weeks, have you felt little interest or pleasure in doing things?"). Patients who screen positive (i.e., those who answer 'yes' to either question) should undergo full diagnostic interview. In addition, anxiety associated with chronic respiratory distress may be a major cause of decreased quality of life for patients with COPD, and appropriate treatment may improve outcomes.

Influenza vaccine (seasonal): Annually for all children aged 6 months through 18 years, adults aged 50 and older, and adults aged 19 through 49 years with chronic pulmonary diseases (including asthma and COPD); chronic cardiovascular diseases (including coronary heart disease and heart failure); and chronic metabolic diseases (including diabetes). In addition, household contacts or caregivers of people in these groups. (Children aged <6 months should not receive influenza vaccination).

Pneumococcal vaccine: All adults aged 65 and older, adults who smoke cigarettes, and adults aged 19 through 64 years who have certain medical conditions, including (not a complete list) chronic pulmonary diseases (including asthma), chronic cardiovascular diseases, and diabetes. A one-time revaccination is recommended five years after the first for some groups, including (not a complete list) patients with chronic kidney disease, those who are immunocompromised, and those vaccinated before age 65.

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Karasu TB, Gelenberg A, Merriam A, and Wang P. Practice Guideline For The Treatment of Patients With Major Depressive Disorder, Second Edition. American Psychiatric Association. 2000:1-78. Available at: http://www.psychiatryonline.com/pracGuide/loadGuidelinePdf.aspx?file=MDD2e_05-15-06

Fochtmann LJ and Gelenberg AJ. Guideline Watch: Practice Guideline for the Treatment of Patients With Major Depressive Disorder, 2nd Edition. *FOCUS: The Journal of Lifelong Learning in Psychiatry*. 2005;3:34-42. Available at: http://focus.psychiatryonline.org/cgi/reprint/3/1/34?maxtoshow=&HIT

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CDC. Vaccines and Preventable Diseases: Pneumococcal Vaccination. 2009. Available at: http://www.cdc.gov/vaccines/vpd-vac/pneumo/default.htm#recs

Clinical Insights:
Effective Care for Patients with Coronary Heart Disease (CHD)

Medications: The following medications may be recommended for patients with CHD, depending on individual circumstances:

- **ACE inhibitors (ACEIs)** (or angiotensin-2 receptor blockers, if ACEI not tolerated): to lower risk of heart attack, stroke, and CHD death.
- **Beta blockers** (or calcium-channel blockers, if beta blockers not tolerated): to lower risk of heart attack, stroke, and CHD death; may also help manage angina.
- **Aspirin (low-dose)** and/or other antiplatelet agent: to lower risk of heart attack.
  - Dual antiplatelet therapy (DAT) with both a thienopyridine (clopidogrel or prasugrel) and aspirin is recommended for at least one year following drug-eluting stent placement and for at least one month (and ideally up to 12 months) following bare-metal stent placement to reduce risk of in-stent thrombosis. Some experts recommend indefinite DAT until data are available to determine the optimal duration; recommendations differ following stent placement for acute coronary syndromes. *Earlier discontinuation should be considered if the risks of bleeding outweigh the anticipated benefit.*
  - In patients receiving clopidogrel, concomitant use of proton-pump inhibitors (PPIs) appears to reduce the risk of gastrointestinal bleeding. However, omeprazole (Prilosec®) reduces the antiplatelet activity of clopidogrel, and the Food and Drug Administration recently recommended against concomitant use of clopidogrel with omeprazole, esomeprazole (Nexium®), as well as the H_2 blocker cimetidine (Tagamet® or Tagamet HB®). It is not yet clear whether all PPIs have this effect, or whether the attenuation of antiplatelet activity definitively results in attenuation of the clinical benefits of clopidogrel**.** Providers may wish to evaluate the necessity of PPI therapy and consider alternatives such as H_2 blockers**,** other than cimetidine; e.g., ranitidine (Zantac®), famotidine (Pepcid®), and nizatidine (Axid®), or antacids, which may be effective alternatives. This issue will continue to be an active area of investigation until the full implications are clarified.
- **Statins:** To reduce risk of heart attack, stroke, and CHD death.
- **Anti-anginal medications** (long- and/or short-acting nitrates, calcium-channel blockers, and/or ranolazine (Ranexa®) in addition to beta blockers): as needed to prevent/treat stable angina.
- **NOTE**: If needed to achieve blood pressure control, **diuretics** may be added to initial therapy.

Written action plan for responding to new, different, or worsening symptoms.

Management of lipid levels: Measure lipid profile at least annually. Repeat lipid profiles at about four to six weeks after hospitalization and two to three months after initiation of or change in lipid-lowering medications.

- Regardless of baseline LDL levels, most patients with CHD will benefit from statin therapy to reduce LDL by 30 to 40 percent.
- Some expert guidelines recommend higher doses of statins (as tolerated) to reach specific LDL targets (e.g., below 100 or below 70), based on trials comparing lower doses vs. higher doses of statins. However, based on current evidence, the majority of the benefit of statins is achieved by lowering LDL by 30 to 40 percent.
- In patients who have achieved their LDL goal but whose triglycerides are 200-499, some expert guidelines (ATP-III and ACC/AHA) recommend additional therapy (e.g., higher-dose statin or add-on fibrates or niacin) to reduce non-HDL cholesterol (total cholesterol minus HDL) to <130 mg/dl (i.e., < target LDL+30).
- Currently, no randomized trials have examined whether efforts to achieve either target LDL or target non-HDL cholesterol levels with add-on fibrates or niacin reduces cardiovascular event rates. Trials have shown some benefit for high-dose statins compared with low-dose statins for reducing CVD events, but have not specifically compared adjusting statin dosing to achieve LDL treatment targets.

Blood pressure management to achieve goal <140/90 (<130/80 with comorbid diabetes) with lifestyle changes and medications as needed. Blood pressure should be measured at each physician visit.

Physical activity: Encourage 30-60 minutes of activity seven days per week (minimum 5 days per week), as tolerated. Cardiac rehabilitation is recommended for those with recent acute coronary syndrome or revascularization.

Weight management to achieve or maintain BMI 18.5 to 24.9 kg/m^2. If weight loss is needed, the initial goal should be to gradually reduce body weight by about 10 percent. When waist circumference equals/exceeds 120 cm in men or 88 cm in women (thresholds may vary by ethnic group), consider lifestyle changes and treatments aimed at elements of the metabolic syndrome, as indicated. (The 2005 AHA/NHLBI Scientific Statement, *Diagnosis and Management of the Metabolic Syndrome,* defines the criteria for clinical diagnosis of metabolic syndrome as elevated waist circumference (noted above); elevated triglycerides greater than/equal to 150 mg/dl or drug treatment for elevated triglycerides; reduced HDL less than 40 mg/dl in men and less than 50 mg/dl in women or drug treatment for reduced HDL; elevated blood pressure greater than/equal to 130/85 mm Hg or on antihypertensive drug treatment in a patient with a history of hypertension; elevated fasting glucose greater than/equal to 100 mg/dl or on drug treatment for elevated glucose. Any 3 of 5 criteria constitute diagnosis of metabolic syndrome)

Smoking cessation: All patients and avoidance of secondary smoke.

Depression: Chronic disease in general, and coronary heart disease in particular, is a risk factor for depression, and depression is associated with worse prognosis and higher risk of cardiac events in patients with CHD. Screening improves the accurate identification of depression in primary care settings, and treatment of depressed adults identified in primary care settings decreases clinical morbidity. Two simple questions may be used as a screening tool ("Over the past two weeks, have you felt down, depressed, or hopeless?" and "Over the past two weeks, have you felt little interest or pleasure in doing things?"). Patients who screen positive (i.e., those who answer 'yes' to either question) should undergo full diagnostic interview.

Influenza vaccine (seasonal): Annually for all children aged 6 months through 18 years, adults aged 50 and older, and adults aged 19 through 49 years with chronic pulmonary diseases (including asthma and COPD); chronic cardiovascular diseases (including coronary heart disease and heart failure); and chronic metabolic diseases (including diabetes). In addition, household contacts or caregivers of people in these groups. (Children aged <6 months should not receive influenza vaccination).

Pneumococcal vaccine: All adults aged 65 and older; adults who smoke cigarettes, and adults aged 19 through 64 years who have certain medical conditions, including (not a complete list) chronic pulmonary diseases (including asthma), chronic cardiovascular diseases, and diabetes. A one-time revaccination is recommended five years after the first for some groups, including (not a complete list) patients with chronic kidney disease, those who are immunocompromised, and those vaccinated before age 65.

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Clinical Insights:
Effective Care for Patients with Diabetes Mellitus (DM)

Medications: The following medications may be recommended for patients with diabetes, depending on individual circumstances:

- Antihyperglycemic agents, including insulin.
- ACE inhibitors (or angiotensin-2 receptor blockers, if ACEI not tolerated): Reduce blood pressure, slow progression of diabetic nephropathy in those with microalbuminuria or macroalbuminuria, and reduce cardiovascular mortality.
- Diuretics, beta blockers and/or calcium-channel blockers: As needed to control hypertension and reduce cardiovascular events.
- Statins (and/or other lipid-lowering agents as needed): Reduce risk of cardiovascular events, including mortality.
- Aspirin (low-dose) (or other antiplatelet agent; i.e., clopidogrel, if aspirin is contraindicated): Primary prevention of cardiovascular (CVD) events in men over age 50 and women over age 60 with at least one additional major risk factor (family history of CVD; hypertension; smoking; dyslipidemia; or albuminuria); secondary prevention in patients with a history of CVD.

Patients with diabetes are at high risk of developing vascular disease including coronary heart disease, peripheral vascular disease, and stroke. In those with diabetes, the mortality benefit from treating hypercholesterolemia and hypertension is greater than the mortality benefit from treating elevated blood glucose. Control of hypertension also reduces the development and progression of diabetic nephropathy and retinopathy.

Blood pressure management for adults: To achieve goal <130/80. Blood pressure should be measured at each physician visit. Regimens including ACEI (or ARB if ACEI not tolerated) are recommended for patients with hypertension and microalbuminuria or macroalbuminuria.

Blood pressure management for pediatrics: Goal is BP $\leq 90^{th}$ percentile for age, sex, and height, or <130/80, whichever is lower. Treatment for BP >90th percentile should focus on lifestyle changes (including physical activity, weight loss). If BP is consistently >95th percentile for age, sex, and height, or if target BP is not reached with 6 to 12 months of lifestyle changes, medication is recommended in addition to lifestyle changes. Regimens including ACEI (or ARB if ACEI not tolerated) are recommended for patients with hypertension and microalbuminuria or macroalbuminuria.

Management of lipid levels for adults: Regardless of baseline LDL levels, most patients over the age of 40 with diabetes will benefit from statins to reduce LDL by ~30 to 40 percent. Some expert guidelines recommend higher doses of statins (as tolerated) to reach specific LDL targets (e.g., below 100 for those without CVD or below 70 for those with CVD). Trials have shown some benefit for high-dose statins compared with low-dose statins for reducing CVD events, but have not specifically compared adjusting statin dosing to achieve LDL targets. The use of combination therapy (statins and other lipid-lowering agents) has not been evaluated for CVD outcomes or safety. Lipid profile should be measured at least annually. Lipid profile may be measured every two years in patients with low-risk lipid values (LDL<100; HDL>50; TG<150).

- Patients with overt CVD: Statin therapy is recommended.
- Patients without CVD over age 40 with one or more other risk factor for CVD: Statin therapy is recommended.
- Patients without CVD under age 40: Consider statin use for those who have LDL above 100mg/dl after lifestyle intervention or for those with more than one CVD risk factor. (Recommendations regarding statins in this group are based on expert opinion rather than clinical trial evidence.)
- Type 1 diabetes: There is little evidence to guide the use of statins or the selection of LDL targets in this group. In patients with other cardiovascular risk factors, lipid goals are similar to those for patients with type 2 diabetes. This recommendation is based on expert opinion only.

Management of lipid levels for pediatrics (type 1 and 2):

- Assess lipid profile soon after diagnosis, but after glycemic control is achieved if there is a family history of high cholesterol (>240) or early coronary heart disease (CVD event before age 55) or if family history is unknown. Otherwise, the initial lipid profile can be done at puberty (age >10). Repeat every 5 years if LDL <100; annually if lipids are abnormal.
- After age 10, if LDL levels do not improve with optimal non-pharmacologic treatment, consider statin therapy in those with:
  - LDL 130-159 and one or more CVD risk factors (family history, hypertension, or smoking).
  - LDL >160.

Glycemic control for adults: A1C levels should be measured at least twice yearly in patients who are achieving glycemic goals; quarterly in patients who are not achieving goals or for whom therapy has changed.

The American Diabetes Association (ADA) guidelines recommend an A1C target of <7 percent for non-pregnant adults with type 1 and type 2 diabetes. There is good evidence that A1C targets around or below 7 percent are associated with lower rates of microvascular and neuropathic complications in type 1 and type 2 diabetes. Tight control primarily benefits patients with early microvascular and/or neuropathic complications. However, A1C targets should be individualized based on discussion about the possible benefits and harms.

There is no evidence in the immediate term that an A1C target of <7percent is associated with fewer macrovascular events. In older patients with long-standing type 2 diabetes (>8-12 years) regimens needed to achieve A1C levels <7 percent have been associated with higher risks of severe hypoglycemia. In one large well designed trial, mortality was higher among those who achieved an A1C of 6.4 percent compared to patients with an A1C of 7.5 percent. One trial suggests that there may be a reduction in long-term CVD events for a selected group of newly diagnosed patients who had three to four years of tight glycemic control.

Less stringent targets (e.g., A1C >7 percent) are appropriate for patients for whom the potential risks (including polypharmacy) of intensive glycemic control may exceed the benefits. This may include those with:

- Life expectancy <10 years.
- Advanced macrovascular complications (e.g., stage III or IV heart failure).
- Multiple comorbid conditions.
- History of severe hypoglycemia.
- Cognitive or functional impairment.
- Frailty from any cause.
- Occupations or activities in which hypoglycemic episodes could lead to injury or death.

Glycemic control for pediatrics: Some studies suggest that both recurrent severe hypoglycemia and chronic hyperglycemia may impair cognitive development in young children. Glycemic goals in children may need to be modified (i.e., relaxed) in order to achieve control while avoiding hypoglycemic episodes.

Nephropathy: Annual screening tests for **microalbuminuria** are recommended starting at diagnosis for all patients with type 2 diabetes. In patients with type 1 diabetes, begin annual screening five years after diagnosis. Annual screening is not necessary in patients on ACEI or ARB therapy. Some experts recommend continued annual screening after detection of microalbuminuria (even in patients on ACEI or ARB); however, this recommendation is controversial and not supported by trial evidence. Experts also recommend annual measurement of **serum creatinine** for estimating GFR.

Pediatric diabetes: Begin annual screening once patients reach age 10 and have had diabetes for five years.

Retinopathy: Dilated and comprehensive eye exams are recommended annually or more frequently if retinopathy is progressing. Less frequent exams (every two to three years) may be considered following one or more normal exams.

- Type 2 diabetes: Begin annual screening shortly after diagnosis.
- Type 1 diabetes: For adults and children aged 10 years and older with diabetes for 3 to 5 years, begin annual screening within five years after diagnosis.

Screening is generally not recommended before age 10. Diabetes-related eye disease that is severe enough to threaten vision is rare before puberty, but the duration of diabetes before puberty may increase the risk of diabetic retinopathy, so it is important to consider each case individually.

Neuropathy, peripheral: Experts suggest comprehensive foot examination, including testing for loss of protective sensation, annually.

- Foot care: Patients, especially those at high risk for foot conditions (e.g., with neuropathy), should examine their own feet daily.

Patient Education: Self-management education that supports patients in gaining the knowledge, skills, and abilities needed for self-care can improve clinical outcomes and quality of life. Current best practices focus on helping patients gain skills to make informed self-management choices. A **Written action plan** for responding to hypoglycemia, hyperglycemia, and sick day management is needed.

Medical Nutrition Therapy and Weight Management: Individualized therapy provided by a registered dietitian or other professional with special expertise can decrease A1C. This may include decreasing saturated and trans fat and cholesterol, and monitoring carbohydrate intake.

- Moderate weight loss (5% to 10% of body weight) in overweight and obese individuals improves glucose tolerance, reduces blood pressure, improves lipid levels, and reduces cardiovascular risks. Caloric restriction, including low-carbohydrate or low-fat diet, is needed.
- Bariatric surgery should be considered in carefully selected patients with type 2 diabetes and BMI ≥ 35.

Physical Activity: Encourage 150 minutes of aerobic physical activity per week and resistance training 3 times per week unless contraindicated.

Smoking cessation: All patients and avoidance of secondary smoke.

Depression: Chronic disease is a risk factor for depression. Screening improves the accurate identification of depression in primary care settings, and treatment of depressed adults identified in primary care settings decreases clinical morbidity. Two simple questions may be used as a screening tool ("Over the past two weeks, have you felt down, depressed, or hopeless?" and "Over the past two weeks, have you felt little interest or pleasure in doing things?"). Patients who screen positive should be referred for further evaluation and diagnosis.

Influenza vaccine (seasonal): Annually for all children aged 6 months through 18 years, adults aged 50 and older, and adults aged 19 through 49 years with chronic pulmonary diseases (including asthma and COPD); chronic cardiovascular diseases (including coronary heart disease and heart failure); and chronic metabolic diseases (including diabetes). In addition, household contacts or caregivers of people in these groups. (Children aged <6 months should not receive influenza vaccination).

Pneumococcal vaccine: All adults aged 65 and older, adults who smoke cigarettes, and adults aged 19 through 64 years who have certain medical conditions, including (not a complete list) chronic pulmonary diseases (including asthma), chronic cardiovascular diseases, and diabetes. A one-time revaccination is recommended five years after the first for some groups, including (not a complete list) patients with chronic kidney disease, those who are immunocompromised, and those vaccinated before age 65.

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Clinical Insights:
Effective Care for Patients with Heart Failure (HF)

NOTE: The material in these insights is primarily intended for use in patients with symptomatic reduced left ventricular ejection fraction (LVEF) (i.e., stage C and D heart failure). Treatment objectives for patients with primarily diastolic dysfunction (i.e., those with normal or near-normal ejection fraction) are similar at this time; trials are under way to determine optimal evidence-based management strategies for this population. Management approaches differ for patients with heart failure secondary to valvular causes; these are not discussed here.

Fluid balance: Changes in volume status often precede onset of clinical exacerbations by several days. Patients are advised to **restrict sodium intake** and **record their weight daily**. A **written action plan** may instruct patients to notify their physician or adjust medication (diuretic) doses in response to predetermined changes in body weight and/or symptoms; this approach may reduce the incidence of clinical deterioration.

Medications: The following medications may be recommended for patients with HF, depending on individual circumstances:

- **Diuretics:** Regulate volume status and improve symptoms and exercise tolerance.
- **Aldosterone antagonist** (e.g., spironolactone): In patients with moderately severe to severe symptoms despite optimal use of other medications. May reduce mortality and hospitalizations. Weigh potential benefits against increased risk of hyperkalemia (ideally creatinine should be <2.5 and supplemental potassium discontinued).
- **ACE inhibitors** (or angiotensin-2 receptor blockers, if ACEI not tolerated): Relieve symptoms, improve clinical status, and reduce mortality and hospitalization.
- **Beta blockers** (specifically bisoprolol, carvedilol, or sustained-release metoprolol): Reduce symptoms, improve clinical status, and reduce mortality and hospitalization.
- **Hydralazine plus a nitrate:**
  - May be added to ACEI and beta blockers in patients who have persistent symptoms.
  - May be reasonable in patients with HF symptoms who cannot take ACEIs or ARBs.
  - Has been found to reduce mortality in patients of African descent who have moderate to severe symptoms while on ACE inhibitors, beta blockers, and diuretics. The effect of this combination in other patients who are on standard therapy is not known, but there is no reason to believe that this benefit is limited to patients of African descent.
- **Digitalis (in many cases):** Improve symptoms, exercise tolerance, and quality of life; and reduce hospitalization in patients with persistent symptoms.
- **Aspirin (low-dose)** or other antiplatelet agent: When otherwise indicated (e.g., HF of ischemic origin or patients with drug-eluting stent) to reduce risk of cardiovascular events. However, aspirin use is controversial in patients with chronic HF because there is some evidence that it may reduce the benefits of ACEI. Clopidogrel may not attenuate ACEI benefits, but has not been shown to improve HF outcomes.
- **Statins:** As appropriate for lipid management per National Cholesterol Education Program guidelines.

Blood pressure management: To achieve goal <130/80, if tolerated. In trials, optimal outcomes are seen at SBP 110 to 130. Blood pressure should be measured at each physician visit. Particularly in elderly patients, care should be taken to avoid postural hypotension. [NOTE: neither JNC-VII nor 2009 ACC/AHA HF guideline specifies a particular BP goal.]

Management of lipid levels with therapeutic lifestyle changes and medications, if needed, in accordance with recommended guidelines. Based on current evidence, the majority of the benefit of statins for patients with co-morbid CHD and CHD-risk equivalents is achieved by lowering LDL by 30 percent to 40 percent. Lipid profile should be measured at least annually.

Physical activity: Improvements in symptoms, exercise capacity, and quality of life have been found in context of formal programs involving 20-45 minutes, 3-5 days a week of aerobic exercise. Alternatively, several short periods per day, as tolerated.

Smoking cessation: All patients and avoidance of secondary smoke.

Devices: In selected patients with clinical indications, consideration of cardiac resynchronization therapy (CRT) and/or implantable cardioverter-defibrillator (ICD) placement may be appropriate.

- ICD: In selected patients (e.g., history of cardiac arrest and sustained ventricular arrhythmias) with reduced LVEF and otherwise good prognosis, ICD placement may be considered to reduce risk of sudden death. The balance of risks and benefits, and the possible reasons and process for future deactivation of the device should be discussed.

- CRT: In selected patients with documented cardiac dyssynchrony, LVEF ≤35%, and persistent symptoms despite optimal medical therapy, CRT use may improve symptoms, exercise capacity, quality of life, and survival, and decrease hospitalization.

Depression: Chronic disease is a risk factor for depression. Screening improves the accurate identification of depression in primary care settings, and treatment of depressed adults identified in primary care settings decreases clinical morbidity. Two simple questions may be used as a screening tool ("Over the past two weeks, have you felt down, depressed, or hopeless?" and "Over the past two weeks, have you felt little interest or pleasure in doing things?"). Patients who screen positive (i.e., those who answer 'yes' to either question) should undergo full diagnostic interview. In addition, anxiety associated with chronic dyspnea may be a major cause of decreased quality of life for patients with HF, and appropriate treatment may improve outcomes.

Influenza vaccine (seasonal): Annually for all children aged 6 months through 18 years, adults aged 50 and older, and adults aged 19 through 49 years with chronic pulmonary diseases (including asthma and COPD); chronic cardiovascular diseases (including coronary heart disease and heart failure); and chronic metabolic diseases (including diabetes). In addition, household contacts or caregivers of people in these groups. (Children aged <6 months should not receive influenza vaccination).

Pneumococcal vaccine: All adults aged 65 and older, adults who smoke cigarettes, and adults aged 19 through 64 years who have certain medical conditions, including (not a complete list) chronic pulmonary diseases (including asthma), chronic cardiovascular diseases, and diabetes. A one-time revaccination is recommended five years after the first for some groups, including (not a complete list) patients with chronic kidney disease, those who are immunocompromised, and those vaccinated before age 65.

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Clinical Insights:
Effective Care for Primary Prevention of Stroke

Individuals with hypertension, diabetes, and atherosclerotic vascular disease (coronary heart disease, heart failure, or peripheral vascular disease) are at increased risk of stroke. Management approaches for these other conditions (e.g., use of statins) can also reduce stroke risk.

Individualized risk assessment: Use of a stroke risk-assessment tool (e.g., Framingham Stroke Profile) to estimate risk of first stroke and guide appropriate use of interventions to modify risk factors and/or further diagnostic testing. Risk assessment should include screening for hypertension and diabetes as per established guidelines. Note that age and sex are important non-modifiable risk factors.

Depending on individual circumstances, management of the following modifiable risk factors can reduce the risk of first stroke:

Blood pressure management, in patients with hypertension (>140/90) or isolated systolic hypertension (SBP >160 and DBP <90) in older adults, according to established guidelines (i.e., JNC-7, which defines optimal BP as <120/80).

Smoking cessation: All patients and avoidance of secondary smoke.

Diabetes screening and management, with emphasis on tight control of hypertension (target <130/80) in patients with diabetes. It is not clear that intensive glycemic control (i.e., target A1C <7 percent) reduces stroke risk. (ACCORD/ADVANCE showed no difference in stroke rates for intensive vs. traditional glycemic control.) For individuals with additional cardiovascular risk factors (e.g., age >40, elevated LDL, etc.), a statin is recommended.

For patients with atherosclerotic vascular disease, management of these other conditions can reduce stroke risk.

Antithrombotic/anticoagulant therapy:

- *Aspirin:* encouraged for women aged 55 to 79 years when the potential benefit of reduction in ischemic stroke outweighs the potential harms of gastrointestinal bleeding; shared decision making should be encouraged when the benefits and risks are closely balanced (Fig. 4 below; USPSTF, 2009). Aspirin is **not recommended** for the primary prevention of stroke in men.
- *Atrial fibrillation with valvular disease:* anticoagulation (warfarin).
- *Atrial fibrillation, nonvalvular (permanent):* Choice of regimen (aspirin vs. warfarin) should be based on risk stratification (e.g., the $CHADS_2$ score, a clinical prediction rule for estimating stroke risk in patients with atrial fibrillation), consideration of the expected net clinical benefit of warfarin (rate of events prevented by warfarin minus intracranial hemorrhages attributable to warfarin), availability of high-quality monitoring services, and patient preference. [See additional information in *Clinical Insights: Atrial Fibrillation*.]
- *Patients with mechanical heart valves (with or without atrial fibrillation):* anticoagulation, with target level depending on location of valves and other patient factors.

Management of lipid levels with therapeutic lifestyle changes and medications, if needed, in accordance with recommended guidelines (i.e., NCEP). In a recent large trial, use of rosuvastatin (Crestor®) in people (average age 66 years) with LDL<130 and hs-CRP (high-sensitivity C-reactive protein) ≥2 mg/L reduced incidence of stroke from about 4 to 2 per 1000 patients per year. At this time, however, it is not clear that routine screening and treatment for elevated hs-CRP in healthy people with normal LDL is warranted.

Physical activity: Recommendations according to established guidelines (i.e., ≥30 minutes of moderate-intensity physical activity most days of the week).

Weight management: According to established guidelines. Weight reduction lowers blood pressure.

Carotid endarterectomy, in carefully selected individuals; i.e., those with high-grade asymptomatic carotid stenosis and life expectancy of at least five years in settings where the peri-procedural risk (i.e., within 30 days) of stroke and death is <3%.

- Patient selection should be guided by assessment of the patient's overall health, life expectancy, and preferences.
- Older age (>80 years) and other comorbidities (such as coronary heart disease and diabetes) can greatly increase the short-term risk of death or stroke due to carotid surgery, and alter the risk-benefit ratio.
- Screening for asymptomatic carotid stenosis is not recommended.

Depression: Screening is always appropriate for patients with any chronic condition. Screening improves the accurate identification of depression in primary care settings, and treatment of adults identified in primary care settings decreases clinical morbidity. Two simple questions may be used as a screening tool ("Over the past two weeks, have you felt down, depressed, or hopeless?" and "Over the past two weeks, have you felt little interest or pleasure in doing things?") Patients who screen positive (i.e., who answer 'yes' to either question) should undergo full diagnostic interview.

Influenza vaccine (seasonal): Annually for all children aged 6 months through 18 years, adults aged 50 and older, and adults aged 19 through 49 years with chronic pulmonary diseases (including asthma and COPD); chronic cardiovascular diseases (including coronary heart disease and heart failure); and chronic metabolic diseases (including diabetes). In addition, household contacts or caregivers of people in these groups. (Children aged <6 months should not receive influenza vaccination).

Pneumococcal vaccine: All adults aged 65 and older, adults who smoke cigarettes, and adults aged 19 through 64 years who have certain medical conditions, including (not a complete list) chronic pulmonary diseases (including asthma), chronic cardiovascular diseases, and diabetes. A one-time revaccination is recommended five years after the first for some groups, including (not a complete list) patients with chronic kidney disease, those who are immunocompromised, and those vaccinated before age 65.

Source: U.S. Preventive Services Task Force, 2009

Aspirin for the Prevention of Cardiovascular Disease

http://www.ahrq.gov/clinic/uspstf09/aspirincvd/aspcvdrs.htm#clinical

Figure 4. Estimated number of strokes prevented and estimated harms of using aspirin for 10 years in a hypothetical cohort of 1000 women on the basis of age and 10-year stroke risk.

As indicated, the estimated number of strokes avoided varies with 10-year stroke risk. The estimated harms of using aspirin vary with age. Therefore, both 10-year stroke risk and age must be considered when determining whether the potential harms of aspirin use outweigh the potential benefit in terms of strokes prevented. The shaded areas indicate the combinations of 10-year stroke risk and age for which the number of harms (GI bleeding) are greater than the number of strokes prevented.*

Variable	Estimated Strokes Prevented (per 1000 Women), *n*		
	Age 55–59 Years	Age 60–69 Years	Age 70–79 Years
10-year stroke risk			
1%	1.7	1.7	1.7
2%	3.4	3.4	3.4
3%	5.1	5.1	5.1
4%	6.8	6.8	6.8
5%	8.5	8.5	8.5
6%	10.2	10.2	10.2
7%	11.9	11.9	11.9
8%	13.6	13.6	13.6
9%	15.3	15.3	15.3
10%	17	17	17
11%	18.7	18.7	18.7
12%	20.4	20.4	20.4
13%	22.1	22.1	22.1
14%	23.8	23.8	23.8
15%	25.5	25.5	25.5
16%	27.2	27.2	27.2
17%	28.9	28.9	28.9
18%	30.6	30.6	30.6
19%	32.3	32.3	32.3
20%	34	34	34
	Estimated Harm, *n*		
Type of event			
GI bleeding	4	12	18

* Calculations of estimated benefits and harms rely on assumptions and are by nature somewhat imprecise. Estimates of benefits and harms, especially at the borders of the shaded and unshaded areas, should be considered in the full context of clinical decision making and used to stimulate shared decision making. The calculations in the table are based on the following assumptions: that there is a 17% risk reduction of strokes with regular aspirin use (3) and that gastrointestinal bleeding includes serious hemorrhage, perforation, or other complications leading to hospitalization or death. Harm of GI bleeding in the table assumes that risk for GI bleeding increases with age and that the women are not taking nonsteroidal anti-inflammatory drugs, do not have upper GI pain, or do not have a history of GI ulcer (2). "Strokes prevented" is the net reduction of strokes, which includes a decrease in ischemic strokes and a small increase in hemorrhagic strokes.

Clinical Insights:
Effective Care for Secondary Prevention of Stroke in Patients with Prior Transient Ischemic Attack or Stroke

The following approaches are appropriate for all patients with ischemic stroke or transient ischemic attack (TIA), regardless of mechanism. About 20 percent of ischemic strokes are associated with cardiogenic cerebral embolism; about half of these occur in patients with a history of atrial fibrillation. (A full discussion of secondary prevention strategies in patients with cardioembolic strokes secondary to conditions such as valvular heart disease, cardiomyopathy, and acute myocardial infarction is outside the scope of this review; see the AHA/ASA Guidelines for Prevention of Stroke in Patients with Ischemic Stroke or Transient Ischemic Attack.)

Risk factor control, including:

- **Blood pressure management:** All patients, including those with no history of hypertension, according to established guidelines (i.e., JNC-7). In general, target BP <140/90 is appropriate; however, the optimal target is uncertain, and benefits are seen with reductions of about 10/5 mm Hg from baseline. Choice of agents should be individualized; available data support the use of diuretics alone or combined with an ACE inhibitor.
  - **Diabetes**: More rigorous blood pressure control should be considered in *patients with diabetes* (target <130/80); a regimen that includes an ACE inhibitor or ARB is recommended for those with hypertension.
- **Management of lipid levels** according to established guidelines for patients with coronary heart disease. (For established guidelines refer to *Management of lipid levels* section of the Clinical Insights: Effective Care for Patients with Coronary Heart Disease (CHD)). For those with atherosclerotic ischemic stroke or TIA and without known CHD, statins are recommended and reduce recurrent stroke rates.
- **Antiplatelet therapy:** Aspirin, alone or with extended-release dipyridamole, or clopidogrel alone, as appropriate based on individual patient characteristics and preferences.
- **For patients with cardioembolic stroke and atrial fibrillation:** warfarin therapy is recommended (aspirin for those who cannot take warfarin). There is no evidence that increasing the intensity of anticoagulation or adding another antiplatelet agent offers additional protection against future ischemic events.
- **Smoking cessation:** All patients and avoidance of secondary smoke.
- **Reduce alcohol consumption:** In patients who consume >five alcoholic beverages per day.
- **Weight management:** Weight reduction may be considered with goal BMI of 18.5 to 24.9 or waist circumference <35 women and <40 men. Weight reduction lowers blood pressure.
- **Physical activity:** For those capable, at least 30 minutes of moderate intensity physical activity on most days. For those with disability after stroke, a supervised rehabilitation program is recommended.

For patients with TIA or stroke and documented carotid artery disease:

- Continued maximal medical therapy: as outlined above.
- Carotid endarterectomy in appropriately selected patients with symptomatic carotid stenosis (>50 percent):
  - In patients with history of carotid TIA or stroke in the past 12 months, carotid endarterectomy reduces the risk of subsequent stroke in settings where the procedure can be done with 30-day stroke and death rates <6 percent.
  - Recommendation for carotid endarterectomy should consider patient age, sex, comorbidities, severity of initial symptoms, and preferences. Older age (>80 years) and other comorbidities (such as coronary artery disease and diabetes) can greatly increase the short-term risk of death or stroke due to carotid surgery, and alter the risk-benefit ratio.

Depression: Screening is always appropriate for patients with any chronic condition. Screening improves the accurate identification of depression in primary care settings, and treatment of adults identified in primary care settings decreases clinical morbidity. Two simple questions may be used as a screening tool ("Over the past two weeks, have you felt down, depressed, or hopeless?" and "Over the past two weeks, have you felt little interest or pleasure in doing things?") Patients who screen positive (i.e., who answer 'yes' to either question) should undergo full diagnostic interview.

Influenza vaccine (seasonal): Annually for all children aged 6 months through 18 years, adults aged 50 and older, and adults aged 19 through 49 years with chronic pulmonary diseases (including asthma and COPD); chronic cardiovascular diseases (including coronary heart disease and heart failure); and chronic metabolic diseases (including diabetes). In addition, household contacts or caregivers of people in these groups. (Children aged <6 months should not receive influenza vaccination).

Pneumococcal vaccine: All adults aged 65 and older, adults who smoke cigarettes, and adults aged 19 through 64 years who have certain medical conditions, including (not a complete list) chronic pulmonary diseases (including asthma), chronic cardiovascular diseases, and diabetes. A one-time revaccination is recommended five years after the first for some groups, including (not a complete list) patients with chronic kidney disease, those who are immunocompromised, and those vaccinated before age 65.

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