Prenatal Care – Adult/Pediatric – Ambulatory Clinical Practice Guideline

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Introduction

Prenatal care is important in promoting a healthy pregnancy and a health birth. This guideline provides evidence-based recommendations for prenatal care on topics such as screening for genetic anomalies, gestational weight gain, immunizations, and diagnosis and management of gestational diabetes. This guideline incorporates recommendations from the US Preventive Services Task Force and other national organizations/societies such as the American Congress of Obstetricians and Gynecologists.

Scope

Intended User(s): Physicians, Advanced Practice Providers, Registered Nurses, Certified Nurse Midwives, Genetic Counselors

Objective(s): To provide evidence-based recommendations regarding prenatal care for UW Health patients in the ambulatory setting

Target Population: Pregnant adolescent and adult patients

Clinical Questions Considered:

- What laboratory tests are recommended for all pregnant patients during the first trimester?
- What laboratory tests are recommended during the initial prenatal visit for patients with hypertension, diabetes, hypothyroidism and/or obesity?
- What are common prenatal screening options for patients?
- What are considerations for carrier screening in pregnant patients?
- When and how should patients be screened for gestational diabetes?
- What are common indications for antepartum fetal surveillance?

Recommendations

Entry of prenatal care

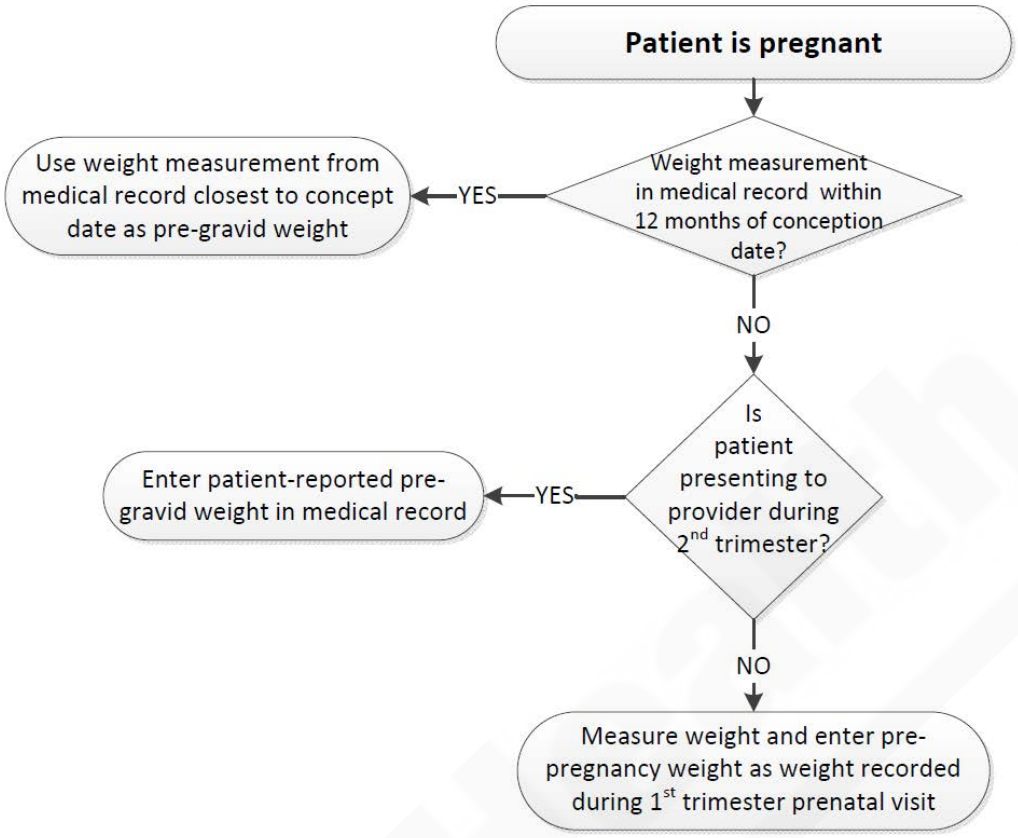
Pregnancy dating

Upon initial notification by the patient regarding confirmed pregnancy by home testing, it is recommended to obtain and document the patient's last reported menstrual period. *(UW Health Low quality evidence, strong recommendation.)* If dating is uncertain, patient may be offered a dating ultrasound which should occur at approximately 7-8 weeks of pregnancy. The dating ultrasound *should not* be scheduled prior to 6 weeks of pregnancy.[1] *(UW Health Low quality evidence, strong recommendation.)*

Documenting patient's pre-gravid weight

It is important to establish a patient's pre-gravid weight to determine what appropriate gestational weight gain will be for the pregnancy. A patient's pre-gravid weight should be documented in the medical chart as outlined in **Figure 1**. *(UW Health Low quality evidence, strong recommendation.)*

Figure 1. Pre-gravid weight recording algorithm



Frequency of prenatal care visits

It is recommended that patients who are of average risk should be seen initially by the prenatal care provider between 6-12 weeks gestation. There after, the frequency of visits should occur on the following schedule:[2] *(UW Health Low quality evidence, strong recommendation.)*

- Every 4-6 weeks through 28 weeks gestation
- Every 2-3 weeks through 36 weeks of gestation and
- Every week thereafter

Initial Visit with Provider (Target 6-12 weeks)

Patient history

It is recommended to document patient's medical history that is relevant to the current pregnancy, including obstetrical history (e.g., history of operative or preterm deliveries, gestational diabetes) and any chronic medical conditions (such as history of hypertension or hypothyroidism.) *(UW Health Low quality evidence, strong recommendation.)* If the patient is diabetic and is not currently seeking obstetric care from Obstetrics/Gynecology, it is recommended that the patient be referred to Obstetrics. *(UW Health Low quality evidence, strong recommendation.)*

Medication history

It is recommended to obtain and document patient's current medication list, including whether or not patient is currently taking a prenatal vitamin. If the patient is not taking a prenatal vitamin, the patient may be offered a prescription for a prenatal vitamin. *(UW Health Low quality evidence, strong recommendation.)*

Folic Acid

A daily supplement of folic acid containing 0.4 to 0.8 mg of folic acid is recommended for all patients planning or capable of pregnancy.[3] *(USPSTF Grade A)* Women at increased risk for a pregnancy with a neural tube defect (i.e., history of a prior child with a neural tube defect or family history of neural tube defect) should be offered a higher dose of folic acid supplementation (4 mg daily) beginning 1 month before trying to conceive and continuing through the first 3 months of pregnancy.[3,4] *(UW Health Low quality evidence, strong recommendation)*

Note: Folic acid supplementation should not be achieved by taking multiple vitamins, due to the risk of vitamin A toxicity.

Physical examination

A routine physical examination, including a pelvic examination which may detect reproductive tract abnormalities, is recommended during the initial visit with the prenatal care provider.[1] *(UW Health Low quality evidence, strong recommendation.)*

Gestational weight gain

It is recommended to measure a patient's weight at each prenatal visit[1] and that providers discuss what appropriate gestational weight gain is with the patient.[5,6] *(UW Health Low quality evidence, strong recommendation)*

The Institute of Medicine guidelines (**Table 1**) outline the recommended maternal weight gain, based upon the patient's pre-pregnancy body mass index (BMI).[5,7]

Table 1. Weight Gain Recommendations for Pregnancy

Prepregnancy Weight Category	**BMI**	**Recommended Total Weight Gain Range** (lbs.)	**Recommended Rates of Weight Gain Second and Third Trimesters** (mean range, lb./week)	**Recommended Total Weight Gain Range** (lbs.)
		Single Fetus	*Single Fetus*	*Twins*
Underweight	Less than 18.5	28-40	1 (1-1.3)	--
Normal weight	18.5-24.9	25-35	1 (0.8-1)	37-54
Overweight	25.0-29.9	15-25	0.6 (0.5-0.7)	31-50
Obese (includes all classes)	≥ 30.0	11-20	0.5 (0.4-0.6)	25-42

Fetal heart rate

It is recommended to auscultate for fetal heart rate at each prenatal visit to confirm viable fetus starting at approximately 10 weeks gestation.[1,8] *(UW Health Low quality of evidence, strong recommendation)*

Lifestyle considerations during pregnancy

It is important to counsel pregnancy patients on lifestyle considerations such as diet, exercise, smoking cessation, alcohol use, and hot tubs and saunas use.[1] *(UW Health Very Low quality evidence, strong recommendation)* **Table X** provides a select list of lifestyle topics in pregnancy to counsel on.

Table 2. Lifestyle considerations in pregnancy

Topic	Counseling points
Caffeine[9,10]	• Limit caffeine consumption to less than 200 mg per day
Diet[1]	• Avoid unpasteurized products (e.g., soft cheese), delicatessen foods, pate and raw eggs. • Avoid seafood with high levels of mercury (e.g., swordfish, tuna steaks, mackerel) and raw fish/shellfish
Tobacco use/smoking cessation[11]	• Counsel current patients who smoke on risks of tobacco use in pregnancy such as miscarriage, premature birth, low birth weight, increased risk for sudden infant death syndrome (SIDS)
Alcohol use[12,13]	• Recommend to avoid alcohol consumption during pregnancy; no amount of alcohol consumption has been proven safe in pregnancy
Dental care[14]	• Counsel patients susceptibility to oral disease such as periodontal disease and association of periodontal disease and adverse pregnancy outcomes (i.e., premature birth, low birth weight) • Advise patient to practice dental hygiene and seek standard dental care evaluation
Exercise[1]	• Encourage physical activity as at least 30 minutes of exercise on most days of the week is reasonable
Hot tubs and saunas[1]	• Advise patients to avoid hot tubs and saunas during first trimester because heat exposure has been associated with neural tube defects and miscarriage
Over the counter medications[1]	• Counsel patients on common OTC medications that are safe to use in pregnancy (i.e., acetaminophen for pain, antacids for acid reflux) and what medications should be avoided

Infections and diseases screening

Asymptomatic bacteriuria

Pregnant women should be screened for asymptomatic bacteriuria with urine culture at 12-16 weeks of gestation or at their first prenatal visit if later.[15] *(USPSTF Grade A)* A urine culture is sufficient for detecting asymptomatic bacteriuria and thus a urinalysis does not need to be ordered at the same time. If the urine culture is positive, the patient should be treated with appropriate antibiotic therapy.[16] *(IDSA A-I)*

Sexually transmitted diseases

Syphilis
It is recommended that all pregnant patients be screened for syphilis at the first prenatal visit. If the patient is at high risk, the patient should be retested early in the third trimester and at delivery.[17] *(UW Health Low quality evidence, strong recommendation.)* This recommendation is consistent with what is recommended by the Centers for Disease Control and Prevention (CDC).

In Illinois, healthcare providers are required by law to screen all pregnant patients for syphilis infection during the first prenatal visit **and** during the third trimester. If any blood test shows a positive or inconclusive result, an additional test or tests should be performed. An infant cannot be discharged from the hospital unless the syphilis status of the mother has been determined at least once during the course of pregnancy and preferably again at delivery.

Chlamydia and Gonorrhea
It is recommended that all prenatal patients be screened for chlamydia/gonorrhea during the first prenatal visit. *(UW Health Low quality of evidence, weak/conditional recommendation)* This recommendation is consistent with the Illinois Department of Public Health. The CDC recommends that all pregnant patients < 25 years of age and pregnant patients >25 years of age who are at increased risk of infection be screened for chlamydia and gonorrhea. These patients should also be retested for chlamydia infection during the third trimester.[17]

Pregnant patients with chlamydial infection should have a test of cure 3-4 weeks after treatment and be retested within 3 months. Pregnant patients with gonorrhea infection should be retested 3 months after treatment. [17]*(UW Health Low quality of evidence, strong recommendation)*

Human Immunodeficiency Virus (HIV)
It is recommended to screen all pregnant patients for Human Immunodeficiency virus during the first prenatal visit.[18-20] *(USPSTF A)*

Per Illinois law, newborns must be screened for HIV if the mother's HIV status is unknown. For patients who are at high risk for infection, it is recommended to retest in the third trimester.[17]

Hepatitis B Virus (HBV)

It is recommended that all pregnant patients be screened for Hepatitis B surface antigen (HBsAg) during the first prenatal visit of *each* pregnancy, even if they have been previously vaccinated or tested.[8,21] Any pregnant patient who was not screened prenatally and any pregnant patient at high risk for Hepatitis B infection should be tested upon admission for delivery. *(UW Health Low quality of evidence, strong recommendation)*

Patients who may be at high risk for Hepatitis B include persons born in countries with ≥ 2% prevalence of HBV, persons who inject drugs, HIV-positive, household and sexual contact with HBV-infected persons, individuals requiring immunosuppressive therapy, end stage renal disease patients, U.S born persons not vaccinated as infants whose parents were born in regions with a high prevalence of HBV infection (≥8%) such as sub-Saharan Africa and Central and Southeast Asia.[22,23]

Hepatitis C virus (HCV)

It is recommended to screen for Hepatitis C virus in pregnant patients with risk factors for Hepatitis C (see **Table 3**) at the first prenatal visit.[17] *(UW Health Low quality of evidence, weak/conditional recommendation)*

Table 3. Criteria for who should receive prenatal screening for Hepatitis C virus[17,24-26]

- Injectable illegal drug use (even if only used once)
- Long-term hemodialysis
- Percutaneous/parenteral exposures in unregulated setting (e.g., tattoo received outside of licensed parlors or medical procedures done in settings without strict infection control policies)
- Recipients of transfusions or organ transplantation before July 1992
- Recipients of clotting factor concentrates produced before 1987
- Recipients of blood products from donor who later tested positive for HCV
- History of incarceration
- Seeking care or evaluation for sexually transmitted infection (including HIV)
- Unexplained chronic liver disease, including persistent elevated alanine aminotransferase (ALT)
- Born to an HCV-infected mother
- Patients born between 1945-1965

Group B Streptococcus

Group B Streptococcus (GBS) can be especially severe for newborn infants causing potentially sepsis, pneumonia or even meningitis. Group B strep can be passed from mother to infant during labor thus screening is vital for preventing infection.

The CDC recommends that all pregnant patients be screened for GBS disease by obtaining a vaginal-rectal swab specimen at 35-37 weeks gestation.[6,27,28] *(CDC Grade AII)* If the patient had a previous positive GBS culture during the current pregnancy (e.g., urine culture) or who had a previous infant with invasive GBS disease and received intrapartum antibiotic prophylaxis, a third trimester vaginal swab screen is not necessary/recommended.[29] *(CDC Grade AII)*

If the patient's GBS status is unknown at the onset of labor or preterm rupture of membranes occurs before 37 weeks gestation with a substantial risk for preterm delivery, then GBS screening should be performed and intrapartum antibiotic prophylaxis should be provided pending culture results (unless a vaginal-rectal GBS screen was performed within the preceding 5 weeks).[28] *(CDC Grade AII)*

The following CDC algorithms[28] may be used as reference:

- GBS Screening/Intrapartum Prophylaxis (Preterm labor) Algorithm
- GBS Screening/Intrapartum Prophylaxis (Preterm Premature Rupture of Membranes) Algorithm
- Intrapartum Antibiotic Prophylaxis Regimens Algorithm

Maternal medical conditions screening

Preeclampsia

Preeclampsia is diagnosed when there is a systolic blood pressure (BP) ≥ 140 mm Hg or a diastolic BP ≥90 on at least two occasions, taken at least four hours apart plus new-onset proteinuria (≥ 300 mg protein in 24-hr urine sample or urinary protein/creatinine ration ≥0.3) and/or one of the following severe features:[30,31]

- Elevated blood pressure (systolic ≥ 160 mm HG, diastolic ≥ 110 mm Hg)
- Elevated creatinine level (> 1.1 mg/dL or ≥ 2 times baseline)
- Hepatic dysfunction (transaminase levels ≥ 2 times upper limit of normal) or right-upper quadrant or epigastric pain
- New onset headache or visual disturbances
- Thrombocytopenia (Platelet count < 100,000/ µL)
- Pulmonary edema

According to the U.S Preventive Services Task Force, it is recommended that all pregnant individuals without a known diagnosis of preeclampsia or hypertension be screened for preeclampsia. *(USPSTF Grade B)* Blood pressure measurement is routinely used for screening and should be measured while the patient is relaxed, quiet and in a sitting position with legs uncrossed and back supported.[32]

For women who are at high risk for preeclampsia, low-dose daily aspirin (i.e., 81 mg daily) is recommended after 12 weeks of gestation.[32] *(USPSTF Grade B)* Increased risk for preeclampsia include a history of eclampsia or preeclampsia (particularly early-onset preeclampsia), previous adverse pregnancy outcome, maternal comorbid conditions such as diabetes or chronic hypertension, multifetal gestation, African-American race, low-socioeconomic status and advanced maternal age.[32]

Anemia

Iron deficiency anemia in pregnancy has been associated with an increased risk of low birth weight, preterm delivery, and perinatal mortality.[33] Screening for iron deficiency may be initiated upon initial notification of pregnancy to clinic. [3,33-35] *(USPSTF Grade B)* Anemia screening should involve a hematocrit or hemoglobin test. *(USPSTF Grade B)* Repeat testing may be done again between 24-28 weeks gestation using a hematocrit or hemoglobin test.[36] (*UW Health Low quality evidence, weak/conditional recommendation*)

Antibody testing

All pregnant women should be tested for ABO blood group (Rh-D type) and screened for the presence of erythrocyte antibodies (type and screen) during the first prenatal visit.[3,6,35,37,38] *(USPSTF Grade A)*

Antibody testing should be repeated in un-sensitized Rh (D)-negative patients at 24-28 weeks of gestation, unless the biological father is known to be Rh (D)-negative.[38] *(USPSTF Grade B)* Patients who are un-sensitized D-negative should receive prophylactic anti-D immunoglobulin (RhoGAM 300 mcg) at 28 weeks, or at the time of any of the following[3,6,37]:

- Ectopic gestation
- Abortion (threatened, spontaneous or induced)
- Procedures associated with possible fetal-to-maternal bleeding, such as chorionic villus sampling or amniocentesis

- Conditions associated with fetal-maternal hemorrhage (i.e., abdominal trauma)
- Unexplained vaginal bleeding during pregnancy
- Delivery of a newborn who is D-positive

Testing should be completed prior to immunoglobulin (RhoGAM) administration.[37] *(UW Health Low quality of evidence, strong recommendation)*

Gestational diabetes

The American College of Obstetricians and Gynecologists (ACOG) recommend that all pregnant individuals be screened for gestational diabetes mellitus (GDM). Screening should ideally occur between 24 and 28 weeks of pregnancy. It is recommended that all pregnant patients be screened for GDM with a 50 gram (non-fasting) oral glucose challenge test (OGTT) with plasma glucose measurement at 1 hour.[39] *(UW Health Moderate quality of evidence, strong recommendation)*

If the plasma glucose level measured at 1 hour is ≥ 140 mg/dL, a 100 gram three-hour OGTT should be performed when the patient has fasted.[39] *(UW Health Low quality of evidence, strong recommendation)* Gestational diabetes is diagnosed if 2 or more plasma glucose measurements (measured fasting, 1 hr, 2 hr, 3 hr after OGTT) listed in **Table 4** are met or exceeded.[40]

Table 4. Diagnostic values for Gestational Diabetes in 100 gram OGTT test

		Carpenter/Coustan
Pre-OGTT	**Fasting**	95 mg/dL
Hours after OGTT	**1 hour**	180 mg/dL
	2 hour	155 mg/dL
	3 hour	140 mg/dL

Initial visit with provider – Special populations

Chronic hypertension

The following laboratory tests are recommended to be obtained during the first prenatal visit for any pregnant patient with chronic hypertension or a history of a hypertensive order of pregnancy (e.g., preeclampsia):[31,41] *(UW Health Low quality of evidence, strong recommendation)*

- Baseline measure of creatinine
- Baseline measure of uric acid
- Baseline liver AST/ALT
- Baseline protein creatinine ratio

It is advised that providers counsel patients on taking low-dose daily aspirin (81 mg/daily) after 12 weeks gestation to prevent preelampsia.[32] *(USPSTF Grade B)*

Hypothyroidism

A Thyroid-stimulating hormone (TSH) and a free thyroid hormone-4 (T4) level are typically needed to appropriately diagnose thyroid disorder/condition (i.e., over hypothyroidism, subclinical hyperthyroidism, hypothyroxinemia.)[42] Therefore, it is recommended that at the first prenatal visit, patients with hypothyroidism have their TSH and T4 levels checked. *(UW Health Moderate quality of evidence, strong recommendation)*

Between 50-85% of hypothyroid patients will require an increased in levothyroxine dosing during pregnancy. It is recommended that pregnant patients with hypothyroidism be advised that

thyroid dose adjustments will likely be needed throughout the first trimester. *(ATA Strong recommendation, high quality evidence)*

The American Thyroid Association recommends that levothyroxine dose be adjusted by approximately 20-30% upon confirmation of pregnancy (i.e., positive home pregnancy test) however providers may choose to increase dose/adjust medication based on TSH and free T4 levels at the first prenatal visit.[42,43]

Pregnant patients with hypothyroidism or at risk for hypothyroidism should be monitored with a serum TSH measurement every 4 weeks until midgestation (~20 weeks) and at least once near 30 weeks gestation.[43]*(ATA Strong recommendation, high quality evidence)*

If trimester-specific reference ranges for TSH are not available in/per the laboratory, the following reference ranges may be used:[44] *(UW Health Moderate quality of evidence, weak/conditional recommendation)*

- 0.1-2.5 mIU/L for first trimester
- 0.2-3.0 mIL/L for second trimester
- 0.3 -3.0 mIL/L for third trimester

Obese patients

Obesity is a risk for gestational hypertension, preeclampsia and gestational diabetes. Congenital malformations including cardiac defects and neural tube defects are more common among obese pregnant patients.[45] Patients who meet criteria listed in **Table 5** should be managed for consideration of maternal obesity.[41]

Table 5. Criteria for consideration of maternal obesity

- Patients with a body mass index ≥30 kg/m^2 (i.e., obese)
- Patients with a body mass index ≥25 kg/m^2 (i.e., overweight) with one of the following risk factors:
  - Family history of Type 2 Diabetes (i.e., 1st degree relative)
  - History of gestational diabetes
  - History of macrosomic infant
  - History of glucose intolerance
  - Polycystic Ovarian Syndrome (PCOS)
  - Metabolic disorder
  - Hypertension
  - Hyperlipidemia
  - Chronic systemic steroid use

For patients with BMI > 35 kg/m^2, consider recommending use of 5 mg folic acid up to 12 weeks to reduce risk of neural tube defects.[46,47] *(UW Health Moderate quality of evidence, weak/conditional recommendation)*

The following labs should be obtained during the initial prenatal visit: *(UW Health Low quality of evidence, strong recommendation)*[48]

- A1 c measurement (if not already ordered)
- Baseline measure of creatinine
- Baseline measure of uric acid
- Baseline AST/ALT
- Baseline protein creatinine ratio

During the initial prenatal care visit, a referral to Nutrition may be offered to the patient too.[46,47] *(UW Health Low level of evidence, strong recommendation)*

Table 6 lists labs and suggested additional interventions depending on the pregnant patient's BMI.[45-47,49,50] *(UW Health Low quality of evidence, strong recommendation)*

Table 6. Labs and additional interventions for pregnant obese patient

BMI > 25-29 kg/m^2 with at least 1 additional risk factor	BMI 30-39 kg/m^2	BMI ≥ 40 kg/m^2
• A1 c measurement (if not already ordered) • Baseline measure of creatinine • Baseline measure of uric acid • Baseline AST/ALT • Baseline protein creatinine ratio	• A1 c measurement (if not already ordered) • Baseline measure of creatinine • Baseline measure of uric acid • Baseline AST/ALT • Baseline protein creatinine ratio • Consider 5 mg folic acid	• A1 c measurement (if not already ordered) • Baseline measure of creatinine • Baseline measure of uric acid • Baseline AST/ALT • Baseline protein creatinine ratio • Consider 5 mg folic acid • Screen for sleep apnea • Consider/order ECHO • Refer to anesthesia for consult

History of gestational diabetes

Any patient with a history of diabetes, gestational diabetes or a history of macrosomic pregnancy (i.e., birthweight > 4000 grams or birthweight) is considered at risk for gestational diabetes in current pregnancy. Additional risk factors for GDM include: [39,40,47]

- BMI > 30
- First or second degree relative with type 2 diabetes
- BMI > 25 and one other risk factor (i.e., history of glucose intolerance defined as A1c > 5.7% or fasting plasma glucose > 100 mg/dL)
- High risk race/ethnicity (e.g., Native American, African American, Latino, Asian American, Pacific Islander)
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovarian syndrome, or small-for-gestational-age birthweight)

If the patient is willing, a fasting glucose test is recommended. However, if the patient is unable to do fasting glucose test, it is strongly recommended to obtain an A1c measure, if one has not been already ordered. [39,40,47] *(UW Health Low quality of evidence, strong recommendation)*

Previous preterm labor (i.e., spontaneous delivery before 37 weeks gestation)

- It is recommended that a patient with a singleton gestation and prior spontaneous preterm birth be offered progesterone supplementation starting at 16-20 weeks of gestation.[51] *(UW Health Moderate quality of evidence, strong recommendation)*
    - 250 mg of 17-alpha-hydroxy-progesterone (17-OHPC) weekly[52]
- Vaginal progesterone is recommended as a preterm labor management option in asymptomatic patients without a previous preterm birth delivery who are identified with short cervical length (≤20 mm) before or after 24 weeks of gestation. [51] *(UW Health Moderate quality of evidence, strong recommendation)*

- Suggested dosing: vaginal progesterone (200 mg or 90 mg gel) nightly starting by 24 weeks until 36 6/7 weeks[52]

For pregnant patients between 24-34 weeks of gestation who are at risk of delivery within 7 days, a single course of corticosteroids is recommended.[53] *(UW Health Moderate quality of evidence, strong recommendation)*

Aneuploidy/Open Neural Tube Defects Screening Options

Aneuploidy/Open neural tube defects screening discussion

It is recommended that all pregnant patients be offered aneuploidy screening or diagnostic testing, regardless of maternal age.[54] *(UW Health Very low quality evidence, strong recommendation)* Screening for aneuploidy should be an informed patient choice. All providers should be familiar with the available screening and testing options and have a standard approach to counseling women, ideally at the initial provider visit.[55] The most common prenatal screening options are: first trimester screen (i.e., nuchal translucency), maternal serum alpha fetoprotein (MS-AFP) screen, Quad screen, 20 week ultrasound and Non-invasive prenatal testing (i.e., cell free DNA testing.) The most common diagnostic tests done are chorionic villus sampling (CVS) and amniocentesis. **Table 7** outlines detection rates and pregnancy risks involved with these screening and diagnostic tests while **Table 8** lists advantages and disadvantages to consider.

"No one screening test is superior to other screening tests in all test characteristics. Each test has relative advantages and disadvantages. It is important that obstetrician–gynecologists and other obstetric care providers be prepared to discuss not only the risk of aneuploidy but also the benefits, risks, and limitations of available screening tests."[55] Patients should also be advised that not all screening options may be covered by insurance without prior authorization. For example, NIPT is often covered one pre-authorization has been obtained for patients who meet the following criteria:

- Maternal age 35 years or older at delivery;
- Fetal ultrasonographic findings indicating an increased risk for aneuploidy;
- History of a prior pregnancy with a trisomy;
- Positive test results for aneuploidy, including first trimester, sequential, integrated or quad screen;
- Parental balanced robertsonian translocation with increased risk for fetal trisomy 13 or 21).[56]

Women with an abnormal screening test should be offered diagnostic testing and if feasible, a referral to genetic counselor should be considered or offered.[54] *(UW Health Low quality of evidence, strong recommendation)* A negative screening test does not rule out the disease that was screened.

Table 7. Detection rates and pregnancy risks involved with select prenatal screening interventions

	Screening					Diagnostic	
	First Trimester Screen[57-64]	**Quad Screen**[65-73]	**AFP**[65]	**20 Week Ultrasound**[74]	**NIPT**[75-78]	**CVS**[79]	**Amniocentesis**[79]
Timing	11 4/7-13 6/7 weeks (IRA- blood 9 0/7)	15 – 22 6/7 weeks	15 – 22 6/7 weeks	20 weeks	> 9-10 weeks	11 4/7 – 13 6/7 weeks	> 15-16 weeks
Detection Rates: Aneuploidy	Trisomy 21: 91-95% Trisomy 18: 95% Trisomy 13: 95% (False Positive 2%)	Trisomy 21: 77-81% Trisomy 18: 60-80% Trisomy 13: N/A (False Positive 6-7%)	N/A	Trisomy 21: 50% Trisomy 18: 75% Trisomy 13: 80% (False Positive 11-17%)	Trisomy 21: 99% Trisomy 18: 99% Trisomy 13: 91% Other (False Positive 0.5%)	> 99%	> 99%
Detection Rates: Open Neural Tube Defects (ONTD)	ONTD: N/A Anencephaly: 90%	80%	80%	ONTD: 95% Anencephaly: 99%	N/A	N/A	98-99%
Pregnancy Risks	None	None	None	None	None	0.1%-0.3% (1/1000 – 1/300)	0.1%-0.3% (1/1000 – 1/300
Turn around time (TAT)	5-7 days IRA- Same day as U/S	4-6 days	3 days	Same day	6-10 days Phone Call	10-14 days Phone Call	7-10 days Phone Call

Table 8. Advantages and Disadvantages of Aneuploidy and Open Neural Tube Defect Screening Options

	Test	Advantages	Disadvantages

Non-invasive	**Cell free DNA screening**	• Screens for Trisomy 21, 18, 13, sex chromosome aneuploidy, +/- microdeletions or triploidy (depending on company)
		• No risk to pregnancy
		• Early (9-10 weeks)
		• Among screening tools:
		  • Highest detection rates (91-99%)
		  • Lowest false positive rates (1% or less)
		• Easy – blood only (can be done at PCP office but at this time many pts referred to genetic counselor)
		• TAT: 6-10 days
			• Not Diagnostic
			• Limited insurance coverage, policies & plans vary
			• Only specific trisomies, +/- microdeletion syndromes
			• Different testing companies with different platforms & costs
			• Not consistent detection rates across diseases
			• New technology, potential lack of understanding among patients and providers
			• Possible no results due to low fetal fraction

	First Trimester Screening (FTS)	• Screens for Trisomy 21, 18, 13 (T13 +/- depending on lab) • No risk to pregnancy • Early (12-14 weeks) • High detection (91-95%) • Quick (TAT ~ 3-5 days)	• Not Diagnostic • Requires referral to certified center • False positives (2-5%) • Does not screen for open neural tube defects (ONTD)
	Quad	• Screens for Trisomy 21, 18 • No risk to pregnancy • Screens for ONTD • Easy – blood only in PCP office • TAT: 4-6 days	• Not Diagnostic • Highest false positives compared to FTS & NIPT • Later in pregnancy (>15-16 weeks)
Invasive	**Chorionic Villus Sampling (CVS)**	• Diagnostic (>99%) • Tests for all aneuploidy (polyploidy) • Test for other chromosome anomalies (e.g. translocations) • Test for other genetic diseases as indicated • Early (12-14 weeks) • TAT 10-14 days (if available, prelims in 48 hours)	• Risk of miscarriage or complication • Does not test for ONTD • Mosaicism • Possible no results due to low sample size
	Amniocentesis	• Diagnostic (>99%) • Tests for all aneuploidy (polyploidy • Test for other chromosome anomalies (e.g. translocations) • Test for other genetic diseases as indicated • Tests for ONTD (98%) • TAT: 7-10 days (if added on, FISH 48 hours)	• Risk of miscarriage or complication • Later in pregnancy (>15-16 weeks)

Carrier Screening for Genetic Disorders

Discussion of Genetic Carrier Screening

It is recommended that the prenatal care provider review carrier screening options for genetic disorders, ideally prior to pregnancy, or at the initial provider visit. *(UW Health Low quality evidence, weak/conditional recommendation)* All patients, "regardless of screening strategy and ethnicity, should be offered carrier screening for cystic fibrosis and spinal muscular atrophy, as well as a complete blood count and screening for thalassemias and hemoglobinopathies." Carrier screening for other diseases may be considered based on family or medical history and ethnicity.[80] Providers should be aware that patients may decline any or all carrier screening. Genetic carrier screening for a specific disease typically does not need to be repeated with subsequent pregnancies. It is recommended a patient's medical record have clear documentation of any completed carrier screening. *(UW Health Very low quality evidence, strong recommendation)*

Patients should be counseled about the limitations of carrier screening, namely that a negative test result does not eliminate risk entirely, but reduces risk. *(UW Health Very low quality evidence, weak/conditional recommendation)* The partner of an identified carrier should be offered carrier screening as well. *(UW Health Very low quality evidence, weak/conditional recommendation)* A referral to genetic counseling should be considered for women identified as carriers or with family histories of genetic disease.

Cystic Fibrosis

Cystic Fibrosis is a genetic disorder that causes a buildup of thick, sticky mucus in the lungs, pancreas and other organs. In the lungs, the mucus clogs the airways and traps bacteria leading to infections, extensive lung damage, and eventually, respiratory failure. In the pancreas, the mucus prevents the release of digestive enzymes that allow the body to break down food and absorb vital nutrients.

As it is increasingly difficult to assign a single ethnicity to individual patients, cystic fibrosis screening may be offered to all patients.[3,81-83] *(UW Health Low quality evidence, weak recommendation)* Screening should be completed using a cystic fibrosis mutation panel and not gene sequencing. Screening is most efficacious in the non-Hispanic white and Ashkenazi Jewish populations, and so a residual risk should be provided to all patients. This disease is also screened for on the newborn screen.

Spinal Muscular Atrophy

Spinal Muscular Atrophy (SMA) is a genetic disorder that results in progressive muscle weakness and paralysis. The most severe type of SMA is usually diagnosed within the first few months of life. Affected children have severe muscle weakness and typically do not survive past the age of 2, if untreated. There are other types of SMA that are less common than the severe type and involve a lesser degree of muscle weakness. Most affected individual need to use wheelchairs or need assistance with walking. Life expectancy for the less severe types ranges from the teenage years to adulthood.

All women who are consider pregnancy or who are pregnant should be offered carrier screening for spinal muscular atrophy (SMA).[84,85] *(UW Health Low quality of evidence, weak/conditional recommendation)* Pretest counseling should include a discussion of the range of severity of the disease, as well as the limitations of carrier screening in different populations. Screening should be completed using a *SMN1* gene dosage assay (i.e., quantitative polymerase chain reaction)

Hemoglobinopathies

Hemoglobinopathies are a group of genetic disorders that affect hemoglobin. Some hemoglobinopathies may cause only mild anemia. Others can cause more significant lifelong health issues and be life-threatening. Sickle cell anemia is one of the most well-known hemoglobinopathies.

It is recommended that all pregnant patients be screened for anemia and risk for hemoglobinopathies via complete blood count with red blood cell indices. Women with a low mean corpuscular hemoglobin or mean corpuscular volume should be offered hemoglobin electrophoreses. Pregnant patients of Southeast Asian, African, West Indian, or Mediterranean descent should be offered hemoglobinopathy screening, as these women are at an increased risk.[6,35,83,86] (*UW Health Moderate quality of evidence, weak/conditional recommendation*) Screening should be offered at the first prenatal visit if it was not offered during pre-conception.

Patients of Southeast Asian, West Indian, or Mediterranean descent
Accurate hemoglobin identification should be completed using a complete blood count (CBC) in patients of non-African descent.[86] *(UW Health Low quality evidence, strong recommendation)* If the results indicate a reduced mean corpuscular volume (MCV < 80 fL) and normal iron studies, a hemoglobin electrophoresis should be ordered. If the MCV is below normal, iron deficiency anemia has been excluded, and the hemoglobin electrophoresis is not consistent with β-thalassemia trait (i.e., there is no elevation of Hb A2 or Hb F), then DNA-based testing should be used to detect α-globin gene deletions characteristic of α-thalassemia.[86] *(UW Health Low quality evidence, weak/conditional recommendation)*

Patients of African descent
For patients of African descent, hemoglobulin testing using a hemoglobin electrophoresis in addition to a CBC is recommended.[86] *(UW Health Low quality evidence, weak/conditional recommendation)* If the MCV is below normal (< 80 fL), iron deficiency anemia has been excluded, and the hemoglobin electrophoresis is not consistent with β-thalassemia trait (i.e., there is no elevation of Hb A2 or Hb F), then DNA-based testing should be used to detect α-globin gene deletions characteristic of α-thalassemia.[86] *(UW Health Low quality evidence, weak/conditional recommendation)*

Fragile X Syndrome

Fragile X Syndrome (FXS) is an X-linked, genetic disorder that causes intellectual disabilities, behavioral and learning challenges and various physical characteristics. Although it can occur in both sexes, males are more frequently affected and more severely affected than females.[87] Carrier females can present with ovarian insufficiency before age 40 years. Male or female carriers of a pre-mutation can present with Fragile-X-associated tremor/ataxia syndrome (FXTAS).[88]

Carrier screening is recommended to women with a family history of fragile X, a family history of unexpected intellectual disability suggestive of fragile X. *(UW Health Low quality evidence, weak/conditional recommendation)* Women with unexplained ovarian insufficiency should be offered carrier screening too. It is reasonable to offer fragile X screening to a woman that requests it but does not have an indication after she has been informed of the benefits, limitation and risks of screening.[83] *(UW Health Very Low quality evidence, weak/conditional recommendation)*

Tay - Sachs disease

Tay-Sachs disease is a progressive neurodegenerative genetic disorder that often presents in infancy. There is regression of skills, seizures, loss of vision and hearing, and severe intellectual disability. Children with the severe form of Tay-Sachs often die within childhood. There are other forms of Tay-Sachs, although they are less common and often less severe.

Carrier screening is recommended to women if either she or her partner is of Ashkenazi Jewish, French-Canadian or Cajun descent, ideally prior to pregnancy or at the initial provider visit.[83,89] Anyone with a family history of the disease should be offered carrier screening. (*UW Health Low quality of evidence, strong recommendation*) Given these ethnicities, screening can occur with use of a Tay-Sachs common mutation panel. Although screening can be completed using the hexosaminidase enzyme level within serum, caution should be exercised as there can false positive in the pregnant woman or the woman taking oral contraceptive.

Genetic Diseases in Patients of Ashkenazi Jewish Descent

For those couple with at least one person of Ashkenazi Jewish descent, further genetic carrier screening can be offered. Recommendations for which diseases should be considered vary amongst professional groups. Referral to a genetic counselor for discussion of carrier screening options is recommended. (*UW Health Very low quality of evidence, weak/conditional recommendation*)

Expanded Carrier Screening

Given advances in technology, a large number of genetic diseases can be screened for simultaneously regardless of ancestry or family history. Expanded carrier screening can screen for several to hundreds of disorders, and it is reasonable to consider this option of carrier screening. Each provider should "establish a standard approach that is consistently offered to and discussed with each patient, ideally before pregnancy."[80] (*UW Health Very low quality of evidence, weak/conditional recommendation*)

Immunizations in pregnancy

Influenza vaccination

Pregnant patients infected with the flu have increased rates of hospitalization, cardiopulmonary complications and death compared with the general population. The Centers for Disease Control recommends that all pregnant patients receive inactivated influenza vaccination during the flu season.[90-92] (*UW Health Moderate quality of evidence, strong recommendation*)
Live attenuated vaccine is contraindicated. It is also recommended that partner, family members and infant caregivers also be vaccinated during the flu season.[90](*UW Health Moderate quality of evidence, strong recommendation*)

Tetanus, diphtheria and pertussis vaccination (Tdap)

It is recommended to administer Tdap vaccine to all pregnant patients during <u>*each*</u> pregnancy, as early as 27-36 weeks gestation.[93,94] (*UW Health Moderate quality of evidence, strong recommendation*) Partners, family members and infant caregivers should be offered Tdap as well, if not previously vaccinated. If vaccination is indicated, it should take place at least 2 weeks before contact with newborn.[90,95](*UW Health Moderate quality of evidence, strong recommendation*)

Labor considerations and planning

Confirm vertex presentation

It is recommended that fetal presentation be assessed and documented beginning at 36 weeks gestation to allow for external cephalic version.[96] If vertex presentation cannot be confirmed, limited ultrasound may be considered.[97] (*UW Health Low quality of evidence, strong recommendation*)

If the fetus is determined to be in breech presentation, patients should be counseled that if spontaneous version is to occur, will likely have taken place by 37 0/7 weeks of gestation. Referral of a patient to Obstetrics for possible external cephalic version or potential scheduled cesarean section should be considered. [96] (*UW Health Low quality of evidence, weak/conditional recommendation*)

Trial of labor after cesarean delivery (TOLAC) discussion

It is recommended to have a thoughtful discussion on labor and delivery plans with patients who are candidates for vaginal birth after cesarean (VBAC). (*UW Health Very low quality of evidence, strong recommendation*) Patients should be informed of the benefits associated with a TOLAC (e.g., shorter recovery period, lower risk of infection and less blood loss) and also the risks as well (i.e., rupture of scar on the uterus or rupture of uterus itself.)[98] Any patient wishing to have a TOLAC should be referred to Obstetrics prior to labor and delivery to ensure informed consent and labor planning is done in a timely manner. (*UW Health Very low quality of evidence, strong recommendation*)

Herpex simplex virus (HSV) suppression

Patients with known recurrent genital herpex simplex virus have a high risk of transmitting HSV to their neonates. It is recommended to offer acyclovir or valacyclovir at 36 weeks gestation to decrease risk of clinical lesions and viral shedding at time of delivery, thereby also reducing need for cesarean section.[99,100] (*UW Health High quality of evidence, strong recommendation*)

Antepartum Fetal Surveillance

The goal of antepartum fetal surveillance is to prevent fetal death. Antepartum fetal surveillance techniques include maternal-fetal movement assessment (i.e., "counting kicks"), contraction stress test, nonstress test, and umbilical artery Doppler velocimetry.[101] **Table 9** provides select indications for antepartum fetal surveillance and suggestions for when to initiate testing and testing frequency.

Table 9. Common Indications for Antepartum Fetal Surveillance[31,101-105]

	Diagnosis	Gestational Age to Initiate Testing	Frequency of testing	UW Recommendation
Maternal conditions	Advanced maternal age (age at delivery ≥ 40 years)	38 weeks	Once a week	*Moderate evidence, strong recommendation*
Pregnancy related conditions	Diabetes, diet controlled	34 weeks	Twice a week	*Low quality evidence, weak/conditional recommendation*
	Diabetes, treated with medication	32 weeks	Twice a week	*Low quality evidence, weak/conditional recommendation*
	Chronic hypertension*	32 weeks*	Twice a week*	*Low quality evidence, weak/conditional recommendation*
	Pregnancy-induced hypertension*	At diagnosis*	Twice a week*	*Low quality evidence, weak/conditional recommendation*
	Preeclampsia	At diagnosis	Twice a week	*Low quality evidence, weak/conditional recommendation*
	Obesity/BMI ≥ 40	32 weeks	Twice a week	*Low quality evidence, weak/conditional recommendation*
	Post-term pregnancy ≥ 41 weeks	41 weeks	Twice a week	*Moderate quality evidence, strong recommendation*
	* *For hypertensive disorders related to pregnancy, consider monitoring with serial growth ultrasounds monthly starting at 28 weeks gestation*			*Low quality evidence, weak/conditional recommendation*
Fetus concerns	Amniotic fluid volume, oligohydramnios (AFI < 5 cm)	At diagnosis	Discussed/determined with maternal fetal medicine provider	*Moderate quality evidence, strong recommendation*
	Growth restricted fetus	28 weeks or at diagnosis	1-2 times per week or at discretion of maternal fetal medicine provider	*Moderate quality evidence, strong recommendation*
	Previous stillbirth/intrauterine fetal demise (IUFD)	32 weeks or 2 weeks prior to previous stillbirth	Twice a week	*Moderate quality evidence, strong recommendation*

Depression in Pregnancy

Depression and anxiety are common in pregnancy and the postpartum period and depression, in particular, is a common complication of pregnancy and in the post-partum period.[106] The exact impact of depression on the fetal environment is not known, however postpartum depression can have a potentially devastating impact on a mother and children. Long term risks associated with post-partum depression include recurrence of peripartum and non-peripartum depression and children of mothers with peripartum depression are at increased risk for development delays and behavioral problems.[107,108] Given depression in pregnancy is a risk factor for peripartum depression, screening for and treating depression in pregnancy is critical.

Risk Factors for Depression

Risk factors are often intertwined and related, and may vary based upon patient age and experiences. Patients with chronic illnesses such as diabetes, cardiovascular disease, and chronic pain are at a higher risk for depression.[109,110] **Table 10** lists risk factors for depression in pregnancy.

Table 10. Risk Factors for depression in pregnancy*[108]

Biological	• Personal history of depression • Unintended pregnancy • Concurrent anxiety
Environmental	• Low socioeconomic status • Exposed to domestic violence • Single • Lack of social support • Stressful life events

**Risk factors for postpartum depression are similar to those for depression in pregnancy. In addition, women with depression during pregnancy have an elevated risk of postpartum depression.[108]*

Screening for depression in pregnancy (12 years or older)

Pregnant adolescents or adults should be screened at the first prenatal visit, during the third trimester (24-32 weeks), and at six weeks postpartum.[109,111-113]*(UW Health Low quality evidence, strong recommendation)* Screening may be completed using the Edinburgh Postnatal Depression Scale (EPDS), Patient Health Questionnaire-9 (PHQ-9) or Patient Health Questionnaire-A (PHQ-A) assessment tools.[111,114]

A total score of 10 points of greater on the EPDS constitutes the need for clinical evaluation and documentation of a follow-up plan. An affirmative response to Question 10 (suicidality) constitutes the need to access crisis intervention services.[115]

Edinburgh Postnatal Depression Scale (EPDS)	
Population	Postpartum patients
Number of Questions	10
Administrator	Self-administered by patient
Scoring:	
Max Score	30 points
Positive Threshold (At-Risk)	**10 points or greater**
Positive Threshold (Suicide Risk)	**Affirmative response to Question 10**

A total score of 10 points or greater on the PHQ-9 or PHQ-A indicates the need for clinical evaluation and documentation of a follow-up plan.[116,117]

Follow-up Plan Documentation

According to the ACO Quality measure, all patients who screen positive on a validated depression screening tool must have a documented follow-up plan on the date of the positive screen. This plan must contain one or more of the following:

- Additional evaluation for depression
- Suicide Risk Assessment
- Referral to a practitioner who is qualified to diagnose and treat depression
- Pharmacological interventions
- Other interventions or follow-up for the diagnosis or treatment of depression.

For additional information on postpartum depression, refer to the UW Health Depression: Diagnosis and Treatment – Adult/Pediatric/ Ambulatory clinical practice guideline.

Treatment of depression in pregnant patient (12 years or older)

The treatment of depression during pregnancy should be completed using a shared-decision making process which weighs the potential risk of fetal exposure to psychotropic medication against the potential adverse effects of an untreated disorder.[109,113,118] *(UW Health Low quality evidence, weak recommendation)* It is important to engage the patient and significant others in this discussion about what is best for their situation (patient's preference), what treatment options are available, and that the ultimate goal is for the patient and baby to be as safe as possible.[119] The treatment decision may also depend on the patient's history of depression prior to pregnancy, past experience with medications, severity of the depression, support available, response to alternative treatment modalities, etc.

Psychotherapy (IPT or CBT) is recommended whenever possible for mild to moderate depression, in patients who have exhibited a positive response in the past, or by patient preference.[118,120] *(APA Grade I)* Interpersonal therapy is considered to be particularly useful during pregnancy as it directly addresses issues associated with role transitions and relationships with the partner.

Patients, who have become significantly depressed while off antidepressant medication in the past, will likely need to continue taking antidepressant medication in pregnancy to prevent recurrence of symptoms. Pregnant patients with new onset of moderate to severe depression in pregnancy may require medication in addition to psychotherapy to ensure the best treatment response.[109,120] *(APA Grade II)* The goal of pharmacotherapy is to treat to remission to avoid exposing the infant to both the antidepressant medication and maternal depression. Refer to **Appendix B** for screening and initial treatment algorithm for depression in pregnancy.

Current evidence is insufficient to establish a direct relationship between antidepressant use during pregnancy and risks or adverse birth outcomes.[118,121] Select serotonin reuptake inhibitors (SSRIs), except for paroxetine and tricyclic antidepressants (TCAs) may be used if preferred by the patient. *(UW Health Low quality evidence, weak/conditional recommendation)* Paroxetine (FDA category D) is not recommended in women who are planning to become pregnant or for use in early pregnancy (i.e., first trimester) as some studies have found increased risk of cardiac defects with more than 25 mg/day of paroxetine use in the first trimester.[118,122,123] *(UW Health Low quality evidence, weak/conditional recommendation)* **Table 11** lists select medications that are considered preferred for treatment of depression in pregnancy. For additional information on

medication dosing and side effects, refer to **Appendix C** or the UW Health Depression: Diagnosis and Management clinical practice guideline.

Table 11. Select medications for pharmacologic treatment of depression in pregnancy

	Pregnancy	Lactation
Preferred	• Sertraline • Citalopram • Escitalopram	• Sertraline • Paroxetine
May Consider	• Fluoxetine • Bupropion (if smoking cessation concurrent issue) • Paroxetine (in late pregnancy/post-partum) • Tricyclic antidepressants	• Fluvoxamine • Citalopram • Venlafaxine • Escitalopram
Limited data	• Venlafaxine • Fluvoxamine • Mirtazapine	• Mirtazapine • Bupropion
Discouraged	• Paroxetine (in 1st trimester)	• Fluoxetine

Electroconvulsive therapy (ECT) is an additional treatment option for patients who are pregnant with depression and psychotic or catatonic feature, moderate to severe depression unresponsive to pharmacotherapy or psychotherapy, or by patient preference.[120] *(APA Grade II)* Any patient who is considering ECT for depression treatment should be referred to and evaluated by Psychiatry prior to ECT initiation. *(UW Health Very low quality evidence, strong recommendation)*

Patient education on depression

It is important to educate patients on depression and the important of adhering to treatment. Patients may not realize that the full effect of medication may not occur for a few weeks despite some immediate side effects of antidepressant medication thus it is important to have a frank discussion with the patient surrounding depression and its treatment. **Table 12** offers some counseling points to discuss with when initiating pharmacotherapy.

Table 12. Suggested counseling points when initiating pharmacotherapy for depression

- Antidepressants must be taken daily for 2-4 weeks for a noticeable effect.
- Educate patient on potential side effects which may occur before full effect of medication is noticed. Many side effects typically resolve after 1-2 weeks and usually by the time medication is in full effect.
- Take medication daily as prescribed. Do not stop taking antidepressant without checking with your provider. Some antidepressants may have uncomfortable withdrawal symptoms.
- Continue to take medication even if you are feeling better due to an increased risk of relapse if stopped before 6 months.
- Contact your provider and/ or pharmacy if you have questions about your medication(s).
- Be sure to make and keep follow-up appointments. This is important to ensure full response to your medication.
- The medication is not addictive and will not change your personality. Depression alters brain functioning and the medication helps restore normal patterns, so you eat and sleep more normally, think more clearly and have more energy.
- The medication should help you benefit from the psychotherapy you are receiving.
- Do not drink alcohol during pregnancy and especially while taking medication.

Methodology

Development Process

Each guideline is reviewed and updated a minimum of every 3 years. All guidelines are developed using the guiding principles, standard processes, and styling outlined in the UW Health Clinical Practice Guideline Resource Guide. This includes expectations for workgroup composition and recruitment strategies, disclosure and management of conflict of interest for participating workgroup members, literature review techniques, evidence grading resources, required approval bodies, and suggestions for communication and implementation.

Methods Used to Collect the Evidence:

The following is a list of various search terms that were used individually or in combination with each other for literature searches on PubMed: depression, pregnancy, antidepressant side effect, lactation, prenatal guideline, antepartum fetal surveillance, hepatitis c screening, prenatal screening, vaccination pregnant, maternal mental heatlh, acog practice bulletin, acog committee opinion, fetal health surveillance, obesity, antenatal testing, hypothyroidism.

Literature Sources:

- Electronic database search (e.g., PubMed)
- Databases of systematic reviews (e.g., Cochrane Library)
- Hand-searching journals, external guidelines, and conference publications
- Medical textbooks/references

Time Period: October 2017 to December 2017

Methods to Select the Evidence:

Literary sources were selected with the following criteria in thought: English language, subject age (i.e., age ≥12 years), publication in a MEDLINE core clinical journal and strength of expert opinion (e.g., professional society guideline).

Methods Used to Formulate the Recommendations:

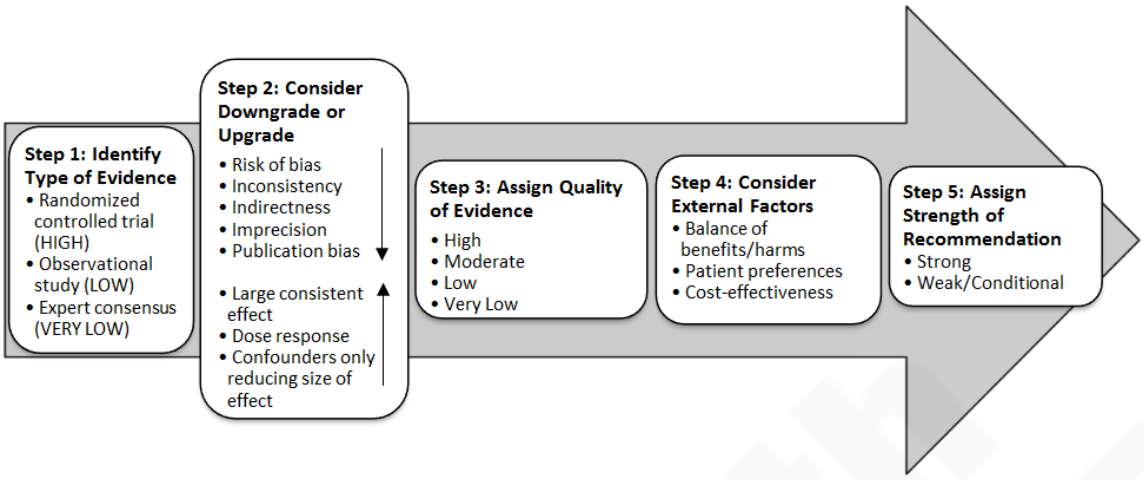
The workgroup members agreed to adopt recommendations developed by external organizations and/or created recommendations internally via a consensus process using discussion of the literature and expert experience/opinion. If issues or controversies arose where consensus could not be reached, the topic was escalated appropriately per the guiding principles outlined in the UW Health Clinical Practice Guideline Resource Guide.

Methods Used to Assess the Quality of the Evidence/Strength of the Recommendations:

Recommendations developed by external organizations maintained the evidence grade assigned within the original source document and were adopted for use at UW Health.

Internally developed recommendations, or those adopted from external sources without an assigned evidence grade, were evaluated by the guideline workgroup using an algorithm adapted from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (see **Figure 1**).

Figure 1. GRADE Methodology adapted by UW Health



Rating Scheme for the Strength of the Evidence/Recommendations:

GRADE Ranking of Evidence

High	We are confident that the effect in the study reflects the actual effect.
Moderate	We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.
Low	The true effect may differ significantly from the estimate.
Very Low	The true effect is likely to be substantially different from the estimated effect.

GRADE Ratings for Recommendations For or Against Practice

Strong	The net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.
Weak/conditional	Recommendation may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.

U.S Preventive Services Task Force (USPSTF) Grades for Recommendations

A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial
B	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.
C	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.
D	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.
I Statement	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.

Infectious Diseases Soceity of America-US Public Health Grading System for Ranking Recommendations in Clinical Guidelines

Category, grade	Definition
A	Good evidence to support a recommendation for use; should always be offered
B	Moderate evidence to support a recommendation for use; should generally be offered
C	Poor evidence to support a recommendation; optional
D	Moderate evidence to support a recommendation against use; should generally not be offered
E	Good evidence to support a recommendation against use; should never be offered
Quality of Evidence	
I	Evidence from ≥ 1 properly randomized, controlled trial
II	Evidence from ≥ 1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studied (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments properly randomized, controlled trial
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports or expert committees

Centers for Disease Control and Prevention Evidence Based Rating System

Category	Definition	Recommendation
A	Strong evidence for efficacy and substantial clinical benefit	Strongly recommended
B	Strong or moderate evidence for efficacy but only limited clinical benefit	Generally recommended
C	Insufficient evidence for efficacy or efficacy does not outweigh possible adverse consequences	Optional
D	Moderate evidence against efficacy or for adverse outcome	Generally not recommended
E	Strong evidence against efficacy or for adverse outcome	Never recommended
Quality of Evidence		
I	Evidence from at least one well-executed randomized, controlled trial or one rigorously designed laboratory-based experimental study that has been replicated by an independent investigator	
II	Evidence from at least one well-designed clinical trial without randomization, cohort or case-controlled analytic studies (preferably from more than one center), multiple time-series studies, dramatic results from uncontrolled studies, or some evidence from laboratory experiments	
III	Evidence from opinions of respected authorities based on clinical or laboratory experience, descriptive studies, or reports of expert committees	

American Thyroid Association (ATA) Recommendations Based on Strength of Evidence

Recommendation strength	Quality of evidence	Description of supporting evidence	Interpretation
Strong recommendation	***High***	RCT without important limitations or overwhelming evidence from observational studies	Can apply to most patients in most circumstances without reservation
	Moderate	RCT with important limitations or strong evidence from observational studies	Can apply to most patients in most circumstances without reservation
	Low	Observational studies/case studies	May change when higher-quality evidence becomes available
Weak recommendation	***High***	RCT without important limitations or overwhelming evidence from observational studies	Best action may differ based on circumstances or patients' values
	Moderate	RCT with important limitations or strong evidence from observational studies	Best action may differ based on circumstances or patients' values
	Low	Observational studies/case studies	Other alternative may be equally reasonable
Insufficient		Evidence is conflicting, or poor quality or lacking	Insufficient evidence to recommend for or against

Recognition of Potential Health Care Disparities: The American College of Obstetricians and Gynecologists (ACOG) recognizes that there may be racial and ethnic disparities in obstetric and gynecologic outcomes between various ethnic groups (e.g., Blacks, Whites, Asians, Hsipanics, Native American, Alaksa Natives.) While examples are prevalent in the literature outlinging differences in outcomes between black and white women, more information is needed to explore disparities among Amerian Indian, Alaska Native and Asian women.[124]

Collateral Tools & Resources

The following collateral tools and resources support staff execution and performance of the evidence-based guideline recommendations in everyday clinical practice.

Metrics

- *Number of patients who had urinalysis and urine culture obtained at initial prenatal visit*
- *Number of pregnant patients with hypothyroidism with thyroid level check at 20 weeks and at 30 weeks gestation*
- *Number of patients who had 50 gram OGTT with level < 140 mg/dL who had 100 gram OGTT ordered*
- *Number of patients who screened positive for GBS prior to third trimester of current pregnancy who had vaginal swab obtained*

Related Guidelines

Depression: Diagnosis and Management – Adult/Pediatric – Ambulatory
Prevention and Management of Obesity – Adult – Ambulatory
Prevention and Management of Obesity – Pediatric – Ambulatory
Preventive Health Care – Adult/Pediatric – Ambulatory

Order Sets & Smart Sets

OB Initial Visit [306]
OB Initial Visit Eau Claire/Augusta [262]
OB Initial Visit – UWHC [2545]
OB PreGravid BMI BPA [4524]
OB Prenatal Intake ACHC [164]
OB Visit [120]
OB Visit Eau Claire/Augusta [292]
OB Visit – UWHC [2548]
Pre-Eclampsia Labs [394]
Bariatric OB Prenatal Care [6544

Patient Resources

HFFY 5457 – Coping with Nausea and Vomiting in Pregnancy
HFFY 5456 – Help for Common Symptoms while Pregnant
HFFY 6687 – Having a VBAC (Vaginal Birth after Cesarean Section)
HFFY 5715 – Group B Streptococcal Infections
HFFY 5811 – Pregnancy, Coping with Nausea and Vomiting (Spanish)
HFFY 5805 – Common Symptoms in Pregnancy (Spanish)
HFFY 7979 – Getting Ready for your Fasting Blood Draw

Clinical Policies

UWHC Policy 3.5.1 – Screening of Possibly Pregnant, or Pregnant Patients Prior to Diagnostic Radiological Exam
UWHC 4.30- Consent for HIV Testing and Release of Protected Health Information

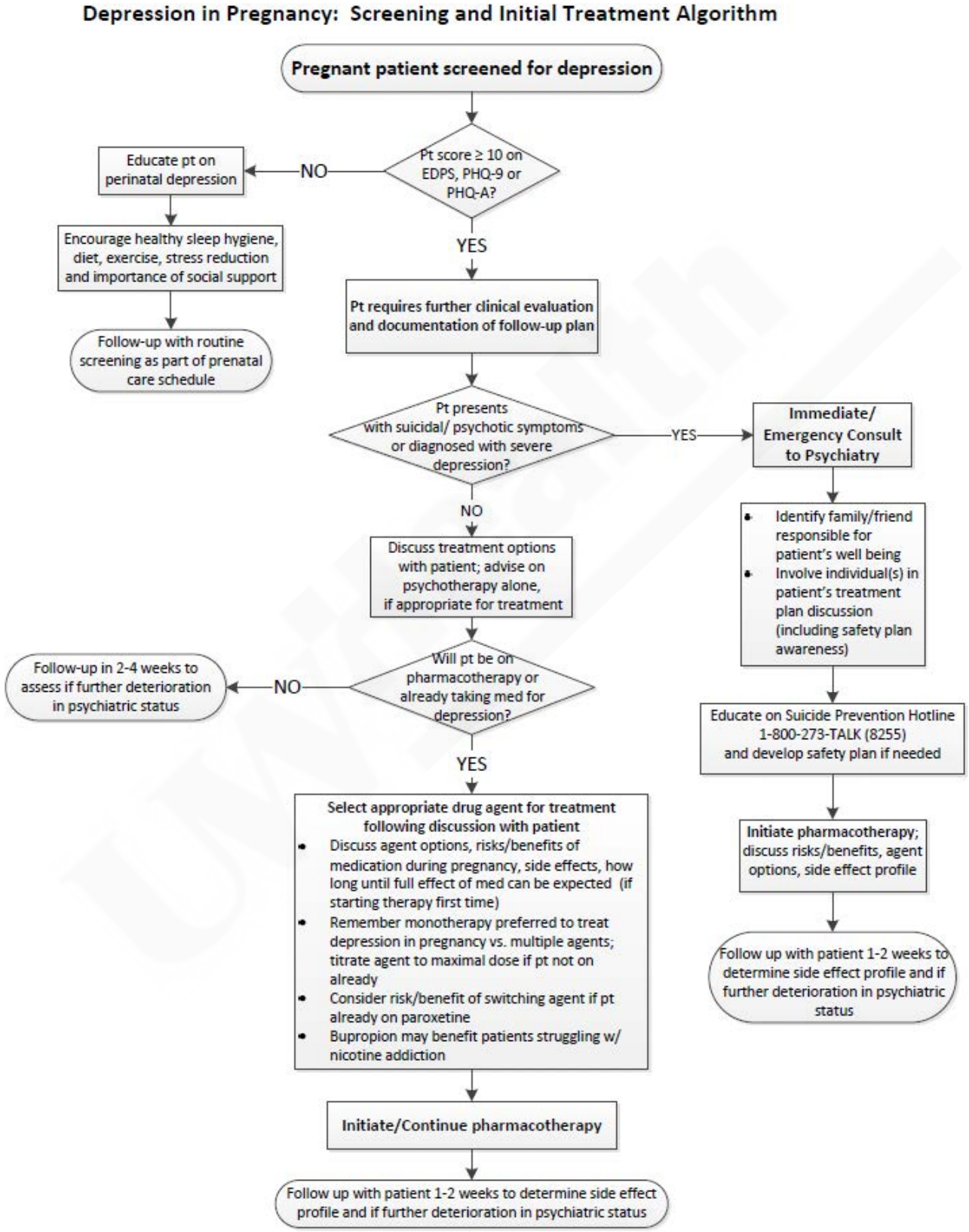
Delegation Protocols
New OB Patient Laboratory and Diagnostic Test Ordering – Adult – Ambulatory [116]
Gestational Diabetes Screening and Treatment – Adult/Pediatric- Ambulatory [22]
Treatment of Nausea in Pregnancy – Adult/Pediatric – Ambulatory [157]
First Trimester Bleeding – Adult/Pediatric – Ambulatory [112]
Treatment of Anemia During Pregnancy – Adult/Pediatric – Ambulatory [68]
Urine Pregnancy Test Ordering – Adult/Pediatric – Ambulatory [113]

Appendix A. Overview of Prenatal Care

Gestational Age	History and Examination	Tests and Immunizations	Counseling/Discussion topics
Entry of prenatal care – 12 weeks	• Document last menstrual cycle; if pregnancy dating unknown, offer dating ultrasound to ideally occur ~7-8 weeks gestation • Document pre-gravid weight • Obtain relevant medical history related to current pregnancy (e.g., hx of preterm deliveries, chronic medical conditions) • Obtain current medication profile including whether or not taking prenatal vitamin/folic acid • Screen for depression • Complete physical exam including height, weight, blood pressure and pelvic examination • Check fetal heart rate	• Complete blood count with differential • Urine pregnancy and screening urine culture • Rubella antibody, IgG • Antibody testing (i.e., ABO and Rh typing, antibody screen) • HIV AB/AG combo • Chlamydia/gonorrhea screen • Syphilis screen • Hepatitis B screen • Pap smear (if indicated) • Hepatitis C screen (if indicated) • Pregnancy dating ultrasound (if indicated) <u>Tests/interventions for special populations (as indicated)</u> • A1c measurement • Creatinine • Uric acid • AST/ALT • Protein/creatinine ratio • TSH, free T4 <u>Prenatal screening tests</u> • Maternal cell free DNA screen/ non invasive prenatal testing (NIPT) • First trimester screen <u>Immunizations</u> • Influenza vaccination	• Weight gain in pregnancy • Lifestyle considerations in pregnancy • Introduce/offer prenatal screening options for aneuploidy and carrier screening • Review pregnancy dating results (if applicable) • Follow-up documentation/treatment options discussion if screen positive for depression
12-16 weeks	• Physical exam including height, weight, blood pressure • Check fetal heart rate	<u>Tests/interventions for special populations (test if indicated)</u> • TSH(every 4 weeks) • Weekly progesterone administration (if history of spontaneous preterm delivery; initiate at 16 weeks) <u>Prenatal screening tests</u> • AFP (recommended if NIPT/First trimester screen) • Quad screen <u>Immunizations</u> • Influenza vaccination	• Review test/ultrasound results • Offer/discuss prenatal screening options with patient (e.g., AFP if had NIPT or First Trimester Screen)
16-22 weeks	• Physical exam including height, weight, blood pressure and fundal height • Check fetal heart rate	• 20 week ultrasound (fetal anatomy) <u>Tests/interventions for special populations (test if indicated)</u> • TSH (every 4 weeks) • Weekly progesterone administration (if history of spontaneous preterm delivery) <u>Prenatal screening tests</u> • AFP • Quad screen <u>Immunizations</u> Influenza vaccination	• Review test/ultrasound results

Gestational Age	History and Examination	Tests and Immunizations	Counseling/Discussion topics
22-28 weeks	• Complete physical exam including height, weight, blood pressure and fundal height • Check fetal heart rate	• 50 gram oral glucose tolerance test (24-28 weeks) • Fasting oral glucose test (as indicated) <u>Tests/interventions for special populations (test if indicated)</u> • TSH (may stop regular assessment if patient is stable) • Weekly progesterone administration (if history of spontaneous preterm delivery) <u>Immunizations</u> • Influenza vaccination	• Review test/ultrasound results • Discuss TOLAC with patient (if candidate) and refer patient to Obstetrics to ensure informed consent obtained in timely manner
28-34 weeks	• Physical exam including height, weight, blood pressure, fundal height • Check fetal heart rate • Screen for depression	• Antepartum fetal surveillance (if indicated) <u>Tests/interventions for special populations (test if indicated)</u> • TSH (check at least once ~30 weeks)) • Weekly progesterone administration (if history of spontaneous preterm delivery) <u>Immunizations</u> • Influenza vaccination • Tdap vaccination (27-36 weeks)	• Discuss TOLAC with patient (if candidate) and refer patient to Obstetrics to ensure informed consent obtained in timely manner
34-38 weeks	• Physical exam including height, weight, blood pressure, fundal height • Check fetal heart rate • Screen for depression	• Group B strep culture (35-37 weeks) • Limited ultrasound (~37 weeks, as needed for vertex presentation confirmation) • Antepartum fetal surveillance (if indicated) <u>Tests/interventions for special populations (test if indicated)</u> • HIV AB/AG combo (if indicated) • Chlamydia/gonorrhea screen (if indicated) • Syphilis screen (if indicated; required in IL) <u>Immunizations</u> • Influenza vaccination • Tdap vaccination (27-36 weeks)	• Offer suppressive anti-viral therapy to patients with recurrent genital HSV at 36 weeks or beyond
38 weeks-delivery	• Physical exam including height, weight, blood pressure, fundal height • Check fetal heart rate • Screen for depression	• Antepartum fetal surveillance (if indicated)	• Discuss potential for labor induction with patient, as necessary

Appendix B. Depression in pregnancy algorithm[108,125,126]



Appendix C. Pharmacotherapy options for Perinatal Depression [106,125,127-132]

Medication	Pregnancy Category*	Lactation Risk Category	Dosage	Pregnancy/Lactation considerations	Side Effects to Consider
Citalopram (Celexa)	C	L3	Start 20 mg daily, may increase to 40 mg daily after 1 week Max 40mg/day	Use in pregnancy: Preferred in pregnancy; When taken at term, 10-30% babies may experience self-limited poor neonatal adaptation syndrome.	Higher risk for sexual dysfunction, QT interval prolongation
Escitalopram (Lexapro)	C	L3 in older infants	Start 10 mg daily; may increase dose after 1 week Max 20mg/day	Use in pregnancy: Limited data	Lowest risk GI side effect and liver toxicity; may help anxiety
Fluoxetine (Prozac)	C	L2 in older infants, L3 if used in neonatal period	Start 20 mg daily (in morning); increase dose after several weeks Max 80 mg/day	Use in pregnancy: Preferred drug Breastfeeding: Decreased weight gain reported but unclear if from drug or depression; Use not recommended during lactation unless it is effective treatment for mother	May worsen anxiety and agitation; lowest risk for sexual dysfunction Long half life; approved for OCD, bulimia and panic disorder
Fluvoxamine (Luvox)	C	L2	Start 50 mg daily (in the evening); may increase by 50 mg/day every 4-7 days Max 300 mg/day	Use in pregnancy: Poor neonatal adaptation syndrome (irritability, poor feeding, respiratory distress) may occur; limited data on use, not recommended Breastfeeding: May be considered	Highest rate GI side effects, lowest risk sexual dysfunction
Paroxetine (Paxil)	D	L2	Start 20 mg twice a day; may increase by 1-mg/day every week Max 50 mg/day	Use in pregnancy: Studies have demonstrated increased risk for cardiac malformations when taken during pregnancy (1st trimester exposure); not recommended in pregnancy or patients trying to conceive Consider fetal echocardiography if paroxetine exposure in early pregnancy Breastfeeding: Preferred for lactation as levels are very low in breastmilk	Weight gain more likely compared to other SSRIs; can be sedating and high risk for sexual dysfunction; approved for OCD, panic disorder, anxiety, and PTSD
Sertraline (Zoloft)	C	L2	Start 25 mg daily for first 3-5 days then 50 mg daily; increase by 25-50 mg/daily every 1-2 weeks Max 200 mg/day	Use in pregnancy: Preferred in pregnancy Neonatal poor adaptation syndrome may occur. Breastfeeding: Preferred for lactation as levels are very low in breastmilk	May help anxiety and sleep quality; more diarrhea relative to other SSRIs
Trazodone (Oleptro)	C	L2	Start at 150 mg/day in divided doses; increase in 50 mg/day increments every 3-4 days Max 600 mg/day	Breastfeeding: Excreted in breast milk, though in very small quantities	Somnolence; dose at night and use in patients with concurrent insomnia

Prior to 2016, U.S Food and Drug Administration classified drug safety with following categories: **A, controlled studies show no risk; **B**, no evidence of risk in humans; **C**, risk cannot be ruled out; **D**, positive evidence of risk; **X**, contraindicated in pregnancy.*

***£** Lactation risk categories are listed as follows: **L1**, safest; **L2**, safer; **L3**, moderately safe; **L4**, possibly hazardous; **L5**, contraindicated.*

Medication	Pregnancy Category*	Lactation Risk Category£	Dosage	Pregnancy/Lactation considerations	Side Effects to Consider
Amitriptyline (Elavil)	C	L2	Start at 25-50 mg/day in a single dose at bedtime or in divided doses; gradually increase if inadequate response Max 300 mg/day	TCAs considered safe in pregnancy however side effect profile may not be desirable to pregnant patients	Anticholinergic side effects (i.e., dry mouth, constipation, blurred vision, drowsiness, orthostatic hypotension)
Desipramine	C	L2	Start at 25-50 mg once daily or in divided doses. Gradually increase if inadequate response Max 300 mg/day		
Nortriptyline (Pamelor)	C	L2	Start at 75-100 mg once daily or in divided doses. Gradually increase if inadequate response. Max 150 mg/day	Breastfeeding: Preferred for lactation	
Doxepin	C	L5	Start at 25-50 mg once daily or in divided doses. Gradually increase if inadequate response Max 300 mg/day	Breastfeeding: Associated with sedation and respiratory depression in case reports of exposed infants; avoid in breastfeeding	
Desvenlafaxine (Pristiq)	C	L3	Start at 50 mg/day. Increase as tolerated. Max 400 mg/day	Breastfeeding: Limited data, not first line for lactation	
Duloxetine (Cymbalta)	C	N/A	Start at 40 to 60 mg daily; dose may be divided (i.e., 20 or 30 mg BID) or given as a single daily dose of 60 mg. Alternatively may start at 30 mg/day and increase to 60 mg/day after at least one week Max 60 mg/day		
Venlafaxine (Effexor)	C	L3	Start at 37.5-75 mg/day in 2 or 3 divided doses; increase by 75 mg/day increments every 4 days Max 375 mg/day	Use in pregnancy: Limited data on use Breastfeeding: May be considered but not first line	Nausea and vomiting common side effect; if used, recommend with food
Bupropion (Wellbutrin)	C	L3	IR tablet - Start at 100 mg twice daily; after 3 days may increase to 100 mg three times daily. After several weeks may increase to 150 mg three times daily Max 450 mg/day	Use in pregnancy/breastfeeding: Bupropion should be avoided in patients due to reduced seizure threshold; avoid in infants with history of seizure, including febrile seizures and parent/sibling history of seizure; may help patients also suffering from nicotine addiction	Considered stimulant antidepressant; take in morning and may exacerbate insomnia
Mirtazapine (Remeron)	C	L3	Start at 15 mg/day; may increase by 15 mg/day increments every 1-2 weeks. Max 45 mg/day	Use in pregnancy: Limited data on use	Weight gain, increased appetite common side effects Somnolence; dose at night and use in patients with concurrent insomnia

Prior to 2016, U.S Food and Drug Administration classified drug safety with following categories: **A, controlled studies show no risk; **B**, no evidence of risk in humans; **C**, risk cannot be ruled out; **D**, positive evidence of risk; **X**, contraindicated in pregnancy.*

***£** Lactation risk categories are listed as follows: **L1**, safest; **L2**, safer; **L3**, moderately safe; **L4**, possibly hazardous; **L5**, contraindicated.*

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