WHO recommendations
Uterotonics for the prevention of postpartum haemorrhage
The global burden of postpartum haemorrhage

Uterotonics for PPH prevention

How were the WHO recommendations updated?

What are the updated WHO recommendations?

So what’s new?

Implementing the WHO recommendations
Method: Developing and applying a ‘living guidelines’ approach to WHO recommendations on Maternal and Perinatal Health*

- Over the past decade, WHO has issued over 400 maternal and perinatal health (MPH) recommendations for global use, and the size of this portfolio presents a major challenge to ensuring that all recommendations are up to date.

- A dynamic ‘living guidelines’ approach has been developed and applied to respond more rapidly to new, important evidence that may affect specific WHO recommendations in MPH.

- The new approach uses an evidence-informed, consultative prioritisation process, rapid updating of prioritised systematic reviews and electronic consultations with ‘living guidelines’ panels.

- Using this approach enables WHO to efficiently use resources to execute its global mandate on normative guidance for MPH.

- Other guideline development organizations can also adapt this approach to facilitate more rapid and efficient updating of recommendations.

What is postpartum haemorrhage?

Postpartum haemorrhage (PPH) is the leading cause of maternal death worldwide. Postpartum haemorrhage (PPH) is commonly defined as a blood loss of 500 ml or more within 24 hours after birth. It affects about 5% of all women giving birth around the world. Globally, nearly one quarter of all maternal deaths are associated with PPH. In most low-income countries, it is the main cause of maternal mortality.

The majority of PPH-associated deaths could be avoided by the use of prophylactic uterotonics during the third stage of labour and appropriate treatment.

Improving health care for women during childbirth to prevent and treat PPH is a necessary step towards achievement of the health targets of the Sustainable Development Goals (SDGs).

99% of all maternal deaths occur in low- and middle-income countries (LMICs).
2. Uterotonics for PPH prevention

New findings on uterotonics for PPH prevention

A Cochrane systematic review and network meta-analysis compared uterotonic options with no uterotonic and other uterotonic options.

- 196 trials (135,559 women) across 53 countries
- Any trial comparing a uterotonic vs placebo, no uterotonic or another uterotonic
- Single agents (oxytocin, carbetocin, misoprostol, ergometrine) or combination agents (oxytocin plus ergometrine, oxytocin plus misoprostol)

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- Single agents (oxytocin, carbetocin, misoprostol, ergometrine) or combination agents (oxytocin plus ergometrine, oxytocin plus misoprostol)

In light of this new evidence, the WHO recommendations on uterotonics for PPH prevention have been updated.

The WHO PPH recommendations were first published in 2012.

These updated recommendations (2018) supersede the previous recommendations on uterotonics for PPH prevention.
3. how were the WHO recommendations updated?

A systematic approach

The recommendations were updated according to the standards of the WHO handbook on guideline development

Updating involves:

1. WHO Steering Group
2. Guideline Development Group (GDG)
3. Executive Guideline Steering Group (GSG)
4. External Review Group
5. Systematic review team
6. External partners and observers

- Identify priority questions and outcomes
- Retrieve, assess and synthesize evidence
- GDG formulates the recommendations
3. how were the WHO recommendations updated?

GDG formulates the recommendations

The Guideline Development Group (GDG) convened in September & October 2018

The GDG comprised 18 external experts and relevant stakeholders with expertise in research, guideline development, policy and programmes on PPH prevention and treatment.

GDG members considered:

- Balance between desirable and undesirable effects
- Overall quality of supporting evidence
- Values and preferences of stakeholders
- Resource requirements
- Cost-effectiveness
- Acceptability
- Feasibility
- Equity
Recommendation 1. The use of an effective uterotonic for the prevention of PPH during the third stage of labour is recommended for all births.

To effectively prevent PPH, only one of the following uterotonics should be used:

- Oxytocin
- Carbetocin
- Misoprostol
- Ergometrine/methylergometrine
- Oxytocin and ergometrine fixed-dose combination
4. What works: efficacy and safety of uterotonics for PPH prevention

**Recommendation 1.** The use of an effective uterotonic for the prevention of PPH during the third stage of labour is recommended for all births.

To effectively prevent PPH, only one of the following uterotonics should be used:

- **Oxytocin**
- Carbetocin
- Misoprostol
- Ergometrine/methylergometrine
- Oxytocin and ergometrine fixed-dose combination

**Recommendation 1.1**

The use of oxytocin (10 IU, IM/IV) is recommended for the prevention of PPH for all births.

- Vaginal birth or caesarean section
- Skilled health personnel required to administer
- At caesarean section: consider dividing doses and avoid a rapid IV bolus
4. What works: efficacy and safety of uterotonics for PPH prevention

**Recommendation 1.** The use of an effective uterotonic for the prevention of PPH during the third stage of labour is recommended for all births.

To effectively prevent PPH, only one of the following uterotonics should be used:

- Oxytocin
- **Carbetocin**
- Misoprostol
- Ergometrine/methylergometrine
- Oxytocin and ergometrine fixed-dose combination

**Recommendation 1.2**

The use of carbetocin (100 µg, IM/IV) is recommended for the prevention of PPH for all births in contexts where its cost is comparable to other effective uterotonics.

- Vaginal birth or caesarean section
- Skilled health personnel required to administer
- For PPH prevention only
Recommendation 1. The use of an effective uterotonic for the prevention of PPH during the third stage of labour is recommended for all births.

To effectively prevent PPH, only one of the following uterotonics should be used:
- Oxytocin
- Carbetocin
- Misoprostol
- Ergometrine/methylergometrine
- Oxytocin and ergometrine fixed-dose combination

Recommendation 1.3

The use of misoprostol (either 400 µg or 600 µg PO) is recommended for the prevention of PPH for all births.

- Alternative routes may be needed at caesarean section, but oral route is preferred by women
- No clear evidence of which dose is superior, but higher doses have more side effects
- Inform women of possible adverse effects
- Can be used in hospital or community
4. What works: efficacy and safety of uterotonics for PPH prevention

**Recommendation 1.** The use of an effective uterotonic for the prevention of PPH during the third stage of labour is recommended for all births.

To effectively prevent PPH, only one of the following uterotonics should be used:

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- Carbetocin
- Misoprostol
- Ergometrine/methylergometrine
- Oxytocin and ergometrine fixed-dose combination

**Recommendation 1.4**

The use of ergometrine (200 µg, IM/IV) is recommended for the prevention of PPH in contexts where hypertensive disorders can be safely excluded prior to its use:

- Vaginal birth or caesarean section
- Skilled health personnel are required
- Inform women of possible side effects - other options may have better side effect profile
4. What works: efficacy and safety of uterotonics for PPH prevention

Recommendation 1. The use of an effective uterotonic for the prevention of PPH during the third stage of labour is recommended for all births.

To effectively prevent PPH, only one of the following uterotonics should be used:

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- Misoprostol
- Ergometrine/methylergometrine
- Oxytocin and ergometrine fixed-dose combination

Recommendation 1.5

The use of oxytocin and ergometrine fixed-dose combination (5 IU/500 µg IM) is recommended for the prevention of PPH in contexts where hypertensive disorders can be safely excluded prior to its use.

- Vaginal birth or caesarean section
- Skilled health personnel are required
4. What works: efficacy and safety of uterotonics for PPH prevention

Recommendation 1. The use of an effective uterotonic for the prevention of PPH during the third stage of labour is recommended for all births.

To effectively prevent PPH, only one of the following uterotonics should be used:

- Oxytocin
- Carbetocin
- Misoprostol
- Ergometrine/methylergometrine
- Oxytocin and ergometrine fixed-dose combination
- Injectable prostaglandins

Recommendation 1.6

Injectable prostaglandins (carboprost or sulprostone) are not recommended for the prevention of PPH
4. Which one: Choice of uterotonic for PPH prevention

**Recommendation 2.** In settings where multiple uterotonic options are available, **oxytocin (10 IU, IM/IV)** is the recommended uterotonic agent for the prevention of PPH for all births.

Vaginal birth or caesarean section

Skilled health personnel are required

Combination of misoprostol and oxytocin may be more effective than oxytocin alone for some priority outcomes, however:

- increases side effects
- not available as a fixed dose combination
- requires parenteral and oral administration
Recommendation 3. In settings where oxytocin is unavailable (or its quality cannot be guaranteed), the use of other injectable uterotonicics (carbetocin, or if appropriate ergometrine/methylergometrine or oxytocin and ergometrine fixed-dose combination) or oral misoprostol is recommended.

Vaginal birth or caesarean section

Skilled health personnel are required
Recommendation 4. In settings where skilled health personnel are not present to administer injectable uterotonics, the administration of misoprostol (either 400 µg or 600 µg PO) by community health care workers and lay health workers is recommended for the prevention of PPH.

If skilled health personnel are not present or have not been trained to administer injectable uterotonics, oral misoprostol is preferred.
6. implementing the updated WHO recommendations

Are skilled health personnel who can administer injectable uterotonics available?

Yes → trained community health workers and lay health workers can administer misoprostol (400 µg or 600 µg PO)

No → use oxytocin (10 IU, IV or IM)

Is oxytocin available?

Yes → oxytocin is not available, or its quality cannot be guaranteed

No → use oxytocin (10 IU, IV or IM)

Is oxytocin of sufficient quality?

Yes → use oxytocin (10 IU, IV or IM)

No → trained community health workers and lay health workers can administer misoprostol (400 µg or 600 µg PO)

Heat-stable carbetocin (100 µg, IM/IV), in contexts where its cost is comparable to other effective uterotonics.

OR

Ergometrine / methylergometrine (200 µg, IM/IV), in contexts where hypertensive disorders can be safely excluded prior to its use.

OR

Fixed-dose combination of oxytocin and ergometrine, in contexts where hypertensive disorders can be safely excluded prior to its use.

OR

Misoprostol (400 µg or 600 µg PO)
6. implementing the updated WHO recommendations

Implementation considerations

- **Update clinical guidance**
  Develop or revise existing clinical guidelines, protocols or job aids

- **Equip health facilities**
  Ensure necessary supplies, equipment and staff to use uterotonics safely

- **Support behaviour change**
  Obtain technical support for implementation, engage stakeholders and partners, and provide training
6. implementing the updated WHO recommendations

Implementation considerations

Quality-certified uterotonics
Regulatory, procurement and logistics processes that work

Cold-chain transport & storage
For heat-sensitive uterotonics (oxytocin, ergometrine)

Effective communication
Ensure women are informed of risks, benefits and alternatives
Contact us

Email: reproductivehealth@who.int

Twitter: @HRPresearch

Facebook: World Health Organization