TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
Obstetric Hemorrhage Due to Uterine Atony
Evidence-Based Guideline

Definition: Obstetric hemorrhage is the loss of blood within 24 hours of a vaginal or cesarean birth that has the potential to produce hemodynamic instability. Uterine atony (UA) is the failure of a uterus to contract adequately. Uterine atony is the most common causative factor in 80% of obstetric hemorrhage cases. [1-4]

Etiology: Most cases of obstetric hemorrhage have no identifiable risk factors. [1-4]

Inclusion Criteria
All postpartum women who hemorrhage due to uterine atony within the first 24 hours of a vaginal or cesarean birth and have the potential to become hemodynamically unstable [3]

Exclusion Criteria
- Secondary obstetric hemorrhage occurring between 24 hours and 12 weeks
- Women hemorrhaging for reasons other than uterine atony
  - Abruption placenta
  - Inherited or acquired coagulopathy
  - Lower genital tract lacerations
  - Retained products of conception
  - Placenta accreta/increta/percreta
  - Placenta previa
  - Uterine inversion
  - Uterine rupture [1-3]

Differential Diagnosis
Inherited or acquired coagulopathy
Lower genital tract laceration
Placenta accreta/increta/percreta
Retained placenta
Uterine inversion
Uterine rupture [1-4]

Diagnostic Evaluation
History: Assess for
- Anemia
- Chorioamnionitis
- Coagulopathies
- Current fetal demise
- Hematoma
- History of postpartum hemorrhage
- Multiparity
- Obesity
- Over distended uterus (macrosomia, twins, hydramnios)
- Placenta abruption
- Prolonged or rapid labor [1-3]

Physical Examination
- Assess signs and symptoms of potential hemodynamic instability:
  - Heart rate >120
  - Weak, thready pulse
  - Oxygen saturation <95%
  - Respiratory rate >24
  - Pulse pressure 30-40
  - Systolic blood pressure <90 mmHg
  - Urine output <30 mL/h for 2 consecutive hours
  - Change in mentation
- Bimanual examination of uterus to rule out uterine inversion, remove placenta, amniotic membrane fragments or blood clots.
- Visual inspection of the lower genital tract to rule out lacerations and/or hematoma [1-4]

Laboratory Tests
- Type and cross for 4 units type specific (estimated time 20-30 minutes)
  - Consider emergency release O negative units (estimated time 5 minutes)
- ABG with metabolites
- Hemoglobin/Hematocrit
- DIC panel (PT/INR, PTT, Fibrinogen, D-dimer, platelet count) [1-4]

Critical Points of Evidence*

Evidence Supports
- Administration of 15 units of oxytocin prior to delivery of the placenta for all births as part of active management of the third stage of labor for prevention of postpartum hemorrhage. [5-19] – Strong recommendation, high quality evidence
- Controlled cord traction as a non-pharmacologic intervention within the active management of the third stage of labor to reduce the need for manual placenta extractions, shorten the duration of the third stage of labor, and lessen pain during placental separation. [20-28] – Strong recommendation, high quality evidence
- Uterine massage following placental delivery, as appropriate, as a non-pharmacologic intervention within the active management of the third stage of labor. [29-33] – Strong recommendation, high quality evidence
- Administration of oxytocin, 10 units and uterine massage as the first-line therapies for treatment of postpartum hemorrhage. [5-12,14-19,34,35] – Strong recommendation, high quality evidence
- Administration of hemabate and/or methergine intramuscularly as second-line therapy for treatment of postpartum hemorrhage, unless contraindicated. If contraindicated, administer 400 mcg of misoprostol, sublingually as second-line therapy for treatment of postpartum hemorrhage. [36-40] – Strong recommendation, moderate quality evidence
- Initiation of intrauterine balloon tamponade as early as possible to control bleeding from PPH due to uterine atony simultaneously or prior to the initiation of second line uterotonic drugs to control bleeding from postpartum hemorrhage. Early balloon deployment before the development of coagulopathy increases its success rate. Balloon tamponade is often successful and is indicated before resorting to more invasive surgical approaches requiring laparotomy. Use of balloon tamponade typically obviates the need for arterial embolization or an open surgical intervention. If bleeding persists, arrangements should be made for definitive treatment. [41-52] - Strong recommendation, moderate quality evidence

- Administration of 1 gram of tranexamic acid intravenously when postpartum hemorrhage is diagnosed and other uterotonics fail to stop bleeding; and to administer 1 gram of tranexamic acid prophylactically when postpartum hemorrhage is anticipated. (51-57) – Strong recommendation, high quality evidence
- Blood transfusions for fibrinogen levels less than 200 mg/dL for women diagnosed with postpartum hemorrhage. (58-63) – Strong recommendation, low quality evidence
- Utilization of a transfusion strategy of 2 units packed red blood cells to 1 unit of fresh frozen plaza and supplementation of platelets and cryoprecipitate as needed for treatment of postpartum hemorrhage. (64,65) – Strong recommendation, low quality evidence
- Administration of fibrinogen concentrate (RiaSTAP) for treatment of hypofibrinogenaemia due to postpartum hemorrhage and treatment target fibrinogen threshold values of 300 to 500 mg/dL. There is considerable evidence in favor of targeting/maintaining a fibrinogen level of 300 mg/dl in patients who experience or who are at-risk for obstetric hemorrhage. This can be accomplished by administration of cryoprecipitate or of RiaStap. (66-70) – Strong recommendation, low quality evidence
- Surgical intervention when uterotonics and other available conservative interventions (e.g., uterine massage, balloon tamponade) fail to stop bleeding. (46,71) – Strong recommendation, very low quality evidence
- The use of compression sutures for postpartum hemorrhage uncontrolled by uterotonics or intrauterine balloon tamponade. (46,72-75,76-81) – Strong recommendation, very low quality evidence
- Uterine vessel ligation as a surgical option prior to hysterectomy for postpartum hemorrhage uncontrolled by uterotonics or intrauterine balloon tamponade. (82-85) – Strong recommendation, very low quality evidence
- To consider uterine artery embolization, when resources are available, as a surgical option prior to hysterectomy for postpartum hemorrhage uncontrolled by uterotonics or intrauterine balloon tamponade. (86-91) – Strong recommendation, very low quality evidence
- Administration of Recombinant Activated FVIIa ONLY for postpartum hemorrhage unresponsive to all uterotonics, conservative treatments and surgical interventions or in the event of life threatening postpartum hemorrhage. (92-97) – Strong recommendation, very low quality evidence

Evidence Against

- Administration of fibrinogen concentrate (RiaSTAP) for treatment of postpartum hemorrhage for women with normofibrinogenaemia (66-70) – Strong recommendation, low quality evidence
- The use of Recombinant Activated FVIIa to control bleeding in non-life threatening postpartum hemorrhage. (92-97) – Strong recommendation, low quality evidence

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

Condition-Specific Elements of Clinical Management

General: The clinical picture of women with primary obstetric hemorrhage is highly variable therefore cumulative blood loss should be formally measured or quantified after every birth utilizing departmental specific processes for the quantification of blood loss. Historically, the definition of obstetric hemorrhage has been blood loss >500 mL for vaginal delivery and >1000 mL for a cesarean delivery but these are average values and do not take into account the woman's initial volume status or pre-existing conditions.

Treatment Recommendations:

- All women should receive either oxytocin 30 units intravenously (5-19) or oxytocin 10 units intramuscularly (1-3,5-19) during the third stage of labor.
- Management of obstetric hemorrhage should involve four components to be undertaken simultaneously: Communication, resuscitation, monitoring, and investigation. (1-2,4)
- Blood loss should be quantified for quantified blood loss (QBL) per departmental process for quantifying blood loss.

Stage 1

- Once identified as obstetric hemorrhage, communicate ongoing significant bleeding and/or signs of hemodynamic instability to team (bedside RN, primary physician, and charge nurse). (1,2,4)
- Notify charge nurse for additional RN.
- Vital signs every 5 minutes.
- Oxygen by non-rebreather mask to maintain oxygen saturation ≥95%. (2,3)
- Bimanual uterine massage to rule out retained placenta fragments and/or to remove blood clots. (1-3)
  - 4 units type specific (estimated time 20-30 minutes)
- Lactated Ringers (LR) for volume resuscitation
- Continue infusing Oxytocin.
- Give hemabate or methergine unless contraindicated, then give misoprostol (1,2) 400 mcg (3) sublingually (preferred), bucally, or rectally.
- Empty bladder. (1-3)
- Prevent hypothermia (2) by using warm blankets for vaginal birth and Bair Hugger® warming blankets for Cesarean birth.
- If uterus is firm and bleeding continues, evaluate for other etiologies (lower genital tract laceration, retained products of conception – note the amount of bleeding and presence of tissue or clots). (1-4)
- If uterus is firm and bleeding does not continue, manage as appropriate to history and clinical findings.
- Administer 1 gram of tranexamic acid intravenously when postpartum hemorrhage is diagnosed and other uterotonics fail to stop bleeding

Stage 2

- Communicate EBL >1000-1500 mL with ongoing significant bleeding and/or signs of hemodynamic instability to team.
- Vital signs every 5 minutes:
  - Heart rate >120 and/or weak thready pulse
  - Respiratory rate >24
  - Oxygen saturation <95%
- Activate Rapid Response Team.
- Start second large bore IV, draw additional laboratory tests, and begin LR volume resuscitation.
- Laboratory Tests
  - Consider emergency release O negative units (estimated time 5 minutes).

  - ABG with metabolites
  - Hemoglobin/Hematocrit
  - DIC panel (PT/INR, PTT, Fibrinogen, D-dimer, platelet count)
- Do not wait for lab results to begin transfusion.
- Continue infusing oxytocin.
- **If no history of asthma,** give Hemabate 0.25 mg intramuscularly, preferably, or intramyometrially every 15 minutes up to a maximum of eight doses AND/OR **if no history of any hypertensive disease,** give Methergine 0.2 mg intramuscularly every 2-4 hours. [36-40]
- Place Foley with urometer.
- Notify OR, and Anesthesia **(1)**, post case in EPIC (move to operating room if not already there).
- If uterus firm and bleeding continues, evaluate for other etiologies (i.e., lower genital tract lacerations, hematoma, retained placenta).
- Vaginal delivery
  - Consider uterine tamponade [1,2,4,41-52] (Bakri or Ebb).
  - Evaluate for laceration/hematoma, pack and repair as needed.
  - Exploratory laparotomy
- Cesarean delivery
  - Consider uterine tamponade [1,2,4,41-52] (Bakri or Ebb).
  - Consider B-Lynch uterine compression suture (without uterine balloon). [1-4,46,72-75,76-81]
- If bleeding continues, activate Mass Transfusion Protocol.
- Prevent hypothermia with Bair Hugger® and Belmont® rapid pressure infusor.

Stage 3

- Communicate EBL >1500 mL with ongoing significant ongoing bleeding and/or signs of hemodynamic instability to team.
- Vital signs every 5 minutes:
  - Heart rate >120
  - Oxygen saturation <95%
  - Respiratory rate >30
  - Decreasing systolic blood pressure
- Continue infusing oxytocin.
  - If no history of asthma, give Hemabate 0.25 mg intramuscularly or intramyometrially every 15 minutes up to a maximum of eight doses in 24 hours AND/OR if no history of hypertensive disease, give methergine 0.2 mg intramuscularly every 2-4 hours if not administered in stage 2.
- Consider arterial or central venous pressure line.
- If patient is hemodynamically stable, fertility is strongly desired, experienced physician and equipment available, consider interventional radiology for one or more of the following: embolization, uterine artery ligation, or hypogastric ligation. [1,3,32,48]
- Proceed to hysterectomy if fertility is not desired OR at any time patient becomes hemodynamically unstable. [1,3]
- Administer Recombinant FVIIa for bleeding uncontrolled by uterotonics, conservative interventions, surgery, hysterectomy or in the event of life-threatening hemorrhage.
- Transfer patient to obstetric intensive care unit for recovery (refer to Texas Children's Pavilion for Women Policy #402).

Measures

Process

- **Assessment**
  - Percentage of patients for whom estimated blood loss (EBL) is quantified/measured
- **Efficiency of Protocol**
  - Time from recognition of obstetric hemorrhage to:
    - 1st medication given
    - 2nd medication given
    - 3rd medication given
    - RRT activation
    - insertion of intrauterine compression device
    - OR (vaginal deliveries)
    - hysterectomy, as applies
    - B-Lynch compression suture
    - uterine artery ligation
    - hypogastric ligation
  - Frequency, timing, dosage, route, and reduction of significant bleeding with:
    - Misoprostol
    - Hemabate
    - Methergine
    - Tranexamic acid
- **Effectiveness of Protocol**
  - Percentage of women successfully treated with:
    - one pharmacologic agent
    - two pharmacologic agents
    - with three pharmacologic agents
    - intrauterine compression device
    - B-Lynch
    - B-Lynch and intrauterine compression device
    - with IR embolization
    - uterine artery ligation
    - hypogastric ligation

- Number of hysterectomies who:
  - desired fertility
  - did not desire fertility

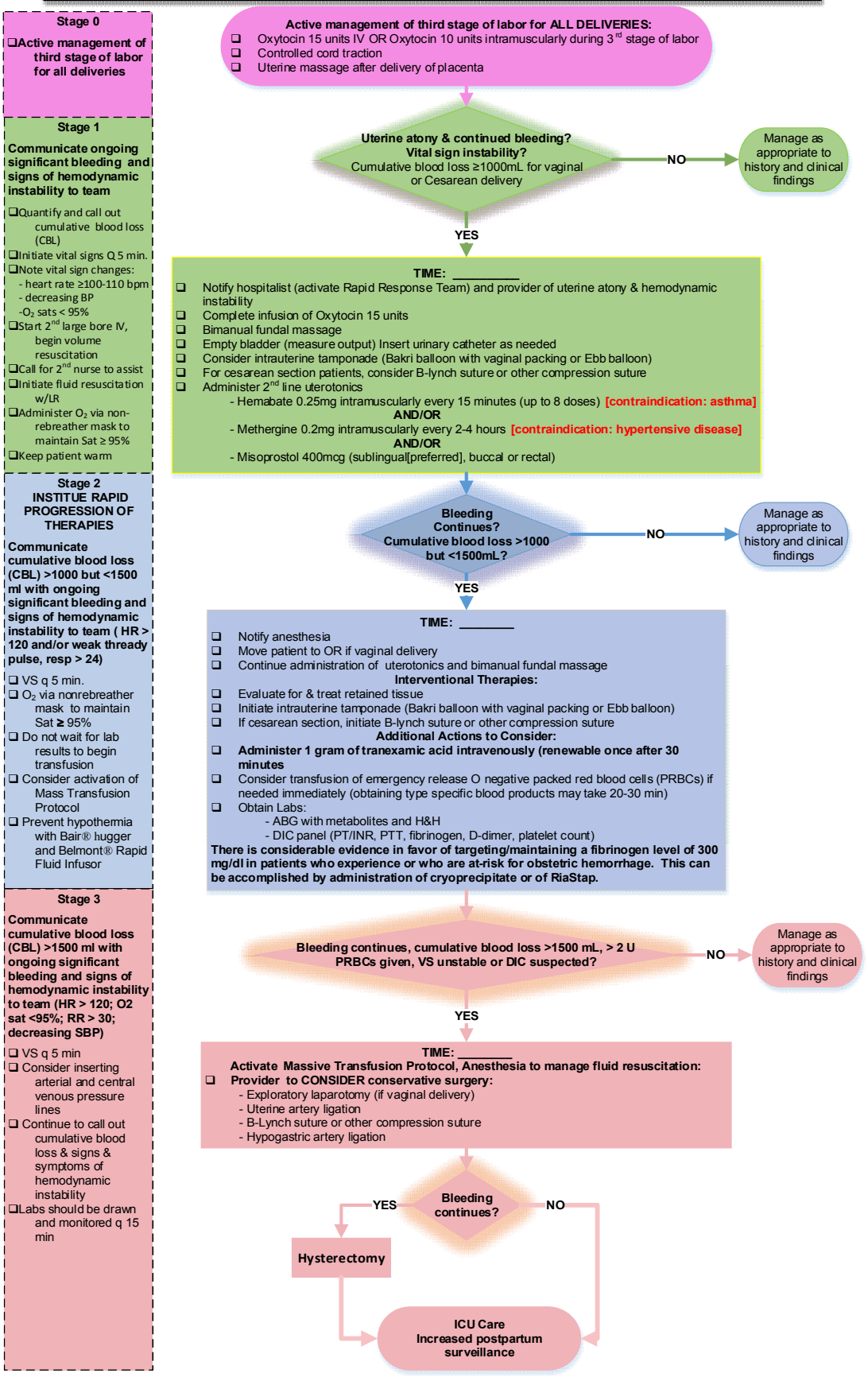
Outcome

- Order set utilization
- Length of stay (OB ICU and inpatient)

Drug	Brand Name	Cost $-$$$$	Dose/Route /Frequency	Absolute Contraindications	Relative Contraindications	Comments
Oxytocin	Pitocin	$	Intramuscularly: Total dose of 10-20 units after delivery IV continuous infusion: 15-20 milliunits/min Intramyometrial: 10 units may be directly injected into the myometrium for the treatment of uterine atony	Hypersensitivity to oxytocin or any component of the formulation		May produce antidiuretic effect (i.e., water intoxication). Severe water intoxication with convulsions, coma, and death is associated with a slow oxytocin infusion over 24 hours.
Misoprostol (prostaglandin E_1 analog)	Cytotec®	$	400 mcg buccal/ sublingual/ rectal, usually given once	None except known allergy	---------	
Carboprost tromethamine (same as 15-methyl $PGF_{2\alpha}$)	Hemabate®	$$$	0.25 mg intramuscularly/intramyometrial, q15-90 minutes. MAX total doses: 8	IV injection	Asthma, cardiac disease	
Methyler-gonovine maleate (same as methylergometrine)	Methergine®	$	0.2 mg IM q2-4 hours	Hypertension, Raynaud's, Coronary artery disease, peripheral vascular disease, arteriovascular shunts	IM is preferred route. IV route is only used for life-threatening situations due to the risk of hypertension. IV administration (slowly over 60 seconds) has greater risk of sudden hypertension and stroke and is generally avoided	
Tranexamic acid	----------	$	IV: 1,000 mg over 10 minutes given within 3 hours of vaginal birth or cesarean section; if bleeding continues after 30 minutes or stops and restarts within 24 hours after the first dose, a second dose of 1,000 mg may be given	Hypersensitivity to tranexamic acid or any component of the formulation; acquired defective color vision; active intravascular clotting; subarachnoid hemorrhage	Should be given prior to fibrinogen supplementation	Tranexamic acid should be administered early in the treatment of postpartum hemorrhage and before fibrinogen supplementation

Texas Children's Hospital Drug Information and Formulary. 11th ed. Hudson (OH): Lexi-Comp; 2017. August 16, 2017

Texas Children's Hospital Evidence-Based Outcomes Center
Clinical Algorithm for Managing Obstetric Hemorrhage due to Uterine Atony (UA)



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Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

Obstetric Hemorrhage due to Uterine Atony
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No relevant financial or intellectual conflicts to report.

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
   - Effective Health Care Program Comparative Effectiveness Review Number 151 Management of Postpartum Hemorrhage
   - Practice Bulletin # 76. Postpartum Hemorrhage
   - Green-top Guideline No. 52. Prevention and Management of Postpartum Haemorrhage
   - Active Management of the Third Stage of Labour: Prevention and Treatment of Postpartum Hemorrhage
   - WHO Guidelines for the Management of Postpartum Haemorrhage and Retained Placenta
   - Clarifying WHO position on misoprostol use in the community to reduce maternal death
   - WHO Recommendations for the Prevention and Treatment of Postpartum Hemorrhage
   - Optimizing Management in Obstetrics, Series 2. Management of Obstetric Hemorrhage
3. Literature Review of Relevant Evidence
   - Searched: PubMed, Cochrane, CINAHL, daily alerts from Texas Medical Center Pro-search alerts, AHRQ, National Guideline Clearing House, NCBI literature bookshelf.
4. Critically Analyze the Evidence
   - Systematic reviews/Meta-analyses, 22
   - Randomized controlled trials, 36
   - Nonrandomized studies, 51
5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in Obstetric Hemorrhage due to Uterine Atony evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.
This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.
"Evidence Supports" provides evidence to support an intervention
"Evidence Against" provides evidence against an intervention.
"Evidence Lacking/Inconclusive" indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence.*
The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the diagnosis/management of obstetric hemorrhage in women When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care.

Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

Version History

Date	Action	Comments
11/2017	Updated	None