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Postpartum Hemorrhage

This Practice Bulletin was developed by the ACOG Committee on Practice Bulletins—Obstetrics with the assistance of William N. P. Herbert, MD, and Carolyn M. Zelop, MD. The information is designed to aid practitioners in making decisions about appropriate obstetric and gynecologic care. These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.



Severe bleeding is the single most significant cause of maternal death worldwide. More than half of all maternal deaths occur within 24 hours of delivery, most commonly from excessive bleeding. It is estimated that, worldwide, 140,000 women die of postpartum hemorrhage each year—one every 4 minutes (1). In addition to death, serious morbidity may follow postpartum hemorrhage. Sequelae include adult respiratory distress syndrome, coagulopathy, shock, loss of fertility, and pituitary necrosis (Sheehan syndrome).

Although many risk factors have been associated with postpartum hemorrhage, it often occurs without warning. All obstetric units and practitioners must have the facilities, personnel, and equipment in place to manage this emergency properly. Clinical drills to enhance the management of maternal hemorrhage have been recommended by the Joint Commission on Accreditation of Healthcare Organizations (2). The purpose of this bulletin is to review the etiology, evaluation, and management of postpartum hemorrhage.

Background

The physiologic changes over the course of pregnancy, including a plasma volume increase of approximately 40% and a red cell mass increase of approximately 25%, occur in anticipation of the blood loss that will occur at delivery (3). There is no single, satisfactory definition of postpartum hemorrhage. An estimated blood loss in excess of 500 mL following a vaginal birth or a loss of greater than 1,000 mL following cesarean birth often has been used for the diagnosis, but the average volume of blood lost at delivery can approach these amounts (4, 5). Estimates of blood loss at delivery are notoriously inaccurate, with significant underreporting being the rule. Limited instruction on estimating blood loss has been shown to improve the accuracy of such estimates (6). Also, a decline in hematocrit levels of 10% has been used to define postpartum hemorrhage, but determinations of hemoglobin or hematocrit concentrations may not reflect the current hematologic status (7). Hypotension, dizziness, pal-

lor, and oliguria do not occur until blood loss is substantial—10% or more of total blood volume (8).

Postpartum hemorrhage generally is classified as primary or secondary, with primary hemorrhage occurring within the first 24 hours of delivery and secondary hemorrhage occurring between 24 hours and 6–12 weeks postpartum. Primary postpartum hemorrhage, which occurs in 4–6% of pregnancies, is caused by uterine atony in 80% or more of cases (7). Other etiologies are shown in the box “Etiology of Postpartum Hemorrhage,” with risk factors for excessive bleeding listed in the box “Risk Factors for Postpartum Hemorrhage.”

If excessive blood loss is ongoing, concurrent evaluation and management are necessary. A number of general medical supportive measures may be instituted, including provision of ample intravenous access; crystalloid infusion; blood bank notification that blood products may be necessary; prompt communication with anesthesiology, nursing, and obstetrician–gynecologists; and blood collection for baseline laboratory determinations.

When treating postpartum hemorrhage, it is necessary to balance the use of conservative management techniques with the need to control the bleeding and achieve hemostasis. A multidisciplinary approach often is required. In the decision-making process, less-invasive methods should be tried initially if possible, but if unsuccessful, preservation of life may require hysterectomy. Management of postpartum hemorrhage may vary greatly among patients, depending on etiology of the bleeding, available treatment options, and a patient’s desire for

future fertility. At times, immediate surgery is required because time spent using other treatment methods would be dangerous for the patient. There are few randomized controlled studies relevant to the management of postpartum hemorrhage, so management decisions usually are made based on clinical judgment.

Evaluation and Management Considerations

In an effort to prevent uterine atony and associated bleeding, it is routine to administer oxytocin soon after delivery. This may be given at the time of delivery of the anterior shoulder of the fetus, or more commonly in the United States, following delivery of the placenta.

It may be helpful to post protocols for hemorrhage management in delivery rooms or operating suites. A sample poster from the New York City Department of Health and Mental Hygiene is available at <http://home2.nyc.gov/html/doh/downloads/pdf/ms/ms-hemorr-poster.pdf>.

Clinical Considerations and Recommendations

- ▶ *What should be considered in the initial evaluation of a patient with excessive bleeding in the immediate puerperium?*

Because the single most common cause of hemorrhage is uterine atony, the bladder should be emptied and a bimanual pelvic examination should be performed. The finding of the characteristic soft, poorly contracted (“boggy”) uterus suggests atony as a causative factor. Compression or massage of the uterine corpus can diminish bleeding, expel blood and clots, and allow time for other measures to be implemented.

If bleeding persists, other etiologies besides atony must be considered. Even if atony is present, there may be other contributing factors. Lacerations should be ruled out by careful visual assessment of the lower genital tract. Proper patient positioning, adequate operative assistance, good lighting, appropriate instrumentation (eg, Simpson or Heaney retractors), and adequate anesthesia are necessary for the identification and proper repair of lacerations. Satisfactory repair may require transfer to a well-equipped operating room.

Genital tract hematomas also can lead to significant blood loss. Progressive enlargement of the mass indicates a need for incision and drainage. Often a single bleeding source is not identified when a hematoma is incised. Draining the blood within the hematoma (sometimes

Etiology of Postpartum Hemorrhage

Primary

- Uterine atony
- Retained placenta—especially placenta accreta
- Defects in coagulation
- Uterine inversion

Secondary

- Subinvolution of placental site
- Retained products of conception
- Infection
- Inherited coagulation defects

Adapted from Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap L 3rd, Wenstrom KD. Obstetric hemorrhage. In: Williams obstetrics. 22nd ed. New York (NY): McGraw-Hill; 2005. p. 809–54 and Alexander J, Thomas P, Sanghera J. Treatments for secondary postpartum haemorrhage. The Cochrane Database of Systematic Reviews 2002, Issue 1. Art. No.: CD002867. DOI: 10.1002/14651858.CD002867.

Risk Factors for Postpartum Hemorrhage

Prolonged labor
Augmented labor
Rapid labor
History of postpartum hemorrhage
Episiotomy, especially mediolateral
Preeclampsia
Overdistended uterus (macrosomia, twins, hydramnios)
Operative delivery
Asian or Hispanic ethnicity
Chorioamnionitis

Data from Stones RW, Paterson CM, Saunders NJ. Risk factors for major obstetric haemorrhage. *Eur J Obstet Gynecol Reprod Biol* 1993;48:15–8 and Combs CA, Murphy EL, Laros RK. Factors associated with hemorrhage in cesarean deliveries. *Obstet Gynecol* 1991;77:77–82.

placing a drain in situ), suturing the incision, and if appropriate, packing the vagina are measures usually successful in achieving hemostasis. Interventional radiology is another option for management of a hematoma. Genital tract hematomas may not be recognized until hours after the delivery, and they sometimes occur in the absence of vaginal or perineal lacerations. The main symptoms are pelvic or rectal pressure and pain.

The possibility that additional products of conception remain within the uterine cavity should be considered. Ultrasonography can help diagnose a retained placenta. Retained placental tissue is unlikely when ultrasonography reveals a normal endometrial stripe. Although ultrasonographic images of retained placental tissue are inconsistent, detection of an echogenic mass in the uterus is more conclusive. Ultrasound evaluation for retained tissue should be performed before uterine instrumentation is undertaken (9). Spontaneous expulsion of the placenta, apparent structural integrity on inspection, and the lack of a history of previous uterine surgery (suggesting an increased risk of abnormal placentation) make a diagnosis of retained products of the placenta less likely, but a curettage may identify a succenturiate lobe of the placenta or additional placental tissue. When a retained placenta is identified, a large, blunt instrument, such as a banjo curette or ring forceps, guided by ultrasonography, makes removal of the retained tissue easier and reduces the risk of perforation.

Less commonly, postpartum hemorrhage may be caused by coagulopathy. Clotting abnormalities should be suspected on the basis of patient or family history

or clinical circumstances. Hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome, abruptio placentae, prolonged intrauterine fetal demise, sepsis, and amniotic fluid embolism are associated with clotting abnormalities. Significant hemorrhage from any cause can lead to consumption of clotting factors. Observation of the clotting status of blood recently lost can provide important information. When a coagulopathy is suspected, appropriate testing should be ordered, with blood products infused as indicated. In some situations, the coagulopathy may be caused or perpetuated by the hemorrhage. In such cases, simultaneous surgery and blood product replacement may be necessary.

Baseline studies should be ordered when excessive blood loss is suspected and should be repeated periodically as clinical circumstances warrant. Clinicians should remember that the results of some studies may be misleading because equilibration may not have occurred. In addition, response to hemorrhage may be required before laboratory results are known. Baseline studies include a complete blood count with platelets, a prothrombin time, an activated partial thromboplastin time, fibrinogen, and a type and cross order. The blood bank should be notified that transfusion may be necessary.

The clot observation test provides a simple measure of fibrinogen (10). A volume of 5 mL of the patient's blood is placed into a clean, red-topped tube and observed frequently. Normally, blood will clot within 8–10 minutes and will remain intact. If the fibrinogen concentration is low, generally less than 150 mg/dL, the blood in the tube will not clot, or if it does, it will undergo partial or complete dissolution in 30–60 minutes.

► *What is the appropriate medical management approach for excessive postpartum bleeding?*

Ongoing blood loss in the setting of decreased uterine tone requires the administration of additional uterotonics as the first-line treatment for hemorrhage (Table 1). Some practitioners prefer direct injection of methylergonovine maleate and 15-methyl prostaglandin (PG) F_{2α} into the uterine corpus. Human recombinant factor VIIa is a new treatment modality shown to be effective in controlling severe, life-threatening hemorrhage by acting on the extrinsic clotting pathway. Intravenous dosages vary by case and generally range from 50 to 100 mcg/kg every 2 hours until hemostasis is achieved. Cessation of bleeding ranges from 10 minutes to 40 minutes after administration (11–14). Concern has been raised because of apparent risk of subsequent thromboembolic events following factor VIIa use (15). Compared with other agents, factor VIIa is extremely expensive. Additional clinical experience in all specialties will help

Table 1. Medical Management of Postpartum Hemorrhage

Drug*	Dose/Route	Frequency	Comment
Oxytocin (Pitocin)	IV: 10–40 units in 1 liter normal saline or lactated Ringer's solution IM: 10 units	Continuous	Avoid undiluted rapid IV infusion, which causes hypotension.
Methylergonovine (Methergine)	IM: 0.2 mg	Every 2–4 h	Avoid if patient is hypertensive.
15-methyl PGF _{2α} (Carboprost) (Hemabate)	IM: 0.25 mg	Every 15–90 min, 8 doses maximum	Avoid in asthmatic patients; relative contraindication if hepatic, renal, and cardiac disease. Diarrhea, fever, tachycardia can occur.
Dinoprostone (Prostin E ₂)	Suppository: vaginal or rectal 20 mg	Every 2 h	Avoid if patient is hypotensive. Fever is common. Stored frozen, it must be thawed to room temperature.
Misoprostol (Cytotec, PGE ₁)	800–1,000 mcg rectally		

Abbreviations: IV, intravenously; IM, intramuscularly; PG, prostaglandin.

*All agents can cause nausea and vomiting.

Modified from Dildy GA, Clark SL. Postpartum hemorrhage. *Contemp Ob/Gyn* 1993;38(8):21–9.

determine factor VIIa's role in the treatment of patients with postpartum hemorrhage.

► ***When is packing or tamponade of the uterine cavity advisable?***

When uterotonics fail to cause sustained uterine contractions and satisfactory control of hemorrhage after vaginal delivery, tamponade of the uterus can be effective in decreasing hemorrhage secondary to uterine atony (Table 2). Such approaches can be particularly useful as a temporizing measure, but if a prompt response is not seen, preparations should be made for exploratory laparotomy.

Packing with gauze requires careful layering of the material back and forth from one cornu to the other using a sponge stick, packing back and forth, and ending with extension of the gauze through the cervical os. The same effect often can be derived more easily using a Foley catheter, Sengstaken-Blakemore tube, or, more recently, the SOS Bakri tamponade balloon (16), specifically tailored for tamponade within the uterine cavity in cases of postpartum hemorrhage secondary to uterine atony.

► ***When are surgical techniques used to control uterine bleeding?***

When uterotonic agents with or without tamponade measures fail to control bleeding in a patient who has given birth vaginally, exploratory laparotomy is indicated. A midline vertical abdominal incision usually is preferred to optimize exposure. Several techniques are

available to control bleeding (Table 3). Hypogastric artery ligation is performed much less frequently than in years past. Its purpose is to diminish the pulse pressure of blood flowing to the uterus via the internal iliac (hypogastric) vessels. Practitioners are less familiar with this technique, and the procedure has been found to be considerably less successful than previously thought (17). Bilateral uterine artery ligation (O'Leary sutures) accomplishes the same goal, and this procedure is quicker and easier to perform (18, 19). To further diminish blood flow to the uterus, similar sutures can be placed across the vessels within the uteroovarian ligaments.

The B-Lynch technique is a newer procedure for stopping excessive bleeding caused by uterine atony (20). The suture provides even pressure to compress the uterine corpus and decrease bleeding. One study reported more

Table 2. Tamponade Techniques for Postpartum Hemorrhage

Technique	Comment
Uterine tamponade	
—Packing	—4-inch gauze; can soak with 5,000 units of thrombin in 5 mL of sterile saline
—Foley catheter	—Insert one or more bulbs; instill 60–80 mL of saline
—Sengstaken-Blakemore tube	
—SOS Bakri tamponade balloon	—Insert balloon; instill 300–500 mL of saline

Table 3. Surgical Management of Postpartum Hemorrhage

Technique	Comment
Uterine curettage	
Uterine artery ligation	Bilateral; also can ligate uteroovarian vessels
B-Lynch suture	
Hypogastric artery ligation	Less successful than earlier thought; difficult technique; generally reserved for practitioners experienced in the procedure
Repair of rupture	
Hysterectomy	

than 1,000 B-Lynch procedures with only seven failures (21). However, because the technique is new, many clinicians have limited experience with this procedure (22).

Hemostatic multiple square suturing is another new surgical technique for postpartum hemorrhage caused by uterine atony, placenta previa, or placenta accreta. The procedure eliminates space in the uterine cavity by suturing both anterior and posterior uterine walls. One study reported on this technique in 23 women after conservative treatment failed. All patients were examined after 2 months, and ultrasound findings confirmed normal endometrial linings and uterine cavities (23).

► ***What are the clinical considerations for suspected placenta accreta?***

Abnormal attachment of the placenta to the inner uterine wall (placenta accreta) can cause massive hemorrhage. In fact, accreta and uterine atony are the two most common reasons for postpartum hysterectomy (24, 25). Risk factors for placenta accreta include placenta previa with or without previous uterine surgery, prior myomectomy, prior cesarean delivery, Asherman's syndrome, submucous leiomyomata, and maternal age older than 35 years (26).

Prior cesarean delivery and the presence of placenta previa in a current pregnancy are particularly important risk factors for placenta accreta. In a multicenter study of more than 30,000 patients who had cesarean delivery without labor, the risk of placenta accreta was approximately 0.2%, 0.3%, 0.6%, 2.1%, 2.3%, and 7.7% for women experiencing their first through sixth cesarean deliveries, respectively. In patients with placenta previa in the current pregnancy, the risk of accreta was 3%, 11%, 40%, 61%, and 67% for those undergoing their first through their fifth or greater cesarean deliveries, respectively (27).

Women with placenta previa or placenta accreta have a higher incidence of postpartum hemorrhage and are more likely to undergo emergency hysterectomy

(28). In the multicenter study cited previously, hysterectomy was required in 0.7% for the first cesarean delivery and increased with each cesarean delivery up to 9% for patients with their sixth or greater cesarean delivery.

In the presence of previa or a history of cesarean delivery, the obstetric care provider must have a high clinical suspicion for placenta accreta and take appropriate precautions. Ultrasonography may be helpful in establishing the diagnosis in the antepartum period. Color Doppler technology may be an additional adjunctive tool for suspected accreta (29). Despite advances in imaging techniques, no diagnostic technique affords the clinician complete assurance of the presence or absence of placenta accreta.

If the diagnosis or a strong suspicion is formed before delivery, a number of measures should be taken:

- The patient should be counseled about the likelihood of hysterectomy and blood transfusion.
- Blood products and clotting factors should be available.
- Cell saver technology should be considered if available.
- The appropriate location and timing for delivery should be considered to allow access to adequate surgical personnel and equipment.
- A preoperative anesthesia assessment should be obtained.

The extent (area, depth) of the abnormal attachment will determine the response—curettage, wedge resection, medical management, or hysterectomy. Uterine conserving options may work in small focal accretas, but abdominal hysterectomy usually is the most definitive treatment.

► ***Under what circumstances is arterial embolization indicated?***

A patient with stable vital signs and persistent bleeding, especially if the rate of loss is not excessive, may be a candidate for arterial embolization. Radiographic identification of bleeding vessels allows embolization with Gelfoam, coils, or glue. Balloon occlusion is also a technique used in such circumstances. Embolization can be used for bleeding that continues after hysterectomy or can be used as an alternative to hysterectomy to preserve fertility.

► ***When is blood transfusion recommended? Is there a role for autologous transfusions or directed donor programs?***

Transfusion of blood products is necessary when the extent of blood loss is significant and ongoing, particularly if vital signs are unstable. Postpartum transfusion

rates vary between 0.4% and 1.6% (30). Clinical judgment is an important determinant, given that estimates of blood loss often are inaccurate, determination of hematocrit or hemoglobin concentrations may not accurately reflect the current hematologic status, and symptoms and signs of hemorrhage may not occur until blood loss exceeds 15% (8). The purpose of transfusion of blood products is to replace coagulation factors and red cells for oxygen-carrying capacity, not for volume replacement. To avoid dilutional coagulopathy, concurrent replacement with coagulation factors and platelets may be necessary. Table 4 lists blood components, indications for transfusion, and hematologic effects.

Autologous transfusion (donation, storage, retransfusion) has been shown to be safe in pregnancy (31, 32). However, it requires anticipation of the need for transfusion, as well as a minimal hematocrit concentration often above that of a pregnant woman. Autologous transfusion generally is reserved for situations with a high chance of transfusion in a patient with rare antibodies, where the likelihood of identifying compatible volunteer-provided blood is very low. Blood donated by directed donors has not been shown to be safer than blood from unknown, volunteer donors. Cell saver technology has been used successfully in patients undergoing cesarean delivery. In a multicenter study of 139 patients using such devices, no untoward outcomes were noted when compared with control patients (33).

► **What is the management approach for hemorrhage due to a ruptured uterus?**

Rupture can occur at the site of a previous cesarean delivery or other surgical procedure involving the uterine wall from intrauterine manipulation or trauma or from congenital malformation (small uterine horn), or it can occur spontaneously. Abnormal labor, operative delivery, and placenta accreta can lead to rupture. Surgical repair is

required, with the specific approach tailored to reconstruct the uterus, if possible. Care depends on the extent and site of rupture, the patient's current clinical condition, and her desire for future childbearing. Rupture of a previous cesarean delivery scar often can be managed by revision of the edges of the prior incision followed by primary closure. In addition to the myometrial disruption, consideration must be given to neighboring structures, such as the broad ligament, parametrial vessels, ureters, and bladder. Regardless of the patient's wishes for the avoidance of hysterectomy, this procedure may be necessary in a life-threatening situation.

► **What is the management approach for an inverted uterus?**

Uterine inversion, in which the uterine corpus descends to, and sometimes through, the uterine cervix, is associated with marked hemorrhage. On bimanual examination, the finding of a firm mass below or near the cervix, coupled with the absence of identification of the uterine corpus on abdominal examination, suggests inversion. If the inversion occurs before placental separation, detachment or removal of the placenta should not be undertaken; this will lead to additional hemorrhage. Replacement of the uterine corpus involves placing the palm of the hand against the fundus (now inverted and lowermost at or through the cervix), as if holding a tennis ball, with the fingertips exerting upward pressure circumferentially (34). To restore normal anatomy, relaxation of the uterus may be necessary. Terbutaline, magnesium sulfate, halogenated general anesthetics, and nitroglycerin have been used for uterine relaxation.

Manual replacement with or without uterine relaxants usually is successful. In the unusual circumstance in which it is not, laparotomy is required. Two procedures have been reported to return the uterine corpus to the abdominal cavity. The Huntington procedure involves

Table 4. Blood Component Therapy

Product	Volume (mL)	Contents	Effect (per unit)
Packed red cells	240	Red blood cells, white blood cells, plasma	Increase hematocrit 3 percentage points, hemoglobin by 1 g/dL
Platelets	50	Platelets, red blood cells, white blood cells, plasma	Increase platelet count 5,000–10,000/mm ³ per unit
Fresh frozen plasma	250	Fibrinogen, antithrombin III, factors V and VIII	Increase fibrinogen by 10 mg/dL
Cryoprecipitate	40	Fibrinogen, factors VIII and XIII, von Willebrand factor	Increase fibrinogen by 10 mg/dL

Modified from Martin SR, Strong TH Jr. Transfusion of blood components and derivatives in the obstetric intensive care patient. In: Foley MR, Strong TH Jr, Garite TJ, editors. Obstetric intensive care manual. 2nd ed. New York (NY): McGraw-Hill; 2004. Produced with permission of The McGraw-Hill Companies.

progressive upward traction on the inverted corpus using Babcock or Allis forceps (35). The Haultain procedure involves incising the cervical ring posteriorly, allowing for digital repositioning of the inverted corpus, with subsequent repair of the incision (36).

► **What is the management approach for secondary postpartum hemorrhage?**

Secondary hemorrhage occurs in approximately 1% of pregnancies; often the specific etiology is unknown. Postpartum hemorrhage may be the first indication for von Willebrand's disease for many patients and should be considered. The prevalence of von Willebrand's disease is reported to be 10–20% among adult women with menorrhagia (37). Hence, testing for bleeding disorders should be considered among pregnant patients with a history of menorrhagia because the risk of delayed or secondary postpartum hemorrhage is high among women with bleeding disorders (38, 39).

Uterine atony (perhaps secondary to retained products of conception) with or without infection contributes to secondary hemorrhage. The extent of bleeding usually is less than that seen with primary postpartum hemorrhage. Ultrasound evaluation can help identify intrauterine tissue or subinvolution of the placental site. Treatment may include uterotonic agents, antibiotics, and curettage. Often the volume of tissue removed by curettage is minimal, yet bleeding subsides promptly. Care must be taken in performing the procedure to avoid perforation of the uterus. Concurrent ultrasound assessment at the time of curettage can be helpful in preventing this complication. Patients should be counseled about the possibility of hysterectomy before initiating any operative procedures.

► **What is the best approach to managing excessive blood loss in the postpartum period once the patient's condition is stable?**

Regardless of the cause of postpartum hemorrhage, subsequent replacement of the red cell mass is important. Along with a prenatal vitamin and mineral capsule daily (which contains about 60 mg of elemental iron and 1 mg folate), two additional iron tablets (ferrous sulfate, 300 mg, each yielding about 60 mg of elemental iron) will maximize red cell production and restoration. Erythropoietin can hasten red cell production in postpartum anemic patients to some extent, but it is not approved by the U.S. Food and Drug Administration for postoperative anemia, and it can be costly (40). Postpartum hemorrhage in a subsequent pregnancy occurs in approximately 10% of patients (8).

Summary of Recommendations and Conclusions

The following recommendations and conclusions are based primarily on consensus and expert opinion (Level C):

- Uterotonic agents should be the first-line treatment for postpartum hemorrhage due to uterine atony.
- Management may vary greatly among patients, depending on etiology and available treatment options, and often a multidisciplinary approach is required.
- When uterotonics fail following vaginal delivery, exploratory laparotomy is the next step.
- In the presence of conditions known to be associated with placenta accreta, the obstetric care provider must have a high clinical suspicion and take appropriate precautions.

Proposed Performance Measure

If hysterectomy is performed for uterine atony, there should be documentation of other therapy attempts.

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The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1901 and June 2006. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and ACOG were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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The American College of Obstetricians and Gynecologists
409 12th Street, SW, PO Box 96920, Washington, DC 20090-6920
12345/09876

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