Screening for Iron Deficiency Anemia and Iron Supplementation in Pregnant Women to Improve Maternal Health and Birth Outcomes: U.S. Preventive Services Task Force Recommendation Statement

Albert L. Siu, MD, MSPH, on behalf of the U.S. Preventive Services Task Force*

Description: Update of the 2006 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for iron deficiency anemia.

Methods: The USPSTF reviewed the evidence on the association between change in iron status as a result of intervention (oral supplementation or treatment) in pregnant women and adolescents and improvement in maternal and infant health outcomes.

Population: This recommendation applies to pregnant women and adolescents living in the United States who do not have symptoms of iron deficiency anemia. It does not address pregnant women who are malnourished, have symptoms of iron deficiency anemia, or have special hematologic conditions or nutritional needs that may increase their need for iron.

Recommendations: The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in pregnant women to prevent adverse maternal health and birth outcomes. (I statement)

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of routine iron supplementation for pregnant women to prevent adverse maternal health and birth outcomes. (I statement)


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* For a list of USPSTF members, see the Appendix (available at www.annals.org).

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The U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

Summary of Recommendations and Evidence

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in pregnant women to prevent adverse maternal health and birth outcomes. (I statement)

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of routine iron supplementation for pregnant women to prevent adverse maternal health and birth outcomes. (I statement)

See the Clinical Considerations section for suggestions for practice regarding the I statements.

See the Figure for a summary of the recommendation and suggestions for clinical practice. Appendix Table 1 describes the USPSTF grades, and Appendix Table 2 describes the USPSTF classification of levels of certainty about net benefit (both tables are available at www.annals.org).

Rationale

Importance

The aims of iron supplementation or screening for and treatment of iron deficiency anemia in pregnant women are to improve maternal and infant health outcomes. Few data are available to estimate the current prevalence of iron deficiency anemia in pregnant women in the United States. Based on older data from 1999 to 2006, an estimated 18.6% of pregnant women have iron deficiency; of those, an estimated 16.2% have

See also:

Summary for Patients ....................... I-23
Related article: Ann Intern Med. 2015;162:566-76
Web-Only Consumer Fact Sheet
anemia (1). Rates may be higher in low-income and minority populations (1, 2).

**Detection and Recognition of Risk Status**

The USPSTF found inadequate evidence that specifically addressed the accuracy of screening tests in asymptomatic pregnant women. The USPSTF found inadequate evidence to evaluate risk prediction tools to identify pregnant women who are at increased risk for iron deficiency anemia.

**Benefits of Early Detection and Treatment Screening**

The USPSTF found inadequate evidence on screening for iron deficiency anemia in asymptomatic pregnant women. No studies evaluated the direct effects of routine screening in asymptomatic pregnant women on maternal health or birth outcomes. The USPSTF also found inadequate evidence on the treatment of iron deficiency anemia in pregnant women because none of the recent studies on treatment were generalizable to the general U.S. population. This represents a critical gap in the evidence.

**Preventive Medication**

Overall, the USPSTF found inadequate evidence on the effect of routine iron supplementation during pregnancy on maternal health or birth outcomes, such as maternal iron deficiency anemia, cesarean delivery, preterm delivery, infant mortality, or low birthweight. Several studies reported inconsistent findings on these health outcomes. The USPSTF found adequate evidence that routine iron supplementation during pregnancy improves intermediate maternal hematologic indexes, such as serum ferritin and hemoglobin levels. The USPSTF found adequate evidence that routine iron supplementation during pregnancy has no effects on the length of gestation and infant Apgar scores at 1 and 5 minutes.

**Change in Iron Status**

No studies were found that directly assessed the association between change in iron status as a result of treatment or supplementation and improvement in maternal or infant health outcomes. This represents a critical gap in the evidence.
Potential Preventable Burden

**I Statement**

Suggestions for Practice Regarding the

current general U.S. population.

### Preventive Medication

The USPSTF found adequate evidence that the
magnitude of the harms of routine iron supplementa-
tion in pregnant women is small to none. Several stud-
ies assessed the harms of iron supplementation in
pregnant women. Most reported no statistically signifi-
cant increase in harms. Of the harms reported, most
were self-limited and transient effects of treatment,
such as nausea, constipation, and diarrhea.

**USPSTF Assessment**

The USPSTF concludes that the evidence of the ef-
effect of routine iron supplementation in pregnant
women on maternal health and birth outcomes is insuffi-
cient. Evidence is lacking, and the balance of benefits and harms cannot be
determined.

The USPSTF concludes that the evidence on the
effect of routine iron supplementation in pregnant
women on maternal health and birth outcomes is insuffi-
cient. Evidence is lacking, and the balance of benefits and harms cannot be
determined.

### CLINICAL CONSIDERATIONS

**Patient Population Under Consideration**

This recommendation addresses screening and
supplementation in pregnant women and adolescents
living in the United States who do not have symptoms of iron deficiency anemia. It does not address pregnant
women who are malnourished, have symptoms of iron
deficiency anemia, or have special hematologic condi-
tions or nutritional needs that may increase their need for iron. Screening for iron deficiency anemia in young
children is addressed in a separate recommendation
statement (available at www.uspreventiveservices

taskforce.org).

**Suggestions for Practice Regarding the**

**I Statement**

**Potential Preventable Burden**

Based on older data, estimates of the prevalence of iron deficiency anemia in pregnant women in the
United States range from 2% to 27%, with higher rates
in later trimesters and minority populations (2). Based
on calculations of total body iron from 1999 to 2006
National Health and Nutrition Examination Survey
(NHANES) data, the estimated prevalence of iron defi-
ciency in pregnant women is 18.6%; of these, 16.2%
also have anemia (1). However, given the physiologic
hemodilution that normally occurs during the later
stages of pregnancy, determining exact prevalence
rates of anemia in pregnant women may be difficult.

Several factors have been identified that may in-
crease a pregnant woman’s risk for iron deficiency ane-
mia, including a diet lacking in iron-rich foods (for ex-
ample, a vegetarian diet with inadequate sources of iron), gastrointestinal disease and/or medications that
can decrease iron absorption (for example, antacids),
and a short interval between pregnancies. Non-
Hispanic black and Mexican American women have
higher prevalence rates of iron deficiency in white
women and women with parity of 2 or more. Evidence
on additional risk factors, such as lower educational
level and family income, has been less consistent. On
the basis of a literature scan, the USPSTF found limited
evidence on the use of risk prediction tools to identify
pregnant women who are at increased risk for iron de-
ficiency anemia.

Many observational studies have explored the as-
association between adverse maternal and infant health
outcomes (such as postpartum hemorrhage, preterm
birth, low birthweight, and perinatal death) and iron
deficiency or iron deficiency anemia in pregnancy, but
findings have been inconclusive (2).

**Potential Harms**

The harms of screening for iron deficiency anemia
have not been well-studied but are likely minor. Poten-
tial harms of screening include false-positive results,
anxiety, and cost. Reported adverse events of iron sup-
plementation or treatment with iron include limited
gastrointestinal symptoms, darkening color of urine or
stool, staining of teeth and gums, and drug interactions
with other medications.

**Current Practice**

Rates of screening for iron deficiency anemia and
iron supplementation in pregnant women by clinicians
are not well-documented. However, based on anec-
dotal evidence, it is probably common. In addition,
there may be other reasons to screen for anemia in
pregnant women, such as to prepare for cesarean de-

delivery or anticipated blood loss during a complicated
delivery. Older data from 1988 show that 97% of preg-
nant women who received prenatal care reported be-
ing advised to take a multivitamin-mineral supplement
(3). Based on 1996 to 2006 NHANES data, 77% of preg-
nant women reported using a supplement within the
previous 30 days and they most frequently used a multi-
vitamin containing 48 mg of iron (4).

**Screening Tests**

Measurement of serum hemoglobin or hematocrit
levels is often the first step used in primary care
practice.

**Treatment**

Treatment of iron deficiency anemia in pregnant
women is similar to that in nonpregnant women and
includes additional iron intake through oral iron pills, prenatal vitamins, and diet. The usual dose is 60 to 120 mg of elemental iron per day (2, 5). Intravenous iron treatment is also used during pregnancy.

Supplementation

Prenatal vitamins often include a low dose of iron; the usual dose prescribed in early pregnancy is 30 mg of elemental iron per day. Higher doses (60 to 100 mg of elemental iron per day) are sometimes prescribed in populations at increased risk for iron deficiency anemia (2).

Other Approaches to Prevention

Dietary Iron

According to the Institute of Medicine, the Recommended Dietary Allowance for iron in pregnant women is 27 mg per day. Natural food sources of iron include certain fruits, vegetables, meat, and poultry. The Institute of Medicine also notes that nonheme iron, which is found in vegetarian diets, may be less well-absorbed than heme iron, which is found in diets containing meat; therefore, the iron requirement may be almost twice as much in women who eat a purely vegetarian diet (6).

Fortified breads and grain products (such as cereal) are also important potential sources of iron (7, 8). Federally regulated iron fortification of U.S. food products began in 1941, and the iron content in enriched grain products has increased over the years (7). It is estimated that more than 50% of the iron in the U.S. food supply comes from iron-fortified cereal grain products (7, 8).

Useful Resources

The USPSTF has published separate recommendation statements on screening for iron deficiency anemia in young children and folic acid supplementation during pregnancy (available at www.uspreventive servicestaskforce.org).

DISCUSSION

Burden of Disease

Iron is necessary for the production of hemoglobin, which is an essential protein found in erythrocytes. During pregnancy, iron is also needed for the development of the fetus and placenta and to expand maternal erythrocyte mass. Iron deficiency occurs when body stores of iron become depleted. It can develop as a result of an increased need for iron (for example, during pregnancy), decreased iron intake and absorption (for example, lack of iron sources in the diet), or a loss of iron (for example, bleeding). Iron deficiency anemia results when iron stores become so low that hemoglobin synthesis is impaired, which causes anemia.

Current data on the prevalence of iron deficiency anemia in pregnant women in the United States are lacking. Based on older data from a cohort of mostly racial or ethnic minorities, the estimated prevalence of iron deficiency anemia in pregnant women ranges from as low as 1.8% during the first trimester to as high as 27.4% during the third trimester (9). Based on calculations of total body iron from 1999 to 2006 NHANES data, the estimated prevalence of iron deficiency in pregnant women is 18.6%, which ranges from 6.9% in the first trimester to 29.5% in the third trimester (1).

The major concern about iron deficiency anemia in pregnant women is whether it has adverse effects on maternal health or infant outcomes. Older observational studies suggest an association between adverse outcomes in infants and anemia in the early stages of pregnancy but not during the third trimester (2). Although iron supplementation and treatment during pregnancy have been observed to improve hemoglobin levels and iron status, the clinical significance of this finding is not clear and the evidence on maternal and infant health outcomes is limited (10). Further, studies evaluating these outcomes are often conducted in countries whose nutritional status and hemoparasite burden vary significantly from those of the United States.

Scope of Review

The USPSTF commissioned a systematic evidence review to update its 2006 recommendation on screening for iron deficiency anemia. The USPSTF focused on reviewing the evidence on the association between change in iron status as a result of intervention (oral supplementation or treatment) in pregnant women and adolescents and improvement in maternal and infant health outcomes. The use of intravenous iron was not assessed. The USPSTF considered studies conducted in settings similar to the United States in rates of malnutrition, hemoparasite burden, and general socioeconomic status. The focus of the current recommendation is on screening and supplementation for the prevention of iron deficiency anemia; however, findings on iron deficiency are also described as reported by individual studies and to provide a better understanding of the potential burden in the U.S. population.
Screening for Iron Deficiency Anemia and Iron Supplementation

**Clinical Guideline**

**Supplementation**

Twelve good- or fair-quality randomized, controlled trials evaluated the effects of iron supplementation on various maternal hematologic indexes, including hemoglobin level, serum ferritin level, anemia, iron deficiency, and iron deficiency anemia. Eight studies were conducted in the United States or Europe, 3 in Iran, and 1 in Hong Kong; sample sizes ranged from 45 to 1164 participants. Supplement doses ranged from 20 to 120 mg per day, and outcomes were measured at various time points, from the second trimester to the postpartum period (2). Overall, the evidence was most consistent on improvement in hemoglobin and ferritin levels. Of the 8 studies (12-19) reporting maternal hemoglobin levels at term or delivery, 6 (12, 13, 15, 17-19) reported a significantly higher mean hemoglobin level in the supplemented versus control groups (122 to 139 g/L vs. 115 to 128 g/L, respectively). Of the 7 studies (13-19) reporting serum ferritin levels at term or delivery, 5 (13, 15, 17-19) reported a significantly higher ferritin level in the supplemented versus control groups (12.0 to 30.0 μg/L vs. 6.2 to 24.9 μg/L, respectively). Although adequate evidence shows that supplementation increases hemoglobin and ferritin levels, the evidence is unclear on whether this increase leads to an improvement in maternal and fetal health outcomes. In most of these studies, the supplemented groups had higher mean hemoglobin levels than the nonsupplemented groups; however, both groups reported values within normal limits. Evidence on the effects of supplementation on maternal iron deficiency anemia and anemia was inconsistent.

Five trials (12, 13, 15, 17, 20) evaluated the effects of iron supplementation during pregnancy on maternal health outcomes (for example, cesarean delivery and quality of life), and 11 trials (12-18, 20-23) evaluated various infant birth outcomes (for example, preterm delivery, low birthweight, small for gestational age, and infant mortality). Studies were conducted in the United States, Australia, Hong Kong, Ireland, Iran, and Norway; sample sizes ranged from 45 to 1164 participants. Studies used varying doses of iron, ranging from 20 to 200 mg per day. Studies on cesarean delivery and maternal quality of life were sparse or reported inconsistent results. Studies on individual infant birth outcomes were sparse, were frequently underpowered, or reported inconsistent findings overall. Only 4 studies reported on infant mortality (12, 13, 17, 20), and none reported a significant difference with prenatal iron supplementation. However, given the relatively low frequency of this outcome, studies were likely underpowered to detect a change and none reported power calculations for this outcome. Evidence on the effects of supplementation on birthweight was mixed. Of the 8 studies (14-18, 21-23) reporting this outcome, 3 (15, 21, 22) found that women receiving iron supplementation during pregnancy gave birth to infants with a significantly higher mean birthweight (95 to 205 g more) than women not receiving iron supplementation; however, both groups reported values within normal limits (2). Of the 6 studies reporting on low birthweight (12, 13, 16, 17, 21, 22), only 1 (21) found a significantly lower rate of low-birthweight infants; however, these studies may have been underpowered to detect a change.

Further, of 4 studies (15, 20-22) reporting on small-for-gestational-age infants, 1 study (22) reported no significant difference in rates between supplemented and nonsupplemented groups, 2 studies (15, 21) reported fewer small-for-gestational-age infants in supplemented groups, and 1 study (20) reported more small-for-gestational-age infants in the supplemented group. Overall, the USPSTF found inadequate evidence on the effectiveness of supplementation during pregnancy.

No good- or fair-quality studies that would be applicable to the current U.S. population (2) evaluated the association between change in iron status as a result of intervention (supplementation or treatment) and improvement in maternal or infant health outcomes.

**Potential Harms of Early Detection and Treatment**

**Screening and Treatment**

No good- or fair-quality studies reported on the harms of screening or early treatment (2). Potential harms of iron treatment include mild reversible gastrointestinal symptoms.

**Supplementation**

Ten trials (12-17, 20-23) reported on the harms of routine iron supplementation during pregnancy. Studies were conducted in the United States, Ireland, Hong Kong, Norway, Iran, and Australia, and sample sizes ranged from 45 to 1164 participants. Supplementation
doses ranged from 20 to 200 mg per day. Most reported harms, including nausea, constipation, and diarrhea, were transient and not serious. In general, no significant difference was found between supplemented and control groups. Reported rates of nausea ranged from 29% to 63% in supplemented groups and 28% to 65% in control groups. Reported rates of vomiting ranged from 12% to 41% in supplemented groups and 15% to 41% in control groups. Reported rates of constipation (or ≤3 bowel movements per week) ranged from 4% to 29% in supplemented groups and 1.6% to 28% in control groups. Evidence on supplementation and maternal hypertension was inconsistent, ranging from 1.4% to 7.5% in supplemented groups and 0% to 9% in control groups (2). Overall, the USPSTF found adequate evidence that the harms of supplementation are small to none.

Estimate of Magnitude of Net Benefit

Screening and Early Detection

Overall, the USPSTF found insufficient evidence on screening for iron deficiency anemia in asymptomatic pregnant women and adolescents. No good- or fair-quality studies were found that evaluated the benefits or harms of screening in this population. There was 1 older poor-quality study on the benefits and harms of treatment, but it was not applicable to the current U.S. population of pregnant women. Given the lack of studies on screening, the USPSTF did not find sufficient evidence to determine the balance of benefits and harms of screening for iron deficiency anemia and thus cannot make a recommendation in favor of or against screening.

Supplementation

Overall, the USPSTF found insufficient evidence on the effects of iron supplementation during pregnancy. Although the USPSTF found adequate evidence on harms and deemed them to be small to none, it found inadequate evidence on benefits. Reported benefits of supplementation were limited to intermediate outcomes (maternal hematologic indexes), and evidence on the benefits of supplementation on maternal and infant health outcomes was inadequate because of inconsistent results and underpowered studies. Given the inconsistent findings and lack of adequately powered studies on the effect of supplementation on maternal and infant health outcomes, the USPSTF did not find sufficient evidence to determine the balance of benefits and harms of supplementation and thus cannot make a recommendation in favor of or against iron supplementation.

Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from 31 March to 27 April 2015. A few comments requested more information on which populations are at increased risk for iron deficiency anemia and to which population the recommendation applies. Existing language describing risk factors for iron deficiency anemia and the target population for this recommendation was inserted earlier in the statement to make this information clearer. Some comments also requested separate analyses of certain high-risk populations. Although the USPSTF sought this information, limitations in the evidence prevented it from performing separate analyses. A few comments noted ambiguity in how the terms “iron deficiency” and “iron deficiency anemia” were used. The recommendation was reviewed to ensure consistent use of each term, and language was added to better explain that the focus of the recommendation is on iron deficiency anemia. The USPSTF also clarified that intravenous iron treatment is a potential therapy that is offered in current practice; however, it was not a focus of the current review.

How Does the Evidence Fit With Biological Understanding?

Based on older observational data, the association between negative iron status during pregnancy and adverse maternal and infant health outcomes is inconsistent. Some findings indicate that anemia occurring earlier in pregnancy may be associated with serious adverse infant outcomes, but anemia occurring during the third trimester may not. Evidence on the association between improvement in maternal iron status and improvement in maternal and infant health outcomes is lacking. Although treatment and supplementation with oral iron can improve maternal hematologic indexes (most often, hemoglobin and serum ferritin levels), subsequent improvement in maternal and infant outcomes has not been well-demonstrated. This raises questions on whether the timing of identification and correction of iron deficiency anemia plays an important role and whether current measures of iron deficiency anemia (primarily hemoglobin, hematocrit, and ferritin levels) are effective in identifying women who may need additional iron during pregnancy, given the normal occurrence of physiologic anemia and the limitations of interpreting ferritin levels.

Update of Previous USPSTF Recommendation

This recommendation is consistent with the 2006 recommendation statement on iron supplementation during pregnancy. Both the 2006 and the current recommendation statements found insufficient evidence to determine the balance of the benefits and harms of iron supplementation during pregnancy (24). Although the 2006 statement recommended screening for iron deficiency anemia in pregnant women, the current recommendation found insufficient evidence to recommend for or against screening. In its review of the evidence to update the 2006 recommendation, the USPSTF found no good- or fair-quality studies on the benefits or harms of screening that would be applicable to the current U.S. population of pregnant women. Since 2006, the USPSTF has updated its methodology to better identify evidence that would be most applicable to the current U.S. population. Therefore, the USPSTF determined that the currently available and applicable evidence on screening for and early treatment of iron deficiency anemia in pregnant women is insufficient.
RECOMMENDATIONS OF OTHERS

In 1998, the Centers for Disease Control and Prevention recommended screening for anemia and initiating low-dose iron supplementation at the first prenatal care visit for all pregnant women (5). The Institute of Medicine recommends screening for anemia in each trimester of pregnancy (25). The American Congress of Obstetricians and Gynecologists recommends screening all pregnant women for anemia and testing those with iron deficiency anemia with supplemental iron. It also states that whether iron supplementation in well-nourished pregnant women without anemia affects perinatal outcomes is unclear (26). Consistent with the USPSTF, the American Academy of Family Physicians concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in pregnant women to prevent adverse maternal health and birth outcomes (27).

From the U.S. Preventive Services Task Force, Rockville, Maryland.

Disclaimer: Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

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Disclosures: Dr. Gillman reports royalties from Cambridge University Press for the book Maternal Obesity. Authors not named here have disclosed no conflicts of interest. Authors followed the policy regarding conflicts of interest described at www.uspreventiveservicestaskforce.org/methods.htm. Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M15-1707.

Requests for Single Reprints: Reprints are available from the USPSTF Web site (www.uspreventiveservicestaskforce.org).

References


**APPENDIX: MEMBERS OF THE U.S. PREVENTIVE SERVICES TASK FORCE**

Members of the U.S. Preventive Services Task Force at the time this recommendation was finalized† are Albert L. Siu, MD, MSPH, Chair (Mount Sinai School of Medicine, New York, and James J. Peters Veterans Affairs Medical Center, Bronx, New York); Kirsten Bibbins-Domingo, PhD, MD, MAS, Co-Vice Chair (University of California, San Francisco, San Francisco, California); David Grossman, MD, MPH, Co-Vice Chair (Group Health, Seattle, Washington); Linda Cicou Baumann, PhD, RN, APRN (University of Wisconsin, Madison, Wisconsin); Karina W. Davidson, PhD, MASc (Columbia University, New York, New York); Mark Ebell, MD, MS (University of Georgia, Athens, Georgia); Francisco A.R. García, MD, MPH (Pima County Department of Health, Tucson, Arizona); Matthew Gillman, MD, SM (Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, Massachusetts); Jessica Herstein, MD, MPH (independent consultant, Washington, DC); Alex R. Kemper, MD, MPH, MS (Duke University, Durham, North Carolina); Alexander H. Krist, MD, MPH (Fairfax Family Practice, Fairfax, and Virginia Commonwealth University, Richmond, Virginia); Ann E. Kurth, PhD, RN,MSN, MPH (New York University, New York, New York); Douglas K. Owens, MD, MS (Veterans Affairs Palo Alto Health Care System, Palo Alto, and Stanford University, Stanford, California); William R. Phillips, MD, MPH (University of Washington, Seattle, Washington); Maureen G. Phipps, MD, MPH (Brown University, Providence, Rhode Island); and Michael P. Pignone, MD, MPH (University of North Carolina, Chapel Hill, North Carolina). Former USPSTF members Virginia Moyer, MD, MPH, and Glen Flores, MD, also contributed to the development of this recommendation.

† For a list of current Task Force members, go to www.uspreventiveservicestaskforce.org/Page/Name/our-members.

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**Appendix Table 1. What the USPSTF Grades Mean and Suggestions for Practice**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
<th>Suggestions for Practice</th>
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<tbody>
<tr>
<td>A</td>
<td>The USPSTF recommends the service. There is high certainty that the net benefit is substantial.</td>
<td>Offer/provide this service.</td>
</tr>
<tr>
<td>B</td>
<td>The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.</td>
<td>Offer/provide this service.</td>
</tr>
<tr>
<td>C</td>
<td>The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.</td>
<td>Offer/provide this service for selected patients depending on individual circumstances.</td>
</tr>
<tr>
<td>D</td>
<td>The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.</td>
<td>Discourage the use of this service.</td>
</tr>
<tr>
<td>I statement</td>
<td>The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.</td>
<td>Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.</td>
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**Appendix Table 2. USPSTF Levels of Certainty Regarding Net Benefit**

<table>
<thead>
<tr>
<th>Level of Certainty*</th>
<th>Description</th>
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<tr>
<td>High</td>
<td>The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.</td>
</tr>
<tr>
<td>Moderate</td>
<td>The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: the number, size, or quality of individual studies; inconsistency of findings across individual studies; limited generalizability of findings to routine primary care practice; and lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.</td>
</tr>
<tr>
<td>Low</td>
<td>The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: the limited number or size of studies; important flaws in study design or methods; inconsistency of findings across individual studies; gaps in the chain of evidence; findings that are not generalizable to routine primary care practice; and a lack of information on important health outcomes. More information may allow an estimation of effects on health outcomes.</td>
</tr>
</tbody>
</table>

* The USPSTF defines certainty as “likelihood that the USPSTF assessment of the net benefit of a preventive service is correct.” The net benefit is defined as benefit minus harm of the preventive service as implemented in a general primary care population. The USPSTF assigns a certainty level on the basis of the nature of the overall evidence available to assess the net benefit of a preventive service.