

# Preconception Care and Reproductive Planning in Primary Care



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## KEYWORDS

- Preconception care • Reproductive life plan • Reproductive planning
- Reproductive-aged women • Primary care

## KEY POINTS

- Primary care for women of childbearing age should include routine assessment of a woman's reproductive goals and pregnancy intentions ("reproductive planning").
- Women who could potentially become pregnant should be assessed for preconception risks and educated about the importance of maternal health in ensuring healthy pregnancies.
- Women may be motivated to address modifiable health risks by learning about the way their health will affect a future pregnancy.
- For women not intending pregnancy in the short term, preconception care should include counseling on effective contraception.
- Women with chronic medical conditions should be counseled about highly effective reversible methods such as intrauterine devices and contraceptive implants, which have few medical contraindications.

*It's not a question of whether you provide preconception care, rather it's a question of what kind of preconception care you are providing.*

—Joseph Stanford and Debra Hobbins

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## INTRODUCTION

The United States has one of the highest rates of maternal mortality in the developed world,<sup>1</sup> with a growing proportion of maternal deaths attributable to chronic medical conditions.<sup>2</sup> In addition, the United States ranks behind most other industrialized nations in infant mortality, primarily because of congenital anomalies and preterm birth.<sup>3</sup> As prenatal care is often initiated too late to meaningfully impact pregnancy outcomes, a growing body of evidence highlights the prepregnancy or preconception period as critical to addressing high rates of maternal and fetal mortality.<sup>4</sup> Preconception care has been defined broadly as a set of interventions to identify and modify biomedical, behavioral, environmental, and social risks to the health of a woman or her baby before pregnancy occurs.<sup>4</sup> Primary care physicians (PCPs) care for large numbers of reproductive-aged women before, between, and after their pregnancies and thus are ideally positioned to help women identify and modify preconception health risks.<sup>5</sup>

Despite national campaigns by organizations such as the Centers for Disease Control and Prevention (CDC),<sup>4,5</sup> many PCPs lack training and knowledge of preconception care. Few PCPs routinely ask women about their pregnancy intentions or discuss how their health status or medications can impact pregnancy.<sup>6,7</sup> For example, one national study found that contraceptive counseling was provided in less than 20% of health care visits that documented use of a potential teratogen by a woman of childbearing age.<sup>8</sup> Furthermore, many women remain unaware of the importance of their prepregnancy health to both maternal and fetal pregnancy health outcomes, and few seek preconception counseling from providers.<sup>9–11</sup>

Given that more than 50% of pregnancies in the United States are unplanned,<sup>12</sup> PCPs should proactively conduct a preconception risk assessment as part of routine primary care for women of childbearing age.<sup>4,13</sup> The substantial overlap between the goals of comprehensive primary care and preconception care suggests that high-quality preconception care need not be viewed as a new set of interventions for PCPs, but rather as a different lens through which to view standard preventive care. This review focuses primarily on aspects of conditions commonly managed by PCPs that may benefit from targeted preconception intervention.

## REPRODUCTIVE PLANNING

The first step in identifying a reproductive-aged woman's need for preconception risk screening and counseling is to assess her pregnancy desires and plans. CDC<sup>4</sup> and the American Congress of Obstetricians and Gynecologists (ACOG),<sup>14</sup> recommend that providers routinely ask women about their reproductive goals and encourage women to create a "reproductive life plan." More recent data indicate that longer term planning may be difficult for many women, therefore asking women about reproductive goals in a shorter time frame, such as 1 year, may be more widely acceptable to women.<sup>15,16</sup> The "Before, Between, and Beyond" provider toolkit recently released by the National Preconception Health and Health Care Initiative recommends the question, "Are you hoping to become pregnant in the next year?" to initiate reproductive planning conversations in routine primary care.<sup>17</sup>

Additional questions to help women think about their reproductive goals and related health needs are listed in [Table 1](#). For women who desire pregnancy in the next year, preconception risk assessment and counseling are indicated. For women who do not desire pregnancy in the next year, information about effective contraception is essential, including information about highly effective reversible contraceptives that

Table 1 Reproductive planning questions	
Questions to Ask if Desires Pregnancy in the Future	Questions to Ask if Never Desires Pregnancy in the Future
How many children would you like to have?	What family planning method will you use to avoid pregnancy?
How long would you like to wait until you (or your partner) become pregnant?	How sure are you that you will be able to use this method without any problems?
What family planning method do you plan to use until you (or your partner) are ready to become pregnant?	People's plans change. Is it possible you or your partner could ever decide to become pregnant?
How sure are you that you will be able to use this method without any problems?	

Adapted from National Preconception Health and Health Care Initiative. Before, between and beyond toolkit. Available at: <http://beforeandbeyond.org/toolkit/reproductive-life-plan-assessment/>. Accessed September 27, 2014.

are safe for virtually all women (eg, intrauterine or subdermal contraceptives). Because women's pregnancy intentions often change over time, a key feature of reproductive planning is the integration of contraceptive and preconception counseling. For example, a woman who desires pregnancy at a later time can benefit from counseling on both effective contraception and preconception risk modification to optimize future pregnancy health. Many women not intending pregnancy in the short term will nonetheless experience unintended pregnancy<sup>12</sup>; PCPs should therefore proactively address a woman's contraceptive plans and preconception health risks whenever possible at each visit. At a minimum, these are important components of annual well-woman visits for this population.<sup>17</sup>

Provision of information on the impact of maternal age on fertility and birth outcomes is an important component of reproductive planning for some women. A large amount of literature describes age-related pregnancy risks and demonstrates a continual increase in risks over the age of 35, rather than a threshold effect.<sup>18</sup> In one meta-analysis, increasing age was significantly associated with miscarriage (adjusted odds ratio [aOR] 2.0 and 2.4 for ages 35–39 years and age 40 years and older, respectively), chromosomal abnormalities (aOR 4.0 and 9.9), congenital anomalies (aOR 1.4 and 1.7), gestational diabetes (aOR 1.8 and 2.4), placenta previa (aOR 1.8 and 2.8), and cesarean delivery (aOR 1.6 and 2.0).<sup>18</sup> Women aged 40 or older also experienced increased risk for abruption (aOR 2.3), preterm delivery (aOR 1.4), low birth weight (aOR 1.6), and perinatal mortality (aOR 2.2).<sup>18</sup> Another important aspect of reproductive planning is the provision of information about recommended interpregnancy intervals (IPIs, defined as the time from delivery to subsequent conception). Data indicate that an IPI shorter than 6 months results in increased risk of preterm birth, low birth weight, and small for gestational age and that an IPI between 18 and 59 months appears to be safest.<sup>19</sup> For women over the age of 35, however, a shorter IPI may be appropriate to balance risks of age-related fertility declines and pregnancy risk.

Reproductive planning conversations are perceived as valuable and important to women from a variety of backgrounds.<sup>16,20,21</sup> Studies suggest that women appreciate having their PCP initiate conversations about reproductive planning that are nonjudgmental (ie, there are no right or wrong answers) and delivered in a caring and supportive manner.<sup>16,20</sup> Women who are not interested in a pregnancy in the next year may find messages related to "being prepared for the unexpected"<sup>16</sup> or "investing in themselves" for a healthy future<sup>22</sup> more relevant than information about

“planning for pregnancy.” Additional information on reproductive life plans and reproductive planning is available on the Before, Between, and Beyond Web site.<sup>17</sup>

## OPTIMIZATION OF CHRONIC CONDITIONS

### *Diabetes*

The prevalence of pregestational diabetes among women in their childbearing years is rising, fueled by the obesity epidemic.<sup>23</sup> One study of nearly 200,000 pregnancies identified an increase in diagnosed pregestational diabetes from 0.81% in 1999 to 1.82% in 2005.<sup>23</sup> Elevated serum glycemic levels are a powerful teratogen,<sup>24</sup> and thus, prepregnancy optimization of glycemic control is critically important to ensure healthy pregnancy outcomes. Women in poor glycemic control during organogenesis (approximately 4–10 weeks of gestation) are at substantially increased risk of spontaneous abortion and of congenital anomalies, including cardiac structural defects, neural tube defects (NTDs), and sacral agenesis.<sup>25–27</sup> The overall risk of one or more congenital anomalies is 6% to 7% among women with pregestational diabetes, more than twice the baseline prevalence,<sup>24</sup> and increases with glycosylated hemoglobin (HgA1c) levels.<sup>28</sup> Later in pregnancy, prepregnancy diabetes is associated with fetal risks including fetal macrosomia (birth weight more than the 90th percentile for gestational age), preterm birth, stillborn, and neonatal death. Maternal risks include worsening of diabetic retinopathy and nephropathy, hypertension, and preeclampsia. Children born to women with diabetes mellitus may be at increased risk of developing diabetes, and hyperglycemia during pregnancy may result in metabolic effects on the fetus that predispose to later life obesity and metabolic syndrome.<sup>29</sup> Data indicate that women who can lower their HgA1c levels to the normal range can reduce their risks to close to that of a nondiabetic woman.<sup>30</sup>

Counseling and education in both inpatient and outpatient settings can improve maternal and fetal outcomes among women with diabetes.<sup>26,31–33</sup> One meta-analysis of 8 retrospective and 8 prospective studies of preconception counseling interventions for type 1 and type 2 diabetic women found reductions in both major congenital anomalies (those involving death such as abortion or intrauterine fetal death, surgical correction, or medical therapy) and minor congenital anomalies as well as in first-trimester HgA1c levels.<sup>34</sup> A second meta-analysis found similar reductions in fetal anomalies and first-trimester HgA1c levels as well as a reduction in rates of preterm delivery.<sup>31</sup>

The American Diabetes Association (ADA) recommends a target HgA1c of less than 7% before conception.<sup>35</sup> Both ADA<sup>36</sup> and the ACOG<sup>37</sup> advise that insulin therapy be the mainstay for glycemic control in pregnancy, although a growing body of literature supports the safety of using metformin during pregnancy.<sup>38</sup> Women with preexisting diabetes who are planning pregnancy should have a comprehensive eye examination, documentation of baseline renal function, thyroid function screening (type 1 diabetes), and baseline cardiovascular risk screening (eg, electrocardiogram). Review of medications should also be performed to address safety in pregnancy (see “Review of medications” section).<sup>36</sup> Angiotensin-converting enzyme (ACE) inhibitors have been associated with congenital anomalies, intrauterine growth restriction, and fetal/neonatal demise. Data are more limited for angiotensin receptor blockers (ARBs) but suggest similar risks to ACE inhibitors; therefore, both classes are contraindicated in pregnancy.<sup>39</sup>

ACOG recommends a minimum of 0.4 to 0.8 mg/d of folic acid for women with pregestational diabetes, with higher doses (4 mg/d) if additional risk factors for NTDs are present.<sup>37</sup> The Society of Obstetricians and Gynaecologists of Canada recommends a higher dose of 5 mg/d of folic acid for women with insulin-dependent pregestational diabetes.<sup>40</sup> Because folic acid is water-soluble and easily excreted, the risks of high

doses are minimal, although evidence suggesting benefit of these doses remains limited.<sup>41</sup> The ADA recommends 0.6 mg/d for women with pregestational diabetes.<sup>36</sup>

Women with pregestational diabetes who do not desire pregnancy should be counseled about effective contraception and encouraged to use highly effective reversible options such as the intrauterine device (IUD) or contraceptive implant. The US Medical Eligibility Criteria (US MEC) for contraceptive use published by the CDC provides specific recommendations regarding safety of contraceptives in women with diabetes in a user-friendly format with summary charts (**Box 1**).<sup>42</sup>

### **Summary of recommendations**

- Women should be educated about the risks of diabetes in pregnancy and advised that normalizing blood glucose before pregnancy will reduce their risks to the level of a nondiabetic woman. ADA recommends target HgA1c of less than 7%.
- All women with preexisting diabetes who are planning pregnancy should be screened for end-organ damage, including retinopathy, nephropathy, and cardiovascular disease.
- Medications should be reviewed to address potential teratogenic risks.
- Women who have elevated HgA1c levels should be counseled about the benefits of short-term use of effective contraception to enable optimization of glycemic control before conception.

### **Hypertension**

Approximately 8% of women of reproductive age have hypertension, according to data from the National Health and Nutrition Examination Survey.<sup>43</sup> Women who have chronic hypertension, whether controlled on antihypertensive drug treatment or not, are more likely to experience fetal and maternal complications, including fetal growth restriction, stillbirth, iatrogenic preterm birth, maternal pulmonary edema and stroke, superimposed preeclampsia, and cesarean delivery.<sup>30,44</sup> Women with moderate or severe renal disease before pregnancy are at risk for developing worsened renal function during pregnancy.<sup>30</sup>

For women with severe hypertension or end-organ damage, continued medical therapy during the preconception period and pregnancy is recommended. Women planning a pregnancy should be transitioned to a regimen that is safe in pregnancy.  $\beta_1$ -selective  $\beta$ -blockers such as atenolol have been associated with growth restriction, and diuretics may prevent physiologic expansion of blood volume in pregnancy; therefore, these drugs are generally not recommended. ACE inhibitors and ARBs are generally contraindicated in pregnancy. ACOG suggests labetalol (a  $\beta$ -blocker with both  $\alpha$ -adrenergic and  $\beta$ -adrenergic blocking activity), nifedipine, or methyldopa

#### **Box 1**

##### **Additional resources**

Before, between, and beyond provider toolkit. Available at: [www.beforeandbeyond.org](http://www.beforeandbeyond.org)

Reprotox information on medication safety. Available at: [www.reprotox.org](http://www.reprotox.org)

CDC Preconception Care. Available at: <http://www.cdc.gov/preconception/index.html>

March of Dimes. Available at: <http://www.marchofdimes.org/pregnancy/get-ready-for-pregnancy.aspx>

US Medical Eligibility Criteria for Contraceptive Use. Available at: <http://www.cdc.gov/reproductivehealth/unintendedpregnancy/usmec.htm>

as first-line options in women who are pregnant or planning pregnancy to achieve a target blood pressure range of 120/80 to 160/105 mm Hg.<sup>45</sup>

Medical therapy in women with mild hypertension may be discontinued with close follow-up if women are planning pregnancy. According to both ACOG and the National High Blood Pressure Education Program Working Group on Blood Pressure in Pregnancy, women with blood pressures less than 160 mm Hg systolic or 105 mm Hg diastolic who have no evidence of end-organ damage do not require treatment during pregnancy.<sup>45,46</sup> The American Heart Association agrees that milder hypertension in pregnancy does not require treatment, but defines systolic pressures greater than 150 mm Hg and diastolic pressures greater than 100 mm Hg as warranting treatment to reduce stroke risk.<sup>47</sup>

Women with hypertension who do not desire pregnancy should be encouraged to use highly effective contraceptive methods such as the IUD and contraceptive implants, which have few medical contraindications. The US MEC for contraceptive use provides specific recommendations on the use of contraceptives among women with hypertension (see **Box 1**).<sup>42</sup>

### **Summary of recommendations**

- Women with chronic hypertension should be counseled about associated pregnancy risks and possible need to change medications when planning a pregnancy.
- Women with mild hypertension can be transitioned off of medication with careful monitoring before pregnancy to ensure pressures remain under SBP less than 150 to 160 mm Hg and DBP less than 100 to 110 mm Hg.
- Women with hypertension of several years' duration should be evaluated for end-organ damage, such as ventricular hypertrophy, retinopathy, and renal disease before pregnancy.
- Medications such as ACE inhibitors and ARBs should be discontinued before attempting pregnancy, with transition to agents with established safety in pregnancy, such as labetalol, nifedipine, or methyldopa.
- For hypertensive women who wish to avoid pregnancy, highly effective reversible methods, such as IUDs and contraceptive implants, are preferred.

### **Obesity**

One-third of reproductive-aged women in the United States are obese,<sup>48</sup> defined as a body mass index (BMI) 30 kg/m<sup>2</sup> or more. Compared with women with a normal BMI (<25 kg/m<sup>2</sup>), obese women are at increased risk of a wide range of adverse pregnancy outcomes, including gestational diabetes mellitus (GDM), pregnancy-related hypertensive disorders such as preeclampsia, iatrogenic preterm delivery, dysfunctional labor, postterm pregnancy, large for gestational age (LGA) infant, shoulder dystocia, fetal and infant death, congenital anomalies, cesarean delivery, and postpartum complications.<sup>49–52</sup> Associated congenital anomalies include NTDs, cardiovascular defects, cleft palate and lip, anorectal atresia, and limb abnormalities.<sup>52</sup> Newborns born to obese mothers are more likely to develop childhood obesity, type 2 diabetes, and cardiovascular disease later in life.<sup>53,54</sup> Obese women also are at increased risk of subfertility and miscarriage.<sup>54</sup>

Weight loss before pregnancy is thus one of the most important preconception lifestyle changes a woman can make. Women should be educated about the pregnancy risks associated with obesity and encouraged to engage in a weight-reduction program before attempting to conceive.<sup>55</sup> Once pregnancy occurs, significant weight loss is no longer a recommended goal, although obese women are encouraged to

avoid excess gestational weight gain.<sup>56</sup> Effective contraception before, between, and after pregnancies to allow women to achieve their weight loss goals is critical.<sup>57</sup> Because the use of depot medroxyprogesterone acetate injections causes undesired weight gain for some women, alternative methods such as the IUD and implant should be considered. Additional information on the safety and efficacy of contraceptives in women with obesity is available in the US MEC for contraceptive use.<sup>42</sup>

Few data exist on whether lifestyle or dietary interventions are effective in helping women to lose weight before conception.<sup>33</sup> Several trials have examined interventions aimed at postpartum weight loss, with mixed results.<sup>58–60</sup> Data from observational cohort studies suggest that decreases in prepregnancy weight between pregnancies are associated with reduced risk in many pregnancy complications, including gestational diabetes, LGA infant, preeclampsia, cesarean delivery, and failed vaginal birth after cesarean.<sup>61–66</sup> The amount of weight loss needed to reduce pregnancy risks is not clear; some studies found risk reductions with change from obese to normal BMI,<sup>61,62</sup> while others found risk reductions with loss of 1 to 2 BMI units (from 2.7 to 5.4 kg for a woman of average height).<sup>63–66</sup>

Women can be counseled that modest to moderate weight loss (5%–15%) can improve health outcomes.<sup>67</sup> The 2013 Obesity Guidelines for Managing Overweight and Obesity in Adults provide guidelines for providers, which can also be applied to women planning pregnancy.<sup>68</sup> These guidelines recommend that overweight individuals engage in comprehensive lifestyle programs for 6 months or more that support low-calorie diets and physical activity with the use of behavioral therapies, including self-monitoring of weight and food, environmental control, contingency planning, and stress management. Programs should be “intensive” and preferably delivered face-to-face or by telephone by a trained interventionist.<sup>68</sup>

Women who have undergone bariatric surgery should be advised to wait 12 to 18 months following surgery to attempt conception, to both allow for optimal postsurgery weight loss and avoid potential adverse effects of nutritional deficiencies.<sup>69</sup> Procedures that may result in malabsorption (such as Roux-en-Y gastric bypass), and to a lesser extent restrictive procedures (such as gastric banding), can cause deficiencies in iron, folate, vitamin B12, calcium, and vitamin D, which can lead to adverse pregnancy outcomes.<sup>70</sup> Nutritional supplementation and monitoring in the preconception period are therefore critical.<sup>69</sup> Specific regimens should be tailored to the individual patient and the type of bariatric procedure performed,<sup>71</sup> with consultation from the bariatric surgeon. Women should be counseled to use effective contraception after surgery, preferable a highly effective reversible method (eg, IUD or implant). Those who undergo malabsorptive procedures should be advised not to use oral contraceptives, because absorption and thus efficacy may be decreased.<sup>42</sup>

### **Summary of recommendations**

1. Women should be educated about obesity-related pregnancy risks and encouraged to pursue weight loss before conception.
2. Women can be encouraged to set achievable goals and counseled that modest reductions in weight can improve both pregnancy and their long-term health outcomes.
3. Women should be counseled to use effective contraception, such as IUDs and implants, to enable them to achieve their weight loss goals before conception.

### **Depressive and Anxiety Disorders**

Depression is a highly prevalent condition among women in the United States.<sup>72</sup> Depression in pregnancy is common, with an estimated period prevalence of perinatal

depression ranging from 11% to 32% from conception to 3 months postpartum.<sup>73</sup> A growing body of evidence suggests that depressive symptoms during pregnancy are associated with poor birth outcomes, including low birth weight, preterm delivery, and postpartum depression.<sup>74–76</sup> Anxiety disorders and symptoms are similarly common among women during pregnancy and the postpartum period<sup>77</sup> and have been linked to adverse perinatal outcomes, including low birth weight and preterm birth.<sup>78</sup>

Psychotropic medications prescribed to women with depression and anxiety may also result in adverse pregnancy outcomes. Studies assessing risks, however, have been observational and of variable quality. Observational studies often cannot adequately control for confounding and can be biased by numerous factors, such as the fact that women with more severe illness are more likely to receive medication. Although certain pregnancy risks may be elevated with psychotropic medications, meta-analysis aggregating the available data suggests that the risks seem to be small and of questionable clinical significance.<sup>79</sup>

The selective serotonin reuptake inhibitors (SSRIs) have been associated with low birth weight, small for gestational age (<10th percentile birth weight), preterm birth, and neonatal effects (increased irritability and persistent pulmonary hypertension of the newborn).<sup>74</sup> SSRIs in general have not been shown to be teratogenic with the exception of paroxetine, which has been linked to a small increased risk of congenital cardiac defects.<sup>80</sup> The risk of congenital anomalies with serotonin-norepinephrine reuptake inhibitors such as venlafaxine seems to be low, although these may increase the risk of preeclampsia.<sup>81</sup> Data are limited on other antidepressants, such as bupropion and tricyclic antidepressants; however, teratogenicity risks seem to be low.<sup>74</sup> Although psychotropic medications are all excreted in low levels in breast milk, levels appear to be lowest with sertraline and paroxetine.<sup>82</sup> Sertraline may therefore be a reasonable first-line SSRI among women initiating therapy given safety data in both pregnancy and breastfeeding.

Although most studies focus on associations between antepartum symptoms and outcomes,<sup>76</sup> one study using national data found that preconception depressive symptoms as well as antepartum symptoms were independently associated with postpartum depression risks.<sup>83</sup> Experts recommend that depression and anxiety be addressed in the preconception period to permit time to review treatment options and to work toward euthymia before conception.<sup>74,76</sup> A joint review from the American Psychiatric Association and ACOG suggests that women with mild or no symptoms for 6 or more months may attempt to taper and discontinue medications before pregnancy, with close follow-up. Patients with serious mental illness, including severe depressive disorders, bipolar disorder, psychosis, and prior history of suicidal ideation or attempts, should generally remain on psychotropics to avoid worsened disease states.<sup>74</sup>

### **Summary of recommendations**

1. Women of reproductive age should be screened for common mental illness such as depression and anxiety.
2. Women with mental illness should be counseled about the risks of untreated conditions and the importance of addressing symptoms before conception.
3. Ideally, women should wait for a period of euthymia (eg, 6–12 months) before attempting conception.
4. Women with mild or no symptoms for 6 or more months may attempt to taper and discontinue medications before pregnancy, with close follow-up.
5. Patients with serious mental illness, including severe depressive disorders, bipolar illness, and psychosis, should generally remain on their medications before and during pregnancy.



### Other Medical Conditions

Multiple other medical conditions treated by PCPs, often in conjunction with specialists, can impact maternal and fetal birth outcomes. Women with chronic conditions should be counseled about the potential impact of their condition on pregnancy, and care should be coordinated with specialists to optimize pre-pregnancy disease control and to choose medication regimens balancing maternal and fetal risks and benefits. **Table 2** provides an overview of selected disease risks and recommendations.

Table 2 Additional selected chronic conditions and preconception recommendations		
Disease	Adverse Effects	Recommendations
Asthma	Preterm birth, low birth weight, preeclampsia, stillbirth, and neonatal death	Counsel regarding importance of asthma control before pregnancy. Inhaled and systemic steroids appear to be low risk, with benefits generally outweighing the pregnancy risks <sup>30</sup>
Cardiovascular disease	Maternal morbidity and mortality. Fetal congenital heart disease is increased among women with congenital heart disease	Counsel about the importance of preconception consultation with maternal-fetal medicine specialist and cardiologist before conception <sup>30</sup>
Seizure disorders	Increased frequency of seizures during pregnancy, congenital anomalies (independent of medication-related anomalies), miscarriage, low birth weight, developmental disabilities Anticonvulsants are known teratogens (see <a href="#">Table 3</a> )	Optimize medication before pregnancy with specialist input. Valproate should be avoided when possible, given its teratogenicity. Monotherapy is preferred with lowest dose needed for seizure prevention. Folic acid supplementation of 4 mg/d is recommended <sup>30</sup>
Systemic lupus erythematosus	Hypertension, preeclampsia, preterm birth, growth restriction, stillborn, and neonatal lupus	A period of quiescence of 6 mo or more is recommended before pregnancy <sup>30</sup>
Thrombophilia	Increased risk of thromboembolic events and preeclampsia during pregnancy and postpartum. Warfarin is teratogenic (see <a href="#">Table 3</a> )	Management of anticoagulation in the preconception period should be addressed with specialist input and generally involves transition to low-molecular-weight heparin or heparin <sup>30</sup>
Thyroid disorders	Hypothyroidism: Preterm birth, preeclampsia, placental abruption, postpartum hemorrhage, low birth weight, stillborn, and impaired neuropsychological development among children Hyperthyroidism: Preeclampsia, maternal heart failure and thyroid crisis, placental abruption, low birth weight, preterm birth, and stillbirth	Universal prepregnancy screening is not recommended, but women with symptoms of thyroid imbalance should be screened. Women with known thyroid disorders should be counseled about the importance of achieving euthyroidism before attempting pregnancy <sup>30</sup>

**Table 3**  
**Common medications with known or suspected teratogenic effects**

Medication	Adverse Effects	Recommendations
ACE inhibitors and ARBs	First-trimester exposure: Cardiovascular and central nervous system defects Second- and third-trimester exposure: Impaired fetal/neonatal renal function leading to oligohydramnios and resulting pulmonary hypoplasia, limb contractures, and skeletal deformations. Hypocalvaria, retinopathy, and prolonged neonatal hypotension	Consider alternative antihypertensives, such as nifedipine, labetalol, or methylopa <sup>45</sup>
Antibiotics	Tetracycline: Bone and teeth staining Trimethoprim: Theoretic risk of NTDs due to lowered folic acid levels	Consider alternatives such as penicillins or cephalosporins
Antidepressants (SSRIs)	First-trimester exposure: Paroxetine may increase risk of some congenital malformations, predominantly congenital heart disease (results not consistent) Third-trimester exposure: Postnatal neurobehavioral effects (long-term effects not known)	Discuss risks and benefits, because risks are low. Consider sertraline as first-line option given good safety profile and low levels secreted in breast milk <sup>74</sup>
Antiepileptics	Valproate: NTDs, facial dysmorphism, autism, atrial septal defect, cleft palate, hypospadias, polydactyly, and craniosynostosis Phenytoin: Risk of fetal hydantoin syndrome, consisting of facial dysmorphism, cleft palate, ventricular septal defect, and growth and mental retardation Carbamazepine: Facial dysmorphism, NTDs, cardiovascular defects, and urinary tract defects	Consult specialist for optimization of medication, including monotherapy and avoidance of valproate <sup>30</sup>
Folic acid antagonists (methotrexate)	Risk of spontaneous abortion, malformations, including microcephaly, meningocele, hydrocephalus, cleft palate, and mental retardation	Women who plan to conceive should discontinue methotrexate and use contraception for at least 3 mo (ideally 6 mo) before conception, with folic acid supplementation <sup>85</sup>

(continued on next page)

<b>Medication</b>	<b>Adverse Effects</b>	<b>Recommendations</b>
Immunosuppressants	Mycophenolate: Miscarriage, abnormalities of the ear, distal limbs, heart, esophagus, kidney, and cleft lip/palate Cyclophosphamide: Inconsistent effect in humans, but may cause malformations	Effective contraception necessary during and for 6 wk to 3 mo after cessation of immunosuppressants <sup>85</sup>
Isotretinoin	Risk of spontaneous abortion and multiple anomalies, including anomalies of the face (facial dysmorphism, cleft palate), central nervous system, and cardiovascular system	Recommend effective contraception and cessation at least 1 mo before attempting conception <sup>86</sup>
Lithium	Low risk of cardiac anomalies, including Ebstein anomaly	Use lowest amount necessary to achieve therapeutic level and consider prenatal cardiac anomaly screening <sup>87</sup>
Nonsteroidal anti-inflammatory drugs (ibuprofen, aspirin)	First trimester: Data on effects not consistent Third trimester: Premature closure of the ductus arteriosus	Avoid use in pregnancy. Alternatives include acetaminophen <sup>85</sup>
Statins (HMG-CoA reductase inhibitors statins)	Decreased cholesterol synthesis may affect fetal development. Animal studies indicate teratogenicity; data in humans are limited	Avoid during pregnancy given paucity of data <sup>88</sup>
Warfarin	Bone and cartilage deformities, mental retardation, and vision problems	Refer to specialist for conversion to heparin or low-molecular-weight heparin <sup>89</sup>

## REVIEW OF MEDICATIONS

One in 6 women of reproductive age receive a prescription for a potentially teratogenic medication each year in the United States.<sup>8</sup> Given high unintended pregnancy rates in the United States,<sup>12</sup> education about the potential teratogenic risks of medications is critical for all women of reproductive age who could become pregnant. Medications with clearly documented teratogenic effects should be avoided in women who desire pregnancy or could become pregnant. For many women, however, medications with some potential teratogenicity also have important benefits, such as psychotropic medications and antiepileptic medications. The benefits of medications with low absolute risk of teratogenicity may outweigh the risks in certain circumstances. Conversations should therefore be individualized and address the risks and benefits of medications to an individual woman. Dietary supplements should also be reviewed with patients to assess for safety in pregnancy, and nonessential supplements without clear safety data should be stopped before attempting conception. **Table 3** includes a list of commonly prescribed medications. Consultation with online resources or experts regarding the risks of medications is recommended (see **Box 1**).

**Table 4**  
**Recommendations for additional preconception risk factors**

<b>Risk Factor</b>	<b>Adverse Effects</b>	<b>Recommendations</b>
Inadequate folic acid consumption	NTDs and other congenital anomalies	Folic acid supplements: 0.4 mg/d for low-risk women and 4 mg/d for women at high risk for NTDs (previous affected child, on anticonvulsants). <sup>90</sup> Some experts recommend 4–5 mg/d for women at intermediate risk, including insulin-dependent diabetes and obesity <sup>40</sup>
Alcohol use	A continuum of adverse outcomes, including birth defects and developmental disabilities, with fetal alcohol syndrome as the most severe (microcephaly, mental retardation, growth retardation, facial dysmorphogenesis, abnormal ears, small palpebral fissures)	Women should be screened for risky drinking. Brief interventions, including education and motivational interviewing, have been shown to be effective in reducing alcohol-exposed pregnancies in randomized controlled trials <sup>33</sup>
Drug use	Marijuana: Data inconclusive, possible childhood neurodevelopmental effects Cocaine: Low birth weight, prematurity, perinatal death, placental abruption Heroin and other narcotics: Spontaneous abortion, placental insufficiency, preterm birth, intrauterine death	Substance use should be obtained in a screening history. Women should be educated and referred to treatment programs that support abstinence and rehabilitation <sup>91</sup>
Tobacco use	Spontaneous abortion, preterm birth, low birth weight, placental previa, placental abruption, and stillbirth	Women should be screened for tobacco use. Provide brief intervention for smoking cessation (eg, the 5 As) and counseling about pharmacotherapies. Few interventions have been studied in the preconception period, although randomized trials of counseling interventions during pregnancy have demonstrated efficacy. <sup>33,92</sup>

Sexually transmitted diseases	HIV, Hepatitis B, and Hepatitis C: Vertical transmission Syphilis: Spontaneous abortion, fetal hydrops, growth restriction, and congenital syphilis Chlamydia/gonorrhea: Pelvic inflammatory disease and resulting impaired fertility. Neonatal eye infections and pneumonia	Screen according to CDC guidelines, which include annual HIV screening for women engaging in unsafe sex and HIV screening for all women not at increased risk of unsafe sex at least once. Women engaging in unsafe sex and all sexually active women <25 should be screened for chlamydia and gonorrhea annually. Women with risk factors should be vaccinated against hepatitis B per CDC recommendations <sup>93</sup>
Other infection exposures	Toxoplasmosis, cytomegalovirus (CMV), rubella, and varicella: Congenital anomalies. Varicella can cause severe pneumonia in pregnant women Listeria: Spontaneous abortion, preterm labor, neonatal sepsis, meningitis, and fetal death	<i>No vaccine available—toxoplasmosis, CMV, listeria</i> Toxoplasmosis: Avoid cat litter, undercooked and raw meats. CMV: Practice frequent hand washing, especially when in contact with children. Listeria: Avoid cold cuts, unpasteurized milk and soft cheeses, and unwashed raw produce. <i>Vaccine available—rubella and varicella</i> Women should be screened if immunization status unknown and vaccinated before pregnancy. Avoid pregnancy for 1 mo after vaccination, as both are live vaccines <sup>94</sup>
Environmental exposures	Lead: Spontaneous abortion, birth defects, and impaired fetal growth and neurodevelopment. Mercury: Impaired neurodevelopment including lower IQ and poor language and motor development	Test serum lead levels in woman with exposure history; consult with environmental health specialist as needed. Lead: Avoid potential sources (paint, construction, ceramics). Mercury: Eat low mercury fish (2 servings/wk). Avoid swordfish, shark, king mackerel, and tile fish <sup>95</sup>
Intimate partner violence and reproductive coercion	Intimate partner violence: Maternal depression, poor pregnancy weight gain, substance abuse, infection, low birth rate, preterm birth, perinatal death Reproductive coercion, including birth control sabotage and pregnancy coercion: Increased risk of unintended pregnancy	Screen all women for intimate partner violence and reproductive coercion. Refer women who screen positive to local or state services dedicated to women with IPV <sup>96</sup>

<b>Risk Factor</b>	<b>Screening Question</b>	<b>Recommendations</b>
Pregnancy history <sup>97</sup>	In your past pregnancy(s), have you had: a. Recurrent miscarriage b. Low birth weight c. Preterm delivery d. GDM e. Baby with NTD (eg, spina bifida) f. Baby with other birth defects g. Stillbirth	Refer to obstetrician/gynecologist For history of GDM, ensure patient has been screened for type 2 diabetes For women with a history of a NTD, prescribe folic acid 4 mg/d
Genetic disease <sup>98</sup>	Do you have a personal or family history of a. $\beta$ -thalassemia or $\alpha$ -thalassemia b. Cystic fibrosis c. Sickle cell disease d. Tay-Sachs disease e. Mental retardation or Fragile X syndrome	Refer to obstetrician/gynecologist or genetic counselor

### SCREEN FOR ADDITIONAL PRECONCEPTION RISK FACTORS

Many routine preventive health interventions provided by PCPs are important for preventing maternal and fetal complications in addition to promoting overall health. Examples include tobacco use screening and cessation interventions and screening for sexually transmitted diseases and intimate partner violence (IPV). Several preventive interventions are specifically relevant to women contemplating a pregnancy, such as counseling about folic acid supplementation and confirming rubella immunization. **Table 4** presents an overview of recommended interventions with potential impact on maternal and fetal health.

### SCREEN FOR PRIOR POOR PREGNANCY OUTCOMES AND GENETIC DISEASE

Women's prior pregnancy history and family history can impact the health of future pregnancies. Although a detailed reproductive and genetic history is outside the scope of many PCPs, brief screening questions can identify women who would benefit from referral to a specialist for preconception evaluation and risk modification. **Table 5** provides a brief list of selected screening questions.

### SUMMARY

Few women present to primary care visits requesting preconception care; however, an estimated 10% of US women of reproductive age become pregnant each year.<sup>84</sup> PCPs who care for women have a critical role to play in helping women to identify preconception risks, both modifiable and nonmodifiable, and to make informed decisions about planning pregnancy and contraception. Screening women for their pregnancy intentions and initiating conversations with women about their pregnancy goals are critical first steps in providing preconception counseling and care. Emphasizing the overlap between a woman's own health goals and preconception goals can help empower women to invest jointly in their own long-term health and the health of their future families.

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