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Guideline No. 431: Postpartum Hemorrhage and Hemorrhagic Shock

(En français : Directive clinique no 431 : Hémorragie post-partum et choc hémorragique)

The English document is the original version. In the event of any discrepancy between the English and French content, the English version prevails.

This clinical practice guideline was prepared by the authors and overseen by the SOGC Clinical Practice Obstetrics committee. It was reviewed by the SOGC Obstetrical Content Review committee and approved by the SOGC Guideline Management and Oversight Committee and SOGC Board of Directors.
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RECOMMENDED CHANGES IN PRACTICE

1. Quantitative blood loss measurement should replace estimated blood loss for all deliveries.
2. Maximum single dose oxytocin doses should be 3 IU IV rapid injection, or 10 IU intramuscular
3. In cases of severe obstetrical hemorrhage, the calculated maximum allowable blood loss and lab-based (or point-of-care−based) factor replacement should guide treatment whenever possible.
4. Misoprostol should only be used sublingually or orally for the prevention and treatment of postpartum hemorrhage.

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KEY MESSAGES

1. Reducing the risk of postpartum hemorrhage begins antenatally and continued vigilance is needed throughout labour to recognize abnormal postpartum bleeding early.
2. Appropriate recognition and treatment of postpartum hemorrhage can prevent serious morbidity while reducing costs to the health care system by minimizing costly interventions and length of hospital stays.
3. Simulation training followed by formal debriefing will improve outcomes in the clinical setting.

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ABSTRACT

Objective: This guideline aims to provide evidence for prevention, recognition, and treatment of postpartum hemorrhage including severe hemorrhage leading to hemorrhagic shock.

Target population: All pregnant patients.

Benefits, harms, and costs: Appropriate recognition and treatment of postpartum hemorrhage can prevent serious morbidity while reducing costs to the health care system by minimizing more costly interventions and length of hospital stays.

Evidence: Medical literature, PubMed, ClinicalTrials.gov, the Cochrane Database, and grey literature were searched for articles, published between 2012 and 2021, on postpartum hemorrhage, uterotonics, obstetrical hemorrhage, and massive hemorrhage protocols.

Validation methods: The authors rated the quality of evidence and strength of recommendations using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. See online Appendix A (Tables A1 for definitions and A2 for interpretations of strong and conditional [weak] recommendations).

Intended Audience: All members of the health care team who care for labouring or postpartum women, including, but not restricted to, nurses, midwives, family physicians, obstetricians, and anesthesiologists.

RECOMMENDATIONS

1. An individualized risk assessment for postpartum hemorrhage should be documented in a checklist upon arrival to a labour unit and updated throughout labour and delivery (*strong, high*). The risk assessment should include a calculation of the maximum allowable blood loss (*good practice point*).
2. Both antenatal and postnatal anemia should be identified and treated aggressively (*strong, high*).
3. Quantitative blood loss measurement should replace estimated blood loss in all patients whenever possible (*strong, moderate*).
4. Staging and management of postpartum hemorrhage should be based on quantitative blood loss (*strong, high*).
5. Active management of the third stage of labour should be offered to all women (*strong, high*).
6. Prophylactic intramuscular oxytocin can be used for patients at low risk for postpartum hemorrhage (*strong, high*).
7. For patients at high risk of postpartum hemorrhage, prophylactic intravenous oxytocin should be used (*conditional, moderate*).
8. When given intravenously, oxytocin can be given either as a rapid infusion (max rate 1 IU/min) for 4 minutes, followed by 7.5−15 IU/h or as a 3 IU intravenous rapid injection (*strong, moderate*)
9. If there is inadequate response to oxytocin within 4 minutes, a second-line uterotonic should be administered (*strong, high*).
10. Carbetocin can be considered as a first-line agent for postpartum hemorrhage prophylaxis at cesarean delivery (*strong, moderate*).
11. Bimanual uterine compression and bladder emptying should be performed as first-line measures while waiting for pharmacologic agents to take effect (*good practice point*).
12. Misoprostol (sublingual/oral) is an effective adjunct to prophylactic or therapeutic oxytocin in high-risk individuals (*strong, high*)
13. Intramuscular ergotamine and intramuscular or intramyometrial carboprost, can both be used to treat active postpartum hemorrhage (*strong, high*).
14. Rectal misoprostol is inferior to other routes (both in onset and in bioavailability) and should not be used (*strong, moderate*).
15. Tranexamic acid can be used in all patients as an adjunct to uterotonics in the setting of postpartum hemorrhage, and can be used as a prophylactic agent in patients at high risk for postpartum hemorrhage (*strong, high*).
16. Uterine tamponade is an effective tool and should be considered for ongoing mild to moderate bleeding (*conditional, moderate*).
17. If the placenta has not been expelled spontaneously in the 30 minutes following delivery, measures should be taken to expedite delivery of the placenta (*strong, high*).
18. When there is ongoing bleeding, examine the patient for the presence of clots, retained placental tissue, or genital tract lacerations (*good practice point*).
19. In the case of uterine inversion, if immediate reversion is not possible, transfer the patient to an operating room for uterine relaxation and patient stabilization, as required (*good practice point*)
20. If pharmacologic interventions have not controlled bleeding, surgical intervention should be undertaken promptly (*strong, high*)
21. Compression sutures, ligation of uterine or internal iliac arteries, and uterine artery embolization are all effective interventions that can be considered; however, hysterectomy should not be delayed in an unstable patient (*strong, high*).
22. Severe obstetrical hemorrhage should be managed by a multidisciplinary team consisting of obstetrics, anaesthesia, nursing, and transfusion medicine (*strong, high*).
23. An obstetrical massive hemorrhage protocol, including defined roles and responsibilities of each team member, should be used (*strong, moderate*).
24. Initial resuscitative and monitoring measures should include intravenous access × 2, electrocardiography, oxygen saturation, blood pressure, placement of an indwelling urethral catheter, euthermia, and volume replacement with balanced crystalloid (*good practice point*).

25. Four units red blood cells should be given prior to other blood products in an actively bleeding patient who is approaching the maximum allowable blood loss, unless the patient has a coagulation defect (*strong, moderate*)

26. Fibrinogen levels should be measured in every moderate to severe case of postpartum hemorrhage, and if <2 g/L, should be replaced accordingly (*strong, high*).

27. A massive hemorrhage protocol with ratios of red blood cells to fresh frozen plasma to platelets of 1:1:1: or 2:1:1 can be used in the absence of timely lab results (*strong, moderate*).

28. Simulation training with all members of the multidisciplinary team should occur on a regular basis, ideally by a trained facilitator (*strong, high*).

INTRODUCTION

Postpartum hemorrhage (PPH) continues to be a significant contributor to maternal morbidity and mortality, even in developed countries.[1] Between 2003 and 2010, the incidence of PPH in Canada was 5.6 per 100 deliveries. International data from high resource countries suggest the rate is closer to 10% when blood loss is actually measured,[2] and this rate continues to rise, with uterine atony being the primary cause.[3,4] The traditional definition of blood loss as ≥500 mL with vaginal delivery or ≥1000 mL with cesarean delivery (CD) is no longer sufficient, as visual estimates have been found to be inaccurate, even for experienced providers.[5,6] In addition, many women of reproductive age maintain normal vital signs despite blood loss beyond these amounts. Since these factors can lead to delays in treatment causing adverse maternal outcomes,[7,8] accurate and cumulative measurement of blood loss has emerged as the new standard of care.[9]

Prevention is key to reducing maternal morbidity from PPH, as 60% of these patients have at least one identifiable antepartum or intrapartum risk factor.[10] Assessment for these risk factors, as well as early intervention, are integral to mitigating potential adverse outcomes.

This guideline provides a new approach to the early identification and management of PPH. Recommendations are based on emerging data that highlight the successes of obstetrical hemorrhage toolkits and care bundles in reducing maternal morbidity and mortality.

The California Maternal Quality Care Collaborative implemented a quality improvement initiative that led to a reduction in PPH of 20.8%, compared with 1.2% in non-participating hospitals.[11] This guideline presents an adapted model to prevent and manage PPH and comprises the following categories:

1. RISK ASSESSMENT

2. RISK REDUCTION

3. RECOGNIZE AND RE-EVALUATE

4. REACT

ABBREVIATIONS

CD	cesarean delivery
MABL	maximum allowable blood loss
MHP	massive hemorrhage protocol
PPH	postpartum hemorrhage
TXA	tranexamic acid

5. RESUSCITATE

6. REVIEW

RISK ASSESSMENT

Causes and Risk Factors

The four Ts (tone, tissue, trauma, thrombin) are well known. Evaluation of risk factors in each of these categories is important to determine a potential cause of PPH (Table 1). *Individualized risk should be documented in a checklist upon arrival to a labour unit and updated throughout labour and delivery* (Appendix B). Patients at high risk for PPH deliver in a facility with easy access to a massive hemorrhage protocol (MHP) that takes into consideration local blood product supply, transport, and access to specialist advice.

Anemia

Women with anemia (Hb <110 g/L) have less reserve to cope with PPH. Anemia may also reduce oxygen delivery to myometrial muscles resulting in uterine atony.[12] In addition, iron is a necessary cofactor for adenosine triphosphate (ATP) production in muscle cells, and iron deficiency itself may contribute to uterine atony.[13]

Iron deficiency anemia is a significant health problem for women worldwide.[14] The prevalence of iron deficiency anemia in pregnancy is estimated at 41%, with higher rates in low socioeconomic populations.[14] A study, conducted in Toronto, Canada, of pregnant women screened for iron deficiency anemia found that 91% of participants were iron deficient (ferritin <50 μg/L), with most having severe iron deficiency with a ferritin < 20 μg/L despite only 25% of participants having a hemoglobin level <110 g/L.[15] These findings highlight the fact that by the time a low hemoglobin is detected, the iron deficiency is profound. Both hemoglobin and ferritin should be measured antenatally.

Anemia and iron deficiency should be assessed and treated at or before 28 weeks gestation. Ferrous salts, taken daily or every other day, on an empty stomach is the ideal method of iron supplementation.[16] There is insufficient evidence to routinely co-administer ascorbic acid (vitamin C).[17] Intravenous iron should be given if there is no response (increase in Hb of 10 g/L) within 2 weeks.[18]

Postpartum anemia contributes to fatigue, postpartum depression, poor bonding, and poor lactation.[19,20] Oral iron supplementation should continue for at least 3 months postpartum and intravenous (IV) iron considered with hemoglobin <80 g/L, regardless of symptoms.[16]

Table 1. Postpartum hemorrhage risk factors

	Etiology	Risk Factors
Tone (uterine atony)	Uterine overdistension	• Polyhydramnios • Multiple gestation • Macrosomia
	Uterine exhaustion	• Precipitous or prolonged labour • Prolonged oxytocin use • High parity • General anaesthesia • Anemia
	Infection	• Prolonged rupture of membranes • Chorioamnionitis
	Dysfunctional uterine activity	• Fibroids • Placenta previa
Tissue	Retained products of conception	Incomplete placental delivery (succenturiate lobe, morbidly adherent placenta)
Trauma	Laceration of cervix, vagina, perineum	• Precipitous or operative delivery • Episiotomy extension • Fetal malposition
	Extension/lacerations at cesarean	• Deep engagement • Prolonged second stage • Fetal malposition
	Uterine rupture	Previous uterine surgery
	Uterine inversion	• Nulliparity with fundal placenta • Excessive cord traction
Thrombin	Pre-existing states	• Hereditary coagulopathies (von Willebrand disease, hemophilia) • Idiopathic thrombotic purpura
	Acquired in pregnancy	• Preeclampsia • Disseminated intravascular coagulopathy • Fetal demise • Severe infection • Abruption • Amniotic fluid embolism
	Iatrogenic	• Therapeutic anticoagulation

RISK REDUCTION

The California Collaborative found that underestimating blood loss and relying on vital signs led to health care providers underestimating the severity of PPH and, more importantly, led to delays in treatment.[11] *Denial is delay* should be the new theme for PPH management strategies.[11] The benefit of one or more PPH bundles (containing key medications, instruments, tamponade devices, sponges, sutures, etc.) can decrease the time to treatment by having all potentially needed materials readily available.

Accurate Measurement of Blood Loss

Since visual estimates grossly underestimate the true volume of blood loss, it is recommended that labour units begin to *accurately monitor and record ongoing bleeding.* Dry weights of sponges, towels, sheets, and other commonly soaked surfaces should be recorded on a standard form that can be accessed at any time to properly evaluate blood loss in any patient. Measuring amniotic fluid in the drape (calibrated cones are available) and wiping the fluid off the floor before active bleeding begins will distinguish it from any postpartum bleeding. Whenever possible, suction the amniotic fluid at CD prior to delivering the infant and document its volume. Everything suctioned after this point should be considered blood loss. Sponges, towels, and drapes should be collected and weighed. A record of cumulative blood loss for the first 24 hours should be kept. Estimated blood loss should be replaced by quantitative (measured) blood loss (Appendices C, D, E, F).

Classification and Management Protocols for Stages of Postpartum Hemorrhage

A staging system based on quantitative blood loss, regardless of vital signs, with detailed management

Table 2. Classification and management of PPH by stage

	Blood loss, mL	BP, mm Hg[a]	HR, bpm[a]	Signs/symptoms	Initial management[b]
Stage 0	• <500 vaginal • <1000 CD	Normal	<100	Asymptomatic	Active or physiologic management of the third stage
Stage 1 (mild)	• 500-1000 vaginal • 1000 CD	Normal	<110	Often asymptomatic, or may have signs of severe PPH	Therapeutic first-line uterotonic
Stage 2 (moderate)	1000-1500	Postural hypotension (SBP 80-100)	>110	May be asymptomatic, or may have signs of severe PPH	• Second-line uterotonic • Look for other causes
Stage 3 (severe)	>1500	SBP <80	>120	• Diaphoresis • Delayed capillary refill time • Tachypnea • Pallor • Oliguria/anuria • Decreased level of consciousness • Agitation • Cool extremities	Full resuscitation protocol

[a]BP and HR may be variable.

[b]Expanded in Appendix G.

BP: blood pressure; CD: cesarean delivery; HR: heart rate; PPH: postpartum hemorrhage; SBP: systolic blood pressure.

protocols for each stage should be implemented.[21] (Classification in Table 2, for a more detailed table including expanded management protocols see Appendix G)

Active Management of the Third Stage of Labour

The SOGC first commented on the active management of the third stage of labour in 2000.[22] Three elements were originally included: a uterotonic after delivery of the anterior shoulder, early cord clamping, and cord traction to deliver the placenta. Since that time, delayed cord clamping has become the standard of care as it improves neonatal outcomes without increasing the incidence of PPH.[23] Furthermore, in multiple trials and reviews, controlled cord traction has been shown to only decrease the length of the third stage by 4-6 minutes and blood loss by <30 mL.[24–28] Since there is limited evidence to suggest that expediting delivery of the placenta before 30 minutes reduces the risk of PPH in an uncomplicated delivery,[22] the definition of active management of the third stage of labour should be confined to the use of a uterotonic. Providers choosing to employ controlled cord traction should only do so after signs of placental separation, and traction should be performed with uterine contraction as these measures reduce the risk of uterine inversion, cord avulsion, and partial detachment of the placenta.

Although prophylaxis with oxytocin for all patients has been common practice, a 2019 Cochrane review found no clear benefit to routine uterotonics in terms of PPH or hemoglobin in women at low risk of PPH, based on low quality evidence.[29] They concluded that women at low risk for PPH should be given the necessary information regarding the benefits and risks of active management of the third stage of labour in order to make informed choices about their care. Skin to skin contact may independently reduce the length of the third stage.[30]

Oxytocin Free Interval Prior to Cesarean Delivery

The longer oxytocin is used for the induction or augmentation of labour, the less responsive the uterus becomes to it. Tran et al. showed a statistically significant association between the length of the oxytocin free interval prior to CD and the total estimated blood loss with the greatest benefit after 1 hour.[31] While the reduction in blood loss in patients with a low BMI was not clinically significant (7 mL/10-min recovery interval), the greatest benefit was seen in women with a BMI >40 kg/m^2, where blood loss was reduced by 45 mL per 10-minute recovery interval up to a maximum of 450 mL at 99 minutes. In these women, higher amounts and longer durations of oxytocin use were associated with an increased need for a second-line uterotonic agent. When maternal and fetal conditions are stable, providing an oxytocin wash-out interval may be beneficial, particularly when the patient's BMI is >40 kg/m^2.

Prophylactic Uterotonics (Table 3)
Oxytocin

Numerous trials over more than 2 decades continue to show that oxytocin is the drug of choice for both the prevention and treatment of PPH.[32] Compared with placebo, ergometrine, carboprost, or misoprostol, oxytocin is

Table 3. Prophylactic and first-line therapeutic uterotonics

	Oxytocin (Syntocinon, Pitocin)		Carbetocin (Duratocin)
Use	Prophylaxis	Prophylaxis AND first-line therapeutic	Prophylaxis
Mechanism of action	Uterotonic, direct stimulation of oxytocin receptors[a]	Uterotonic, direct stimulation of oxytocin receptors[a]	Stimulation of oxytocin receptors
Dose and route	• 3 IU IV rapid injection • 10 IU IM	20−40 IU/L infusion − rapid × 4+ min, then 7−15 IU/h once tone achieved	• 100 μg slow IV injection (≥30 s) • 100 μg IM
Onset of clinical action	• 1−2 min (IV) • 3−7 min (IM)	4 min with rapid infusion	• 1−2 min IV • 3−4 min IM
Half-life	• 4−10 min (IV) • 15−30 min (IM)	Ongoing	40 min
Duration of action	• 15−20 min (IV) • 1−2 h (IM)	Ongoing	1 h

Adverse effects	• IV:
	  o <1 IU − none
	  o 1−3 IU − minimal
	  o >3 IU − dose-related increase ST depression, increase in HR, drop in BP
	• IM: minimal
		• Water retention
		• Note: rate above 15 IU/h ineffective after 3 IU in circulation
			100 μg dose side effects equivalent to 5 IU slow IV rapid injection oxytocin

Note: misoprostol and TXA may be given concurrently with these first-line uterotonics for patients at high risk for PPH.

[a]Decreased effect with prolonged use. Increased effect after oxytocin free interval.

either more effective, has fewer adverse effects, or both.[33−35] While the uterus is increasingly responsive to oxytocin as pregnancy progresses, there are fewer receptors in the lower uterine segment than in the fundus, and oxytocin has no direct effects on the cervix.[36] Oxytocin is most commonly given by IV or intramuscular injection, though some research has been done on the inhaled and intramyometrial routes.[37,38] For low-risk patients, prophylaxis via any route is sufficient; for high-risk patients, the IV route is preferred.[39]

Much research has been done on the effects of IV oxytocin at the time of CD. In an elective CD (no labour), as little as 1 IU of oxytocin can achieve uterine tonus. While similar studies have not been done in the context of a vaginal birth, it is reasonable to assume that the uterus will be at least as responsive after vaginal delivery than after an intrapartum CD, where studies show an IV bolus of 3 IU is sufficient to cause maximal uterine tonus by 4 minutes.[40] Interestingly, a rapid IV infusion will provide the same benefit at 4 minutes, when approximately 3−4 IU of oxytocin has entered the circulation.[41,42]

In order to avoid overdosing oxytocin, the infusion should be put through a pump, hung as a separate mini-infusion with only 4 IU in 100 mL. At this point, an infusion of 7.5−15 IU/h is sufficient to maintain uterine tone; a higher infusion rate or additional IV boluses will not provide any additional benefit. For high-risk patients, or ongoing bleeding, a second-line agent should be added.

Oxytocin has known hemodynamic and cardiac side effects (mainly ST depression from vasoconstriction of coronary arteries) that are seldom recognized after vaginal birth, primarily because patients are not monitored to detect them and because the clinical signs are attributed to other causes. Fortunately, these side effects are short lived; however, they have contributed to maternal death in developed countries.[43,44] When oxytocin is given quickly, hypotension and ST changes begin to appear after as little as 1 IU is administered but do not become noticeable until 3 IU is administered; these signs are significant at ≥5 IU.[40] At 10 IU, 50% of women will experience ST depression, even non-pregnant, non-anesthetized control patients.[45] These effects disappear when the 5 IU bolus is given over 5 minutes. Rapid IV bolus should therefore be restricted to 3 IU or less, and an IV infusion is preferred.

Carbetocin
Carbetocin is a synthetic, long-acting, heat stable, analogue of oxytocin with equivalent affinity for the oxytocin receptor. A single prophylactic 100 μg dose given IV over 30 seconds to 1 min provides similar or better clinical effects

Table 4. Pharmacokinetics of misoprostol

	AUC rank[a]	Onset of action,[b] min	Tmax,[c] min	Cmax,[d] pg/mL (averaged)	Duration of action,[e] h
Sublingual	1	11	30	500	3
Vaginal	2	20	75	300	4
Oral	3	8	30	300	2
Buccal	4	20	75	200	4
Rectal	5	100	75	100	4

[a]AUC: area under the (concentration vs time) curve; reflects bioavailability from highest (1) to lowest (5)

[b]How rapidly clinical effect is seen.

[c]Tmax: how rapidly the drug is completely absorbed.

[d]How completely the drug is absorbed.

[e]How long clinical effect is seen.

and similar side effects as a 5 IU IV bolus of oxytocin given at the same rate,[46,47] and some studies have shown smaller doses to be equally effective.[48] In addition, its long half-life of 40 minutes reduces the need for additional uterotonics when compared with oxytocin. The product monograph states that severe preeclampsia/eclampsia is a contraindication to its use; however, clinical trials in women delivering vaginally or by cesarean found carbetocin to be both safe and effective in this setting.[49,50] While carbetocin has not been studied as a therapeutic agent for active PPH, it should be considered a first-line agent for prophylaxis at CD. Emerging evidence suggests the use of carbetocin may also be considered as a first-line prophylactic uterotonic at vaginal delivery.[51]

RECOGNIZE AND RE-EVALUATE

It is crucial for care providers to rapidly recognize when initial measures have not adequately controlled bleeding. Failure to discern both the extent and source of bleeding will needlessly delay appropriate intervention. Recording quantitative blood loss and vital signs for every postpartum patient will help health care providers recognize when blood loss has moved between stages and can prompt intervention (Appendix G)

RE-EVALUATE TONE

Bimanual Uterine Compression and Bladder Emptying

The basic manoeuvre of manually compressing the uterus simultaneously through the abdomen and the vagina can be life-saving and should be actively used until the pharmacologic agents take effect, or surgical intervention is initiated. The lower uterine segment must be cleared of clots to allow the uterus to contract. Catheterization should be an initial step in management of PPH as a full bladder can impair the uterus' ability to contract.

Special Agents

Misoprostol

PG_{E1} is available in 100 and 200 μg tablets and can be given sublingually, orally, buccally, vaginally, and rectally. However, an understanding of the pharmacokinetics of misoprostol, borne out in clinical trials, will quickly eliminate most of these routes for treatment of PPH[52] (Table 4).

The 2018 Cochrane review of all uterotonic agents found misoprostol alone was superior to placebo but inferior to oxytocin for preventing PPH; however, adding misoprostol to oxytocin prevented the need for additional uterotonics.[47,53] When used as an adjunctive treatment, misoprostol should be given sublingually as this route offers the highest bioavailability with a rapid onset and a moderate duration of action. Doses above 400 μg are not needed, and, in fact, 200 μg may be sufficient.[54] Misoprostol should not be given rectally as this route offers the lowest bioavailability and is associated with a maximum serum concentration that may not reach clinically significant levels.[52,55] While misoprostol is a valuable adjunct to both prophylactic and therapeutic uterotonics, the injectable agents (oxytocin, ergometrine, carboprost, and TXA) have a more rapid onset and may be more useful as an independent agent in active PPH. The main side effects of misoprostol, which are dose dependent, are shivering and fever, nausea, vomiting, and diarrhea.

Tranexamic Acid

TXA is an antifibrinolytic agent that inhibits the activation of plasminogen to plasmin. Given intravenously, it has a half-life of 2 hours.[56] Side effects include nausea, vomiting, diarrhea, seizures, deep vein thrombosis, and pulmonary embolism, though seizures and thrombosis have not been demonstrated in clinical trials of PPH.[57] Two separate randomized trials showed prophylactic IV TXA (after cord clamping in 1 trial, and preoperatively in the other)

Table 5. Special agents

	Misoprostol (Cytotec)	Tranexamic acid (TXA)
Indication	• Adjunct for prophylaxis with first-line agents in high-risk patients • Adjunct for treatment with second-line uterotonics in all patients with active PPH	• Adjunct for prophylaxis with first-line agents in very high-risk patients • Adjunct for treatment with second-line uterotonics in all patients with active PPH
Mechanism of action	Uterotonic; binds prostaglandin receptors	Antifibrinolytic; inhibits activation of plasminogen to plasmin
Dose/route/rate	• 200–400 μg sublingual • 200–400 μg oral	1 g IV over 30–60 s
Onset of action	• 11 min (sublingual) • 8 min (oral) 　o both peak at 30 min	—
Half-life	• 2 h (sublingual) • 1.5 h (oral)	2 h
Duration of action	• 3 h (sublingual) • 2 h (oral)	—
Repeat dosing	—	Every 30 min; max 2 doses
Adverse effects	• Fever (especially with doses ≥600 μg) • Shivering, nausea/vomiting, diarrhea	Nausea/vomitingdiarrhea, Headache
Caution	—	VTE has not been seen in obstetrical clinical trials

IV: intravenous; PPH: postpartum hemorrhage; VTE: venous thromboembolism.

reduced the blood loss at CD,[58,59] and 2 separate large meta-analyses, as well as one randomized controlled trial showed that 1g of IV TXA given in the setting of ongoing PPH after vaginal delivery decreases blood loss, rate of hysterectomy, and mortality.[60–62] In particular, when given over 30–60 seconds, there was no difference in systolic or diastolic blood pressures compared with placebo.[61] TXA should be given whenever a second-line uterotonic is administered. Every 15-minute delay results in a 10% reduction of TXA efficacy and immediate treatment improves survival by over 70% ($P < 0.0001$).[63] Prophylactic use (in addition to a prophylactic uterotonic agent) in individuals at high risk of PPH (cesarean or vaginal delivery) is a reasonable option. For a summary of special agents, see Table 5.

Uterotonics for Treatment of Postpartum Hemorrhage

Additional agents should be used whenever the initial agent has not produced sufficient uterine tone by 4 minutes, or concurrently with a prophylactic agent in patients with increased risk for PPH based on the ongoing checklist (Table 6).

Ergometrine

Ergometrine, or ergonovine is an ergot alkaloid which directly stimulates uterine and vascular smooth muscle to contract. It can be given intramuscularly or, in life-saving circumstances, as a slow IV injection.[64] It is a potent uterotonic, but in the setting of anemia and hypovolemia, ergometrine can rarely precipitate coronary artery vasospasm and myocardial ischemia, even in patients without pre-existing cardiovascular risk factors.[65] Ergometrine should not be used in patients with essential or gestational hypertension,[66] or in patients on HIV protease inhibitors.[47,67,68] Though undisputedly extremely effective, potential adverse effects limit ergometrine to a second-line agent.

Carboprost

Carboprost is a prostaglandin $F_{2\alpha}$ that causes contractions in myometrial and intestinal smooth muscle cells.[69] It can be given by intramuscular or intramyometrial injection but cannot be given intravenously. Its efficacy is equivalent to oxytocin after either cesarean or vaginal delivery but common adverse effects, including nausea, vomiting, diarrhea, and fever limit its use to a second-line agent.[34,70] Loperamide should be given concurrently with carboprost to counteract its diarrheal effects. As a member of the F class of prostaglandins, carboprost can cause bronchospasm and should not be used in patients with asthma.[71]

Mechanical Options

Tamponade

Intrauterine compression may control mild to moderate blood loss. The Bakri balloon was designed for this purpose and its use prevents the need for further non-pharmacologic intervention in 75%–95% of cases.[72,73] It should be filled with 300–500 mL of sterile solution, left in situ for 8–48 hours and then gradually deflated. Antibiotics should be considered if they have not already been

Table 6. Second-line uterotonics for treatment of postpartum hemorrhage

	Ergometrine/ergonovine	Carboprost (Hemabate, PGF$_{2\alpha}$)
Mechanism of action	Uterotonic; non-specific activation of adrenergic and dopaminergic receptors in uterine and vascular smooth muscle	Uterotonic; binds prostaglandin receptors
Dose and route	• 250 μg IM (preferred) • 250 μg IV over 1 min (only in life-saving circumstances)	250 μg IM or IMM
Onset of action	• 2−5 min (IM) • 1−2 min (IV)	5 min
Half-life	• T1/2α = 10 min[a] • T1/2β = 2 h[b]	30 min
Duration of action	120 min	60 min
Repeat dosing	Every 2 h, max 5 doses	Every 15 min, max 5 doses
Adverse effects	Nausea/vomiting, hypertension, vasoconstriction causing ST depression and chest pain	Diarrhea
Caution	• Hypertension • HIV medications (NNRTIs or protease inhibitors) • Macrolide antibiotics	Can cause bronchospasm in patients with asthma

[a]T1/2α = time for the drug to redistribute to other tissues;

[b]T1/2β = time for the drug to re-enter and then be cleared from the circulation

IM: intramuscular; IMM: intramyometrial; IV: intravenous; NNRTI: non-nucleoside reverse transcriptase inhibitors; PGF$_{2\alpha}$: prostaglandin F$_{2\alpha}$.

given, and a pack can be placed in the vagina if the balloon is hourglassing through the cervix. If a Bakri balloon is not available, any balloon device can be used. Alternatively, systematically packing the uterus from cornua to cornua with laparotomy packs tied end to end may be considered; however, this procedure requires more experience, more anaesthesia, and a second procedure to remove. It may also mask blood loss and increase the risk of infection. Packing should be used as a last resort until more definitive treatment can be initiated. A running record of accumulated quantitative blood loss and interventions should be easily accessible and visible to all members of the care team (Appendix E, F, H, I).

RE-EVALUATE SOURCE

Retained Placenta

Retained placenta occurs in 1%−3% of vaginal deliveries and is the second leading cause of PPH.[74] Risk factors are uterine atony, an adherent placenta, succenturiate lobe, and a trapped placenta behind a closed cervix. Internationally, recommendations for manual removal of the placenta vary between 30 and 60 minutes, based on studies from the 1990s showing no increase in PPH until at least 30 minutes had passed.[74] The majority of placentas (95%) will deliver spontaneously by 18 minutes. A 2012 randomized controlled trial confirmed a previous observational study that found patients who had manual removal of the placenta earlier than 30 minutes had less blood loss.[75] Similarly, a large retrospective study (n >28 000) showed

waiting more than 30 minutes for placental separation increased the risk of blood transfusion more than three-fold.[76] More studies need to be done to be able to recommend the ideal time for manual removal of the placenta in a stable patient.

Intraumbilical oxytocin (20 IU in 30 mL saline), misoprostol (800 μg in 30 mL saline), or ergometrine (0.2 mg in 30 mL saline), as well as IV carbetocin (100 μg), or sublingual misoprostol (400 μg) all have similar efficacy for expelling the placenta within 30 minutes of administration (62%−72%).[77,78] In the presence of heavy bleeding, transfer to an operating room for manual removal of the placenta should be expedited and curettage with a large curette may be needed. There is insufficient evidence to recommend routine treatment with antibiotics.[74]

Lacerations

Lacerations of the vagina or cervix, or disruption of a uterine scar should be ruled out by a formal examination under anaesthesia, and surgical repair of the injury should be completed. Vaginal packing may be required when generalized bleeding from a deep venous plexus precludes proper repair. Re-opening the abdominal incision after CD to look for surgical bleeding should not be delayed.

Uterine Inversion

This rare but potentially life-threatening condition is thought to be caused by excessive cord traction on a

fundal placenta or fundal pressure without a uterine contraction; however, there are no risk factors in most cases.[79] Clinical diagnosis is based on the presence of brisk vaginal bleeding, a mass in the vagina, and vasovagal syncope. If still attached, the placenta should not be removed prior to reversion. Prompt replacement may be attempted; however, hypovolemic shock occurs rapidly, and the patient should be urgently transferred to an operating room if reversion cannot be accomplished immediately. Uterine relaxation with IV nitroglycerine in addition to vasopressors may be required to revert the uterus and reverse hemodynamic instability. If reversion is unsuccessful, laparotomy may be required. Antibiotics and oxytocin should be given after reversion.

REACT

If previous measures fail to control bleeding, urgent abdominal surgical exploration is required. Bimanual compression should be continued while preparations in the operating room are being made and surgery is about to begin. Uterine compression sutures (B-Lynch, Cho), uterine artery ligation, internal iliac artery ligation, embolization, and hysterectomy are possible interventions. This guideline is not an instruction manual for those not skilled at performing these procedures. Additional expertise should be sought urgently if the necessary procedure is beyond the skill set of the care provider.

Compression Sutures

The B-Lynch technique uses an absorbable suture on a large needle to create compression "suspenders," which successfully treat intractable uterine atony 75% of the time.[80] Adding a second suture can further decrease the need for hysterectomy.[81] Cho square compression sutures, incorporating both anterior and posterior walls of the uterus, have similar efficacy.[82]

Uterine Artery Ligation

The purpose of uterine artery ligation is not to obliterate blood flow to the uterus, but to temporarily slow it. Key aspects include bladder retraction (to prevent traction on both bladder and ureters caused by the suture) and use of an absorbable suture on a large needle to secure the uterine artery at the level of the isthmus (or 2–3 cm below the uterine incision at CD). Ensuring 2 cm of myometrium is incorporated into the suture will bundle the uterine artery and vein and prevent complete occlusion of the uterine artery. A second suture can be used superiorly to further compress ascending branches of the uterine artery. Alternatively, if bleeding is predominantly coming from the lower uterine segment or cervical branches, a second stitch placed 3 cm inferior to the first can be used to compress descending branches of the uterine artery. This location increases the risk of ureteric entrapment, and further bladder dissection should be performed. Radiologic or cystoscopic evaluation of ureteral patency is recommended.

Bilateral Internal Iliac Artery Ligation

Bilateral internal iliac artery ligation is extremely effective at controlling obstetrical hemorrhage (including following hysterectomy), with numerous case series reporting success rates of 75% or higher.[83-85] Unfortunately, bilateral internal iliac artery ligation requires more skill and experience. Retroperitoneal dissection to identify the bifurcation of the common iliac artery is followed by ligation of the internal branch at least 2 cm distal to the bifurcation with an absorbable suture. Bilateral internal iliac artery ligation reduces pelvic blood flow by 49% but immediate increased retrograde flow in collateral vessels prevents pelvic ischemia. Resumption of menses and demonstration of flow in distal uterine arteries in 90% of women within 6 months suggests that fertility is preserved.[86]

Uterine or Internal Iliac Artery Embolization

Embolization of either uterine or internal iliac arteries is highly effective and fertility sparing. When compared with hysterectomy, blood loss and operative time are significantly less.[87,88] The main drawbacks of embolization are the availability of an interventional radiology department and a patient with a stable blood pressure. If these conditions are met and bleeding is ongoing, uterine artery embolization can be considered before proceeding to hysterectomy. Uterine artery embolization can also be considered post-hysterectomy for ongoing bleeding, where a contributing vessel can be identified. Uterine artery embolization is particularly useful for cases where bleeding is expected to be high and/or surgical treatment is expected to be difficult (e.g., placenta previa, accreta, severe obesity, or suspected intra-abdominal adhesions). In these cases, an interventional radiology consult should be obtained pre-delivery and a plan established, including the possibility of pre-delivery placement of arterial balloons.

Hysterectomy

In cases of massive obstetric hemorrhage, hysterectomy can be life-saving, and the biggest risk is waiting too long to perform it. Successive clamping of pedicles without tying them until the uterine arteries have been secured will allow faster control of bleeding. Conflicting opinions on subtotal versus total hysterectomy preclude a

recommendation, and clinical judgment on the source of bleeding and type of hysterectomy is required.[89]

Abdominal Packing

When surgical hemostasis has been achieved, but ongoing bleeding persists, disseminated intravascular coagulation, acidosis, and hypothermia are often contributing factors. Packing the pelvis tightly with warm, moist packs and leaving them in place for 24–48 hours can provide the necessary time to reverse these factors.

RESUSCITATE

Resuscitation requires ongoing communication and teamwork involving the obstetrical care provider and anaesthesia and nursing teams. An algorithm, including clinical signs and symptoms of PPH and hypovolemic shock and their treatments, should clearly outline the responsibilities of various team members in order to optimize maternal outcome[11] (Appendix G).

PPH is an active, ongoing process; lab results represent a point in time that has invariably passed. While formal lab tests can help tailor therapy, waiting for results to initiate treatment can worsen patient outcomes.[90] Most parturients are able to maintain hemodynamic stability despite considerable blood loss. The recommended hemoglobin level at which to transfuse has decreased over time. In 2003, the threshold was 80 g/L, and as of 2021 the consensus is 70 g/L; however, with many patients able to tolerate hemoglobin as low as 50 g/L, this threshold may change in the future. Patients with pre-existing anemia may tolerate lower hemoglobin levels better than those with acute anemia. Current recommendations suggest that vital sign changes and accurate measurements of ongoing blood loss should trigger resuscitation efforts. Escalation of care (with or without transfusion) should occur at blood loss intervals of 500, 1000, and 1500 mL (mild/moderate/severe blood loss) so the team can respond appropriately if the patient is not tolerating the blood loss.

Maximum allowable blood loss (MABL)[91] is an invaluable tool to customize treatment of PPH and should be calculated for each individual patient and documented on the risk assessment form. This formula uses the patient's most recent hemoglobin level as the initial hemoglobin (Hbi) and the hemoglobin at which transfusion may occur, if clinically indicated, as the final hemoglobin (Hbf); it incorporates the patient's weight and total circulating blood volume and provides an individualized estimate of the patient's tolerable blood loss before transfusion should

occur. The equation assumes that volume losses have been replaced with balanced crystalloid. In a healthy pregnancy, the total circulating blood volume is 100 mL/kg (range 90–200 mL/kg.) In obesity, or volume-contracted states such as severe preeclampsia, total blood volume should be estimated at 70 mL/kg.[92]

The actual calculation is:

$$\frac{(Hbi\text{-}Hbf) \times Pt's\ Weight\ (kg) \times Total\ Blood\ Volume\ (mL/kg)}{[(Hbi + Hbf) \times 0.5]}$$

The following simplified and more user-friendly version of this formula can be used to calculate MABL:

$$MABL = \frac{Wt\ (kg) \times 100 \times [Hbi\text{-}70]}{(Hbi + 70) \times 0.5}$$

Hypotension, tachycardia, oliguria, and altered mental status indicate hypovolemic shock and should be treated aggressively. The "lethal triad" of coagulopathy, acidosis, and hypothermia, which occurs in hemorrhagic shock, compounds the loss of volume and blood components.[8] (Appendix J)

Initial Steps

Establish the following:

- Two large bore IV catheters
- Frequent BP monitoring (consider arterial line)
- Continuous EKG
- O$_2$ saturation monitor
- Temperature probe
- Foley catheter

Oxygen, Temperature, Volume

Oxygen supplementation of 8–10 L/min will slow the onset of tissue hypoxia. Hypothermia increases the risk of mortality; keeping the patient dry, using warmed blankets or forced air warmers, and warming all fluids will help maintain euthermia.[93] Initial volume resuscitation should use Ringer's lactate in a ratio of 1–2 mL per 1 mL blood loss.[94] Higher volumes of crystalloid have been associated with poor maternal outcomes due to dilutional coagulopathy. At this time, there is no evidence to promote the use of colloids over crystalloids, as colloids are also associated with impaired coagulation. In the setting of ongoing massive hemorrhage, red blood cell (RBC) administration should occur before total blood loss equals MABL.

Blood Products

Red Blood Cells

RBCs are the first step in the transfusion process, unless the patient has a known coagulation defect. Transfusing RBCs is not without risk, and ongoing transfusion medicine trials continue to demonstrate that the decision to transfuse must take into account the potential for harm.[92] Patients at high risk for PPH should have a blood type and screening on admission to cross match blood, if needed. O negative, Kell negative emergency blood is the next best alternative to cross-matched blood. There is no absolute hemoglobin level at which transfusion must occur, but maintaining a level between 70 and 90 g/L during active hemorrhage is recommended.[95]

Transfusion should occur when hemorrhage is unresponsive to uterotonic measures *and* blood loss exceeds 150 mL/min *or* total loss is rapidly approaching the calculated MABL *or* when the patient develops symptoms of inadequate perfusion, such as shortness of breath or tachycardia unresponsive to fluid in the presence of hemoglobin less than 90 g/L.

Fatigue alone is not a symptom that warrants transfusion.[96] Each unit of packed RBCs should increase the hemoglobin by 10 g/L. If 4 units of RBCs have been given, and blood loss is ongoing, activation of a MHP should be considered. Hemorrhage caused by uterine atony or birth-related trauma rarely requires additional coagulation factors or platelets, unless the volume of blood loss is significantly greater than the MABL and/or dilutional coagulopathy occurs. Hemorrhage due to placental abruption, amniotic fluid embolism, or disseminated intravascular coagulation consumes platelets and factors rapidly and replacement may be beneficial earlier in resuscitation.[97] Cell salvage does not increase the risk of amniotic fluid embolism and should be considered when the risk for severe PPH is high.[19] Intravenous iron is an important adjuvant for a hemoglobin level <80 g/L once bleeding has settled.[16,98,99]

Platelets

Platelet transfusion is necessary if blood loss is severe or if a consumptive coagulopathy develops. During active hemorrhage, platelets should be transfused at a level of 75×10^9/L in order to maintain a level above 50×10^9/L.[19] There is no evidence to support a fixed ratio of platelets in obstetric hemorrhage; however, it is acceptable to give 1 pooled dose of adult platelets (4 U platelets, or 5 U in Québec) per 8—10 U of RBCs, transfused in the absence of lab data and with ongoing

hemorrhage.[100] Each dose should raise the platelet count by $15-25 \times 10^9$/L.

Fresh Frozen Plasma

The goal of transfusion is to keep the INR <1.8. Donor plasma has less fibrinogen than the 5 g/L typically seen in the plasma of healthy parturients and is not the first choice for its replacement.[19] Although plasma provides additional clotting factors, most healthy women with moderate obstetric hemorrhage do not require these factors. However, using plasma in a ratio to RBCs of 1:2 or 1:1, as a global replacement, may improve outcomes in severe hemorrhage in trauma patients, particularly if timely lab values are not available. Large volumes of plasma increase the incidence of transfusion-related acute lung injury (TRALI) and transfusion-associated cardiorespiratory overload (TACO).[101]

Fibrinogen

Fibrinogen levels <2 g/L are associated with poor outcomes and direct replacement below these levels is recommended. Testing for fibrinogen levels when blood loss is <1500 mL is not predictive of severe PPH, and routine administration of fibrinogen in the absence of hypofibrinogenemia does not improve outcomes. Levels will drop more rapidly in the setting of abruption and amniotic fluid embolism than in the setting of atony.[94,96,97]

Each unit of cryoprecipitate contains 150—350 mg of fibrinogen and a typical dose is 8—10 U. Thawing is required prior to use, and multiple donors are required for sufficient amounts, which increases the risk of transfusion reactions.[102,103]

Fibrinogen concentrates (RiaSTAP and FIBRYGA) do not require thawing, provide accurate dosing, and decrease both the requirement for other blood products and the incidence of circulatory overload.[104] Fibrinogen concentrates also undergo viral inactivation and removal of antigens and antibodies. Four grams of fibrinogen concentrate is equivalent to 10 units of cryoprecipitate and typically raises plasma fibrinogen levels by 1 g/L (60 mg/kg dosing).[102,103]

Massive Hemorrhage Protocol

Originally designed for trauma patients, MHP is now often used in the setting of obstetrical hemorrhage. In the trauma literature, transfusing fixed ratios of RBCs to fresh frozen plasma to platelets of either 1:1:1 or 2:1:1 after the first 4 units of packed RBCs has been shown to decrease mortality.[94,96,97,105,106] Therapy based on lab values

(including viscoelastography, where available [rotational thromboelastometry, thromboelastography]) is superior to ratio-based approaches as it reduces the number of products transfused, reduces transfusion overload and transfusion-related complications, and tailors therapy to the underlying coagulopathy.[107,108]

The amount of blood loss that should trigger an MHP can be markedly different based on the patient's size, etiology of hemorrhage, and underlying health issues (i.e., pre-eclampsia). Using a single blood loss volume to initiate an MHP may result in some patients being transfused too early and others too late. Whenever the blood loss is approaching the MABL and there is ongoing bleeding, RBCs should be considered first.[94,96,97,105,106] Canadian standard of care recommendations indicate that an MHP should be able to be mobilized and products delivered within 10 minutes.[109] If local resources cannot reliably meet this timeline, consider initiating an MHP sooner. If the patient is stable and the bleeding is controlled after the initial 4 units of RBCs, the MHP products can be returned.

Coagulopathy does not occur in every PPH including massive PPH. When there is no coagulopathy, there is no benefit to transfusion of coagulation products. The etiology of the bleed matters, as atony and trauma are less likely to require coagulation factor replacement than abruption, abnormal placentation, or amniotic fluid embolism. Testing for coagulopathy rarely demonstrates abnormalities when the blood loss is <1.5−2 L. When coagulopathy is present in PPH, hypofibrinogenemia is the most common etiology,[102,103] and commonly coexists with hypocalcemia. Ionized calcium less than 1.16 mmol/L (rather than routine or corrected calcium which may be normal) is the most accurate way to measure calcium status in a hemorrhaging patient and may be at least as important as fibrinogen in terms of risk reduction.[110] Calcium chloride is the agent of choice to replace calcium as it contains 3 times the elemental calcium of calcium gluconate and does not require liver metabolism. Fresh frozen plasma and platelets are less commonly needed, but may be included in the MHP, particularly after 4 to 8 units of RBCs, respectively.

Frequent monitoring of all these components (CBC, PTT, INR, fibrinogen, ionized calcium), as well as magnesium, electrolytes, hypothermia, and overall volume status are necessary components of any MHP. Tailoring therapy as early as feasible results in a patient-centred approach that is in keeping with the most up-to-date recommendations in transfusion medicine.

Prothrombin Complex Concentrate

Prothrombin complex concentrate contains vitamin K−dependent clotting factors and is indicated for reversal of vitamin K antagonists (warfarin). Apart from patients with known factor II or X deficiencies, in which case, a hematologist should be consulted, there is currently no role for prothrombin complex concentrate in the treatment of PPH.[96,97,105]

Recombinant Activated Factor VII

Recombinant activated factor VII (rFVIIa) provides a thrombin burst and stabilizes clots, and should only be administered to patients with a fibrinogen level >1g/L, platelets $>20 \times 10^9$/L, and a near normal pH (7.4) and temperature (35.9°C). Given the absence of strong evidence of benefit and the serious risk of thrombosis, rFVIIa should only be used in PPH as a last resort and in consultation with a transfusion medicine specialist or hematologist.[96,97,105]

REVIEW

Quality care initiatives in many centres have clearly shown that strong teamwork and communication, along with simulation training and debriefing after any significant PPH, improve outcomes. Key components of teamwork include a process for standard and structured communication, effective use of clear language, psychological safety where team members are not fearful of speaking up, situational awareness, and effective leadership[111] (Appendix K).

Debriefing after simulation led by a trained facilitator promotes improved learning outcomes and enhances future performance in the clinical setting.[112] Debriefing is more than feedback, it is "an interactive, bidirectional and reflective conversation,"[113] which will foster better communication and teamwork in subsequent clinical scenarios. As experiencing PPH can be traumatic, care providers should have a conversation with the patient and their family to explain the events and answer any questions they have. Debriefing after a significant PPH should occur and should include all involved members of the health care team, as well as a separate discussion with the patient and her family.

CONCLUSION

Although the acute treatment of PPH is key for any single patient, the ongoing review practices is most important for

future patients. While standardized approaches for the identification and management of PPH may need to vary between sites based on the availability of resources, best practices include:

- a risk assessment for every patient, including calculation of the MABL
- a standardized approach for collecting, weighing, and reporting blood loss
- stage-based management strategies, including protocols specifically designed for massive blood loss
- 'hemorrhage carts' for storing medications and supplies
- regular multidisciplinary staff training and simulation
- debriefing with formal review of adverse events.

Templates for all these recommendations can be found in the supplementary toolkit.

SUPPLEMENTARY TOOLKIT

A supplementary toolkit related to this article can be found in the Online Appendix.

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APPENDIX A

Table 1. Key to Grading of Recommendations, Assessment, Development and Evaluation Quality of Evidence

Grade	Definition
Strength of recommendation	
Strong	High level of confidence that the desirable effects outweigh the undesirable effects (strong recommendation for) or the undesirable effects outweigh the desirable effects (strong recommendation against)
Conditional [a]	Desirable effects probably outweigh the undesirable effects (weak recommendation for) or the undesirable effects probably outweigh the desirable effects (weak recommendation against)
Quality of evidence	
High	High level of confidence that the true effect lies close to that of the estimate of the effect
Moderate	Moderate confidence in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Limited confidence in the effect estimate: The true effect may be substantially different from the estimate of the effect
Very low	Very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]Do not interpret conditional recommendations to mean weak evidence or uncertainty of the recommendation.

Adapted from GRADE Handbook (2013), Table 5.1.

Table 2. Implications of Strong and Conditional recommendations, by guideline user

Perspective	Strong Recommendation • "We recommend that…" • "We recommend to not…"	Conditional (Weak) Recommendation • "We suggest…" • "We suggest to not…"
Authors	The net desirable effects of a course of action outweigh the effects of the alternative course of action.	It is less clear whether the net desirable consequences of a strategy outweigh the alternative strategy.
Patients	Most individuals in the situation would want the recommended course of action, while only a small proportion would not.	The majority of individuals in the situation would want the suggested course of action, but many would not.
Clinicians	Most individuals should receive the course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that patient choices will vary by individual and that clinicians must help patients arrive at a care decision consistent with the patient's values and preferences.
Policymakers	The recommendation can be adapted as policy in most settings.	The recommendation can serve as a starting point for debate with the involvement of many stakeholders.

Adapted from GRADE Handbook (2013), Table 6.1.