Selecting a Rational Mix of Uterotonic Drugs for Prevention and Treatment of Postpartum Hemorrhage (PPH)

A guide for policymakers, pharmacy managers and Ministries of Health

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Integrated Program

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Acknowledgments

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ABOUT MCHIP

The Maternal and Child Health Integrated Program (MCHIP) is the USAID Bureau for Global Health's flagship maternal, neonatal and child health (MNCH) program. MCHIP supports programming in maternal, newborn and child health, immunization, family planning, malaria and HIV/AIDS, and strongly encourages opportunities for integration. Cross-cutting technical areas include water, sanitation, hygiene, urban health and health systems strengthening.

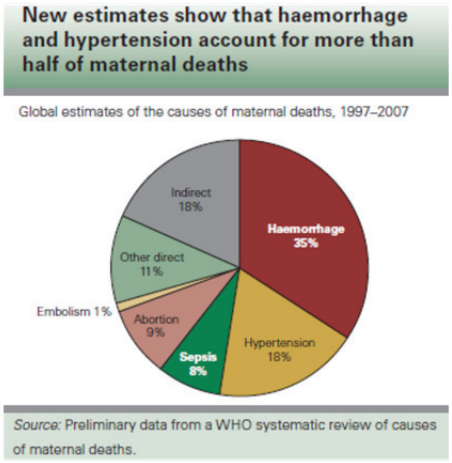
Abbreviations

AMTSL	Active management of the third stage of labor
CCT	Controlled cord traction
EML	Essential Medicines List
FIGO	*d'Obstétrique/ of* Gynecology and Obstetrics
ICM	International Confederation of Midwives
MOH	Ministry of Health
NK	Not known
NLMIS	National Logistics Management Information Systems
OiU	Oxytocin in the Uniject device
PPH	Postpartum hemorrhage
SBA	Skilled birth attendant
TBA	Traditional birth attendant
TTI	Time temperature indicator
WHO	World Health Organization

Background

The leading cause of maternal deaths remains postpartum hemorrhage (PPH) (see Figure 1), in spite of the fact that morbidity and mortality due to PPH are largely preventable through skilled care during childbirth. Delays in identifying hemorrhage, delays in transport to the appropriate point of care, and delays in receiving the recommended treatment all contribute to high rates of maternal mortality and morbidity due to PPH. These delays are exacerbated when women give birth without any assistance, or alternatively, even when a relative, member of the community or a traditional birth attendant (TBA), often without formal training, attends the birth. Thus, women giving birth in the community without a skilled attendant may not have access to interventions either to prevent or treat PPH. In some cases, women may give birth in facilities where skilled birth attendants lack the necessary skills, equipment or supplies to prevent and manage PPH and shock.

Figure 1.



http://www.countdown2015mnch.org/reports-publications/2010-report/2010-report-downloads)

Fortunately, there are two profoundly effective prevention strategies to reduce PPH by more than 60% that are endorsed by the World Health Organization (WHO),[1] the International Federation of Gynecology and Obstetrics (FIGO), and the International Confederation of Midwives (ICM)[2,3]:

- Active management of the third stage of labor (AMTSL),* when skilled birth attendants are at the birth, regardless of where they practice
- Provision of a uterotonic drug (oxytocin or misoprostol) during the third stage of labor without controlled cord traction (CCT) in situations where oxytocin is not available or birth attendants' skills are limited

While up to 60% of PPH cases may be prevented[4] by applying AMTSL or administering a uterotonic drug during the third stage of labor, women may still hemorrhage in the postpartum period. Seventy-five to ninety percent of PPH is due to uterine atony (failure of the uterus to contract adequately after birth).[5] It is therefore imperative that women also have access to uterotonic drugs that contract the uterus to treat PPH should it occur.

Government initiatives can improve maternal outcomes and meet [objectives of] Millennium Development Goal 5 (improve maternal health), by quickly increasing coverage of uterotonic drugs for prevention and treatment of PPH and correct use of AMTSL when birth is attended by a skilled attendant. Although AMTSL is a critical component of PPH prevention, the WHO recommends AMTSL only be performed by a skilled birth attendant because of the skills it requires. All women regardless of delivery location or type of birth attendant present should have access to an effective uterotonic to prevent PPH. This requires the development of a comprehensive PPH strategy that addresses prevention and management in situations both with and without a skilled provider, and in births occurring in and outside the facility. Although it is preferable that all women give birth in a facility with skilled birth attendants, Ministries of Health (MOHs) must address the needs of women who live in settings where geographical and socioeconomic restrictions do not allow them to reach health centers.

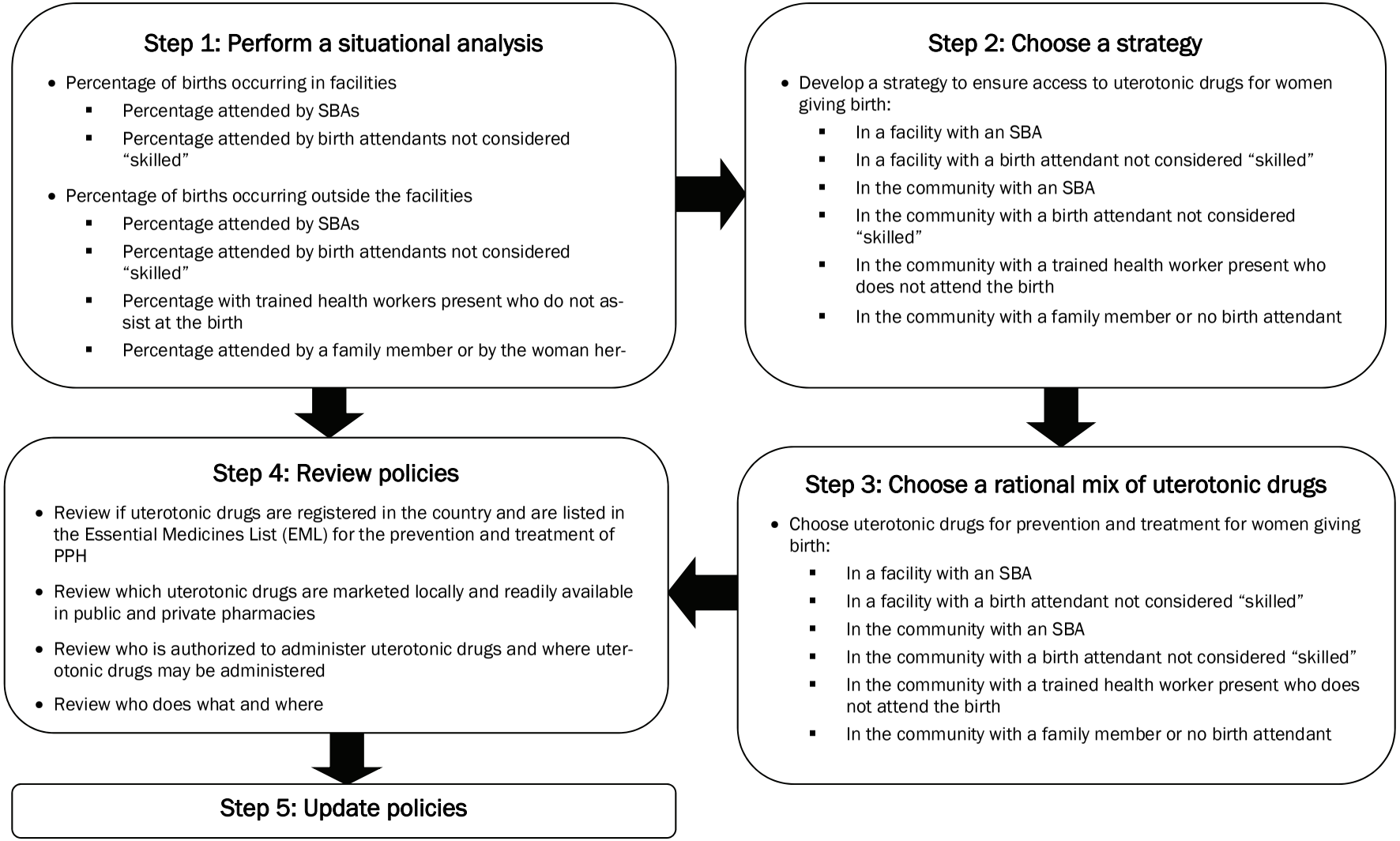
* AMTSL consists of three steps: 1) administration of a uterotonic agent within 1 minute of birth; 2) controlled cord traction; and 3) uterine massage after delivery of the placenta.

The goal for PPH control initiatives is to increase uterotonic coverage with the most appropriate uterotonic drug. Each country must evaluate the most cost-effective scenarios for use of each uterotonic based on: 1) place of birth, 2) type of birth attendant, and 3) availability of a sustainable cold chain. This tool provides essential information to assist an MOH in selecting the most appropriate uterotonic drug for each point of care and by each cadre of birth attendant.

DEVELOPING A STRATEGY FOR USE OF UTEROTONIC DRUGS

To ensure maximum access to uterotonic drugs to prevent and treat PPH, the MOH will need to choose both a comprehensive strategy to address community- and facility-based births and a rational mix of uterotonic drugs for each point of care and type of birth attendant. The process of selection involves five key steps: 1) perform a situational analysis to assess points of care needing uterotonic drugs; 2) choose a strategy; 3) choose a rational mix of uterotonic drugs; 4) review policies and clinical guidelines; and 5) update policies and clinical guidelines as needed (see Figure 2).

Figure 2. Overview of steps to take when selecting a rational mix of uterotonic drugs for the prevention and treatment of PPH



1. Perform a Situational Analysis

The first step in the selection of a rational mix of uterotonic drugs is an assessment of where births occur and who attends the births. Understanding where births are occurring and the type of birth attendant present during the births will give decision-makers an idea of where access to uterotonic drugs is needed.

Before completing this part of the analysis, it will be helpful to first define who is a "skilled birth attendant" (SBA). The WHO defines an SBA as someone "trained to proficiency in the skills needed to manage normal (uncomplicated) pregnancies, childbirth and the immediate postnatal period, and in the identification, management and referral of complications in women and newborns."[6] In most countries, the MOH will define an SBA by a cadre: doctor, midwife, obstetric nurse, etc. In some countries, the shortage of nurses, midwives and doctors has meant that non-professional cadres of health care providers attend normal births in facilities. These birth attendants may or may not be considered "skilled" birth attendants by the MOH and may be restricted in what they can do; for example, they may not be authorized to apply AMTSL or administer oxytocin.

To complete this step, you will need access to data on vaginal births occurring in both the facility and the community. If data are available only by "facility" and "community" and not by type of birth attendant, you may have to rely on your understanding of the reality in your country and estimate the percentage of births attended by each type of provider.

Table 1 below provides a matrix for completing information about vaginal births occurring in the facility and the community. To complete Table 1, you should write in the numbers of annual vaginal births by place of birth and type of birth attendant. If you do not have the information, either write in "Not Known" (NK) or make an educated estimate. If the cadre of birth attendant does not exist, simply make a line through the row.

Table 1. Numbers of vaginal births by place of birth and type of birth attendant

Place of birth	Type of birth attendant	Number of vaginal births attended annually	Percentage of vaginal births attended in facility / community	Percentage of all vaginal births
Facility	Skilled birth attendant	A: _____	A divided by C multiplied by 100: _____%	
	Birth attendant not considered "skilled"	B: _____	B divided by C multiplied by 100: _____%	
	Total number of vaginal births occurring in the facility	C: _____		C divided by (C plus H) multiplied by 100: _____%

Place of birth	Type of birth attendant	Number of vaginal births attended annually	Percentage of vaginal births attended in facility / community	Percentage of all vaginal births
Community	Skilled birth attendant	D: _____	D divided by H multiplied by 100: _____%	
	Birth attendant not considered "skilled"	E: _____	E divided by H multiplied by 100: _____%	
	Trained health worker who does not attend the birth	F: _____	F divided by H multiplied by 100: _____%	
	Woman/Family member	G: _____	G divided by H multiplied by 100: _____%	
	Total number of vaginal births occurring in the community	H: _____		G divided by (C plus H) multiplied by 100: _____%

After completing Table 1, the figures for total number of vaginal births by cadre and point of care can be transferred to fill in the boxes in Figure 3, below.

Figure 3. Situational analysis of where vaginal births occur and who is the birth attendant

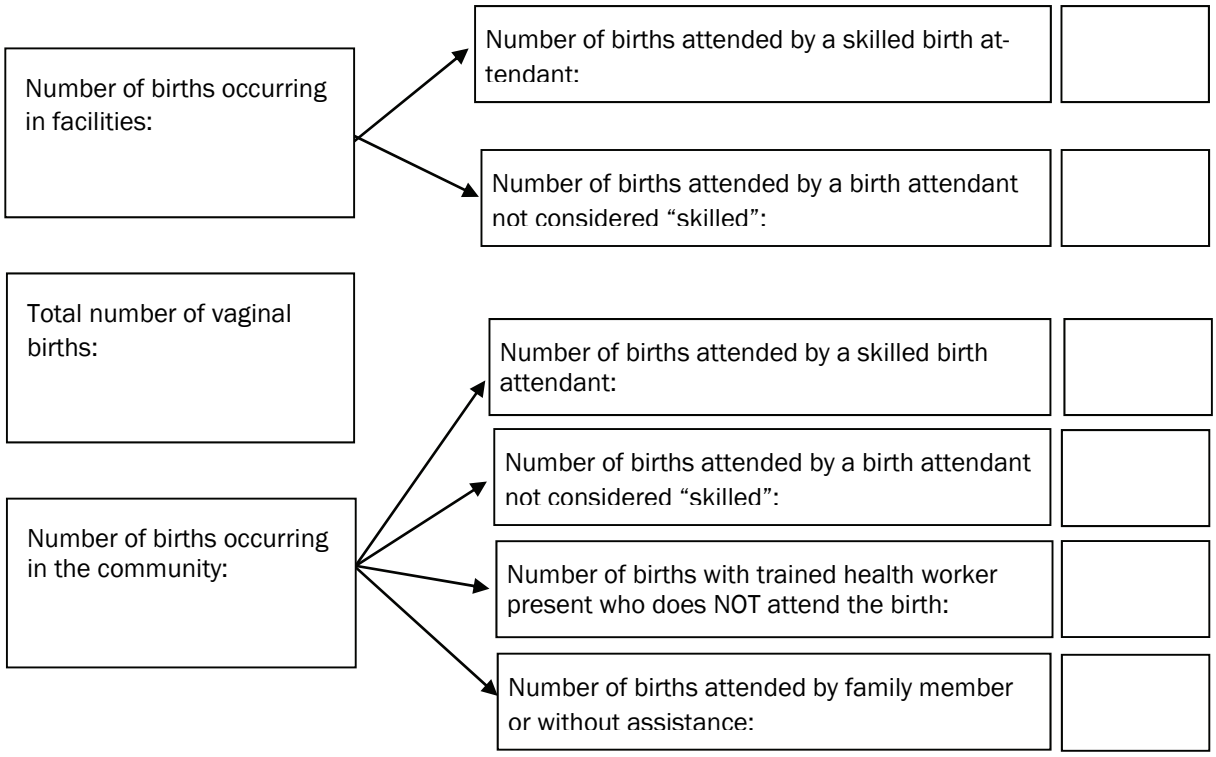


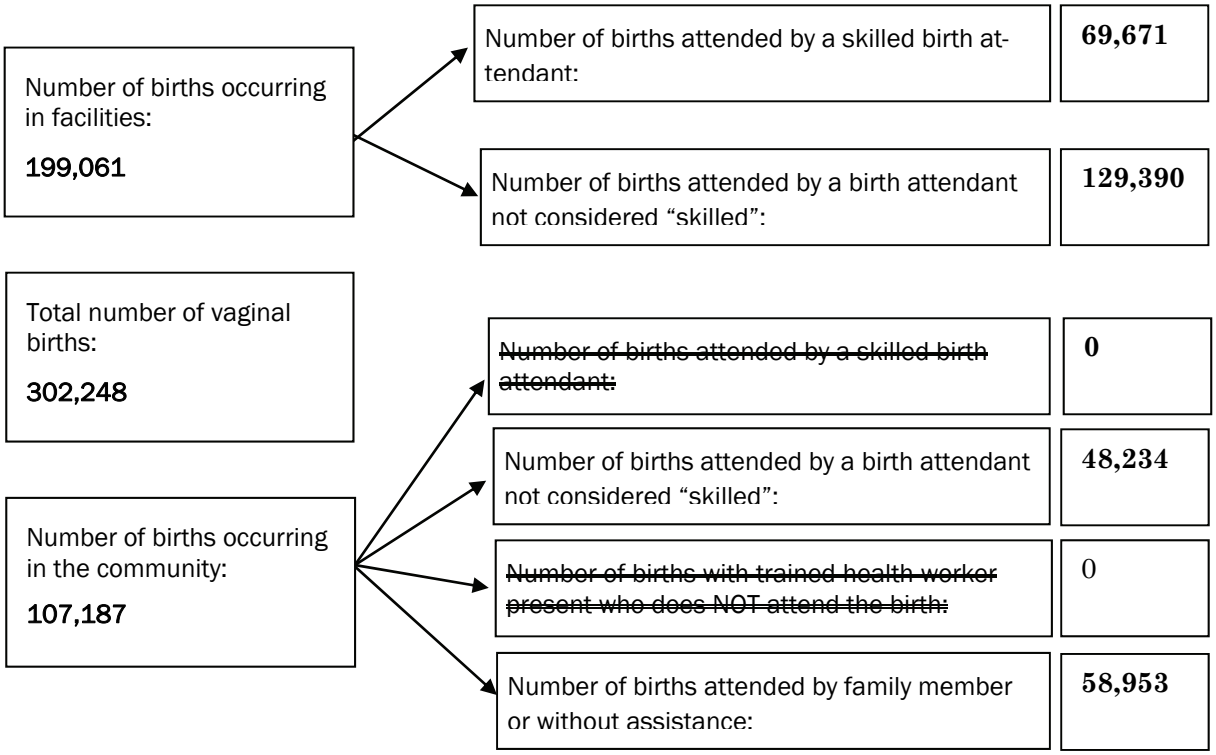
Table 2, below, gives an example for Country Make-Believe. Country Make-Believe had 306,248 vaginal births in 2010. Of these births, 199,061 occurred in facilities. Although the national statistics show that all births occurring in facilities were attended by SBAs, the MOH knows that approximately 65% of vaginal births in facilities are attended by midwifery assistants, who are not considered SBAs. SBAs are not authorized to attend births in the community, and Country Make-Believe does not have a cadre of trained health workers working in the community, so they will strike these two categories out in the table. Data on the type of birth attendants assisting women who give birth in the community are not consistently gathered, but TBAs provide data to facilities about births they attend, and these account for approximately 55% of births in the community. The remaining births are attended by a family member or the woman herself.

Table 2. Country Make-Believe: Numbers of vaginal births by place of birth and type of birth attendant

Place of birth	Type of birth attendant	Number of vaginal births attended annually	Percentage of vaginal births attended in facility / community	Percentage of all vaginal births
Facility	Skilled birth attendant	69,671 (35% of vaginal births)	0.35 x 199,061 = 69,671	
	Birth attendant not considered "skilled"	129,390 (65% of vaginal births)	0.65 x 199,061 = 129,390	
	Total number of vaginal births occurring in the facility	199,061		[199,061 / (107,187 + 199,061)] x 100 = 65%
Community	~~Skilled birth attendant~~			
	Birth attendant not considered "skilled"	48,234 (55% of vaginal births)	0.55 x 107,187 = 48,234	
	~~Trained health worker who does not attend the birth~~			
	Woman/Family member	58,953 (45% of vaginal births)	0.45 x 107,187 = 58,953	
	Total number of vaginal births occurring in the community	107,187		[107,187 / (107,187 + 199,061)] x 100 = 35%

Decision-makers from Country Make-Believe took the numbers from Table 2 and filled in the boxes in Figure 4, on the next page. They now have an approximate number of births each type of birth attendant is assisting in both facilities and the community.

Figure 4. Country Make-Believe: Situational analysis of where vaginal births occur and who is the birth attendant



Please complete Exercises 1a and 1b in your workbook, using statistics from your country.

2. Choose a Strategy

The goal in developing a strategy for use of uterotonic drugs is to achieve as high a **population-level** uterotonic coverage as possible. This means that the strategy must ensure that all women, regardless of where they give birth, have access to a uterotonic drug in the immediate postpartum period. While any MOH would hope that every woman gives birth with an SBA in a well-equipped facility, this may not be attainable in the short term for some countries. In countries where births are occurring outside a facility, a balanced strategy using a facility-based and community-based model will increase uterotonic protection for all women. A woman may give birth:

- In a facility with an SBA
- In a facility with a birth attendant not considered "skilled"
- In the community with an SBA
- In the community with a birth attendant not considered "skilled"
- In the community with a trained health worker present who does not attend the birth
- In the community with a family member or no birth attendant

To achieve a high population-level uterotonic coverage, all women, regardless of where they give birth, must have access to a uterotonic drug in the immediate postpartum period.

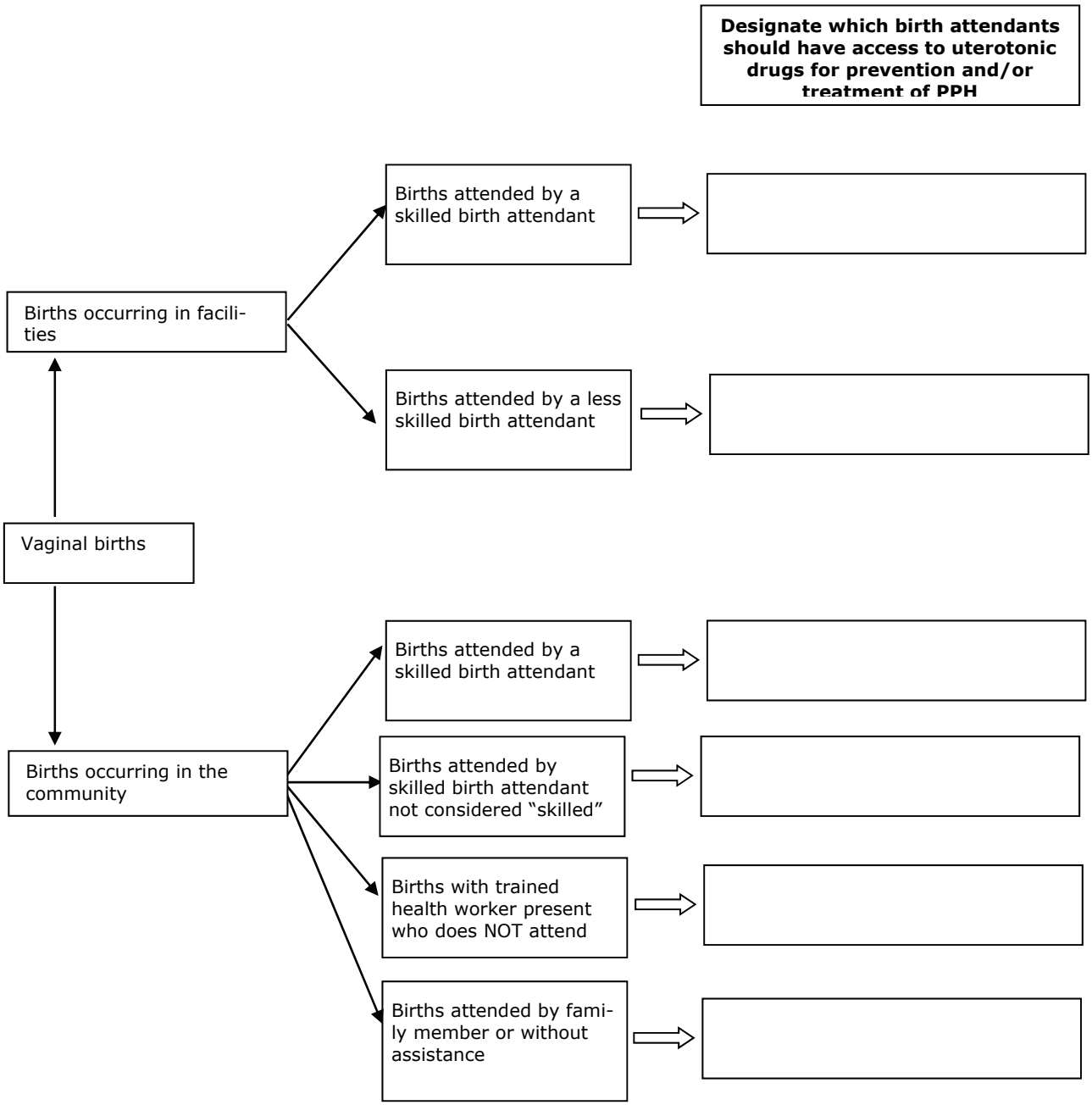
There are a series of "yes/no" questions in Table 3, below, about whether or not decision-makers believe that uterotonic drugs should be available for prevention and/or treatment for all the possible scenarios in which a laboring woman may find herself. Decision-makers will circle "yes" for each type of birth attendant and place of birth where they feel a strategy should be developed to make uterotonic drugs available; they will circle "no" for each type of birth attendant and place of birth where they feel a strategy should **NOT** be developed to make uterotonic drugs available. If the cadre does not exist, decision-makers will either leave the row blank or simply cross out the row for that cadre.

Table 3. Deciding whether a strategy should be developed for making uterotonic drugs accessible by type of birth attendant and place of birth

Place of birth	Type of birth attendant	Should uterotonic drugs be available for prevention?	Should uterotonic drugs be available for treatment?
Facility	Skilled birth attendant	Yes / No	Yes / No
	Birth attendant not considered "skilled"	Yes / No	Yes / No
Community	Skilled birth attendant	Yes / No	Yes / No
	Birth attendant not considered "skilled"	Yes / No	Yes / No
	Trained health worker who does not attend the birth but is present at the time of birth	Yes / No	Yes / No
	Woman/Family member	Yes / No	Yes / No

Decisions about which providers should have access to uterotonic drugs for prevention and treatment of PPH can be put on a tree like Figure 5, below.

Figure 5. Situational analysis of where vaginal births occur and who is the birth attendant



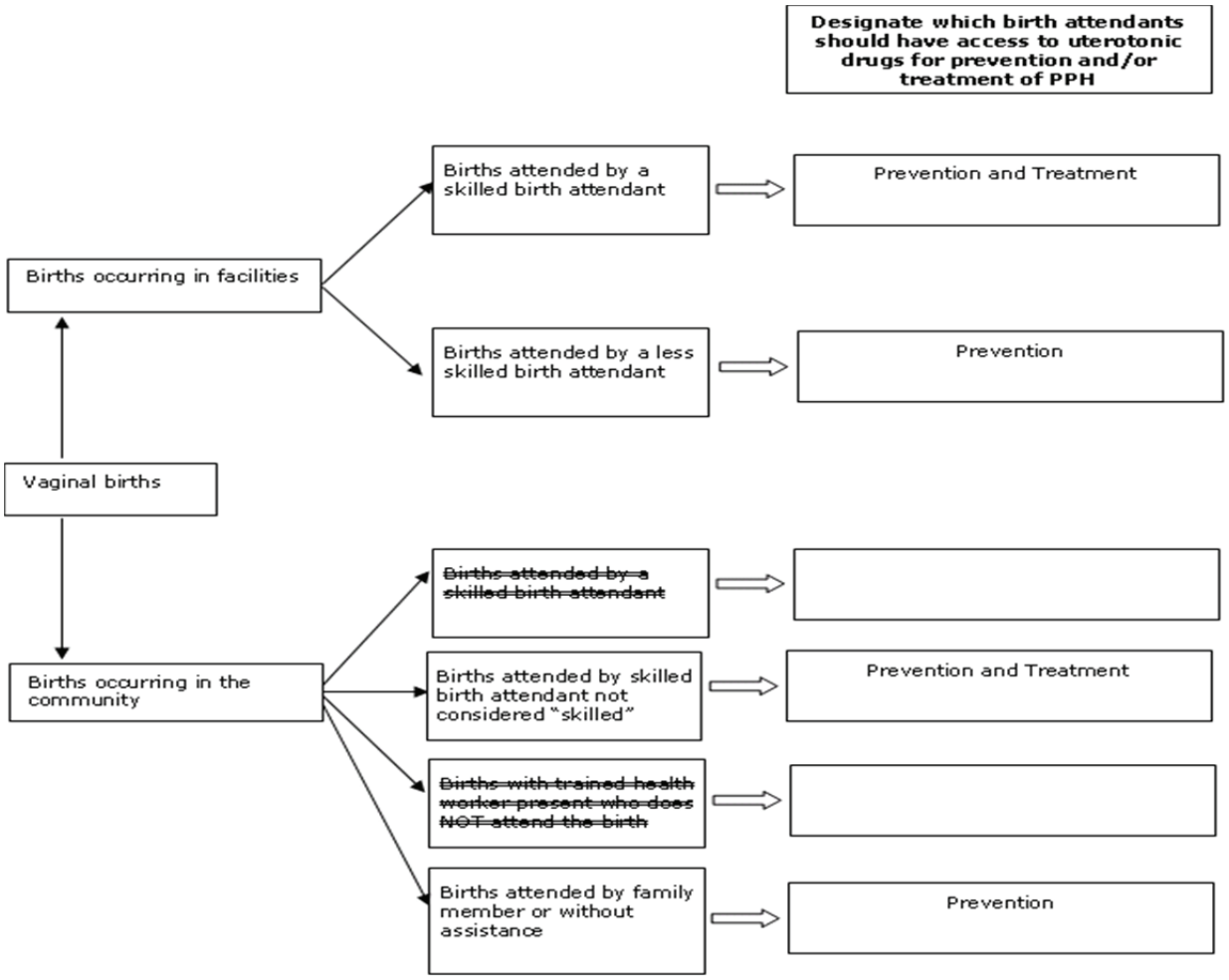
On the following pages, you can see how country Make-Believe completed Table 3 and Figure 5. The decision-makers in country Make-Believe would like to make uterotonic drugs available:

- For prevention and treatment for women giving birth with SBAs in the facility
- For prevention only for women giving birth in facilities with birth attendants not considered "skilled"
- For prevention and treatment for women giving birth in community with birth attendants not considered "skilled"
- For prevention only for women giving birth in the community without any assistance or with the assistance of a family member
- Country Make-Believe does not have trained health workers in the community and does not allow SBAs to attend births in the community, so these cadres have been crossed out.

Table 4. Country Make-Believe strategy for making uterotonic drugs accessible by type of birth attendant and place of birth

Place of birth	Type of birth attendant	Should uterotonic drugs be available for prevention?	Should uterotonic drugs be available for treatment?
Facility	Skilled birth attendant	(Yes) / No	(Yes) / No
	Birth attendant not considered "skilled"	(Yes) / No	Yes / (No)
Community	~~Skilled birth attendant~~	~~Yes / No~~	~~Yes / No~~
	Birth attendant not considered "skilled"	(Yes) / No	(Yes) / No
	~~Trained health worker who does not attend the birth but is present at the time of birth~~	~~Yes / No~~	~~Yes / No~~
	Woman/Family member	(Yes) / No	Yes / (No)

Figure 6. Country Make-Believe: Situational analysis of where vaginal births occur and who is the birth attendant



NOTE: Please complete Exercises 2a and 2b in your workbook, completing the table and figure with information for your country.

3. Choose a Rational Mix of Uterotonic Drugs for Prevention and Treatment of PPH

3.1. REVIEW INFORMATION ON UTEROTONIC DRUGS USED FOR PREVENTION AND TREATMENT OF PPH

Once the MOH develops a strategy for increasing access to uterotonic drugs, it must choose a rational mix of uterotonic drugs by point of care and by type of birth attendant. Choosing uterotonic drugs should not be seen as an "either/or" choice—for example, "if we choose misoprostol, then we can't use oxytocin." Rather, a mix of uterotonic drugs should be chosen that maximizes cost-effectiveness and minimizes loss of uterotonic drugs (due to expiration or loss of active ingredient due to exposure to heat and light) while increasing access to them at the largest number of points of care when needed.

The decision on which uterotonic drugs to use will depend on many factors, including:

- Safety
- Cost
- Availability
- Efficacy
- Response time
- Stability
- Storage requirements
- Adverse effects
- Contraindications
- Presentation
- Requirements for administering the drug

Safety

Ergometrine (and the fixed drug combination of oxytocin and ergometrine) is contraindicated in women with a history of hypertension, heart disease, pre-eclampsia or eclampsia. A provider must be able to ascertain if these conditions exist before administering ergometrine. Therefore, to safely use ergometrine or the fixed drug combination of oxytocin and ergometrine, the birth attendant must have a functional blood pressure (BP) machine and stethoscope, be able to competently measure BP, and be able to ascertain if there are contraindications to its use before administering it.

In many countries, there have been reports of all types of health workers in all types of settings inappropriately and/or unsafely using oxytocin for labor induction and augmentation, and inappropriately and/or unsafely using misoprostol for abortions and labor induction and augmentation. While inappropriate and/or unsafe use of these uterotonic drugs is an important public health issue, the fear of potential misuse should not limit women's access to lifesaving uterotonic drugs. Rather, any strategy for increasing access to uterotonic drugs should include a strategy on how best to limit and control their potential inappropriate and/or unsafe use.

Cost

The acquisition costs of the different uterotonic drugs will vary from country to country, and by manufacturer, and it is therefore difficult to give actual cost estimates for each of the uterotonic drugs. In any consideration of uterotonic drug costs, acquisition, administration and storage costs should all be evaluated and compared.

In a calculation of the **acquisition cost** for ergometrine, oxytocin and Syntometrine, the cost of a sterile syringe and needle should be added to the cost of an ampoule of the product. Because oxytocin in the Uniject™ device (OiU) is supplied as a unit, acquisition cost will be the cost of

the unit. In general, the acquisition costs for oxytocin in ampoules and ergometrine are essentially the same,[7] while the fixed drug combination of oxytocin and ergometrine (Syntometrine) and OiU, with or without the time temperature indicator (TTI), are likely to be more expensive in most countries than oxytocin in ampoules or ergometrine alone. The cost of misoprostol tablets is usually somewhat more than ampoules of oxytocin or ergometrine and less than OiU.

Administration costs of oxytocin in ampoules, ergometrine, and the fixed drug combination of oxytocin and ergometrine are likely to be generally equivalent. Administration costs of OiU will be less than uterotonic drugs supplied in ampoules because the syringe is pre-loaded and can easily be used by a less skilled birth attendant authorized to give injections. Administration costs of misoprostol will be less because it does not require a syringe and needle, a skilled birth attendant trained and authorized to administer injections, or consumables and supplies to ensure safe injection and infection prevention practices.

Storage costs may be higher for ergometrine (and the fixed drug combination of oxytocin and ergometrine) because it requires temperature-controlled transport and storage and protection from light. Oxytocin is more stable and storage costs may be less than ergometrine.[8] OiU takes up more room in the cold chain because of packaging. If the TTI is fixed on the OiU, the acquisition cost would be higher, but this difference could be made up by the cold chain flexibility afforded by the TTI. Costs for storage of misoprostol will be minimal because it is the most stable of the three uterotonic drugs and can be stored at room temperature. However, there is evidence that packaging of misoprostol can have a degrading effect, and misoprostol products using aluminum blister packs appear to have the least degradation and should be recommended where available.

Availability

The availability of the uterotonic drug may be an important consideration when choosing which uterotonic drug to use. A uterotonic drug is more "available" if it is:

- Locally manufactured
- Readily available in public and private pharmacies
- Registered
- Listed on the Essential Medicines List (EML) for prevention and treatment of PPH

The availability of each uterotonic drug will vary from country to country.

Efficacy

Prevention

The evidence for comparison of oxytocin and ergometrine used for the prevention of PPH is based on a systematic review conducted by the WHO[9] of studies that compared ergometrine (or derivatives) and oxytocin, or ergometrine alone versus the fixed dose combination of ergometrine and oxytocin. For the outcomes related to blood loss and transfusion, the results of the trials do not show a difference between lower doses of oxytocin and the recommended dose of ergometrine. The fixed drug combination of oxytocin and ergometrine was associated with less use of additional uterotonic drugs. The available comparisons are limited, but while a major difference in the benefits of oxytocin and ergometrine appears unlikely, there are numerous advantages to using oxytocin rather than ergometrine, including cost, stability, lack of contraindications and few adverse effects.

The evidence for comparison of oxytocin and misoprostol used for the prevention of PPH is based on a systematic review conducted by the WHO[1] of studies that compared use of oxytocin and misoprostol for AMTSL. Blood loss of 1000 mL or more was increased with misoprostol

when compared to oxytocin 10 IU IM; there was no statistically significant difference in the use of blood transfusion with misoprostol compared with oxytocin. However, there was more use of additional uterotonic drugs with misoprostol.

Based on results of efficacy studies, the WHO[1] recommends that when choosing a uterotonic drug for prevention of PPH:

1) Oxytocin should be the uterotonic drug of choice for prevention of PPH during the third stage of labor
2) Syntometrine and ergometrine should be the uterotonic drugs of choice when oxytocin is not available and there are no contraindications to their use
3) Misoprostol should be the uterotonic of choice when injectable uterotonic drugs are not available or the person administering the drug is not authorized to give injections.

Treatment

The WHO assessed the value of oxytocin, ergometrine, fixed dose combination of oxytocin and ergometrine, and misoprostol (tablet form used via oral, sublingual and rectal routes). Based on their assessment, they made the following recommendations concerning use of uterotonic drugs for treatment of PPH[10]:

1) For management of PPH, oxytocin should be preferred over ergometrine alone, a fixed-dose combination of ergometrine and oxytocin, carbetocin and prostaglandins.
2) If oxytocin is not available, or if the bleeding does not respond to oxytocin, ergometrine or oxytocin-ergometrine fixed-dose combination should be offered as second-line treatment.
3) If the above second-line treatments are not available, or if the bleeding does not respond to the second-line treatment, a prostaglandin should be offered as the third line of treatment.
4) Misoprostol may be considered as a third line of treatment for the management of PPH, because of its ease of administration and low cost compared with injectable prostaglandins.
5) There is no added benefit of offering misoprostol as adjunct treatment for PPH in women who have received oxytocin during the third stage of labor. Where oxytocin is available, and is used in the management of the third stage of labor, oxytocin alone should be used in preference to adjunct misoprostol for the management of PPH.

Response time

Of the injectable uterotonic drugs, oxytocin acts the most rapidly, while ergometrine has the benefit of sustained action. The fixed drug combination of oxytocin and ergometrine combines the rapid action of oxytocin with the sustained action of ergometrine.

Oral misoprostol acts moderately quickly, within 8–11 minutes, and has a moderately long sustained action of up to 2 hours. Table 5 reviews response time and length of action for the most common route used when administering uterotonic drugs for prevention and initial management of PPH.

Table 5. Response time and length of action of selected uterotonic drugs

Uterotonic drug	Route	Response time and length of action
Oxytocin	Intramuscular injection	• Onset of action: 2–3 minutes • Duration of action: ≈15–20 minutes
	Intravenous injection	• Onset of action: 1 minute • Duration of action: ≈15–20 minutes
Misoprostol*	Oral†	• Onset of action: 8 minutes • Duration of action: ≈2 hours
	Sublingual	• Onset of action: 11 minutes • Duration of action: ≈3 hours
	Vaginal	• Onset of action: 20 minutes • Duration of action: ≈4 hours
	Rectal	• Onset of action: 100 minutes • Duration of action: ≈4 hours
Ergometrine**	Intramuscular injection	• Onset of action: 6–7 minutes • Duration of action: 2–4 hours
Syntometrine	Intramuscular injection	• Onset of action: 2–3 minutes • Duration of action: 2–4 hours

* Oral and sublingual routes for misoprostol are preferred for prevention and treatment of PPH.
** IV and oral routes for ergometrine are not recommended.

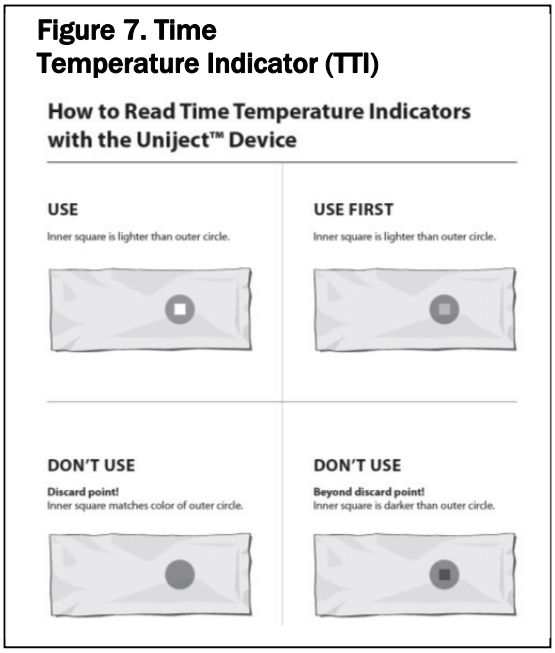
Stability

The stability of a drug is defined by how well it maintains active ingredient potency (and other measures such as pH) when stored over time. Two factors can influence the effectiveness of injectable uterotonic drugs: temperature and light. Of the injectable drugs, oxytocin is more stable than ergometrine (and the fixed drug combination of oxytocin and ergometrine) when exposed to heat and light (when cold/dark storage is not possible).

While misoprostol does not require special transport or storage requirements to protect it from heat or light, manufacturers recommend protecting the product from humidity. Double-alu blisters protect misoprostol the best from humidity, and are therefore recommended for misoprostol products.

Oxytocin in the Uniject™ device is the first uterotonic drug to use TTIs (Figure 7). TTIs, similar to

Figure 7. Time Temperature Indicator (TTI)



† Information on oral, sublingual, vaginal and rectal misoprostol is from: Tang OS, Gemzell-Danielsson K and Ho PC. 2007. Misoprostol: Pharmacokinetic profiles, effects on the uterus and side effects. *International Journal of Gynecology and Obstetrics* 99: S169–S167.

vaccine vial monitors used in immunization programs, allow precise monitoring of cumulative temperature exposure. They assure quality and potency of the uterotonic drug at the time that the drug is administered. Use of the TTI does not increase stability or negate the need for cold chain, but allows some flexibility in the cold chain as providers will know if the oxytocin has been exposed to heat to a point where potency can no longer be guaranteed.

Storage of uterotonic drugs

Pharmaceutical companies conduct stability studies to determine the appropriate shelf-life, storage conditions and expiration dating for safe storage of the uterotonic drug they produce. A manufacturer will recommend storage conditions based on the conditions under which it has performed stability studies, and will set the expiry date to be consistent with this. It is therefore important to read storage recommendations made by the manufacturer.

Since ergometrine and Syntometrine are sensitive to heat and light, and oxytocin is sensitive to heat, following storage guideline is critical to ensure the optimal effectiveness of injectable uterotonic drugs. When drugs are inadequately stored, drug effectiveness can diminish, posing serious consequences for the postpartum woman.

Recommended guidelines for transporting and storing specific uterotonic drugs are noted in Table 6.

Table 6. Recommended guidelines for transport and storage of uterotonic drugs

Drug	Transport	Storage
Oxytocin	May stay out of the cold chain for up to 3 months if temperature is 30° C or less	• Keep refrigerated at 2–8°C • Check manufacturer's recommendations – some manufacturers are producing oxytocin that is more heat stable than previously available • May stay out of the cold chain for up to 3 months if temperature is 30° C or less
Misoprostol	Protect from humidity	• Store at room temperature in closed container and protected from humidity
Ergometrine	Unrefrigerated transport **in the dark** is possible if no more than 1 month at 30°C or less; Protect from freezing	• Store in the dark • Keep refrigerated at 2–8°C • Store in closed container • Protect from freezing
Syntometrine	Unrefrigerated transport **in the dark** is possible if no more than 1 month at 30°C or less; protect from freezing	• Store in the dark • Keep refrigerated at 2–8°C • Store in closed container • Protect from freezing

Storage practices in health care facilities vary widely and may not follow guidelines for correct storage. For example, vials of uterotonic drugs might be kept on open trays or containers in the labor ward, leaving them exposed to heat and light. Pharmacists, pharmacy managers and birth

attendants using the oxytocin must carefully read and follow recommended guidelines for transporting and storing uterotonic drugs.

Adverse effects

All of the uterotonic drugs have a side effect profile. However, a comparison of oxytocin versus the fixed drug combination (5 IU oxytocin + 0.5 mg ergometrine) showed a higher rate of adverse effects in women treated with the combination drug: nausea, vomiting and high blood pressure. A lower rate of manual removal of placenta was seen in women treated with oxytocin. Overall, ergometrine alone or in combination with oxytocin is associated with more adverse effects, especially with regard to causing high blood pressure.

Misoprostol is associated with an increase in shivering, diarrhea and temperature higher than 38°C. However, these adverse effects are transient, usually mild, tolerable to women and easily managed by providers.

Ergometrine alone or in combination with oxytocin is associated with serious and potentially fatal results if used in women with existing hypertension, heart disease, or pre-eclampsia/ eclampsia.

Contraindications

Misoprostol and oxytocin have no known contraindications for use for prevention and treatment of PPH in the immediate postpartum period.

Ergometrine (and the fixed drug combination of oxytocin and ergometrine) is contraindicated in women with a history of hypertension, heart disease, pre-eclampsia or eclampsia.

Presentation

Oxytocin, ergometrine and the fixed drug combination of oxytocin and ergometrine (Syntometrine) are supplied in glass ampoules. Oxytocin is available in ampoules containing 3 IU/mL, 5 IU/mL and 10 IU/mL. Ergometrine is available in ampoules containing 200 mcg/mL or 500 mcg/mL.‡ Syntometrine injection contains synthetic oxytocin 5 IU/mL and ergometrine maleate 0.5 mg/mL and is supplied in 1 mL ampoules. Providers must first break open the ampoules and then draw up the required dose into a syringe. If oxytocin is supplied in 5 IU/mL ampoules, two ampoules are required to get the recommended dose for AMTSL; if ergometrine is supplied in 500 mcg/mL ampoules, then 0.4 mL will need to be drawn up to get the recommended dose for AMTSL. Ampoules are sometimes very hard to open, which may result in providers getting cuts from broken glass and/or wastage of ampoules. In addition, users of uterotonic drugs supplied in ampoules must be able to read the strength of the drug in the ampoule, calculate the number of milliliters required to get the correct dose, open a sterile needle/syringe and measure out the correct dose.

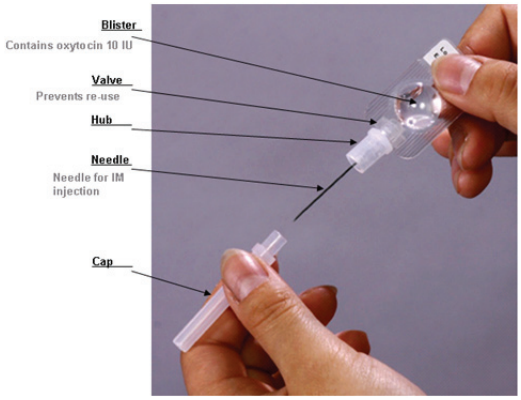
Oxytocin is also available in an auto-disable, prefilled, single-dose injection device, called Uniject™ (Figure 8). The Uniject™ device with pre-filled with 10 IU of oxytocin has an intramuscular needle, and is packaged in a foil pouch. The Uniject™ device was designed with the following features:

- **Single dose**—to minimize wastage and facilitate outreach to individual patients
- **Prefilled**—to ensure that the correct dose is given, and to simplify procurement and logistics

‡ The recommended dose of ergometrine for AMTSL is 200 mcg.

- **Nonreusable**—to minimize patient-to-patient transmission of blood-borne pathogens
- **Easy to use**—to allow use by health workers who do not normally give injections
- **Compact size**—for easy transport and disposal

Figure 8. Uniject™ device



Some cadres may find it challenging to break ampoules, load syringes without contaminating the product or the needle/syringe, or measure the correct dose. If these cadres are going to be authorized to practice AMTSL, having access to the Uniject™ device may increase the likelihood that women assisted by them have access to oxytocin for prevention and/or treatment. One disadvantage of the Uniject™ device is that it takes up more room in the cold chain than an ampoule.

Misoprostol is supplied in 200 mcg tablets for prevention and treatment of PPH.

3.2. REVIEW REQUIREMENTS FOR ADMINISTRATION OF A UTEROTONIC DRUG

Administering any uterotonic will require:

- A health worker authorized and trained to distribute and/or provide the drug
- A health worker who understands the timing and dose of the drug
- A health worked trained to recognize and manage side effects of the drugs
- Application of manufacturer-specific storage recommendations

Please note: In settings where health care providers distribute misoprostol to women during pregnancy or to community health workers for use in the third stage of labor, the only requirement will be that providers are trained to educate health workers, women and their families about the correct and safe use of misoprostol after birth of the baby.

In addition to the above requirements, administering injectable uterotonic drugs will also require:

- A health worker authorized and trained to give injections

Please note: A health worker may be an SBA, a birth attendant not considered "skilled," or a community-based provider who may not attend the birth but is present at the time of birth to administer a uterotonic drug.

- Consumables and supplies to ensure adequate infection prevention and injection safety measures
- Cold chain

- For ergometrine or Syntometrine: a health worker able to measure BP and a functioning BP machine and stethoscope

3.3. COMPARE ALTERNATIVE DRUG OPTIONS FOR PREVENTION AND TREATMENT OF PPH

The table below provides an overview of advantages, disadvantages and requirements of the most commonly available uterotonic drugs.

Table 7. Advantages, limitations and requirements of uterotonic drugs

Drug	Route	Advantages	Disadvantages	Requirements

Oxytocin in ampoule	Injectable (needle and syringe)	• Recommended by WHO as the preferred uterotonic for PPH
		• No contraindications for postpartum use
		• Few side effects
		• Acts within 2–3 minutes after IM administration
		• Inexpensive
		• Takes little space in the cold chain
		• May stay out of the cold chain for up to 3 months if temperature is 30° C or less
			• Effect lasts only about 15–30 minutes
			• Requires cold chain (recommendation is to store at 2–8°C)
			• Needle and syringe could potentially be re-used
			• Needle and syringe take up relatively more space in the sharps disposal box
				• **Infrastructure:**
				  • Cold chain
				• **Provider:**
				  • Authority to administer injections
				  • Training in injection administration
				  • Ability to safely break ampoules and measure the dose into the syringe
				  • Training in evidence-based regimen and identification and management of side effects
				• **Consumables:**
				  • Infection prevention measures
				  • Injection safety
				• **Logistics:**
				  • Requires two logistics systems: oxytocin and needles/syringes

Drug	Route	Advantages	Disadvantages	Requirements

Oxytocin-Uniject™ (OiU)	Injectable, Uniject™ device	• Recommended by WHO as the preferred uterotonic for PPH
		• No contraindications for postpartum use
		• Few side effects
		• Acts within 2–3 minutes after IM administration
		• Simplifies dosing and administration
		• Cannot be re-used
		• May stay out of the cold-chain for up to 3 months if temperature is 30° C or less
		• Uses less space in safety boxes when disposed of
		• Needle/syringe and oxytocin are procured together
		• If TTI included, assures quality and allows use in facilities with limited or no cold chain availability
			• Effect lasts only about 15–30 minutes
			• Cost
			• Uses relatively more space in the cold chain
				• **Administrative:**
				  • Requires registration in many countries
				• **Infrastructure:**
				  • Cold chain
				• **Provider:**
				  • Authority to administer injections
				  • Training in injection administration
				  • Training in evidence-based regimen and identification and management of side effects
				• **Consumables:**
				  • Infection prevention measures
				  • Injection safety
				• **Logistics:**
				  • Only one logistics system required

Drug	Route	Advantages	Disadvantages	Requirements

Misoprostol	Oral, sublingual	• Recommended by WHO in the absence of AMTSL by health workers trained in its use
		• Acts within 3–5 minutes
		• Effect lasts 75 minutes
		• Tablet—does not require injection
		• Does not require refrigeration
		• No known contraindications for postpartum use
			• Common side effects include shivering and elevated temperature
			• Less effective than oxytocin and ergometrine
			• Price varies from one country to another
				• **Administrative:**
				  • Requires registration for PPH prevention and treatment in many countries
				• **Infrastructure:**
				  • No cold chain requirements
				• **Provider:**
				  • Training in evidence-based regimen and identification and management of side effects
				  • Training in misoprostol use and in how to educate women / families to use it
				• **Logistics:**
				  • Only one logistics system required

Drug	Route	Advantages	Disadvantages	Requirements

Ergometrine (Methergine)	Injectable*	• Recommended by WHO as the second line uterotonic for PPH, if injectable uterotonic drugs are available
		• Effect lasts 2–4 hours.
		• Inexpensive
		• Takes little space in the cold chain
			• Acts within 6–7 minutes IM
			• Contraindicated in women with a history of hypertension, heart disease, retained placenta, pre-eclampsia or eclampsia
			• Causes tonic contractions (may increase risk of retained placenta)
			• Side effects: nausea, vomiting, headaches, and hypertension
			• Needle and syringe could potentially be re-used
			• Takes up relatively more space in the sharps disposal box
				• **Infrastructure:**
				  • Cold chain
				• **Provider:**
				  • Authority to administer injections
				  • Training in injection administration
				  • Ability to safely break ampoules and measure the dose into the syringe
				  • Knowledge of contraindications, side effects and management of side effects
				  • Able to measure BP
				• **Equipment:**
				  • BP machine / stethoscope
				  • Consumables:
				  • Infection prevention measures
				  • Injection safety
				• **Logistics:**
				  • Two logistics systems required: ergometrine and needles/syringes

Drug	Route	Advantages	Disadvantages	Requirements
Syntometrine (Fixed drug combination of 5 IU oxytocin plus 0.5 mg ergometrine)	Injectable	• Recommended by WHO as the second line uterotonic for PPH • Combined advantages of oxytocin and ergometrine	• Combined disadvantages of oxytocin and ergometrine • Relatively more expensive than ergometrine and oxytocin	• All requirements are the same as for ergometrine

*Oral ergometrine is no longer recommended.

3.4. MAKE A DECISION ABOUT WHICH UTEROTONIC DRUGS TO MAKE AVAILABLE FOR PREVENTION AND TREATMENT OF PPH AT EACH POINT OF CARE

You have now reviewed: 1) the number of vaginal births occurring in the facility and community, and 2) the types of birth attendants assisting women during both facility- and community-based births. You have also made a decision about where uterotonic drugs should be available; review Table 3 on deciding whether a strategy should be developed for making uterotonic drugs accessible by type of birth attendant and place of birth. Based on your strategy, you must now choose first-, second- and third-line uterotonic drugs for women giving birth:

- In a facility with an SBA
- In a facility with a birth attendant not considered "skilled"
- In the community with an SBA
- In the community with a birth attendant not considered "skilled"
- In the community with a trained health worker present at the time of birth but who does not attend the birth
- In the community with a family member or no birth attendant

When choosing a mix of uterotonic drugs, you must take into consideration the availability of a sustainable cold chain and the type of birth attendant assisting the woman during labor, childbirth and the immediate postpartum period.

Recommendations for the situations where constraints of type of birth attendant or a sustainable cold chain may be present include, but are not limited to, the following:

- If a functional blood pressure machine and stethoscope and/or a birth attendant able to measure BP and respond to obstetric complications are not available, then ergometrine or the fixed combination of ergometrine and oxytocin should NOT be used.
- If a sustainable cold chain is not available, the preference will be for uterotonic drugs that are either heat stable or have the TTI affixed to show when the drug has been exposed to excessive heat over time. Theoretically, all injectable uterotonic drugs would benefit from having a TTI to assure potency. However, at this point in time (2011), only the oxytocin in the Uniject™ device has the TTI added to the packaging of each oxytocin dose.
- If a birth attendant is alone during birth, the preference will be for uterotonic drugs that are relatively easy to use.
- If a birth attendant who is not considered skilled is attending the birth, the preference will be for uterotonic drugs that are either relatively easy to use or do not require injection skills.
- If no birth attendant is available (that is, the woman is alone during birth or a family member assists her), the preference will be for uterotonic drugs that do not require injection skills.

Using data you have collected and information about uterotonic drugs, decision-makers may complete Figures 9 and 10 by writing in the first-line, second-line and third-line, etc., uterotonic drugs of choice for each type of birth attendant for both prevention and treatment of PPH in both community- and facility-based births.

Figure 9. First-, second- and third-line uterotonic drugs for community-based births

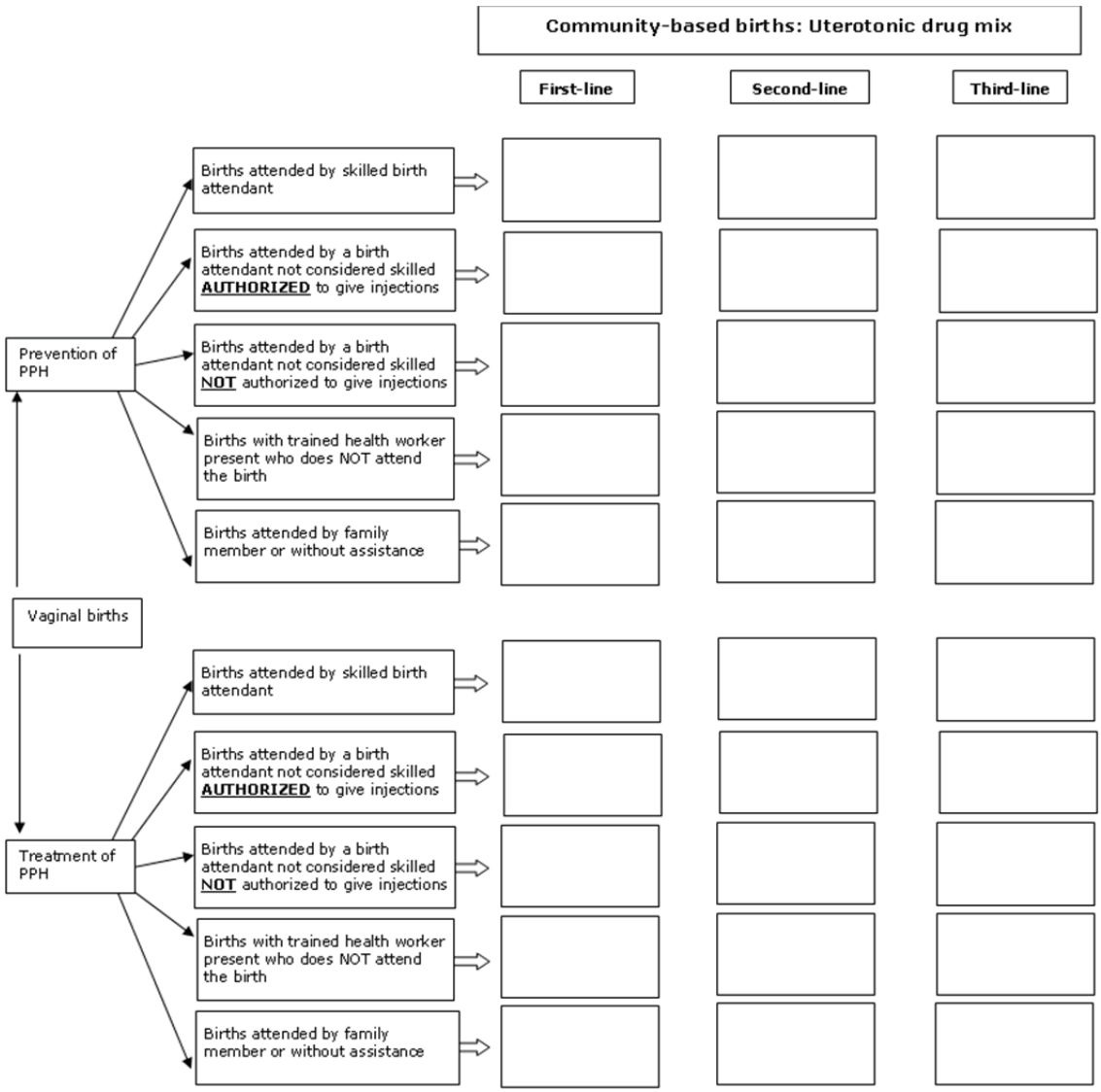
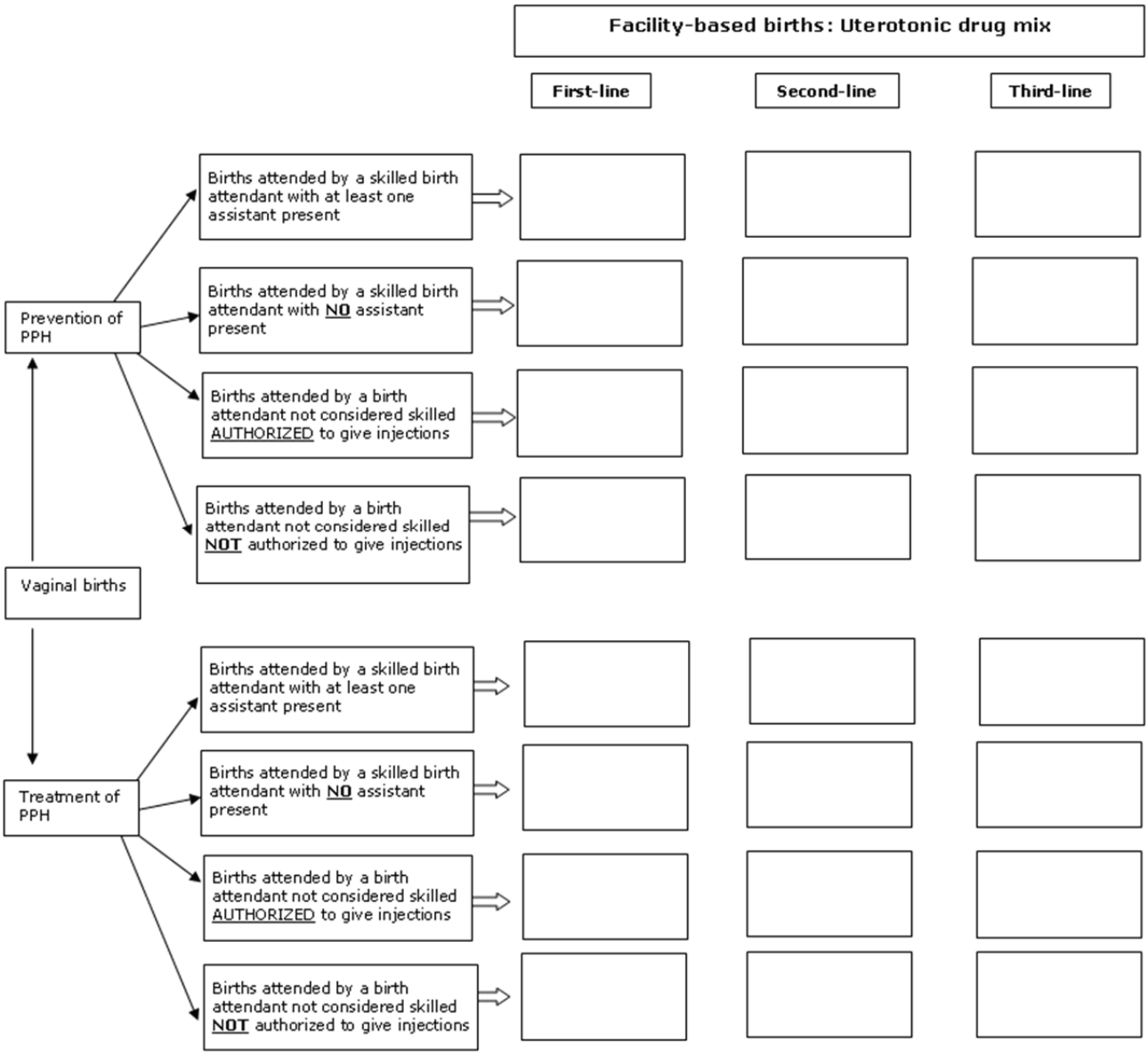


Figure 10. First-, second- and third-line uterotonic drugs for facility-based births



Country Make-Believe decided to make uterotonic drugs available (review Table 4 and Figure 6):

- For prevention and treatment for women giving birth with SBAs in the facility
- For prevention only for women giving birth in facilities with birth attendants not considered "skilled"
- For prevention and treatment for women giving birth in community with birth attendants not considered "skilled"
- For prevention only for women giving birth in community without any assistance or with the assistance of a family member

Country Make-Believe does not have trained health workers in the community and does not allow SBAs to attend births in the community. They have completed Figures 11 and 12, indicating first-, second- and third-line uterotonic drugs for prevent and treatment by each cadre of birth attendant and place of birth.

You will notice that decision-makers from Country Make-Believe have taken considerations of ease of use, stability and contraindications/adverse effects of the different uterotonic drugs when choosing a mix of uterotonic drugs that is dependent on the number and type of birth attendants present at the birth and the place of birth.

Figure 11. Country Make-Believe: First-, second- and third-line uterotonic drugs for community-based births

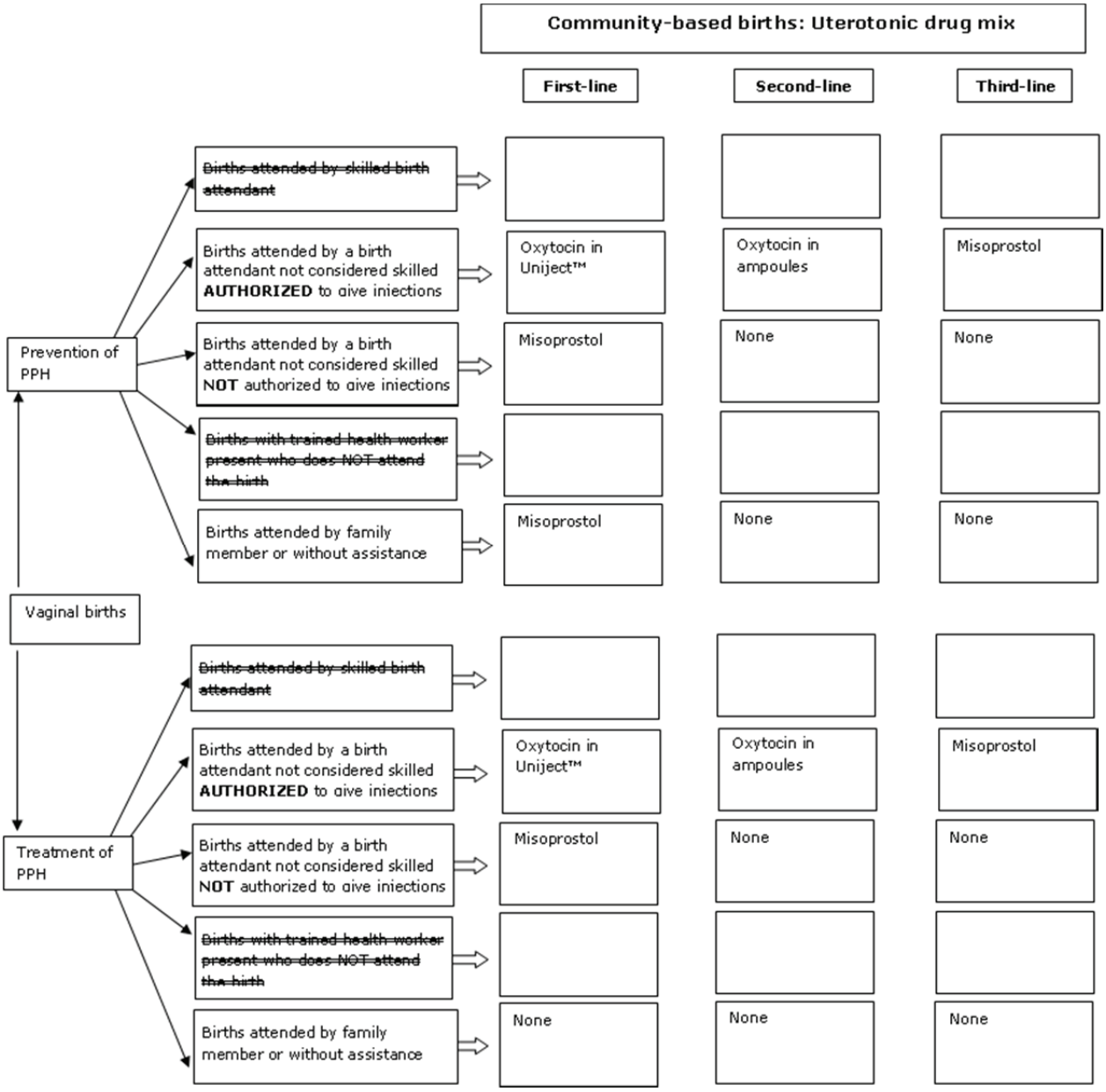
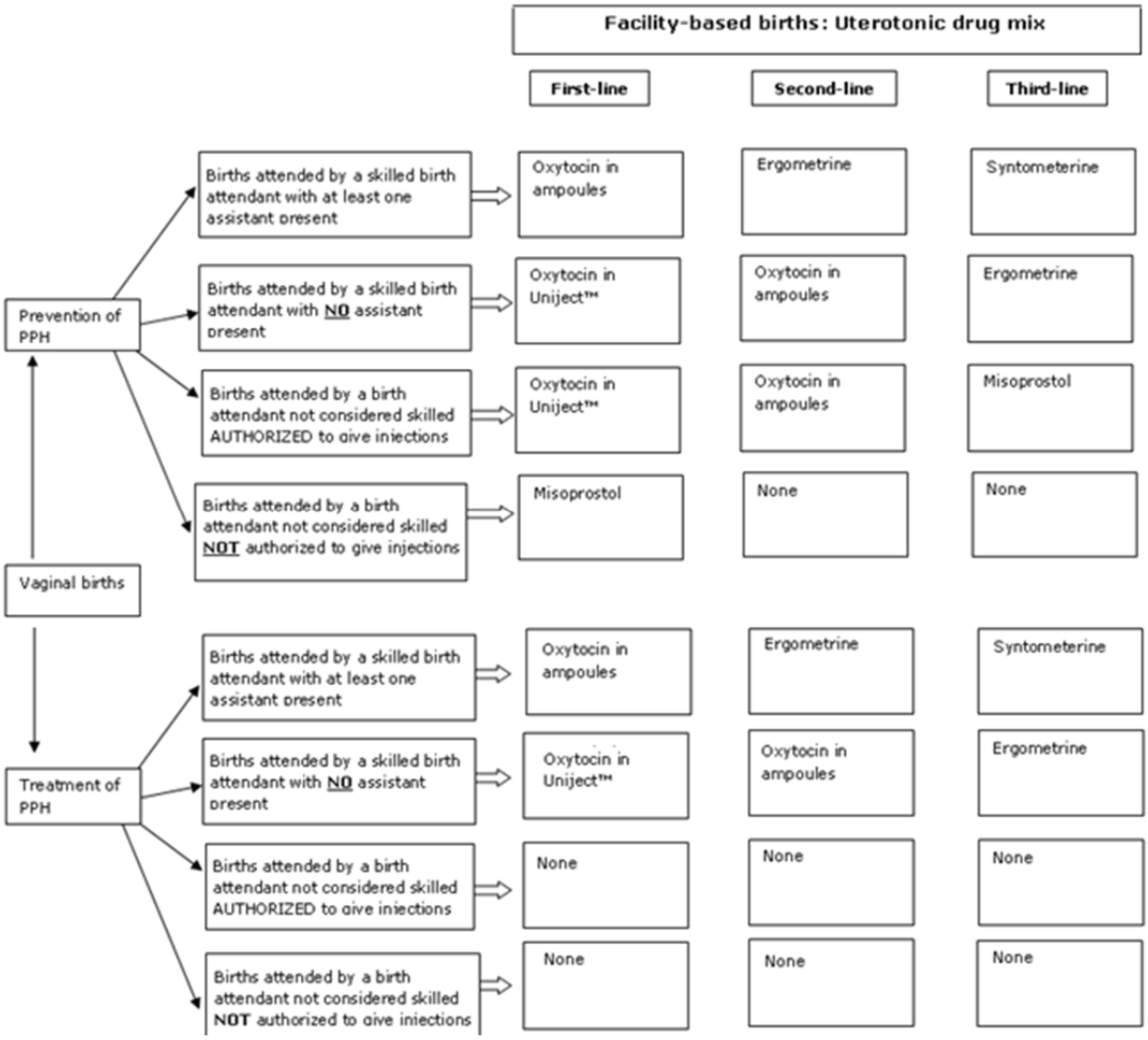


Figure 12. Country Make-Believe: First-, second- and third-line uterotonic drugs for facility-based births



NOTE: Please complete Exercise 3 in your workbook, completing the figures based on the strategy you developed in Exercises 2a and 2b.

4. Review Policies

The next step in the selection of a rational mix of uterotonic drugs is the review of policies and clinical guidelines relating to their use to ensure that they are in line with the strategy developed. This analysis will help decision-makers identify enabling and limiting factors to ensuring access to uterotonic drugs.

The first part of this step will involve reviewing which uterotonic drugs are locally manufactured, readily available in public and private pharmacies, registered in the country and listed in the EML for the prevention and treatment of PPH. This information can be gathered using Table 8. There is a series of "yes/no" questions about uterotonic drugs in Table 8 below. Decision-makers will circle "yes" or "no" for each question and each type of uterotonic drug. If certain uterotonic drugs or presentations that are part of the mix you have selected are not registered, not readily available or not listed on the EML for the prevention and treatment of PPH, a plan will need to be made to update the EML and seek registration.

Table 8. Important questions to ask about uterotonic drugs

	Oxytocin in ampoules	Oxytocin in Uniject™	Ergometrine	Syntometrine*	Misoprostol
Is the uterotonic drug locally manufactured?	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
Does the manufacturer follow Current Good Manufacturing Practices (C-GMP) standards?	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
Is the uterotonic drug readily available in public pharmacies?	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
Is the uterotonic drug readily available in private pharmacies?	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
Is the uterotonic drug registered in the country?	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
Is the uterotonic drug listed in the EML for prevention of PPH?	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
Is the uterotonic drug listed in the EML for treatment of PPH?	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No

*Syntometrine is the fixed drug combination of oxytocin (5 IU) and ergometrine (0.5 mg).

Country Make-Believe reviewed the status of uterotonic drugs in its country by completing Table 9. Decision-makers note that misoprostol and OiU are part of the strategy but are not registered in the country. The EML also does not include prevention and treatment of PPH indications for misoprostol. Of all the uterotonic drugs available in Country Make-Believe, oxytocin, ergometrine and misoprostol are the most readily available uterotonic drugs in the country.

Table 9. Country Make-Believe: List of uterotonic drugs registered and listed on the EML for prevention and/or treatment of PPH

	Oxytocin in ampoules	Oxytocin in Uniject™	Ergometrine	Syntometrine*	Misoprostol
Is the uterotonic drug locally manufactured?	(Yes) / No	Yes / (No)	(Yes) / No	Yes / (No)	Yes / (No)
Does the manufacturer follow Current Good Manufacturing Practices (C-GMP) standards?	(Yes) / No	(Yes) / No	(Yes) / No	(Yes) / No	(Yes) / No
Is the uterotonic drug readily available in public pharmacies?	(Yes) / No	Yes / (No)	(Yes) / No	Yes / (No)	(Yes) / No
Is the uterotonic drug readily available in private pharmacies?	(Yes) / No	Yes / (No)	(Yes) / No	Yes / (No)	(Yes) / No
Is the uterotonic drug registered in the country?	(Yes) / No	Yes / (No)	(Yes) / No	(Yes) / No	Yes / (No)
Is the uterotonic drug listed in the EML for prevention of PPH?	(Yes) / No	(Yes) / No	(Yes) / No	(Yes) / No	Yes / (No)
Is the uterotonic drug listed in the EML for treatment of PPH?	(Yes) / No	(Yes) / No	(Yes) / No	(Yes) / No	Yes / (No)

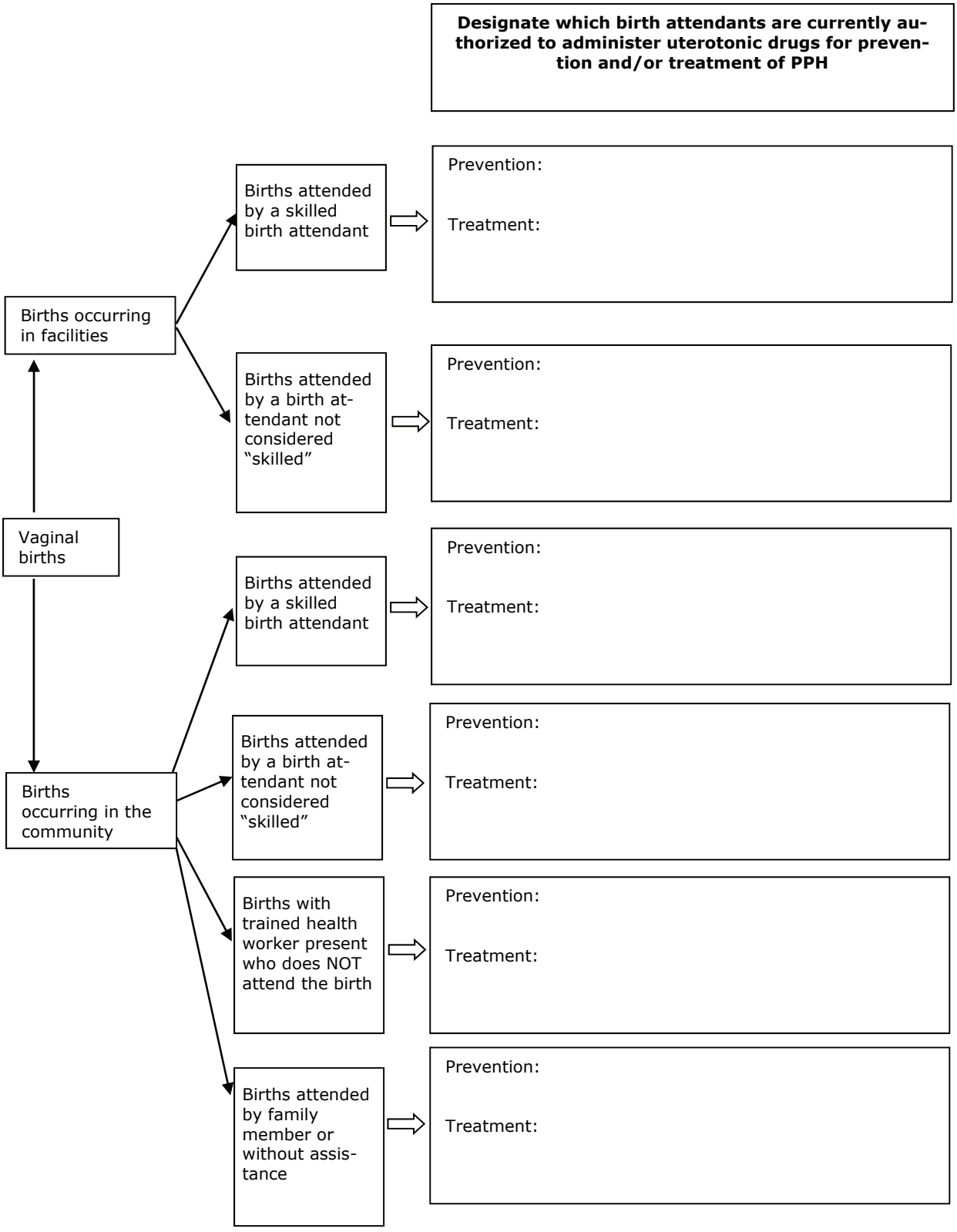
NOTE: Please complete Exercise 4a in the Workbook.

This second part of this step is an analysis to understand which type of birth attendant is authorized to administer which uterotonic drugs at each point of care (community and facility). If existing policies are not in line with your strategy—for example, only physicians may use misoprostol, birth attendants not considered "skilled" are not authorized to give injections, birth attendants not considered "skilled" are not authorized to administer oxytocin, etc.—a plan will

need to be made to promote policies that allow task shifting and ensure maximum access to uterotonic drugs.

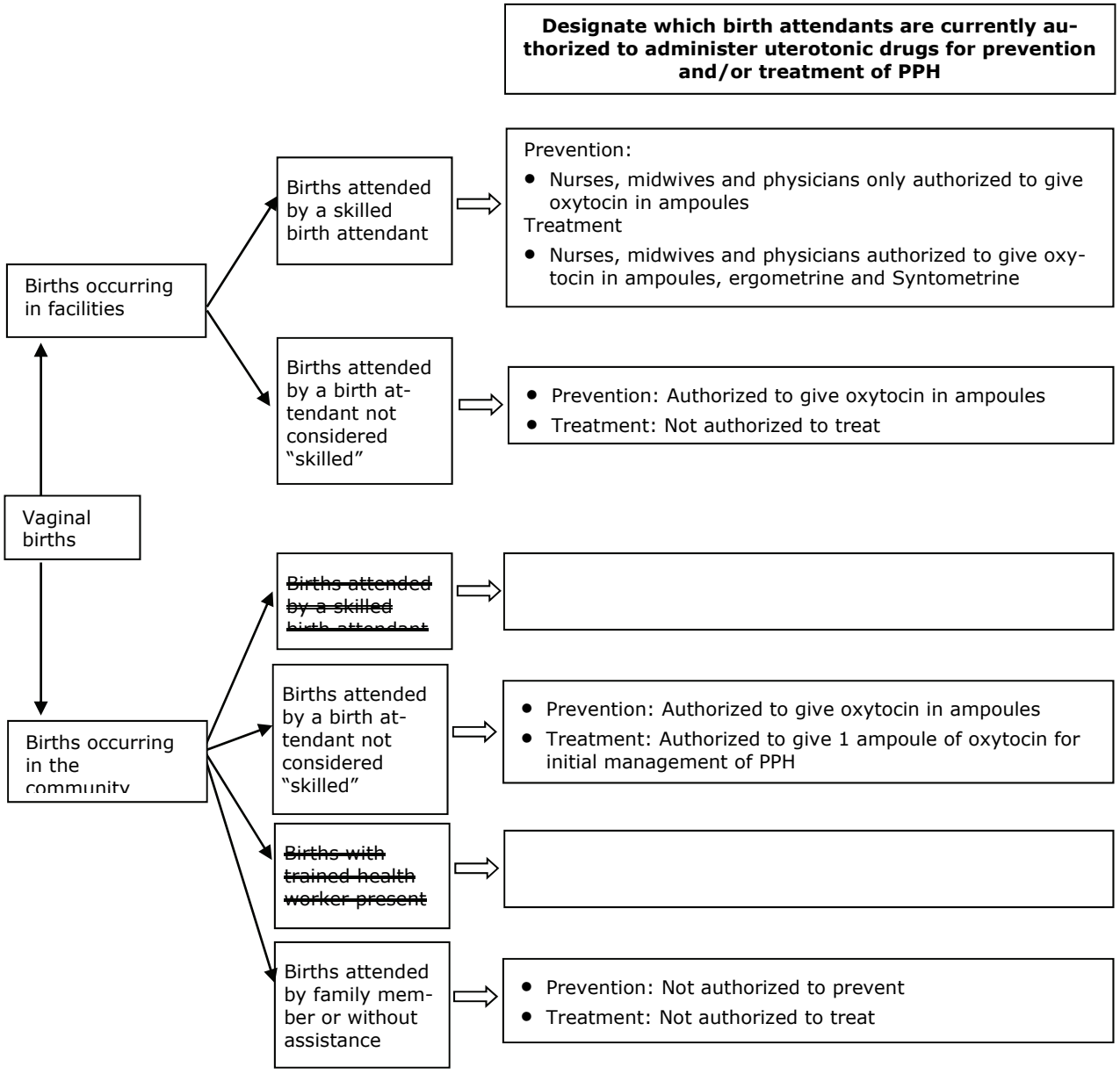
Gathering this information will require a review of policies and standards for provision of maternal care services and may require finding informed experts to complete Figure 13, on the next page, regarding administration of uterotonic drugs. For each type of birth attendant assisting births in either the facility or community, list the uterotonic drugs they are currently authorized to administer for prevention and treatment of PPH. This exercise will give you a complete picture of **who** (type of birth attendant) **does what** (administration of uterotonic drugs) **where** (community/facility), and will assist you in understanding if policies and standards regarding administration of uterotonic drugs are in line with your strategy. If policies and standards are not in line with your strategy, you will develop a plan for promoting standards and policies that are in line with international standards and evidence-based practices.

Figure 13. Birth attendants authorized to administer uterotonic drugs and points of care where administration of uterotonic drugs is authorized



Decision-makers from Country Make-Believe filled in Figure 14 to understand who currently does what and where—that is, which birth attendants are authorized to administer which uterotonic drugs at which points of care. Country Make-Believe currently has very restrictive policies concerning administration of uterotonic drugs (see Figure 14). The only uterotonic drug authorized for prevention of PPH is oxytocin. Only SBAs may use oxytocin, ergometrine or Syntometrine for treatment. And misoprostol is currently not being used for either prevention or treatment of PPH by any of the birth attendants.

Figure 14. Country Make-Believe: Situational analysis of WHO (type of birth attendant) DOES WHAT (administration of uterotonic drugs) WHERE (community/facility)



NOTE: Please complete Exercise 4b in the Workbook.

Existing policies should be consistent with a strategy that is based on international recommendations and scientific evidence. When existing policies for uterotonic drug use serve as barriers to access, efforts must be made to revise and update them. In some cases, restrictive policies may require advocacy efforts to change them. In other cases, experts will simply need to update the policies and/or guidelines based on international recommendations and scientific evidence. Certain uterotonic drugs and devices may also require registration in the country and will need to be added to the EML.

To understand which policies, guidelines and standards need to be aligned with your strategy that reflects best practices, you must compare your strategy with your analysis of "who does what where."

If existing policies, standards and clinical guidelines are already aligned with best practices but maternal morbidity and mortality due to PPH are still high, then a careful review of other factors influencing use of uterotonic drugs is in order. These could include, but are not limited to, pre- and in-service education programs, logistics and supply systems, supervision, and monitoring and evaluation systems.

If existing policies, standards and clinical guidelines are not aligned with your strategy, you will need to make a list of what should be changed so that they are aligned with best practices. These could include, but are not limited to:

- Addition of uterotonic drugs and/or presentations of uterotonic drugs to the EML
- Addition of PPH prevention and treatment indications for certain uterotonic drugs in the EML
- Registration of certain uterotonic drugs/presentations
- Broadening of the number of different uterotonic drugs that can be used for prevention and treatment
- Modification of scopes of practice for birth attendants not considered "skilled" who attend births in facilities and the community (e.g., authorization to give injections, authorization to administer uterotonic drugs for prevention and/or treatment of PPH, etc.)
- Authorization of the distribution of misoprostol by health workers trained in its use for prevention of PPH

Decision-makers in Country Make-Believe compared their strategy to increase access to uterotonic drugs (Figures 10 and 11) with the situational analysis of uterotonic drugs (Table 9) and the analysis of who currently does what where (Figure 14) and developed the following list of changes they will advocate for:

- Registration of misoprostol and OiU
- Addition of Uniject™ presentation of oxytocin and misoprostol in the EML
- Addition of PPH prevention and treatment indications for misoprostol in the EML
- Addition of ergometrine and Syntometrine as second- and third-line uterotonic drugs for prevention of PPH when an SBA is assisting the birth
- Provision of a uterotonic drug (oxytocin or misoprostol) during the third stage of labor without CCT in situations where no oxytocin is available or birth attendants' skills are limited

NOTE: Please complete Exercise 4c in the Workbook.

5. Update Policies

The most difficult and time-consuming element of ensuring access to uterotonic drugs is changing policies, standards and guidelines to align them with best practices. Changing these policies, standards and guidelines can be approached using a two-step process: 1) advocate with evidence for addressing the problem, and 2) create an enabling policy environment.[11]

Advocate with evidence for addressing the problem

The first step in the process will involve informing policymakers and giving them an evidence base with which to make decisions about changing policy. Useful activities include, but are not limited to:

Develop champions for PPH prevention and treatment
To ensure that PPH is on the national agenda, it is helpful to have champions at the national level who are convinced of the evidence and can persuasively advocate to decision-makers for PPH interventions. Key government officials, members of professional associations, pre-service and in-service educational programs and influential clinicians can all be powerful champions.

Demonstrate that PPH is a public health priority

- Hemorrhage is a leading direct cause of maternal deaths in the world.1
- PPH is preventable through use of simple interventions that should be offered to all women at the time of birth.
- PPH is treatable—but requires rapid recognition and care to prevent life-threatening consequences. A woman can die from PPH in just 2 hours.
- PPH is unpredictable, so every pregnant woman needs care during childbirth from an SBA. Yet, in developing countries, two-thirds of deliveries occur at home without an SBA. Women giving birth at home without a skilled provider are at increased risk of dying from complications, including PPH.

Provide evidence to key stakeholders and decision-makers to assist in shaping policy. This can be done by:

- Organizing information sessions providing the evidence base for recommended use of uterotonic drugs for PPH prevention and treatment.
- Conducting a series of technical updates presenting data on: country- or region-specific PPH prevalence and rates of skilled attendance at birth; global evidence on PPH prevention and management; and results from PPH prevention and management research and projects.
- Conducting surveys that study existing practices, policies and training curricula to understand where the country is in terms of PPH prevention and/or treatment.
- Designing research to help policymakers, program managers, and health service administrators understand factors that inhibit access to adequate, affordable uterotonic drugs for PPH preventions and treatment, especially for vulnerable populations.
- Identifying innovative interventions and approaches that can be tested and evaluated to demonstrate safety and program feasibility in their context, e.g., OiU, distribution of misoprostol during antenatal care visits, and training of birth attendants not considered skilled to use uterotonic drugs for prevention and/or treatment. Governments should choose a strategic approach that suits their situation, such as beginning with a demonstration project or pilot.

Create an enabling policy environment

The second step in the process will involve changing policy, standards and guidelines to align them with best practices. Useful activities include, but are not limited to:

Develop policies that allow a range of providers to offer PPH-related care
Policies need to be in place that ensure access to PPH prevention and treatment interventions by all women giving birth, regardless of the type of birth attendant or the place the woman chooses to give birth. To do this, policies must support authorization of different cadres of providers to deliver defined interventions for prevention and treatment of PPH. For example, in 2009 the Ministry of Health in Mali decreed that AMTSL and oxytocin can be used for the prevention of PPH by doctors, midwives, obstetric nurses and matrones (auxiliary midwives)—increasing national coverage of AMTSL.

Ensure that service delivery guidelines are up to date
National service delivery guidelines should reflect state-of-the-art and evidence-based interventions for prevention and treatment of PPH. These may be adapted from global reference materials, such as publications developed by the WHO. MOHs need to disseminate copies to all levels of the health care system to ensure compliance with the guidelines.

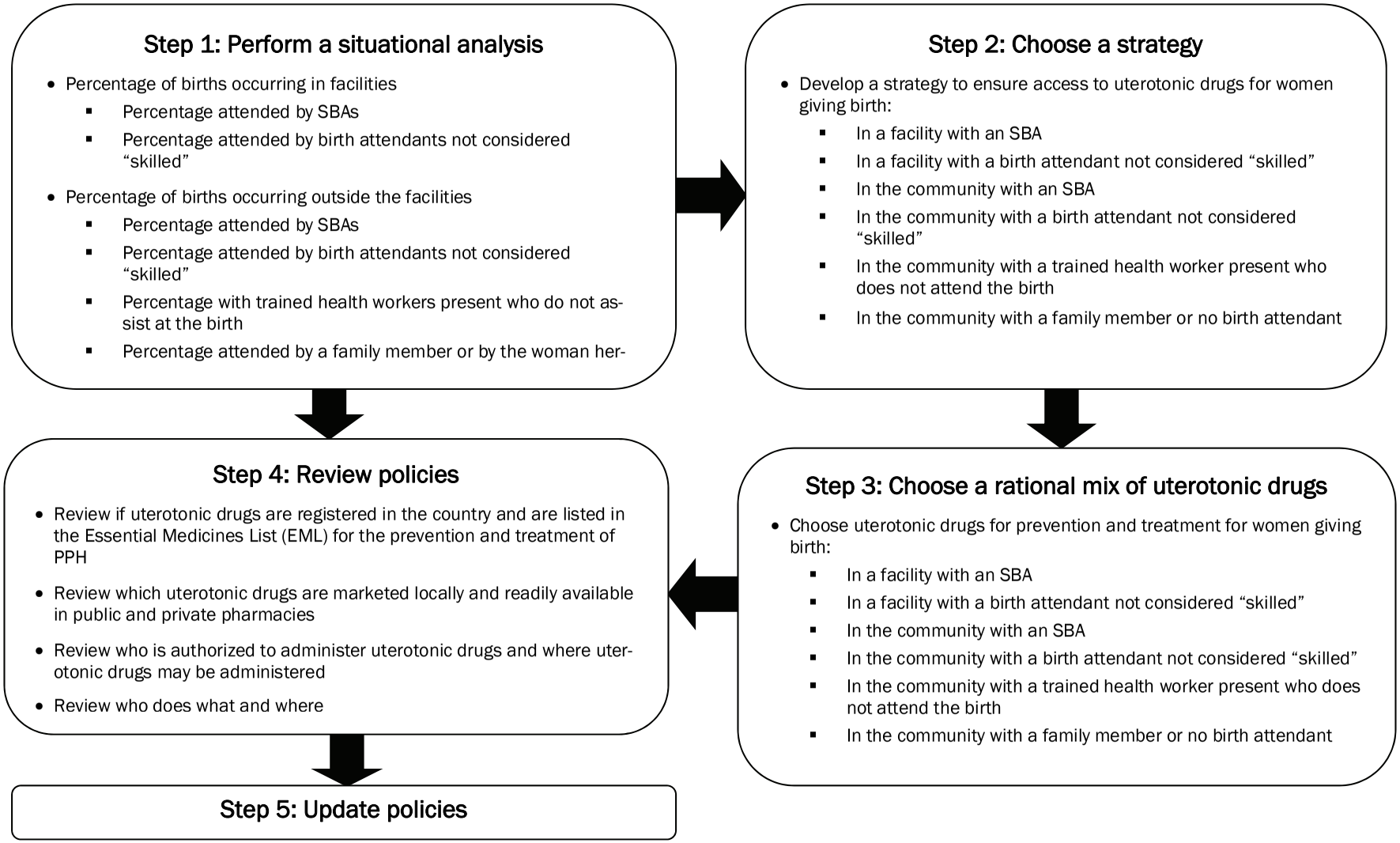
Address logistics needs for drugs, instruments and equipment
Ensure that both oxytocin and misoprostol are on the national EML and are tracked through national logistics management information systems (NLMIS). Although misoprostol is often available in countries for other uses, registration of the drug for importation and use for PPH prevention and treatment is needed.

NOTE: Please complete Exercise 5 in the Workbook.

Conclusion

The selection of a rational mix of uterotonic drugs for the prevention and treatment of PPH is essential for ensuring access to lifesaving interventions. This document, while not exhaustive, has attempted to guide policymakers, pharmacy managers, and Ministries of Health through the process of choosing uterotonic drugs for each type of birth attendant and at each point of care. Once a strategy for distribution of uterotonic drugs has been established, it is essential to link it with logistics systems to ensure that quantification, procurement, supply chain management and quality assurance of uterotonic drugs are integrated with drug procurement systems.

Overview of steps to take when selecting a rational mix of uterotonic drugs for the prevention and treatment of PPH



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