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Asthma in Pregnancy

Asthma is a common, potentially serious medical condition that complicates approximately 4–8% of pregnancies (1, 2). In general, the prevalence of and morbidity from asthma are increasing, although asthma mortality rates have decreased in recent years. The purpose of this document is to review the best available evidence about the management of asthma during pregnancy.

This Practice Bulletin was developed by the ACOG Committee on Practice Bulletins—Obstetrics with the assistance of Mitchell P. Dombrowski, MD and Michael Schatz, MD, MS. The information is designed to aid practitioners in making decisions about appropriate obstetric and gynecologic care. These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

Background

Asthma is characterized by chronic airway inflammation, with increased airway responsiveness to a variety of stimuli, and airway obstruction that is partially or completely reversible (3). The pathogenesis of asthma involves airway inflammation in nearly all cases. Current medical management for asthma emphasizes treatment of airway inflammation in order to decrease airway responsiveness and prevent asthma symptoms.

The National Asthma Education and Prevention Program has found that “it is safer for pregnant women with asthma to be treated with asthma medications than it is for them to have asthma symptoms and exacerbations” (4). Mild and well-controlled moderate asthma can be associated with excellent maternal and perinatal pregnancy outcomes (5–7). Severe and poorly controlled asthma may be associated with increased prematurity, need for cesarean delivery, preeclampsia, growth restriction, other perinatal complications, and maternal morbidity and mortality (8–12). The ultimate goal of asthma therapy in pregnancy is maintaining adequate oxygenation of the fetus by preventing hypoxic episodes in the mother. Optimal management of asthma during pregnancy includes objective monitoring of lung function, avoiding or controlling asthma triggers, educating patients, and individualizing pharmacologic therapy to maintain normal pulmonary function. The step-care therapeutic approach uses the lowest amount of drug intervention necessary to control a patient’s severity of asthma.



Medications

Asthma medications generally are divided into long-term control medications and rescue therapy. Long-term control medications are used for maintenance therapy to prevent asthma manifestations and include inhaled corticosteroids, cromolyn, long-acting β -agonists, and theophylline. Rescue therapy, most commonly inhaled short-acting β -agonists, provides immediate relief of symptoms. Oral corticosteroids can either be used as a form of rescue therapy to treat an asthma exacerbation or as long-term control therapy for patients with severe persistent asthma.

Certain medications, possibly used during labor and delivery, have the potential to worsen asthma. Nonselective β -blockers, carboprost (15-methyl prostaglandin $F_{2\alpha}$) and ergonovine may trigger bronchospasm. Magnesium sulfate is a bronchodilator, but indomethacin can induce bronchospasm in patients who are sensitive to aspirin. Prostaglandin E_2 or prostaglandin E_1 can be used for cervical ripening, the management of spontaneous or induced abortions, or the management of postpartum hemorrhage (13).

Asthma Severity Classification

In 2004, the National Asthma Education and Prevention Program Working Group on Asthma and Pregnancy defined mild intermittent, mild persistent, moderate persistent, and severe persistent asthma according to daytime and nighttime symptoms (wheezing, coughing, or dyspnea) and objective tests of pulmonary function (4). The most commonly used pulmonary function parameters are the peak expiratory flow rate (PEFR) and forced expiratory volume in the first second of expiration (FEV_1). Current National Asthma Education and Prevention Program guidelines suggest classifying the

degree of asthma severity in patients who are not taking controller medication and the degree of asthma control in patients who are taking controller medication (Table 1).

Effects of Pregnancy on Asthma

In a large prospective study, pregnant patients with mild asthma had exacerbation rates of 12.6% and hospitalization rates of 2.3%, those with moderate asthma had exacerbation rates of 25.7% and hospitalization rates of 6.8%, and those with severe asthma had exacerbation rates of 51.9% and hospitalization rates of 26.9% (14). The effects of pregnancy on the course of asthma are variable—the symptoms of 23% of women studied improved and the symptoms of 30% became worse during pregnancy (14). Because many pregnant women have increased symptoms, pregnant patients who have asthma, even those with mild or well-controlled disease, need to be monitored with PEFR and FEV_1 testing as well as by observing their symptoms during pregnancy.

Effects of Asthma on Pregnant Women and Fetuses

There has been considerable consistency among results of prospective studies of the effects of asthma during pregnancy. Eight prospective studies, reporting maternal and infant outcomes with at least 100 participants in locations at or near sea level, have been published (5–7, 15–20). These studies show that the gravid patient with mild or moderate asthma can have excellent maternal and infant outcomes. However, suboptimal control of asthma during pregnancy may be associated with increased maternal or fetal risk (7). In fact, a significant relationship has been reported between decreased FEV_1 during pregnancy and increased risk of low birth weight and prematurity (21). Results of the two largest studies

Table 1. Classification of Asthma Severity and Control in Pregnant Patients

Asthma Severity* (Control†)	Symptom Frequency	Nighttime Awakening	Interference With Normal Activity	FEV_1 or Peak Flow (Predicted Percentage of Personal Best)
Intermittent (well controlled)	2 days per week or less	Twice per month or less	None	More than 80%
Mild persistent (not well controlled)	More than 2 days per week, but not daily	More than twice per month	Minor limitation	More than 80%
Moderate persistent (not well controlled)	Daily symptoms	More than once per week	Some limitation	60–80%
Severe persistent (very poorly controlled)	Throughout the day	Four times per week or more	Extremely limited	Less than 60%

Abbreviation: FEV_1 , forced expiratory volume in the first second of expiration

*Assess severity for patients who are not taking long-term-control medications.

†Assess control in patients taking long-term-control medications to determine whether step-up therapy, step-down therapy, or no change in therapy is indicated.

indicate that classification of asthma severity and therapy tailored according to asthma severity can result in excellent infant and maternal outcomes (6, 7).

There are important caveats when interpreting the study results of asthma in pregnancy. Fewer considerable adverse associations have been found in the results of prospective studies, possibly because of better asthma surveillance and treatment. The excellent maternal and infant outcomes were achieved at centers that tended to manage asthma in pregnancy actively. In addition, women who enroll in research studies tend to be more motivated and adhere to therapeutic regimens more than the general public. The lack of more adverse outcomes among women with severe asthma also may be a function of the relatively small number of participants in this cohort and the resulting lack of power to find adverse outcomes that were statistically significant. Although the results of these prospective studies are reassuring in their consensus of good pregnancy outcomes, they do not indicate that asthma should be considered a benign condition because active asthma management was a part of these studies and may have had a positive impact on the outcomes.

Clinical Considerations and Recommendations

► *How is asthma diagnosed during pregnancy?*

Diagnosis of asthma in a pregnant patient is the same as that for a nonpregnant patient. Asthma typically includes characteristic symptoms (wheezing, chest cough, shortness of breath, chest tightness), temporal relationships (fluctuating intensity, worse at night), and triggers (eg, allergens, exercise, infections). Wheezing on auscultation would support the diagnosis, but its absence does not exclude the diagnosis. Ideally, the diagnosis of asthma would be confirmed by demonstrating airway obstruction on spirometry that is at least partially reversible (greater than a 12% increase in FEV₁ after bronchodilator). However, reversible airway obstruction may not be demonstrable in some patients with asthma. In patients with a clinical picture consistent with asthma, in whom reversible airway obstruction cannot be demonstrated, a trial of asthma therapy is reasonable. In such patients, a positive response to asthma therapy can be used to diagnose asthma during pregnancy.

In patients presenting with new respiratory symptoms during pregnancy, the most common differential diagnosis would be dyspnea of pregnancy. Dyspnea of pregnancy usually can be differentiated from asthma by its lack of cough, wheezing, chest tightness, or airway obstruction. Other differential diagnoses include gastroe-

sophageal reflux, chronic cough from postnasal drip, and bronchitis.

► *How should patients with asthma be assessed during pregnancy?*

Clinical evaluation includes subjective assessments and pulmonary function tests. Because pulmonary function and asthma severity may change during the course of pregnancy, routine evaluation of pulmonary function in pregnant women with persistent asthma is recommended. For pulmonary function assessment during outpatient visits, spirometry is preferable, but peak expiratory flow measurement with a peak flow meter also is sufficient. Patients with worsening symptoms should be evaluated with peak flow measurement and lung auscultation. Severity and control of asthma should be assessed in terms of symptom exacerbation and pulmonary impairment. It is important to identify a history of prior hospitalization (especially hospital stays that required intensive care unit admission or intubation), emergency department or other unscheduled visits for asthma treatment, or oral corticosteroid requirements. In patients who are not taking controllers, it is useful to assess pulmonary impairment based on severity classification (Table 1). Patients with two or more episodes of symptom exacerbation requiring the use of oral corticosteroids in the prior 12 months also should be considered to have persistent asthma. In patients who are taking controllers, it is useful to assess control (Table 1). Assessing the impairment domain of control consists of determining the frequency of daytime symptoms, nocturnal symptoms, activity limitation, frequency of rescue therapy, and FEV₁. The assessment in a pregnant patient with asthma also should include the effect of any prior pregnancies on asthma severity or control because this may predict the course of the asthma during subsequent pregnancies.

► *Can allergy shots be started or continued during pregnancy?*

The use of allergen immunotherapy, or “allergy shots,” has been shown to be effective in improving asthma in patients with allergies (4). In two studies, no adverse effects of immunotherapy during pregnancy have been found (22, 23). However, anaphylaxis is a risk of allergen injections, especially early in the course of immunotherapy when the dose is being escalated, and anaphylaxis during pregnancy has been associated with maternal death, fetal death, or both. In a patient who is receiving a maintenance or near-maintenance dose, not experiencing adverse reactions to the injections and apparently deriving clinical benefit, continuation of immunotherapy is recommended. In such patients, a

dose reduction may be considered to further decrease the chance of anaphylaxis. Risk–benefit considerations do not usually favor beginning allergen immunotherapy during pregnancy.

► **What is appropriate rescue therapy for asthma during pregnancy?**

Inhaled short-acting β_2 -agonists are the rescue therapy of choice for asthma during pregnancy. Inhaled albuterol is the first-choice, short-acting β_2 -agonist for pregnant women, although other agents also may be appropriate. In general, patients should use up to two treatments of inhaled albuterol (two to six puffs) or nebulized albuterol at 20-minute intervals for most mild to moderate symptoms; higher doses can be used for severe symptom exacerbation. To avoid maternal and fetal hypoxia, patients should be counseled to start rescue therapy at home when they have an exacerbation of symptoms, such as coughing, chest tightness, dyspnea, wheezing, or a 20% decrease in the PEFr. With a good response (ie, symptoms reduce or resolve, and the PEFr reaches 80% of personal best) the patient can continue normal activity. If the patient does not have a good response or if she notices a decrease in fetal activity, she should seek medical attention quickly.

► **What is first-line controller therapy for asthma during pregnancy?**

For those with mild, intermittent asthma, no controller therapy is indicated. Use of inhaled corticosteroids is first-line controller therapy for persistent asthma during pregnancy. For patients with mild, persistent asthma, the use of low-dose inhaled corticosteroids is recommended (see the box). For patients with moderate persistent asthma or whose symptoms are not controlled with the use of low-dose inhaled corticosteroids, the use of medium-dose inhaled corticosteroids or low-dose inhaled corticosteroids and long-acting β -agonists are indicated. See Table 2 for typical inhaled corticosteroid regimens. Budesonide is the preferred inhaled corticosteroid for use during pregnancy (4). However, there are no data indicating that the other inhaled corticosteroid preparations are unsafe during pregnancy. Therefore, the use of any inhaled corticosteroids may be continued in patients whose asthma was well controlled by these agents before pregnancy (4).

► **What is appropriate add-on controller therapy for asthma during pregnancy?**

Use of long-acting β_2 -agonists is the preferred add-on controller therapy for asthma during pregnancy. This therapy should be added when patients' symptoms are

Step Therapy Medical Management of Asthma During Pregnancy

Mild Intermittent Asthma

- No daily medications, albuterol as needed

Mild Persistent Asthma

- Preferred—Low-dose inhaled corticosteroid
- Alternative—Cromolyn, leukotriene receptor antagonist, or theophylline (serum level 5–12 mcg/mL)

Moderate Persistent Asthma

- Preferred—Low-dose inhaled corticosteroid and salmeterol or medium-dose inhaled corticosteroid or (if needed) medium-dose inhaled corticosteroid and salmeterol
- Alternative—Low-dose or (if needed) medium-dose inhaled corticosteroid and either leukotriene receptor antagonist or theophylline (serum level 5–12 mcg/mL)

Severe Persistent Asthma

- Preferred—High-dose inhaled corticosteroid and salmeterol and (if needed) oral corticosteroid
- Alternative—High-dose inhaled corticosteroid and theophylline (serum level 5–12 mcg/mL) and oral corticosteroid if needed

not controlled with the use of medium-dose inhaled corticosteroids. Alternative add-on therapies are theophylline or leukotriene receptor antagonists (montelukast, zafirlukast). However, the use of long-acting inhaled β_2 -agonists is preferred because it has been shown to be a more effective add-on therapy in nonpregnant patients than leukotriene receptor antagonists or theophylline. Long-acting inhaled β_2 -agonists have fewer side effects than theophylline, which has a narrow therapeutic index and requires serum monitoring, and there are few data on the use of leukotriene receptor antagonists in humans during pregnancy. See Table 2 for typical medication dosages. Because long-acting and short-acting inhaled β_2 -agonists have similar pharmacology and toxicology, long-acting inhaled β_2 -agonists are expected to have a safety profile similar to that of albuterol. Two long-acting inhaled β_2 -agonists are available: 1) salmeterol and 2) formoterol. Limited observational data exist on their use during pregnancy. A step-wise approach to management is advised in order to achieve control. See the box for specific therapy.

For patients whose symptoms are not well controlled (Table 1) with the use of medium-dose inhaled corticosteroids and long-acting inhaled β_2 -agonists, treatment should be advanced to high-dose inhaled corticosteroids

Table 2. Comparative Daily Doses for Inhaled Corticosteroids*

Corticosteroid	Amount	Low Dose	Medium Dose	High Dose
Beclomethasone HFA	40 mcg per puff	2–6 puffs	More than 6–12 puffs	More than 12 puffs
	80 mcg per puff	1–3 puffs	More than 3–6 puffs	More than 6 puffs
Budesonide	200 mcg per inhalation	1–3 puffs	More than 3–6 puffs	More than 6 puffs
Flunisolide	250 mcg per puff	2–4 puffs	4–8 puffs	More than 8 puffs
Fluticasone HFA	44 mcg per puff	2–6 puffs		
	110 mcg per puff	2 puffs	2–4 puffs	More than 4 puffs
	220 mcg per puff		1–2 puffs	More than 2 puffs
Fluticasone DPI	50 mcg per inhalation	2–6 puffs		
	100 mcg per inhalation	1–3 puffs	3–5 puffs	More than 5 puffs
	250 mcg per inhalation	1 puff	2 puffs	More than 2 puffs
Mometasone	200 mcg per inhalation	1 puff	2 puffs	More than 2 puffs
Triamcinolone	75 mcg per puff	4–10 puffs	10–20 puffs	More than 20 puffs

*Total daily puffs is usually divided into a twice-per-day regimen.

Abbreviations: DPI, dry powder inhaler; HFA, hydrofluoroalkane

Adapted from National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert panel report 3: guidelines for the diagnosis and management of asthma. NIH Publication No. 07-4051. Bethesda (MD): NHLBI; 2007. Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>. Retrieved September 10, 2007.

(Table 2) and long-acting inhaled β_2 -agonists (salmeterol, one puff twice daily). Some patients with severe asthma may require regular oral corticosteroid use to achieve adequate asthma control. For patients whose symptoms are very poorly controlled (Table 1), a course of oral corticosteroids may be necessary to attain control, along with a step up in therapy, as described previously and in the box.

► *What nonpharmacologic approaches should be used for asthma during pregnancy?*

Identifying and controlling or avoiding factors, such as allergens and irritants, that contribute to asthma severity, particularly tobacco smoke, can lead to improved maternal well-being with less need for medication (4). If gastroesophageal reflux is exacerbating the patient's asthma, nonpharmacologic measures, such as elevating the head of the bed, eating smaller meals, not eating within 2–3 hours of bedtime, and avoiding triggering foods, may help. Asthma control is enhanced by ensuring access to education about asthma, the interrelationships between asthma and pregnancy, and the skills necessary to manage asthma. These skills include self-monitoring, correct use of inhalers, following a plan for long-term management of asthma, and promptly handling signs of worsening asthma (4). Specific measures to reduce mold, dust mite exposure, animal dander, cockroaches, and other environmental triggers may be important. Animal dander control entails removing the animal from the home or, at a minimum, keeping the animal out of the patient's bed-

room. Cockroaches can be controlled by poison or bait traps and eliminating exposed food or garbage.

► *How should asthma therapy be adjusted during pregnancy?*

The step-care therapeutic approach increases the number and dosage of medications with increasing asthma severity (see the box). At each step of therapy, medications are considered to be “preferred” or “alternative” based on efficacy and safety considerations. Patients whose symptoms are not optimally responding to treatment should receive a step up in treatment to more intensive medical therapy. Once control is achieved and sustained for several months, a step-down approach can be considered, but a change in therapy should be undertaken cautiously and administered gradually to avoid compromising the stability of the asthma control. For some patients, it may be prudent to postpone, until after birth, a reduction of therapy that is effectively controlling the patient's asthma (4).

► *How should acute asthma be assessed during pregnancy?*

Initial assessment of a pregnant patient presenting with acute asthma includes obtaining a brief medical history, performing a physical examination, and examining physiologic measures of airway function and fetal well-being. Pulmonary physiologic assessment includes measuring FEV₁ or PEF and oxygen saturation. Fetal assessment

depends on the stage of pregnancy, but continuous electronic fetal monitoring or biophysical profile or both should be considered if the pregnancy has reached the stage of fetal viability.

After initial treatment, repeat assessments of the patient and fetus will determine the need for continuing care. Patients with FEV₁ or PEF_R measurements greater than or equal to 70% sustained for 60 minutes after last treatment, no distress, and reassuring fetal status may be discharged. For an incomplete response (FEV₁ or PEF_R measurements greater than or equal to 50% but less than 70%, mild or moderate symptoms), the disposition (continued treatment in the emergency department, discharge home, or hospitalization) will need to be individualized. For patients with a poor response (FEV₁ or PEF_R measurements less than 50%), hospitalization is indicated. For patients with a poor response and severe symptoms, drowsiness, confusion, or PCO₂ level greater than 42 mm Hg, intensive care unit admission is indicated and intubation should be strongly considered.

► ***What should be the discharge regimen after an acute asthma episode?***

Patients discharged after an acute asthmatic episode should continue treatment with short-acting β₂-agonists, two to four puffs every 3–4 hours as needed. Oral corticosteroids should be continued at a dose of 40–60 mg in a single dose or two divided doses for 3–10 days. Inhaled corticosteroids should be initiated or continued until review at medical follow-up. Outpatient follow-up should be arranged within 5 days of the acute visit.

► ***What are considerations for fetal surveillance in pregnancies complicated by asthma?***

Ultrasound examinations and antenatal fetal testing should be considered for women who have moderate or severe asthma during pregnancy. First-trimester ultrasound dating should be performed, if possible, to facilitate subsequent evaluations of fetal growth restriction and the risk of preterm birth. Serial ultrasound examinations to monitor fetal activity and growth should be considered (starting at 32 weeks of gestation) for women who have poorly controlled asthma or moderate-to-severe asthma and for women recovering from a severe asthma exacerbation. All patients should be instructed to be attentive to fetal activity.

► ***What intrapartum concerns are unique to pregnant women with asthma?***

Asthma medication use should not be discontinued during labor and delivery. The patient should be kept hydrated

and should receive adequate analgesia in order to decrease the risk of bronchospasm. Women who are currently receiving or recently have taken systemic corticosteroids should receive intravenous administration of corticosteroids (eg, hydrocortisone 100 mg every 8 hours) during labor and for 24 hours after delivery to prevent adrenal crisis (4).

Cesarean delivery for acute exacerbation of asthma is rarely needed. Maternal and fetal compromise usually will respond to aggressive medical management. However, delivery may benefit the respiratory status of a patient with unstable asthma who has a mature fetus. Lumbar anesthesia can reduce oxygen consumption and minute ventilation during labor (24). Regional anesthesia was reported to incur a 2% incidence of bronchospasm (25). Obstetric, anesthetic, and pediatric staff should communicate to coordinate intrapartum and postpartum care.

► ***How should women with asthma be counseled about breastfeeding?***

In general, only small amounts of asthma medications enter breast milk. The National Asthma Education and Prevention Program found that the use of prednisone, theophylline, antihistamines, inhaled corticosteroids, β₂-agonists, and cromolyn is not contraindicated for breastfeeding (4, 26).

Summary of Recommendations and Conclusions

The following recommendations and conclusions are based on limited or inconsistent scientific evidence (Level B):

- It is safer for pregnant women with asthma to be treated with asthma medications than it is for them to have asthma symptoms and exacerbations.
- Clinical evaluation of asthma includes subjective assessments and pulmonary function tests.
- The ultimate goal of asthma therapy in pregnancy is maintaining adequate oxygenation of the fetus by preventing hypoxic episodes in the mother.
- The step-care therapeutic approach increases the number and dosage of medications with increasing asthma severity.
- Inhaled corticosteroids are first-line controller therapy for persistent asthma during pregnancy.

- ▶ Budesonide is the preferred inhaled corticosteroid for use during pregnancy.
- ▶ Inhaled albuterol is recommended rescue therapy for pregnant women with asthma.
- ▶ Identifying and controlling or avoiding factors such as allergens and irritants, particularly tobacco smoke, can lead to improved maternal well-being with less need for medication.
- ▶ Continuation of immunotherapy is recommended in patients who are at or near a maintenance dose, not experiencing adverse reactions to the injections, and apparently deriving clinical benefit.
- ▶ Use of prednisone, theophylline, antihistamines, inhaled corticosteroids, β_2 -agonists, and cromolyn is not contraindicated for breastfeeding.

The following recommendations and conclusions are based primarily on consensus and expert opinion (Level C):

- ▶ Asthma self-management skills, including self-monitoring, correct use of inhalers, and following a plan for long-term management of asthma and promptly handling signs of worsening asthma, enhance asthma control.
- ▶ For pulmonary function assessment of patients during outpatient visits, spirometry is preferable, but peak expiratory flow measurement with a peak flow meter also is sufficient.
- ▶ Ultrasound examinations and antenatal fetal testing should be considered for women who have moderate or severe asthma during pregnancy.
- ▶ Pregnant patients with asthma, even those with mild or well-controlled disease, need to be monitored with PEF_R and FEV₁ testing as well as by observing their symptoms during pregnancy.
- ▶ Routine evaluation of pulmonary function in pregnant women with persistent asthma is recommended.
- ▶ Because pulmonary function and asthma severity may change during the course of pregnancy, routine evaluation of pulmonary function in pregnant women with persistent asthma is recommended.

Proposed Performance Measure

The percentage of pregnant patients with persistent asthma who have undergone pulmonary function testing

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The MEDLINE database, the Cochrane Library, and ACOG’s own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985 and March 2007. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

- Level A—Recommendations are based on good and consistent scientific evidence.
- Level B—Recommendations are based on limited or inconsistent scientific evidence.
- Level C—Recommendations are based primarily on consensus and expert opinion.

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