

Kayle S. Shapero, MD, PhD
Yale-New Haven Health System,
New Haven, CT

Nihar R. Desai, MD, MPH
Section of Cardiovascular Medicine, Department of
Medicine, Yale School of Medicine, New Haven, CT;
Center for Outcomes Research and Evaluation,
New Haven, CT

Robert W. Elder, MD
Section of Cardiovascular Medicine, Department of
Medicine, Yale School of Medicine, New Haven, CT;
Department of Pediatrics, Yale School of Medicine,
New Haven, CT

Heather S. Lipkind, MD
Department of Obstetrics and Gynecology,
Yale School of Medicine, New Haven, CT

Josephine C. Chou, MD, MS
Section of Cardiovascular Medicine, Department of
Medicine, Yale School of Medicine, New Haven, CT

Erica S. Spatz, MD, MHS
Section of Cardiovascular Medicine, Department of Medicine,
Yale School of Medicine, New Haven, CT; Center for Outcomes
Research and Evaluation, New Haven, CT

Cardio-obstetrics: Recognizing and managing cardiovascular complications of pregnancy

ABSTRACT

Pregnancy can exacerbate known cardiovascular disorders and unmask previously unrecognized problems. Patients with congenital heart disorders, valvular disease, primary pulmonary hypertension, hypertensive disorders of pregnancy, and acquired peripartum cardiomyopathy need a collaborative interdisciplinary team that includes a cardiologist with specialty training in obstetrics.

KEY POINTS

Several trends are increasing cardiovascular risk in pregnancy. The average maternal age at first pregnancy is increasing, survival in congenital heart disease has improved, and cardiovascular risk factors are developing at younger ages.

Maternal morbidity and mortality are increasing, with cardiovascular diseases accounting for over one-quarter of peripartum and postpartum deaths.

Rates of maternal mortality from cardiovascular disease are highest among low-income women and women of color.

The emergence of new cardiovascular complications during pregnancy is often considered a failed stress test and can increase the risk of future cardiovascular disease. Women should be monitored closely after pregnancy in order to improve maternal outcomes and prevent the development of future cardiovascular disease.

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CARDIOVASCULAR COMPLICATIONS during and after pregnancy are on the rise, but traditional cardiology and obstetric training programs do not adequately cover this topic. As a result, many family clinicians, obstetricians, and cardiologists are uncomfortable managing pregnant women with cardiovascular conditions.

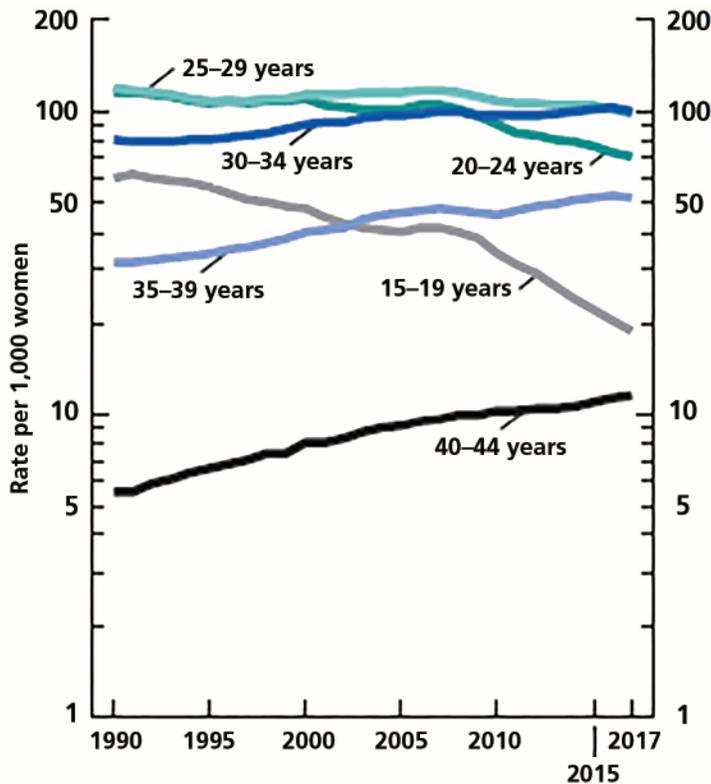
In this review, we describe populations of women at risk for heart disease in pregnancy and discuss the most commonly encountered preexisting and incident types, with a focus on recognition, risk assessment, and management.

■ MATERNAL MORTALITY RATES RISING

In the United States, between the years 2000 and 2014, the maternal death rate increased by 6.6%.¹ In the years 1998–2005, the rate of death during or within 1 year of pregnancy attributed to cardiovascular causes was 3.48 per 100,000 live births²; in 2006–2010 it was 4.23.^{3,4}

A study in Hawaii from 1991 to 2007 found that 4.2% of all deaths occurred within 1 year of pregnancy, and heart disease was the leading cause of pregnancy-associated death (20.5%). The most prominent causes of maternal death were peripartum cardiomyopathy, myocardial infarction, and arrhythmias.⁵ Similar findings were reported in a 2002–2006 review in California.⁶

Ethnic and racial disparities in maternal outcomes exist in the United States: eg, in black women, the risk of pregnancy-related death is 3 times higher than in women of oth-



NOTE: Rates are plotted on a logarithmic scale.
Source: NCHS, National Vital Statistics System, Natality.

Figure 1. Birth rates by selected age of mother, United States, 1900–2017.

From reference 12.

er races.³ This may partially be due to higher rates of preexisting cardiovascular disease and higher rates of new-onset hypertension of pregnancy and peripartum cardiomyopathy.^{7,8} Disparities may also result from poorer quality of care and provider bias.^{9,10}

REASONS FOR THE INCREASE IN CARDIOVASCULAR RISK

Three major trends are contributing to the increase in maternal cardiovascular risk.

Older women are having children

Women are waiting longer to have children (Figure 1).^{11,12} Between 2000 and 2015, pregnancy rates increased from 40 to 52.3 per 1,000 in women ages 35 to 39 and from 8 to 11.6 per 1,000 in women ages 40 to 45.^{13,14} The average age of first-time mothers in the United States rose from 24.9 in 2000 to 26.8 in 2017.^{12,14} This trend is not limited to the United States—the mean age for first preg-

nancies is increasing around the world.¹⁵

Reasons for delaying pregnancy likely include increased availability and efficacy of contraception, more women pursuing higher education and careers, and economic uncertainty among younger women.¹⁶

More children with congenital heart disease now survive into adulthood

Thanks to advances in surgery and medical care, most children with congenital heart disease now survive to childbearing age.¹⁷

An estimated 1% of women giving birth in the United States have congenital heart disease.¹⁸ Between 2000 and 2010, the prevalence of maternal congenital heart disease increased from 6.4 to 9.0 per 10,000 hospitalizations for childbirth.¹⁹

Congenital heart diseases in adults range in severity from simple abnormalities such as atrial septal defects (17%) and ventricular septal defects (14%) to moderate ones such as repaired tetralogy of Fallot (11%) and more severe disease such as transposition of the great arteries (5%) and Ebstein anomaly (2%).²⁰

Cardiovascular risk factors are increasing in young people

Rates of obesity, diabetes, hypertension, and atherosclerosis are increasing in the United States in younger adults,²¹ including women of childbearing age, placing them at risk of pregnancy complications.

PREGNANCY INCREASES CARDIOVASCULAR RISK

Hemodynamic and hormonal factors in pregnancy contribute to cardiac risk and exacerbate preexisting conditions.

Increased cardiac output

During pregnancy, plasma volume expands, leading to increased stroke volume, which may increase cardiac output by 30% to 50%.²² Cardiac output is further increased during labor—by 15% in the first stage, and by up to 50% in the second stage, due to pain, anxiety, and “autotransfusion” of blood into the circulation during uterine contractions, increasing the circulating volume by 300 to 500 mL (Table 1).²³ Cardiac output also increases by 25% to 40% after delivery in addition to the increases during pregnancy and delivery, due to

reduced vena cava compression and to uterine contractions, and then declines rapidly over the next hours.²⁴

Other hemodynamic changes of pregnancy include increased heart rate, reduced systemic vascular resistance, and complex changes in systolic blood pressure, all of which contribute to a rise in cardiac output.²⁵

Physiologic anemia

In conjunction with increased cardiac output, blood volume increases by about 1.5 L during pregnancy. Although red blood cell mass also increases, the increase is not proportionate to the plasma volume, resulting in physiologic anemia.²⁶

Hormonal changes

Estrogen and progesterone levels rise during pregnancy, which increases sympathetic tone and can increase the risk for plaque rupture and thrombosis.²⁷

CONGENITAL HEART DISEASE AND PREGNANCY

Congenital heart disease accounts for about 75% of cases of heart disease in pregnancy,²⁸ and this percentage is increasing.

While some congenital heart problems (eg, atrial septal defect, patent ductus arteriosus) may be well tolerated during pregnancy, complex syndromes such as pulmonary hypertension from Eisenmenger physiology are associated with a risk of maternal death as high as 50%.²⁹

Metabolic and physiologic changes of pregnancy may precipitate new heart failure or exacerbate existing cardiac disease, especially in women who underwent repair of congenital heart lesions as children. Even if the defect has been repaired, a patient can still be vulnerable to later complications such as heart failure, arrhythmia, pulmonary hypertension, and residual structural concerns.

Congenital heart disease also increases the risk of medical and obstetric complications during delivery.¹⁹

Management guidelines available

The 2008 American College of Cardiology and American Heart Association guidelines for managing adults with congenital heart disease include topics in pregnancy such as frequency of follow-up, stress testing, anticoagulation, anesthesia, monitoring during delivery,

TABLE 1

Physiologic changes of pregnancy

Arterial compliance increases throughout pregnancy

Cardiac output begins to increase by 5 weeks and plateaus at 20 weeks

Heart rate increases throughout pregnancy

Systolic blood pressure increases at 20 weeks

Systemic vascular resistance decreases early on, continues to decrease, and plateaus toward the end of pregnancy

Stroke volume peaks at 24 weeks

Relative anemia: Red blood cell mass increases but relatively less than plasma volume, which expands by 10% to 15% by 6–12 weeks

During labor: Cardiac output increases 15% to 50% with contractions, and circulating volume increases

pregnancy counseling, genetic evaluation, review of medications, and fetal echocardiography.³⁰ The following are a few highlights:

General risk. In general, if a patient's functional class and systolic function are normal or near-normal, pregnancy tends to be uncomplicated. Nonetheless, all women with congenital heart disease who are considering pregnancy should be seen by an adult congenital heart disease specialist before conceiving.

Anticoagulation. The risks and benefits of continuing anticoagulation during pregnancy should be discussed with the patient. Warfarin is teratogenic and should be avoided during the first trimester. Warfarin should also be avoided during delivery, given the increased risk of fetal intracranial hemorrhage; low molecular weight heparin and unfractionated heparin should be used instead. The efficacy and safety of the direct-acting oral anticoagulants in pregnancy are still unknown, as data are scarce.³¹

Delivery method. In general, vaginal delivery is preferable for women with congenital heart disease unless cesarean delivery is indicated for obstetric reasons.

Breastfeeding is considered safe in patients with heart disease, although many cardiac medications may cross into breast milk. These issues should be discussed with the patient before restarting medications after delivery.

Traditional training does not adequately cover pregnant women with cardiovascular conditions

■ **PREEXISTING ACQUIRED HEART DISEASE IN PREGNANCY**

The prevalence of preexisting acquired heart disease (eg, valvular heart disease, pulmonary hypertension, arrhythmia) in pregnancy is difficult to ascertain, given that pregnancy can unmask previously unknown disease. A nationwide 2003–2012 study found 81,295 women with heart disease, representing 0.2% of all pregnant women in the sample. Of these women, 30.9% had valvular heart disease and 6.5% had pulmonary hypertension, both of which require specific management during pregnancy.³²

Acquired valvular disease

Acquired valvular disease can lead to complications during pregnancy owing to hemodynamic changes. In some situations, valvular disease is first diagnosed during pregnancy, when hemodynamic changes may cause heart failure and arrhythmias.

Women with a stenotic valve can safely undergo balloon dilation by percutaneous catheter; cardiac surgery should be considered only in severe cases.³³

Primary pulmonary hypertension

Primary pulmonary hypertension can cause right heart failure. Women with severe pulmonary hypertension have the highest maternal death rate, approaching 50%, which is attributed to high fixed pulmonary vascular resistance and an inability to increase pulmonary blood flow.³⁴ Given the high risk, most providers and guidelines recommend against pregnancy for women with established pulmonary hypertension.

Pregnancy management. A woman who decides to continue her pregnancy should be followed closely with at least monthly visits. Given the dearth of data, it is unknown if patients with lower pulmonary pressures have a lower risk of complications; even some women with mild to moderate pulmonary hypertension deteriorate during pregnancy. Efforts should be made to reduce oxygen demand with rest and to use supplemental oxygen when indicated. Frequently, patients with severe pulmonary hypertension are admitted to the hospital in the second trimester and followed as inpatients.

It is often recommended that women continue their pulmonary hypertension medica-

tions during pregnancy, except for bosentan, a dual endothelin receptor antagonist with teratogenic effects. Other advanced therapies such as prostacyclin analogues and sildenafil are considered safe.³⁵

Delivery. The preferred delivery method in patients with pulmonary hypertension is highly debated. Vaginal delivery increases cardiac output, and pushing during the second stage of labor can reduce venous return to the right side of the heart, both of which may be particularly dangerous for these patients. Additionally, because patients with pulmonary hypertension tend to go into labor early, induction of labor may be associated with increased length of labor and a likelier need for an emergency cesarean delivery, which entails additional risks.

For these reasons, many institutions (including ours) recommend elective cesarean delivery to avoid emergency procedures and minimize blood loss. General anesthesia is not recommended because of reports of cardiac failure owing to adverse effects of intubation and positive pressure ventilation on venous return. Instead, regional anesthesia with a combination of epidural and low-dose spinal anesthesia is preferred to avoid vasodilation and the associated risk of hypotension. During delivery, it is imperative to closely follow arterial and venous hemodynamics including blood pressure; in addition, the mother should be observed in the hospital after delivery for several days until stable.^{36–38}

Preexisting hypertension

A physiologic drop in blood pressure in pregnancy may allow women with preexisting hypertension to avoid medication use early in pregnancy, although they should be monitored closely. Those who require ongoing medication should switch to a drug deemed safer for pregnancy such as labetalol, metoprolol, or a calcium channel blocker; labetalol and nifedipine are most commonly used. Angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and direct renin inhibitors are contraindicated in pregnancy.

Hypertensive patients of African or Caribbean family origin should be treated with a calcium channel blocker as a first-line agent³⁹ and should be carefully monitored for progression to preeclampsia or eclampsia.⁴⁰

In 2017, the average age of first-time US mothers was 26.8

INCIDENT CARDIOVASCULAR DISEASE IN PREGNANCY

Cardiovascular disease can arise during pregnancy in women without preexisting conditions.

Hypertensive disorders of pregnancy

New-onset hypertension and maternal placental disorders such as preeclampsia occur in 1% to 5% of pregnancies. They are defined as blood pressure higher than 140/90 mm Hg arising after 20 weeks of gestation.

Risk factors for hypertensive disorders of pregnancy include genetics^{41,42} and, for preeclampsia, elevated body mass index ($> 24 \text{ kg/m}^2$).⁴³

Future risk. Developing a hypertensive disorder of pregnancy has been compared to failing a stress test, in that it often presages later cardiovascular disease.⁴⁴ Underlying or unrecognized risk factors may contribute not only to the development of hypertensive conditions in pregnancy, but also to subsequent cardiovascular disease.

Hypertensive disorders in pregnancy have been shown in numerous studies to increase the risks for metabolic syndrome, subsequent diagnosis of hypertension, and lifetime risk of cardiovascular disease.⁴⁵⁻⁴⁸ Problems may reveal themselves soon after giving birth: a study of all births in New York City from 1995 to 2004 found that women with gestational hypertension had a higher rate of hospitalizations in the year after delivery related to heart failure (adjusted odds ratio 2.6), and women with preeclampsia had higher rates of hospitalization for cardiovascular disease and stroke.⁴⁹

The American Heart Association considers preeclampsia to be a cardiac risk factor and recommends monitoring women with preeclampsia for the first few years after delivery.^{50,51} Women with this condition have at least double the risk of stroke, cardiac ischemia, or venous thromboembolism for up to 20 years after pregnancy.

Peripartum cardiomyopathy

Peripartum cardiomyopathy occurs in about 1 in 1,000 to 4,000 live-birth pregnancies. Proposed causes include autoimmunity, genetics, nutritional deficiencies, and vascular dysfunction.⁵² Advanced maternal age, preeclampsia, gestational hypertension, multiparity, and African American race have been identified as

risk factors.

Presentation. Peripartum cardiomyopathy classically presents during the first 6 months after delivery, but it may also present during the second or third trimester of pregnancy. The typical presentation is consistent with that of heart failure (eg, orthopnea, paroxysmal nocturnal dyspnea, significant peripheral edema, elevated jugular venous distention). This is often difficult to distinguish from signs and symptoms of normal pregnancy, especially during the third trimester, so a high index of suspicion is required.

Diagnosis. Other possible causes of heart failure (ie, ischemic, congenital) should first be ruled out. Echocardiography is required for evaluation.⁵²

Pregnancy management. Patients are managed similarly to pregnant women with other forms of heart failure in pregnancy: beta-blockers and volume control agents, including diuretics, to reduce afterload are the mainstays of therapy.

Postpartum care. After delivery, patients should be managed with standard therapy consisting of beta-blockers, angiotensin-converting enzyme inhibitors, mineralocorticoid receptor antagonists, and diuretics. Patients with severe hemodynamic compromise and depressed left ventricular function may require inotropic support or mechanical circulatory devices.⁵³

Prognosis. Most women recover from peripartum cardiomyopathy. The Investigations of Pregnancy-associated Cardiomyopathy study found that after 12 months, left ventricular ejection fraction had increased to greater than 50% in more than two-thirds of women. However, 13% had major events or persistent heart failure (ejection fraction $< 35\%$).⁵⁴ Even with full left ventricular recovery, there is a risk of recurrence with subsequent pregnancies, and this risk is higher in women with persistent left ventricular dysfunction. There are currently no firm recommendations to guide women on subsequent pregnancies,⁵⁵ but they should be advised of the risks.⁵²

Ischemic heart disease

New ischemic heart disease of pregnancy, which includes plaque rupture and thrombosis, spontaneous coronary artery dissection, coro-

Most children with congenital heart disease now survive to childbearing age

TABLE 2

The Cardiac Disease in Pregnancy (CARPREG II) modified risk score

Predictor	Points
Prior cardiac events or arrhythmias	3
Baseline New York Heart Association functional class II or III heart failure or cyanosis	3
Mechanical valve	3
Ventricular systolic dysfunction	2
High-risk left-sided valve disease or left ventricular outflow obstruction	2
Pulmonary hypertension	2
Coronary artery disease	2
High-risk aortopathy	2
No prior cardiac intervention	1
Late pregnancy assessment	1
Total points	Risk
0–1	5%
2	10%
3	15%
4	22%
> 4	41%

Data from reference 62.

nary embolism, and vasospasm, is estimated to occur in 1 to 6.2 per 100,000 deliveries,⁵⁶ a rate 3 to 4 times higher than in nonpregnant women of comparable age.⁵⁷ The most common causes of new ischemic heart disease are coronary artery dissection and coronary artery thrombosis.

Spontaneous coronary artery dissection. Pregnancy-related spontaneous coronary artery dissection occurs by intimal rupture causing medial dissection, or by a spontaneous disruption of the vasa vasorum, which causes intramedial hemorrhage and separation within the arterial wall. Proposed underlying causes include hormonally mediated structural changes of decreased collagen synthesis and increased polysaccharide content, which weakens the tunica media, predisposing it to dissection; underlying connective tissue disorders such as Marfan syndrome or Ehlers-Danlos syndrome; and inflammatory conditions such as lupus

erythematosus. Such factors, when combined with the increased hemodynamic effects of pregnancy and labor, are thought to precipitate spontaneous artery dissection.⁵⁸

Risk factors for ischemic heart disease during pregnancy are similar to those outside of pregnancy, ie, smoking, diabetes, family history, hyperlipidemia, and chronic hypertension. While rare, women with preexisting but undiagnosed coronary atherosclerosis have the greatest risk of myocardial ischemia during pregnancy,⁵⁹ followed by those with pregnancy after age 40.⁶⁰ Patients with congenital heart disease (eg, uncorrected anomalous origins of the coronary arteries) or severe aortic stenosis or those who have undergone previous surgical coronary manipulation are also at increased risk for ischemia.⁶¹

Pregnancy management. The goal of managing ischemic heart disease during pregnancy is to reduce oxygen demand to avoid progression to infarction. In the absence of ST-segment elevation acute coronary syndrome, patients can be managed with watchful waiting and medical therapy with beta-blockade and low-dose aspirin.

Infarction management. Should myocardial infarction occur, percutaneous coronary intervention is advised, given the risk of hemorrhage with thrombolysis. After percutaneous coronary intervention, routine management with dual antiplatelet inhibitors and beta-blockers is generally well tolerated. Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers are contraindicated due to embryonic toxicity.

Delivery. Vaginal delivery is preferred over cesarean delivery to avoid the hemodynamic changes of anesthesia and the potential for blood loss. Epidural analgesia is advised for pain control, given its effects on reducing afterload, pain, stress, and anxiety.

RISK ASSESSMENT

Several tools have been developed to estimate morbidity and mortality risk in pregnant women with cardiac disease.

The Cardiac Disease in Pregnancy Study (CARPREG) risk score, developed in 1997, has been validated in several retrospective studies and is widely used. Applicable to pregnant wom-

en with acquired or congenital heart disease, the score stratifies risk according to the presence of poor functional class (New York Heart Association class III or IV), cyanosis, arrhythmias, prior cardiovascular events (heart failure, transient ischemic attack, stroke), left heart obstruction, and ejection fraction less than 40%.¹⁹

The CARPREG II study refined the initial score in 2018 by incorporating general characteristics with lesion-specific risk estimates (such as systemic right ventricle or peripartum cardiomyopathy with residual left ventricular dysfunction) to improve predictive accuracy (Table 2).⁶²

The Pregnancy in Women With a Congenital Heart Defect (ZAHARA) risk score was developed in 2010 based on data from a retrospective study of 1,300 pregnancies (Table 3).⁶³ It differs from the original CARPREG score by incorporating more specific details of prepregnancy cardiac disease, including valvular heart disease, and cardiac medications.

The World Health Organization (WHO) risk classification (Table 4), devised by the Task Force on the Management of Cardiovascular Diseases During Pregnancy of the European Society of Cardiology,⁴⁰ the Working Group on Pregnancy and Contraception, and others, integrates congenital and acquired heart disease data with other comorbidities. It may better reflect the diversity of at-risk pregnant women and thus be more useful. One especially useful feature of the WHO score is that it has a 100% negative predictive value of cardiovascular events for class I patients (ie, uncomplicated or mild defect, repaired simple lesions, isolated premature ventricular beats and atrial ectopic beats), indicating that risk of pregnancy for that group is considered equivalent to that of the general population.

Based on studies comparing the 3 scores, the WHO's appears to best estimate the risk of cardiovascular events in pregnant women with preexisting heart disease. However, studies were performed using the first CARPREG model, so it is unclear how the CARPREG II model compares.^{64,65}

■ SUBSEQUENT PREGNANCIES

Many women with cardiovascular complications in pregnancy, regardless of severity,

TABLE 3

The Pregnancy in Women With a Congenital Heart Defect (ZAHARA) risk score

Predictor	Points
History of arrhythmias	1.5
Cardiac medication before pregnancy	1.5
New York Heart Association functional class before pregnancy \geq II	0.75
Left heart obstruction (peak gradient $>$ 30 mm Hg, or aortic valve area $<$ 1.0 cm ²)	2.5
Systemic aortic valve regurgitation (moderate or severe)	0.75
Mechanical heart prosthesis	4.25
Cyanotic heart disease (corrected or uncorrected)	1.0
Total points	Risk
0–0.5	2.9%
0.51–1.50	7.5%
1.51–2.50	17.5%
2.51–3.50	43.1%
$>$ 3.50	70.0%

Data from reference 63.

desire additional pregnancies. The provider should engage the patient in shared decision-making with the goal of making as informed a decision as possible. Predicting outcomes for subsequent pregnancies can be challenging, and other than for preeclampsia and peripartum cardiomyopathy, few data exist regarding recurrent pregnancies in the setting of cardiac disease. With no firm guidelines or recommendations, guidance must rely heavily on a patient's diagnosis and previous experience.

Women with structural or congenital heart disease that has remained stable can be managed similarly through subsequent pregnancies.

Preeclampsia. Published rates of recurrent preeclampsia range widely, from 5% to nearly 50%. Blood pressure and proteinuria should be monitored during subsequent pregnancy for early detection and consideration of aspirin use.^{48,51}

Peripartum cardiomyopathy. Risk of relapse may be as high as 20% to 50% and is highest in patients with persistent left ventricular dysfunction from prior pregnancies. To reduce the risk of additional complications,

TABLE 4

World Health Organization classes of pregnancy risk

Class 1: Risk is considered equivalent to that in the general population

Uncomplicated, small, or mild pulmonary stenosis, patent ductus arteriosus, mitral valve prolapse

Repaired simple lesions, eg, atrial septal defect, ventricular septal defect, patent ductus arteriosus, total anomalous pulmonary vein drainage

Isolated premature ventricular beats and atrial ectopic beats

Class 2: Small increased risk of morbidity and death

Unoperated atrial septal defect

Repaired tetralogy of Fallot

Most arrhythmias

Class 2 or 3: Moderate increased risk of morbidity and death, depending on the patient

Mild left ventricular impairment

Hypertrophic cardiomyopathy

Native or tissue valvular heart disease (not including class IV valvular disease)

Marfan syndrome without aortic dilation

Heart transplant

Class 3: Significantly increased risk of morbidity and death

Mechanical valves

Systemic right ventricle (ie, repaired congenital lesions)

Cyanotic heart disease

Post-Fontan operation

Complex congenital heart disease

Class 4: Pregnancy contraindicated

Pulmonary hypertension

Severe systemic ventricular dysfunction (left ventricular ejection fraction < 30%)

Severe left heart obstruction

Marfan syndrome with dilated aorta (> 40 mm)

Previous peripartum cardiomyopathy with residual impaired left ventricular function

Adapted from information in reference 33.

women should be advised to wait until their left ventricular function has completely recovered before attempting pregnancy again.⁵⁵

IMPROVING MATERNAL OUTCOMES

Cardiologists with expertise in managing cardiovascular disease in pregnancy are increasingly needed, as are multidisciplinary teams that can facilitate care for complex patients.

Lacking specific guidelines for pregnant women with a cardiovascular disorder, clinical practice varies, and knowledge is limited regarding best practices for detection and management. More research and opportunities for shared learning are needed, including establishing registries of pregnant women at risk of heart disease or with a known condition. Clinical trials of effective management approaches should be done.

Academic institutions should promote learning opportunities (eg, conferences, didactics, or specialized cross-disciplinary training). Our program at Yale has a monthly management conference attended by specialists in maternal fetal medicine, adult congenital heart disease, and cardiology.

The American College of Cardiology and American Heart Association recommend that patients with congenital heart disease be closely followed by a specialized team of providers, including specialists in adult congenital heart disease and maternal-fetal medicine, to assist in managing their pregnancies.³⁰ Hospitals should organize and support collaborative multidisciplinary pregnancy care teams that include clinicians from the fields of family medicine, pediatrics, obstetrics, cardiology, endocrinology, and emergency medicine to facilitate care of complex patients.

In view of racial disparities in rates of maternal death, with especially high rates in black women, focused efforts are needed that engage health systems, providers, and communities to understand breakdowns in care.

Finally, better care systems need to be developed to focus on maternal health after delivery. Typically, medical attention tends to pivot toward the baby, resulting in missed opportunities for education, surveillance, and possible intervention for women at risk. ■

REFERENCES

- MacDorman MF, Declercq E, Cabral H, Morton C. Recent increases in the US maternal mortality rate: disentangling trends from measurement issues. *Obstet Gynecol* 2016; 128(3):447–455. doi:10.1097/AOG.0000000000001556
- Berg CJ, Callaghan WM, Syverson C, Henderson Z. Pregnancy-related mortality in the United States, 1998 to 2005. *Obstet Gynecol* 2010; 116(6):1302–1309. doi:10.1097/AOG.0b013e3181fd11b1
- Creanga AA, Berg CJ, Syverson C, Seed K, Bruce FC, Callaghan WM. Pregnancy-related mortality in the United States, 2006–2010. *Obstet Gynecol* 2015; 125(1):5–12. doi:10.1097/AOG.0000000000000564
- Freedman RL, Lucas DN. MBRACE-UK: saving lives, improving mothers' care—implications for anaesthetists. *Int J Obstet Anesth* 2015; 24(2):161–173. doi:10.1016/j.ijoa.2015.03.004
- Burlingame J, Horiuchi B, Ohana P, Onaka A, Sauvage LM. The contribution of heart disease to pregnancy-related mortality according to the pregnancy mortality surveillance system. *J Perinatol* 2012; 32(3):163–169. doi:10.1038/jp.2011.74
- Hameed AB, Lawton ES, McCain CL, et al. Pregnancy-related cardiovascular deaths in California: beyond peripartum cardiomyopathy. *Am J Obstet Gynecol* 2015; 213(3):379.e1–e10. doi:10.1016/j.ajog.2015.05.008
- Williams RA. Cardiovascular disease in African American women: a health care disparities issue. *J Natl Med Assoc* 2009; 101(6):536–540. pmid:19585921
- Creanga AA, Bateman BT, Kuklina EV, Callaghan WM. Racial and ethnic disparities in severe maternal morbidity: a multistate analysis, 2008–2010. *Am J Obstet Gynecol* 2014; 210(5):435.e1–e8. doi:10.1016/j.ajog.2013.11.039
- Harper M, Dugan E, Espeland M, Martinez-Borges A, McQuellon C. Why African-American women are at greater risk for pregnancy-related death. *Ann Epidemiol* 2007; 17(3):180–185. doi:10.1016/j.annepidem.2006.10.004
- Nelson A. Unequal treatment: confronting racial and ethnic disparities in health care. *J Natl Med Assoc* 2002; 94(8):666–668. pmid:12152921
- Ventura SJ, Mosher WD, Curtin SC, Abma JC, Henshaw S. Trends in pregnancies and pregnancy rates by outcome: estimates for the United States, 1976–96. *Vital Health Stat* 21 2000; (56):1–47. pmid:10740440
- Mathews TJ, Hamilton BE. Mean age of mothers is on the rise: United States, 2000–2014. *NCHS Data Brief* 2016; (232):1–8. pmid:26828319
- Martin JA, Hamilton BE, Osterman MJ, Driscoll AK, Mathews TJ. Births: final data for 2015. *Natl Vital Stat Rep* 2017; 66(1):1. pmid:28135188
- Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Drake P. Births: final data for 2017. *Natl Vital Stat Rep* 2018; 67(8):1–50. pmid:30707672
- Central Intelligence Agency. The World Factbook. Mother's mean age at first birth. <https://www.cia.gov/library/publications/the-world-factbook/fields/352.html>. Accessed December 10, 2019.
- Barclay K, Myrskylä M. Advanced maternal age and offspring outcomes: reproductive aging and counterbalancing period trends. *Population and Development Review* 2016; 42(1):69–94.
- Gilboa SM, Devine OJ, Kucik JE, et al. Congenital heart defects in the United States: estimating the magnitude of the affected population in 2010. *Circulation* 2016; 134(2):101–109. doi:10.1161/CIRCULATIONAHA.115.019307
- Hoffman JJ, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol* 2002; 39(12):1890–1900. pmid:12084585
- Thompson JL, Kuklina EV, Bateman BT, Callaghan WM, James AH, Grotegut CA. Medical and obstetric outcomes among pregnant women with congenital heart disease. *Obstet Gynecol* 2015; 126(2):346–354. doi:10.1097/AOG.0000000000000973
- Verheugt CL, Uiterwaal CS, van der Velde ET, et al. Mortality in adult congenital heart disease. *Eur Heart J* 2010; 31(10):1220–1229. doi:10.1093/eurheartj/ehq032
- Benjamin EJ, Virani SS, Callaway CW, et al; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics—2018 Update: A Report From the American Heart Association. *Circulation* 2018; 137(12):e67–e492. doi:10.1161/CIR.0000000000000558.
- Hunter S, Robson SC. Adaptation of the maternal heart in pregnancy. *Br Heart J* 1992; 68(6):540–543. doi:10.1136/hrt.68.12.540
- Nelson-Piercy C. *Handbook of Obstetric Medicine*. 2nd Ed. London, UK: Taylor & Francis Group; 2002.
- James CF, Banner T, Caton D. Cardiac output in women undergoing cesarean section with epidural or general anesthesia. *Am J Obstet Gynecol* 1989; 160(5 Pt 1):1178–1184. pmid:2729392
- Crapo RO. Normal cardiopulmonary physiology during pregnancy. *Clin Obstet Gynecol* 1996; 39(1):3–16. pmid:8635306
- Fujitani S, Baldisseri MR. Hemodynamic assessment in a pregnant and peripartum patient. *Crit Care Med* 2005; 33(10 suppl):S354–S361. pmid:16215359
- Heidemann BH, McLure JH. Changes in maternal physiology during pregnancy. *CEPD Reviews*. *Br J Anaesth* 2003; 3(3):65–68. doi:10.1093/bjacepd/mkg065
- Siu SC, Sermer M, Harrison DA, et al. Risk and predictors for pregnancy-related complications in women with heart disease. *Circulation* 1997; 96(9):2789–2794. pmid:9386139
- Clark SL. Cardiac disease in pregnancy. *Crit Care Clin* 1991; 7(4):777–797. pmid:1747800
- Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease. *J Am Coll Cardiol* 2008; 52(23):e143–e263. doi:10.1016/j.jacc.2008.10.001
- Sessa M, Mascolo A, Callréus T, Capuano A, Rossi F, Anderson M. Direct-acting oral anticoagulants (DOACs) in pregnancy: new insight from VigiBase. *Sci Rep* 2019; 9:7236.
- Lima FV, Yang J, Xu J, Stergiopoulos K. National trends and in-hospital outcomes in pregnant women with heart disease in the United States. *Am J Cardiol* 2017; 119(10):1694–1700. doi:10.1016/j.amjcard.2017.02.003
- Anthony J, Sliwa K. Decompensated heart failure in pregnancy. *Card Fail Rev* 2016; 2(1):20–26. doi:10.15420/cfr.2015.24.2
- Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. *Heart* 2006; 92(10):1520–1525. doi:10.1136/hrt.2006.095240
- Olsson KM, Channick R. Pregnancy in pulmonary arterial hypertension. *Eur Respir Rev* 2016; 25(142):431–437. doi:10.1183/16000617.0079-2016
- Bonnin M, Mercier FJ, Sitbon O, et al. Severe pulmonary hypertension during pregnancy: mode of delivery and anesthetic management of 15 consecutive cases. *Anesthesiology* 2005; 102(6):1133–1137. pmid:15915025
- Kiely DG, Condliffe R, Wilson VJ, Gandhi SV, Elliot CA. Pregnancy and pulmonary hypertension: a practical approach to management. *Obstet Med* 2013; 6(4):144–154. doi:10.1177/1753495X13495193
- Pieper PG, Hoendermis ES. Pregnancy in women with pulmonary hypertension. *Neth Heart J* 2011; 19(12):504–508. doi:10.1007/s12471-011-0219-9
- Webster LM, Myers JE, Nelson-Piercy C, et al. Labetalol versus nifedipine as antihypertensive treatment for chronic hypertension in pregnancy: a randomized controlled trial. *Hypertension* 2017; 70(5):915–922. doi:10.1161/HYPERTENSIONAHA.117.09972
- European Society of Gynecology (ESG); Association for European Paediatric Cardiology (AEPC); German Society for Gender Medicine (DGesGM); Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, et al. ESC Guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). *Eur Heart J* 2011; 32(24):3147–3197. doi:10.1093/eurheartj/ehr218
- Ness RB, Markovic N, Bass D, Harger G, Roberts JM. Family history of hypertension, heart disease, and stroke among women who de-

- velop hypertension in pregnancy. *Obstet Gynecol* 2003; 102(6):1366–1371. pmid:14662228
42. **Irgens HU, Reisaeter L, Irgens LM, Lie RT.** Long term mortality of mothers and fathers after pre-eclampsia: population based cohort study. *BMJ* 2001; 323(7323):1213–1217. doi:10.1136/bmj.323.7323.1213
 43. **O'Brien TE, Ray JG, Chan WS.** Maternal body mass index and the risk of preeclampsia: a systematic overview. *Epidemiology* 2003; 14(3):368–374. pmid:12859040
 44. **Williams D.** Pregnancy: a stress test for life. *Curr Opin Obstet Gynecol* 2003; 15(6):465–471. doi:10.1097/01.gco.0000103846.69273.ba
 45. **Forest JC, Girouard J, Masse J, et al.** Early occurrence of metabolic syndrome after hypertension in pregnancy. *Obstet Gynecol* 2005; 105(6):1373–1380. doi:10.1097/01.AOG.0000163252.02227.f8
 46. **Ray JG, Vermeulen MJ, Schull MJ, Redelmeier DA.** Cardiovascular health after maternal placental syndromes (CHAMPS): population-based retrospective cohort study. *Lancet* 2005; 366(9499):1797–1803. doi:10.1016/S0140-6736(05)67726-4
 47. **Smith GN, Pudwell J, Walker M, Wen SW.** Ten-year, thirty-year, and lifetime cardiovascular disease risk estimates following a pregnancy complicated by preeclampsia. *J Obstet Gynaecol Can* 2012; 34(9):830–835. doi:10.1016/S1701-2163(16)35381-6
 48. **Veerbeek JH, Hermes W, Breimer AY, et al.** Cardiovascular disease risk factors after early-onset preeclampsia, late-onset preeclampsia, and pregnancy-induced hypertension. *Hypertension* 2015; 65(3):600–606. doi:10.1161/HYPERTENSIONAHA.114.04850
 49. **Savitz DA, Danilack VA, Elston B, Lipkind HS.** Pregnancy-induced hypertension and diabetes and the risk of cardiovascular disease, stroke, and diabetes hospitalization in the year following delivery. *Am J Epidemiol* 2014; 180(1):41–44. doi:10.1093/aje/kwu118
 50. **Wilson BJ, Watson MS, Prescott GJ, et al.** Hypertensive diseases of pregnancy and risk of hypertension and stroke in later life: results from cohort study. *BMJ* 2003; 326(7394):845. doi:10.1136/bmj.326.7394.845
 51. **LeFevre ML; US Preventive Services Task Force.** Low-dose aspirin use for the prevention of morbidity and mortality from preeclampsia: US Preventive Services Task Force recommendation statement. *Ann Intern Med* 2014; 161(11):819–826. doi:10.7326/M14-1884
 52. **Arany Z, Elkayam U.** Peripartum cardiomyopathy. *Circulation* 2016; 133(14):1397–1409. doi:10.1161/CIRCULATIONAHA.115.020491
 53. **Hilfiker-Kleiner D, Haghikia A, Nonhoff J, Bauersachs J.** Peripartum cardiomyopathy: current management and future perspectives. *Eur Heart J* 2015; 36(18):1090–1097. doi:10.1093/eurheartj/ehv009
 54. **McNamara DM, Elkayam U, Alharethi R, et al; IPAC Investigators.** Clinical outcomes for peripartum cardiomyopathy in North America: results of the IPAC Study (Investigations of Pregnancy-Associated Cardiomyopathy). *J Am Coll Cardiol* 2015; 66(8):905–914. doi:10.1016/j.jacc.2015.06.1309
 55. **Elkayam U.** Risk of subsequent pregnancy in women with a history of peripartum cardiomyopathy. *J Am Coll Cardiol* 2014; 64(15):1629–1636. doi:10.1016/j.jacc.2014.07.961
 56. **Ginz B.** Myocardial infarction in pregnancy. *J Obstet Gynaecol Br Commonw* 1970; 77(7):610–615. pmid:5433480
 57. **Petitti DB, Sidney S, Quesenberry CP Jr, Bernstein A.** Incidence of stroke and myocardial infarction in women of reproductive age. *Stroke* 1997; 28(2):280–283. pmid:9040675
 58. **Vijayaraghavan R, Verma S, Gupta N, Saw J.** Pregnancy-related spontaneous coronary artery dissection. *Circulation* 2014; 130(21):1915–1920. doi:10.1161/CIRCULATIONAHA.114.011422
 59. **Burchill LJ, Lameijer H, Roos-Hesselink JW, et al.** Pregnancy risks in women with pre-existing coronary artery disease, or following acute coronary syndrome. *Heart* 2015; 101(7):525–529. doi:10.1136/heartjnl-2014-306676
 60. **James AH, Jamison MG, Biswas MS, Brancazio LR, Swamy GK, Myers ER.** Acute myocardial infarction in pregnancy: a United States population-based study. *Circulation* 2006; 113(12):1564–1571. doi:10.1161/CIRCULATIONAHA.105.576751
 61. **Nolan TE, Hankins GD.** Myocardial infarction in pregnancy. *Clin Obstet Gynecol* 1989; 32(1):68–75. pmid:2661081
 62. **Silversides CK, Grewal J, Mason J, et al.** Pregnancy outcomes in women with heart disease: the CARPREG II Study. *J Am Coll Cardiol* 2018; 71(21):2419–2430. doi:10.1016/j.jacc.2018.02.076
 63. **Drenthen W, Boersma E, Balci A, et al; ZAHARA Investigators.** Predictors of pregnancy complications in women with congenital heart disease. *Eur Heart J* 2010; 31(17):2124–2132. doi:10.1093/eurheartj/ehq200
 64. **Balci A, Sollie-Szarynska KM, van der Bijl AG, et al; ZAHARA-II investigators.** Prospective validation and assessment of cardiovascular and offspring risk models for pregnant women with congenital heart disease. *Heart* 2014; 100(17):1373–1381. doi:10.1136/heartjnl-2014-305597
 65. **Lu CW, Shih JC, Chen SY, et al.** Comparison of 3 risk estimation methods for predicting cardiac outcomes in pregnant women with congenital heart disease. *Circ J* 2015; 79(7):1609–1617. doi:10.1253/circj.CJ-14-1368

Address: Erica S. Spatz, MD, MHS, Section of Cardiovascular Medicine, Department of Medicine, Yale School of Medicine, 789 Howard Avenue, Dana 3, New Haven, CT 06520; erica.spatz@yale.edu