Prenatal Care Screening and Testing Guideline

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Last guideline approval: April 2018

Guidelines are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.
Major Changes as of April 2018

<table>
<thead>
<tr>
<th>New</th>
<th>Previous</th>
</tr>
</thead>
<tbody>
<tr>
<td>We now recommend more frequent screening for depression in pregnant women: once per trimester (at initial visit and at 16 and 32 weeks) and at the 6-week postpartum visit.</td>
<td>Previously, we recommended that pregnant women be screened only at the initial prenatal visit.</td>
</tr>
<tr>
<td>Ultrasound is recommended at the initial prenatal visit for all pregnant women to determine gestational age and identify multiple gestations, and will be available at all KPWA primary care clinics by the end of 2018.</td>
<td>Previously, ultrasound was not available at all KPWA primary care clinics, so some women were sent to Radiology for this service.</td>
</tr>
<tr>
<td>We now recommend using the 2-step screening test for gestational diabetes (GDM).</td>
<td>Previously, we recommended using the 1-step screening test for GDM.</td>
</tr>
</tbody>
</table>

**Note:** The Prenatal Care Screening and Testing Guideline is targeted to primary care/family medicine clinicians.

Visit Schedule

<table>
<thead>
<tr>
<th>Table 1. Visit schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Visit</strong></td>
</tr>
<tr>
<td>All visits are with an MD/APP except where noted.</td>
</tr>
<tr>
<td>Initial visit with a <strong>registered nurse</strong></td>
</tr>
<tr>
<td>Initial visit</td>
</tr>
<tr>
<td>Early second trimester</td>
</tr>
<tr>
<td>Late second trimester</td>
</tr>
<tr>
<td>Third trimester</td>
</tr>
<tr>
<td>Postpartum care</td>
</tr>
</tbody>
</table>
Initial Visit

Timing
The optimal timing for the initial prenatal visit with an MD or advanced practice provider (APP) is at or before 10 weeks’ gestation, as several of the recommended screening tests may be performed during this period. In addition, holding initial visits at this time may lead to earlier identification of multiple gestations, potentially improving pregnancy outcomes.

History
Initiate transfer of the patient’s outside medical records from prior births involving cesarean delivery and/or complicated pregnancies.

Update the patient’s history in the medical record to include all active problems and medical/surgical history, including prior cesarean or chronic hypertension.

- Current pregnancy history
- Past obstetric history
- Menstrual history
- Sexual history
- Contraceptive history
- Medical and surgical history
- Infection history
- Genetics history
- Immunization status
- Medications and allergies
- Exposure to teratogens
- Sociodemographic data
- Pregnancy readiness
- Nutrition
- Housing/finances
- Social support
- HIV/STI risk
- Tobacco use history
- Alcohol use history
- Drug use history

Consider using a tool to review important medical/surgical history, such as:
- The OB Care Visit questionnaire
- The U.S. Surgeon General’s My Family Health Portrait Tool: www.hhs.gov/familyhistory/

Behavior, lifestyle and social issues
If the patient:
- Smokes, advise to quit and refer to Quit For Life® or other tobacco cessation program.
- Discloses intimate partner violence, complete safety assessment and supply information regarding support services.
- Reports, or provider suspects, that she is drinking any alcohol, do a brief intervention.
- Has screened positive on the AUDIT-C for unhealthy drinking, offer a referral to a behavioral health professional.
- Has HIV/STI risk, perform risk-reduction counseling.

Connect patients to resources for family assistance and information. Offer information about nonprofit statewide programs in Washington state:
- Within Reach: http://withinreachwa.org/
- ParentHelp123: www.parenthelp123.org

Physical examination
Lactation assessment should be included in the physical exam.

Ultrasound is preferred at the initial visit to determine gestational age and estimated date of delivery (EDD), and to identify multiple gestations, in alignment with community standards. All pregnant women will be able to receive this service at their preferred KPWA primary care clinic by the end of 2018.

Once the estimated due date (EDD) has been established, it should not be changed unless there is a significant discrepancy between ultrasound dating and last menstrual period dating (see Table 2). Traditional EDD is set at 280 days after the LMP, or determined based on the crown-rump length when measured by ultrasound during the first trimester (up to and including 13 6/7 weeks of gestation).
**Table 2. Recommendations for changing estimated due date (EDD) based on ultrasound (US)**

*Source: ACOG*

<table>
<thead>
<tr>
<th>Gestational age based on last menstrual period (LMP)</th>
<th>Difference between LMP and US dating that supports changing to US dating</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 8 weeks 6 days ¹</td>
<td>&gt; 5 days</td>
</tr>
<tr>
<td>9 weeks 0 days – 13 weeks 6 days ¹</td>
<td>&gt; 7 days</td>
</tr>
<tr>
<td>14 weeks 0 days – 15 weeks 6 days ²</td>
<td>&gt; 7 days</td>
</tr>
<tr>
<td>16 weeks 0 days – 21 weeks 6 days ²</td>
<td>&gt; 10 days</td>
</tr>
<tr>
<td>22 weeks 0 days – 27 weeks 6 days ²</td>
<td>&gt; 14 days</td>
</tr>
<tr>
<td>≥ 28 weeks ², ³</td>
<td>&gt; 21 days</td>
</tr>
</tbody>
</table>

1 Measurement method: crown-rump length.
2 Measurement method: biparietal diameter, head circumference, abdominal circumference, or femur length.
3 Because of the risk of redating a small fetus that may be growth restricted, management decisions based on third-trimester US alone are especially problematic and need to be guided by careful consideration of the entire clinical picture and close surveillance.

**Logistical issues**

If the designated birthing facility has a weight limit and the patient is above that maximum weight, initiate discussion regarding an alternative delivery location.

**Immunizations**

**Table 3. Immunizations for pregnant women, their families, and caregivers ¹**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Eligible population</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Preservative-free influenza vaccine ¹</td>
<td>All pregnant women</td>
</tr>
<tr>
<td>• Tdap ²</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B vaccine</td>
<td>Pregnant women not previously immunized who have any of these characteristics:</td>
</tr>
<tr>
<td></td>
<td>• More than one sex partner during the previous 6 months</td>
</tr>
<tr>
<td></td>
<td>• Previous evaluation or treatment for an STI</td>
</tr>
<tr>
<td></td>
<td>• Recent or current injection drug use</td>
</tr>
<tr>
<td></td>
<td>• HBsAg-positive sex partner</td>
</tr>
</tbody>
</table>

Before the patient gives birth:

| • Influenza vaccine | |
| • Tdap if not previously administered | Patient’s family members and potential caregivers for newborns |

¹ CDC Guidelines for Vaccinating Pregnant Women: [https://www.cdc.gov/vaccines/pregnancy/hcp/guidelines.html](https://www.cdc.gov/vaccines/pregnancy/hcp/guidelines.html)

² Tdap should be given to pregnant women in each pregnancy (preferably at between 27 and 36 weeks’ gestation), regardless of the number of years since prior Td or Tdap vaccination.

**Pregnant women who have never been vaccinated** against tetanus should receive three vaccinations containing tetanus and reduced diphtheria toxoids. The recommended schedule is 0, 4 weeks, and 6–12 months. Tdap should replace one dose of Td, preferably during the third or late second trimester (after 20 weeks’ gestation) of pregnancy (CDC 2013).

The following vaccines are **contraindicated** during pregnancy:

- HPV
- Influenza in live attenuated influenza vaccine (LAIV) form; pregnant patients should receive inactive form.
- MMR or its component vaccines (measles, mumps, rubella)
- Varicella
- BCG (tuberculosis vaccine given for travel)
# Initial screening and testing

## Table 4. Initial prenatal screening and testing

<table>
<thead>
<tr>
<th>Test</th>
<th>Eligible population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood type and Rh</td>
<td>All pregnant women</td>
</tr>
<tr>
<td>Antibody screen</td>
<td></td>
</tr>
<tr>
<td>CBC</td>
<td></td>
</tr>
<tr>
<td>HbA1c&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Depression, PHQ-9&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Alcohol use, AUDIT-C&lt;sup&gt;3&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>HIV, with patient counseling</td>
<td></td>
</tr>
<tr>
<td>Syphilis</td>
<td></td>
</tr>
<tr>
<td>Chlamydia testing&lt;sup&gt;4&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B surface antigen</td>
<td></td>
</tr>
<tr>
<td>Rubella immunity</td>
<td></td>
</tr>
<tr>
<td>Varicella immunity</td>
<td></td>
</tr>
<tr>
<td>Urine testing followed by urine culture</td>
<td>for positive results</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxoplasmosis screening</td>
<td>Women with risk factors for toxoplasmosis, such as high risk of exposure to contaminated undercooked meat, untreated drinking water, or cat litter boxes</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Gonorrhea testing</td>
<td>Women with risk factors for sexually transmitted infections (STIs) such as age under 25, multiple sexual partners, history of prior STI</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Herpes simplex virus (HSV)</td>
<td>Women with risk factors for STI and women who are immunocompromised</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Tuberculosis (TB) screening</td>
<td>Women with risk factors for TB, such as poverty, drug use, and HIV, and immigrants from TB-endemic areas</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytomegalovirus (CMV)</td>
<td>Women with risk factors for CMV, such as day care workers, NICU nurses, and adolescents with multiple sexual partners or a history of STI</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis C antibody testing</td>
<td>Women with a history of injection drug use or a history of blood transfusion or organ transplantation prior to 1992</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Pap test</td>
<td>Women older than 21 who are due or overdue for a Pap test</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid-stimulating hormone (TSH) testing&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Women with diagnosed hypothyroidism only. Routine screening not recommended</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug misuse screening, DAST-10</td>
<td>Women in whom there is clinical suspicion of drug misuse</td>
</tr>
</tbody>
</table>

<sup>1</sup> If HbA1c is negative but diabetes is suspected due to symptoms, BMI, or ultrasound findings, a two-step screening test for gestational diabetes is recommended. See the [Gestational Diabetes Guideline](#).

<sup>2</sup> See the [Depression Guideline](#).

<sup>3</sup> Any alcohol use is unhealthy in pregnancy. See the [Adult Unhealthy Drinking Guideline](#).

<sup>4</sup> Screen all pregnant women under age 25 and women age 25 or older with risk factors for STI.

<sup>5</sup> TSH reference range for pregnant patients:

- First trimester (0–14 weeks) 0.3–3.70 µIU/mL
- Second trimester (15–28 weeks) 0.3–4.35 µIU/mL
- Third trimester (28–40 weeks) 0.41–5.18 µIU/mL
Screening for carrier status, aneuploidy risk, and neural tube defects

The following screenings may be offered and ordered only by MD/APPs.

- **Carrier status screening** should be offered for certain high-risk populations (see Table 5).
- **Screening for aneuploidy and neural tube defects** should be offered to all pregnant women.
  - Women at **average risk** of aneuploidy should be offered the integrated screen or prenatal risk quad screen (see Table 6).
  - Women at **high risk** of aneuploidy can be offered screening with cell-free DNA, plus separate neural tube defect screening with AFP (see Table 7 and Figure 1).

### Carrier status screening

<table>
<thead>
<tr>
<th>Condition</th>
<th>Test</th>
<th>Eligible population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalassemias</td>
<td>Thalassemia screen, including hemoglobin electrophoresis</td>
<td>Asian, Mediterranean, African, African American, Caribbean, Middle Eastern, or South American descent</td>
</tr>
<tr>
<td>Hemoglobinopathies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Ashkenazi panel</td>
<td>Ashkenazi Jewish descent</td>
</tr>
<tr>
<td>Tay-Sachs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canavan disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Familial dysautonomia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bloom syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fanconi anemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gaucher disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucolipidosis type IV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Niemann-Pick type A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tay-Sachs</td>
<td>Tay-Sachs WBC</td>
<td>French Canadian or Cajun descent</td>
</tr>
<tr>
<td>Cystic fibrosis ³</td>
<td>Cystic fibrosis carrier testing</td>
<td>All pregnant women</td>
</tr>
<tr>
<td>Spinal muscular atrophy</td>
<td>Spinal muscular atrophy carrier screening</td>
<td>Women at high risk of carrying spinal muscular atrophy³</td>
</tr>
</tbody>
</table>

¹ Some women might elect not to do this screening.
² If family history is unknown (e.g., due to adoption), do all of the carrier screening tests listed in Table 5.
³ See Clinical Review Criteria: Genetic Screening and Testing.
Aneuploidy and neural tube defect screening: women at AVERAGE RISK of aneuploidy

Both the integrated screen and the prenatal risk quad screen (PRS), which is often referred to as the "quad" screen, are reasonable options for estimating patient-specific risk for chromosome abnormalities (see Table 6). The integrated screen has a higher detection rate (96% vs. 81%) than the PRS (Malone 2005), but other factors such as timing, maternal preference, and availability may favor the PRS screen.

Whichever screening test is used, the patient should be advised that the screening provides an individual risk assessment, but it is not diagnostic. A positive screening test must be followed by an invasive diagnostic test (chorionic villus sampling or amniocentesis) to definitively diagnose chromosome abnormalities.

Table 6. First and second trimester screening for aneuploidy and neural tube defects: WOMEN AT AVERAGE RISK

<table>
<thead>
<tr>
<th>Condition</th>
<th>Timing</th>
<th>Test</th>
<th>Eligible population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integrated screen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Trisomy 21 (Down syndrome)</td>
<td>11–14 weeks</td>
<td>Nuchal translucency screening (NTS) ultrasound</td>
<td>All pregnant women</td>
</tr>
<tr>
<td>• Trisomy 18</td>
<td></td>
<td>PAPP-A</td>
<td></td>
</tr>
<tr>
<td>• Neural tube defects</td>
<td></td>
<td>and</td>
<td></td>
</tr>
<tr>
<td>• Alpha-fetoprotein (AFP)</td>
<td>15–22 weeks</td>
<td>Unconjugated estriol (UE)</td>
<td></td>
</tr>
<tr>
<td>• Unconjugated estriol (UE)</td>
<td></td>
<td>Human chorionic gonadotropin (hCG)</td>
<td></td>
</tr>
<tr>
<td>• Inhibin-A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prenatal risk quad screen (PRS)</td>
<td>15–22 weeks</td>
<td>Alpha-fetoprotein (AFP)</td>
<td>All pregnant women</td>
</tr>
<tr>
<td>• Trisomy 21</td>
<td></td>
<td>Unconjugated estriol (UE)</td>
<td></td>
</tr>
<tr>
<td>• Trisomy 18</td>
<td></td>
<td>Human chorionic gonadotropin (hCG)</td>
<td></td>
</tr>
<tr>
<td>• Neural tube defects</td>
<td></td>
<td>Inhibin-A</td>
<td></td>
</tr>
</tbody>
</table>

1 Some women might elect not to do this screening.

Aneuploidy and neural tube defect screening: women at HIGH RISK of aneuploidy

Patients at increased risk of aneuploidy (see Table 7) can be offered testing with cell-free DNA (also called cell-free fetal DNA, or non-invasive prenatal testing [NIPT]). This technology can be expected to identify approximately 99% of cases of trisomy 21 (Down syndrome), with a false-positive rate of less than 0.5%. The screening test provides information on the most common aneuploidies—trisomy 21, 18 and 13. Some versions of this test can also detect monosomy X and sex chromosome aneuploidies. Because false-positive results can occur, confirmation by amniocentesis or chorionic villus sampling (CVS) is recommended. Note that patients screened with the cell-free DNA test will need a separate alpha-fetoprotein (AFP) test to screen for neural tube defects (American College of Obstetricians and Gynecology Committee on Genetics 2012; Akkerman 2012).
Clinicin counseling before and after the cell-free DNA screening test is recommended. Key points to include are:

- The cell-free DNA test has high sensitivity and specificity, but it is not diagnostic.
- Positive results should be followed up with an invasive diagnostic test (amniocentesis or CVS).
- Negative (“normal”) results do not guarantee a chromosomally normal fetus.
- The test will only screen for the common trisomies and monosomy X. It does not include risk assessment for neural tube defects or for other structural or developmental anomalies.

For a flow chart guide to shared decision making around cell-free DNA screening, see Figure 1 on the following page.

**Note:** There is insufficient evidence at this time to support a recommendation regarding cell-free DNA screening in AVERAGE-RISK women. For women at average risk, refer to the recommendations on the previous page.

<table>
<thead>
<tr>
<th>Table 7. First and second trimester screening for aneuploidy and neural tube defects: WOMEN AT HIGH RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Condition</strong></td>
</tr>
<tr>
<td><strong>Cell-free DNA</strong></td>
</tr>
<tr>
<td>• Trisomy 21 (Down syndrome)</td>
</tr>
<tr>
<td>• Trisomy 18</td>
</tr>
<tr>
<td>• Trisomy 13</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Alpha-fetoprotein (AFP)</strong></td>
</tr>
<tr>
<td>Neural tube defects</td>
</tr>
</tbody>
</table>

1 Some women might elect not to do this screening.
Figure 1. Screening for aneuploidy and neural tube defects: shared decision making for women at high risk

* High risk for aneuploidy as indicated by one of the following:
- Advanced maternal age (≥ 35 years at expected time of delivery)
- Previous pregnancy affected with a trisomy
- Positive conventional prenatal screening test (integrated or PRS)
- Fetal ultrasound findings indicating an elevated risk of aneuploidy
- Previously identified chromosome 21, 18, or 13 translocation in self or partner

Pregnant woman at high risk for aneuploidy?*

Yes

Provide clinician counseling on cell-free DNA test; offer test at 10–22 weeks.

Patient accepts?

Yes

Cell-free DNA test (trisomy 21, 18, and 13) per Table 7.

AND

Alpha fetoprotein (neural tube defects) per Table 7.

Positive: high chance of trisomy
Negative: low chance of trisomy

Share test results and provide clinician counseling.

Either test positive?

Yes

Refer to perinatologist for diagnostic amniocentesis or chorionic villus sampling per Table 8.

Negative

Ultrasound at 18–22 weeks.

No

No

Refer to perinatologist for diagnostic amniocentesis or chorionic villus sampling per Table 8.

 Negative

Offer screening per Table 6 (trisomy 21 and 18, neural tube defects).

Positive

Refer to perinatologist for diagnostic amniocentesis or chorionic villus sampling per Table 8.

Both negative
Diagnostic follow-up of positive screening results

Table 8. Invasive diagnostic tests for follow-up of any positive screening result: ALL WOMEN
Both tests may be used to definitively diagnose aneuploidy. The choice of test is based on timing, maternal preference, and the need for further neural tube defect testing. Referral to a perinatologist is required for all invasive diagnostic testing. 

<table>
<thead>
<tr>
<th>Condition</th>
<th>Timing</th>
<th>Test</th>
<th>Eligible population</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Aneuploidy</td>
<td>10–13 weeks</td>
<td>Chorionic villus sampling (CVS)</td>
<td>Women at increased risk for genetic birth defects due to advanced maternal age, family history, or abnormal first trimester screening</td>
</tr>
<tr>
<td>• Inherited disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Neural tube defects</td>
<td>15–22 weeks</td>
<td>Amniocentesis</td>
<td>Women at increased risk for genetic birth defects due to advanced maternal age, family history, or abnormal first or second trimester screening</td>
</tr>
<tr>
<td>• Aneuploidy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Inherited disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 Additional testing that may be ordered by the perinatologist includes:

- FISH: provides information on chromosomes 21, 18, and 13; sex chromosomes; and specific microdeletion/duplication syndromes which may be suspected on certain ultrasound findings.
- Microarray: detects genomic imbalances that may account for abnormal ultrasound findings that do not follow a specific pattern. Parental studies may be needed to interpret uncertain microarray results.
- Mendelian disorders testing: may be offered based on a pattern of specific ultrasound findings.
Second Trimester Visits (14–28 Weeks)

Screening for aneuploidy and neural tube defects
See recommendations for average-risk women (Table 6) and high-risk women (Table 7) for information on screening during the second trimester.

Physical examination (14–16 weeks)
- Weight
- Blood pressure
- Auscultation of fetal heart tones

Depression screening, using the PHQ-9, should be repeated for all pregnant women at their first visit in their second trimester (about 16 weeks).

Ultrasound (18–22 weeks)
The second trimester ultrasound is designed to detect structural anomalies and growth. Structural anomalies should be followed up by a referral for high-resolution ultrasound and/or maternal-fetal medicine consultation to a tertiary perinatal center for confirmation, consultation, and discussion of risks/available testing options/therapeutic options. When desired by the patient before 23 weeks’ gestation, consultation for pregnancy termination should be facilitated by the patient’s MD/APP.

Physical examination (24–28 weeks)
- Weight
- Blood pressure
- Auscultation of fetal heart tones
- Measurement of fundal height

Screening and testing (24–28 weeks)

<table>
<thead>
<tr>
<th>Test</th>
<th>Eligible population</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hematocrit</td>
<td>All pregnant women</td>
</tr>
<tr>
<td>• 2-step gestational diabetes screening</td>
<td></td>
</tr>
<tr>
<td>• PIH (pregnancy-induced hypertension)</td>
<td>Women with risk factors for gestational hypertension, such as first pregnancy or high blood pressure or kidney disease prior to pregnancy</td>
</tr>
</tbody>
</table>

1 See the [Gestational Diabetes Guideline](#) for more details.
Third Trimester Visits (28–41 Weeks)

Physical examination

- Weight
- Blood pressure
- Auscultation of fetal heart tones
- Measurement of fundal height
- Determination of fetal lie at 36 weeks and subsequent visits
- Cervical examination by 42 weeks

Depression screening, using the PHQ-9, should be repeated for all pregnant women at their first visit in their third trimester (about 32 weeks).

Interventions

If fetus is breech at 36 weeks, offer external cephalic version.

Routine topics to discuss

- Breastfeeding and formula supplementation during the first 6 months
- Skin-to-skin contact and infant feeding cues
- Rooming in with baby after birth

Screening and testing

<table>
<thead>
<tr>
<th>Table 10. Third trimester (28–41 weeks): screening and testing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Test</strong></td>
</tr>
<tr>
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<tr>
<td>Group B strep vaginal and rectal culture at 35–37 weeks</td>
</tr>
<tr>
<td>Non-stress test (or alternative test for fetal well-being) by 42 weeks</td>
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<tr>
<td>Antibody screen 1</td>
</tr>
<tr>
<td>Chlamydia</td>
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<tr>
<td>Gonorrhea</td>
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<tr>
<td>Syphilis</td>
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<tr>
<td>HIV</td>
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<tr>
<td>Herpes</td>
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<tr>
<td>Hepatitis B surface antigen</td>
</tr>
<tr>
<td>MRSA screening at 34–38 weeks</td>
</tr>
</tbody>
</table>

1 Rh(D) negative women should receive anti(D)immune globulin as indicated.
Postpartum Visit

The routine postpartum visit should take place approximately 3–4 weeks after delivery, but no later than 6 weeks; however, an early postpartum visit at 1–2 weeks after delivery should also be considered for women who delivered by cesarean section or are at high risk for postpartum depression.

Physical examination

- Weight
- Blood pressure
- Thyroid
- Breasts
- Abdomen
- Pelvic

Routine topics to discuss

- Breastfeeding
- Return to sexual activity
- Contraceptive plan
- Emotional status

Screening and testing

<table>
<thead>
<tr>
<th>Test</th>
<th>Eligible population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postpartum depression, PHQ-9 (^1)</td>
<td>All postpartum women</td>
</tr>
<tr>
<td>HbA1c (^2) (Place order at 4-week postpartum visit.)</td>
<td>All women with gestational diabetes</td>
</tr>
</tbody>
</table>

\(^1\) See the [Depression Guideline](#).

\(^2\) The recommendation to use HbA1c as the standard screening test is different from that of ACOG. HbA1c is thought to be a more accurate screening test with less variability between patients. See the [Gestational Diabetes Guideline](#).
Evidence Summary and References

The Prenatal Care Guideline was developed using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis. The guideline team adapted recommendations from externally developed evidence-based guidelines and/or recommendations of organizations that establish community standards. The guideline team reviewed additional evidence in the areas of cell-free DNA screening, integrated screening, early combined screening, sequential screening, quad screening, early ultrasound screening, carrier screening for spinal muscular atrophy, and estimating due dates.

Key questions addressed in the KPWA guideline

1. Should cell-free DNA be offered to women at low or average risk of aneuploidy?
2. What is the accuracy of early combined screening?
3. What is the accuracy/effectiveness of sequential screening?
4. What is the performance of early ultrasound screening?
5. What is the effectiveness of integrated screening?
6. What is the effectiveness of quad screening?
7. What is the effectiveness of thyroid screening?
8. What is the effectiveness/performance of carrier screening for spinal muscular atrophy?
9. What is the best method for estimating due date?
10. What is the effectiveness of early second-trimester anatomy scan (13–16 weeks) in combination with cfDNA in women at high or average risk of aneuploidy?
11. What is the residual risk of structural anomaly of aneuploidy among women with negative cfDNA?
12. Is there value added by completing nuchal translucency (NT) after negative cfDNA? Or, what is the role of NT measurement after negative cfDNA or low-risk result?
13. What proportions of anomalies are missed without early anatomy scan (13–16 weeks) ultrasound (in the context of cfDNA with early second trimester scan)?
14. What is the role of NT when cfDNA is being used?

External guidelines meeting KPWA criteria for adaptation/adoptions

2015 ACOG No. 640.
2017 ACOG No. 691. Carrier Screening for Genetic Conditions.
2017 Society for Maternal Fetal Medicine. The role of ultrasound in women who undergo cell-free DNA screening.
2017 American Thyroid Association. 2017 Guidelines for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum.

Key question 1: Should cell-free DNA be offered to women at low or average risk of aneuploidy?

Two systematic reviews were reviewed (Iwarsson 2017, Taylor-Phillips 2016); 32–41 studies were included in the systematic reviews. Study designs were retrospective for the most part. Sampling occurred in the first trimester. A reference test (invasive genetic test) was used in all studies. Gestational age at sampling ranged from 8 to 34 weeks, and age varied between 18 to 46 years. Cell-free DNA showed high performance (sensitivity, specificity, negative predictive value, positive predictive value) in detecting trisomy 21, 18, and 13 in women at average risk of aneuploidy. Limitations included heterogeneity, moderate to high risk of bias, role of sponsor, applicability of findings, and issues with follow-up.

Conclusion: Moderate evidence suggests that cell-free fetal DNA has high accuracy in detecting trisomy 21, 18, and 13 in pregnant women with average risk of aneuploidy. However, accuracy is lower for trisomy 18 and 13 compared to trisomy 21.
Key question 2: What is the accuracy of early combined screening?
Three studies (Park 2016, Santorum 2017, Baer 2015) were reviewed; two were retrospective in design and one was a prospective validation study. The tests consisted of ultrasound, free beta-hCG, and PAPP-A. Combined screening consisted of integrated or sequential screening. Gestational age ranged from 10 to 13+6 weeks and maternal age ranged from 21 to 41 years; median maternal weight was 55 kg (34–96.9kg). Sensitivities were high across studies, and ranged from 75 to 100%. However, there was a high false-positive rate ranging from 4 to 7%. Specificity was reported in one study and was high for trisomy 21 and 18. Positive predictive value and negative predictive value were also reported in one study, and were low (4–7%).

Conclusion: Low to moderate evidence suggests that combined screening’s accuracy is high in detecting trisomy 21, 18, and 13 in all pregnant women, with a high false-positive rate.

Key question 3: What is the accuracy/effectiveness of sequential screening?
Two studies (Norton 2016, Benn 2007) were extensively reviewed. The Norton study compared cell-free DNA with sequential screening and the Benn study did not make any comparison. In the study that compared cell-free DNA with sequential screening, patients underwent sequential screening and its performance was compared with that of expected cfDNA (if primary screening).

Population characteristics of the Norton study included: N of 452,901; age < 35 years (73.6%). Results showed that sequential screening had a higher detection rate of all chromosomal abnormalities than expected cfDNA (81% vs. 70%). The results should be interpreted with caution. Major limitation resides in the study design (non-randomized trial). The study quality was fair.

Conclusion: Fair-quality study suggests that sequential screening has high performance. Its detection rate seems to be higher than cfDNA but results should be interpreted with caution.

Key question 4: What is the performance of early ultrasound screening?
One moderate-quality prospective study (Wiechec 2016) was reviewed. The risk was determined by Nuchal translucency (NT) alone and NT in combination with secondary markers. Characteristics included: N of 5,696 patients; majority of patients were at low risk of aneuploidy; median maternal BMI varied from 17.6 to 35.2 kg; gestation of 11–13 weeks. Outcomes suggested that the performance of ultrasound alone in the first trimester without biochemical markers was high among patients with low risk of aneuploidy (73.8%). When secondary markers were added to NT, the performance became higher (91.7%).

Conclusion: Early ultrasound screening has high detection rates; however, the ultrasound with secondary markers has higher detection rates.

Key question 5: What is the effectiveness of integrated screening?
One study was reviewed (Guanzial-Franchi 2011). Combined and sequential risks were calculated retrospectively for patients in whom integrated test had been performed. First-trimester testing included nuchal translucency, pregnancy-associated plasma protein-A, and free beta-hCG; the second-trimester tests were alpha-fetoprotein, hCG, and unconjugated estriol. Population characteristics included: N of 7292; mean age 32 years; majority aged less than 35 years; population with high risk. The authors reported an increase in net detection rate for trisomy 21 with a reduction of false-positive rate, after the addition of second-trimester screening in women who had received combined first-trimester screening. In addition, integrated screening tests may have a higher detection rate than sequential and contingent screening tests.

Conclusion: One moderate-quality retrospective study shows that integrated screening as well as sequential and contingent tests have a higher detection rate with a lower false-positive rate over combined first-trimester screening. This confers higher efficacy for these tests in high-risk women.

Key question 6: What is the effectiveness of quad screening?
One comparative study (Ball 2007) assessed different strategies and reported that contingent screening was the most cost-effective for detecting trisomy 21. Screening tests included quad screen, first-trimester screening, triple screening, integrated screening, and sequential screening. Population characteristics: Patients were 16 years old, 10–13 weeks gestation for first-trimester screening and 15–18 weeks for
second-trimester screening. Data in this study derived from the FASTER trial. Sensitivity was superior to 80% for most of the tests except for triple screening, which had a sensitivity of 69%.

**Conclusion:** One comparative study shows that sequential screening is the most cost-effective for detecting Down syndrome.

**Key question 7: What is the effectiveness of thyroid screening?**
No new studies that challenge the above guidelines were identified.

**Guidelines:** ACOG 2015 indicated that universal screening for thyroid disease in pregnancy is not recommended due to the lack of association between treatment of maternal subclinical hypothyroidism and improvement in neurocognitive function in offspring. The American Thyroid Association 2017 postulated that there is insufficient evidence to recommend for or against universal screening for abnormal TSH concentrations.

**Conclusion:** The 2017 American Thyroid Association guidelines should be adopted.

**Key question 8: What is the effectiveness/performance of carrier screening for spinal muscular atrophy?**
Five studies were reviewed (MacDonald 2014, Qu 2013, Su 2011, Ben-Shachar 2011, Gitlin 2010). However, none challenged the ACOG 2017 recommendation. The sensitivity and negative predictive value were high in the population assessed, except in Black women, for whom the sensitivity was 70.6% (69–71%).

**Guidelines:** ACOG 2017 (Committee Opinion No. 691) indicated that all pregnant women or women who are considering pregnancy should be offered carrier screening for spinal muscular atrophy.

**Conclusion:** No new studies that challenge the ACOG 2017 recommendation were identified. Sensitivity/detection and carrier rates were high in the population assessed. ACOG 2017 should be adopted.

**Key question 9: What is the best method for estimating due date?**

**Guidelines:** ACOG 2017 indicated that ultrasound measurement of embryo or fetus in the first trimester is the most accurate method to confirm or establish gestational age. Changes to the estimated due dates should be performed in rare circumstances.

**Conclusion:** ACOG 2017 guideline should be adopted.

**Key question 10: What is the effectiveness of early second-trimester anatomy scan (13–16 weeks) in combination with cfDNA in women at high and average risk women of aneuploidy?**
No studies allowed evaluation of early second-trimester anatomy scan in combination with cfDNA in women at high and average risk of aneuploidy. However, three studies compared early second-trimester ultrasound with mid second-trimester ultrasound. Of these studies, only one (Lim 2013) reported the performance of early second-trimester anatomy scan: sensitivity: 83%; specificity: 95%; false positives: 4%; and false negatives: 17% (proportion of anomalies missed).

**Conclusion:** There was no evidence that allowed assessment of early second-trimester anatomy scan (13–16 weeks) in combination with cfDNA in women at high and average risk of aneuploidy.

**Key question 11: What is the residual risk of structural anomaly of aneuploidy among women with negative cfDNA?**
Only one study (Reiff 2016) was relevant. The study was a retrospective cohort study of women with negative cfDNA for T21, 18, 13. It included women with high risk of aneuploidy who underwent 11–14 weeks ultrasound and obstetrical care. Ultrasound included nuchal translucency measurements and early anatomic imaging. Population characteristics consisted of sample size of 1739; average maternal age of 38.3; mean GA at 11–14 weeks of 12.5 (11–14); 99% anatomy scan was performed; mean GA cfDNA of 12.5 (9–34.4); 4.5% underwent Dx testing; 0.6% CVS; 3.9% amniocentesis; prior trisomy: 58; advanced
maternal age: 1721. The authors reported low structural abnormality in this population of women with negative cfDNA and 3.5% of abnormal findings (60/1739).

**Conclusion:** Low-quality evidence shows that the residual risk of structural abnormality after a negative cfDNA is low in high-risk women who underwent ultrasound at 11–14 weeks.

**Key question 12:** Is there value added of completing nuchal translucency (NT) after negative cfDNA? Or, what is the role of NT measurement after negative cfDNA or low-risk result?

Two observational studies were identified (Reiff 2016, Khalil 2015). The first study suggested that after a negative cfDNA, ultrasound identified abnormal findings in 1 in 28 women. The second study was of low quality and had a serious risk of bias.

**Guidelines:** SMFM 2017 (Norton 2017) recommended against NT in women who have already received a negative cell-free DNA screening result. ACOG 2015 concluded that NT for detection of aneuploidy risk is not required at the time of cfDNA screening in the first trimester.

**Conclusion:** SMFM 2017 should be adopted.

**Key question 13:** What proportions of anomalies are missed without early anatomy scan (13–16 weeks) ultrasound (in the context of cfDNA with early second-trimester scan)?

No studies were identified.

**Key question 14:** What is the role of NT when cfDNA is being used?

Four studies were reviewed. The first (Jackson 2014), which was a non-randomized study, assessed outcomes of nuchal translucency (NT) followed by non-invasive prenatal testing (NIPT) in average-risk women. NT followed by NIPT detected 15 of the 16 major abnormalities. Also, only four invasive tests were performed to confirm false-positive NIPT outcomes compared to 30 invasive tests in the year preceding the study. The authors indicated that NT with NIPT increased detection of fetal abnormalities compared to either option alone. The second study, which was a retrospective study (O'Brien 2017), indicated that abnormal NT scan alone, in the first trimester, did not identify aneuploidy. The third study was a cohort study (Reiff 2016) of 1739 patients that investigated the role of ultrasound (11–14 weeks) in women with high risk of aneuploidy with negative cfDNA. Thirty patients (1.7%) had positive NT measurement or cystic hygroma and of these patients, none had health issues at birth. Four had cystic hygroma and three did not have aneuploidy; the last one was lost in utero. The authors reported 3.5% of abnormalities on ultrasound. The fourth study was a retrospective cohort study (Vora 2017); the authors reported that 16% of patients who were eligible for cfDNA screening had an abnormality on ultrasound (anomaly, incorrect dating, multiple gestations, and non-viable pregnancy) that would change prenatal screening method. In addition, ultrasound before cfDNA screening in women of advanced maternal age was recommended. Limitations included study design, selection bias, weak or no information on confounders, and possible measurement bias. Overall, there was serious risk of bias.

**Conclusion:** NT with cfDNA may increase detection of fetal abnormalities compared to either option alone. NT may not be useful for aneuploidy when cfDNA is being offered. Ultrasound may be recommended prior to cfDNA screening in women of advanced maternal age.
References


Guideline Development Process and Team

Development process
To develop the Prenatal Care Guideline, the guideline team adapted recommendations from externally developed evidence-based guidelines and/or recommendations of organizations that establish community standards. The guideline team reviewed additional evidence in the areas of cell-free DNA screening, integrated screening, early combined screening, sequential screening, quad screening, early ultrasound screening, carrier screening for spinal muscular atrophy, and estimating due dates. For details, see Evidence Summary and References.

This edition of the guideline was approved for publication by the Guideline Oversight Group in April 2018.

Team
The Prenatal Care Guideline development team included representatives from the following specialties: clinical lab, family medicine, genetics, obstetrics/gynecology, midwifery, nursing, preventive care, and residency.

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Disclosure of conflict of interest
Kaiser Permanente requires that team members participating on a guideline team disclose and resolve all potential conflicts of interest that arise from financial relationships between a guideline team member or guideline team member's spouse or partner and any commercial interests or proprietary entity that provides or produces health care-related products and/or services relevant to the content of the guideline.

Team members listed above have disclosed that their participation on the Prenatal Care Guideline team includes no promotion of any commercial products or services, and that they have no relationships with commercial entities to report.