Economic Evaluation of Oxytocin in Uniject™ Injection System versus Standard Use of Oxytocin for the Prevention of Postpartum Hemorrhage in the Active Management of the Third Stage of Labor in Latin America and the Caribbean

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Abstract

TITLE

Economic evaluation of oxytocin in Uniject injection system versus standard use of oxytocin for the prevention of postpartum hemorrhage in Latin America and the Caribbean

BACKGROUND

Postpartum hemorrhage (PPH) is a leading cause of maternal death. Despite strong evidence showing the efficacy of oxytocin in preventing PPH, use of the drug for this purpose remains suboptimal. The Uniject injection system prefilled with oxytocin (OiU) has the potential advantage, due to its ease of use, to increase oxytocin coverage rates (OCR).

OBJECTIVES

To evaluate the cost-effectiveness of OiU in Latin America and the Caribbean (LAC).

METHODS

An epidemiological model was built to estimate the impact of replacing oxytocin in ampoules with OiU on the incidence of PPH, quality-adjusted life years (QALYs), and costs, from a health care perspective. A systematic search for data on epidemiology and cost studies was undertaken. A consensus panel among LAC experts was performed to quantify the expected increase in OCR as a consequence of making OiU available. Deterministic and probabilistic sensitivity analyses were performed.

RESULTS

In the threshold analysis the minimum required increment in the OCR to make OiU a cost-effective strategy ranged from 1.3% in Suriname to 15.8% in Haiti. In more than 60% of the countries, the required increment was below 5%. OiU could prevent more than 40,000 PPH episodes annually in LAC. In 27% of the countries, OiU was found to be cost saving. In the remaining 22 countries, OiU was associated with a net cost increment (0.005 to 0.847 2013 US dollars per delivery). OiU strategy ranged from being dominant to having an incremental cost-effectiveness ratio (ICER) of US$ 8,990 per QALY gained. In the great majority of countries these ICERs were below one GDP per capita.

CONCLUSIONS

OiU was cost-saving or very cost-effective in almost all countries. Even if countries can achieve only small increases in OCR by incorporating OiU, this strategy could be considered an efficient use of resources. These results were robust in the sensitivity analysis under a wide range of assumptions and scenarios.

Abbreviations

AMTSL	active management of third stage labor
BEmONC	basic emergency obstetric and newborn care
CEmONC	comprehensive emergency obstetric and newborn care
DALY	disability-adjusted life year
DHS	Demographic and Health Survey
GDP	gross domestic product
GDPPC	gross domestic product per capita
ICER	incremental cost-effectiveness ratio
IM	intramuscular
IMF	International Monetary Fund
IV	intravenous
LAC	Latin America and the Caribbean
LCU	local currency units
NGO	nongovernmental organization
OCR	oxytocin coverage rate
OiU	Oxytocin in Uniject
POPPHI	Prevention of Postpartum Hemorrhage Initiative
PPH	postpartum hemorrhage
PSA	probabilistic sensitivity analysis
PPP	purchasing power parity
QALY	quality-adjusted life years
SBA	skilled birth attendant
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
WHO	World Health Organization

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Introduction

Maternal health is one of the main global health priorities. One of the eight United Nations Millennium Development Goals (MDGs) is to reduce the maternal mortality rate by three-quarters between 1990 and 2015 *(1)*. According to World Health Organization (WHO) estimations, the maternal mortality rate (the number of maternal deaths per 100,000 live births) in South America ranges from 20 to 226, and from 16 to 523 in Central America and the Caribbean*(2)*.

Postpartum hemorrhage (PPH) is one of the leading causes of maternal death. In its severe form, it occurs in around 2%–3% of deliveries, with wide variation among regions. WHO statistics show that globally 14 million cases of PPH led to 127,000 deaths per year *(3–7)*. Besides its death toll, severe PPH (greater than 1,000 mL of blood loss) is associated with significant short- and long-term morbidity, including, among others, shock, coagulopathy, respiratory distress syndrome, and need for a hysterectomy, all of which may involve a prolonged hospital stay, admission to an intensive care unit, and higher health care costs. Twelve percent of women who survive PPH have severe anemia *(4)* and all women who survive severe PPH are significantly more likely to die in the year following the PPH *(8)*.

Clinical guidelines universally recommend active management of the third stage of labor (AMTSL) to prevent PPH *(9, 10)*. Active management of the third stage of labor (AMTSL) reduces incidence of PPH, length of the third stage of labor, need for blood transfusion, and need for uterotonic drugs to manage PPH. AMTSL includes routine administration of a uterotonic drug after birth of a baby and before delivery of the placenta, controlled cord traction to deliver the placenta, and uterine massage after delivery of the placenta *(11)*. In 2007 WHO initiated a randomized non-inferiority controlled trial comparing a simplified package of oxytocin 10 IU IM/IV without controlled cord traction and uterine massage versus AMTSL and found that the most important component of AMTSL is the administration of a uterotonic drug *(12)*. Oxytocin is the recommended drug of choice for prevention of PPH and the recommended dose is 10 IU by intramuscular (IM) injection or 5 IU as an intravenous (IV) bolus *(13, 14)*. A systematic review published by Chelmow et al. in 2010 showed that both AMTSL (with oxytocin) and the use of oxytocin alone had benefits in preventing PPH, reducing the need for blood transfusions, and reducing the number of women with postpartum anemia *(15)*. A Cochrane systematic review published by Cotter et al. showed that oxytocin given prophylactically resulted in blood loss reduction (RR 0.5; 95% CI 0.43–0.59) compared to no uterotonics *(16)*.

Although there is strong evidence showing the efficacy of oxytocin/AMTSL in preventing up to 60% of PPH cases *(17)*, its use in real-life settings, and thus its effectiveness, is suboptimal and heterogeneous *(18–23)*. Several barriers have been proposed for this "know-do gap": home deliveries, practitioner bias against the proposed interventions, lack of availability of oxytocin in delivery rooms, lack of skills to administer injections, and the need for oxytocin to be kept out of heat exposure *(24)* are some of the variables that might contribute to the variation in the utilization of oxytocin *(3)*.

The successful administration of oxytocin in ampoules requires a provider authorized to administer injections; a procurement system that adequately orders syringes, needles, and oxytocin; and a system to appropriately store oxytocin. Once assured that the material is available in the delivery room a series of steps should be followed: opening the ampoules, loading the syringe, administering the injection, and discarding the needle and syringe. The relative complexity of this process, particularly in those settings where only one skilled health provider attends the delivery, has also been proposed as an important barrier to achieving the desired rate of 100% oxytocin use *(25)*.

To increase the use of oxytocin to prevent PPH and overcome some of these barriers, a novel technology for the administration of oxytocin was developed in the last decade based on the Uniject™ injection system (Uniject). Uniject is an auto-disable injection system that received US patents between 1989 and 1993. It has been used as a means of delivering a variety of drugs *(25)*. The oxytocin in the Uniject injection system (OiU) offers some advantages over a standard ampoule and needle-syringe delivery format for the administration of oxytocin. OiU is prefilled with 10 IU of oxytocin, the recommended IM dose for the prevention and initial management of PPH. It combines a single dose with a syringe and sterile needle that cannot be reused (auto-disable). In addition, only the total loaded dose, 10 IU, can be administered. The Uniject injection system makes it easier, faster, and potentially safer to administer oxytocin by eliminating the need to open small glass vials of oxytocin, open a sterile syringe, and measure the correct dose of the drug before administration. This user-friendly product is well suited for use by less-skilled health workers in community and facility settings and by birth attendants who are alone when conducting a birth. For these reasons it is proposed that it could simplify the administration of oxytocin and thus increase the use of oxytocin by health care providers for prevention of PPH.

This ease of use of Uniject was evaluated in several studies. Tsu et al. published two surveys performed in a group of Indonesian and Vietnamese midwives in which 98% and 99% of all respondents stated that Uniject was easier to use and more practical than the conventional use of oxytocin in syringes. The great majority, 96% and 100% respectively, responded that they preferred Uniject over the regular syringes *(26, 27)*. Althabe et al. published a before-and-after quasiexperimental study in 2011 in Argentina, and 96% of the birth attendants responded that they believed that Uniject facilitated the administration of oxytocin *(28)*.

The clinical effectiveness of oxytocin, if correctly stored and properly administered, is equivalent whether the oxytocin is in the Uniject injection system or in ampoules. The main advantage of OiU would be its potential, due to its ease of use, to increase utilization of oxytocin, expand uterotonic protection, and increase the proportion of women who receive oxytocin for prevention of PPH.

This potential advantage of OiU versus oxytocin in ampoules has not yet been evaluated by any controlled trial. Strand et al. compared AMTSL using Uniject with physiological management. PPH was reduced from 40.4% to 8.2%, and severe PPH was reduced from 7.5% to 1% in the AMTSL group ($p < 0.01$) *(29)*. However, it is not possible to attribute this effect exclusively to Uniject, as the control arm did not use oxytocin. There are other studies (such as Althabe et al. *[28]*) in which Uniject oxytocin was compared with oxytocin in ampoules and in which a significant increase in the proportion of women who received oxytocin was observed in the Uniject arm. However, in these studies, the Uniject arm was accompanied by other measures to increase the use of oxytocin (reminders, medical training, or clinical practice guidelines), and therefore the benefit attributable to the use of Uniject itself cannot be isolated. Additionally, Glenton et al. concluded in a systematic review in 2013 that no studies evaluated the effects and safety of using compact, prefilled, auto-disable devices delivered by lay health workers *(30)*.

The reasons for the heterogeneous use and underutilization of oxytocin for the prevention of PPH vary according to country, birth setting, and other variables. In large hospitals health care providers have adequate training to administer IV or IM injections; therefore, the barriers to utilization of oxytocin are probably more related to practitioner bias if stock-outs of oxytocin are not a problem. Home birth attendants are less likely to be authorized to or have the skills needed to administer IV or IM injections, thus oxytocin use would be limited or absent. Thus, there are several reasons for heterogeneity in oxytocin use, and the potential impact on uterotonic coverage of using Uniject, if any, will likely vary.

To summarize, it can be assumed that OiU, once administered, is as effective as standard oxytocin, because the active molecule and route of administration are the same. However, the potential additional benefits of Uniject are related to its potential to expand use and increase

utilization rates by health care providers (i.e., though efficacy is the same, using Uniject could have greater effectiveness). However, no high-quality evidence exists that allow for the quantification of this potential benefit, as in most of the aforementioned studies, Uniject was part of a complex intervention that included several measures in addition to Uniject. In addition, even if there were an increase in oxytocin use that results from to the use of Uniject, it is uncertain whether this incremental benefit would justify its potential incremental costs and thus whether it could be deemed a cost-effective intervention.

To evaluate the cost-effectiveness of promoting the use of oxytocin in the Uniject injection system versus oxytocin in ampoules/vials, the differential effectiveness has to be compared to the differential cost of these strategies. Previous economic evaluations showed that Uniject was a cost-effective intervention in the settings where these studies were performed. In 2006 Seligman et al. published an economic evaluation of interventions for reducing PPH in developing countries (with data from Argentina, Bangladesh, India, and Nigeria, and regional estimates) *(31)*. In this study, all uterotonics proved cost-effective, and the cost per disability-adjusted life year (DALY) was found to be very similar between them.. Therefore, it was recommended that the selection of interventions assign relatively more weight to the criteria of access and associated health impacts and relatively less weight to economic efficiency. Results also indicate that oxytocin in Uniject was marginally more cost-effective than oxytocin monodose. Another economic evaluation, published by Tsu et al., showed a net incremental cost of AMTSL that suggested that the introduction of AMTSL in Vietnam could reduce the incidence of PPH without significantly increasing national health care costs; the cost to avert a case of PPH was US$ 2.10 with ampoules and US$ 4.52 with Uniject *(32)*. To date, there have been no economic evaluations of Uniject oxytocin in Latin America and the Caribbean (LAC) that allow concluding that a strategy of using Uniject oxytocin is good value for money, or cost-effective from the different countries´ perspective *(31)*.

The objective of this activity is to perform a full economic evaluation from the health care system perspective of countries in LAC that compares the cost-effectiveness of the current practice (oxytocin in ampoules administered by health care providers by syringe/ needles) as compared with the use of Uniject to administer oxytocin. In this study, the potential higher effects of Uniject relate exclusively to its potential capacity to increase the proportion of women receiving oxytocin for the prevention of PPH. We want to evaluate what would be expected in a given health system if oxytocin in ampoules was replaced entirely by Uniject, without mediating any significant educational measure or other specific intervention aimed at increasing the use of oxytocin.

Due to the lack of published scientific evidence to quantify how much of this effect (increased use of oxytocin) can be attributed to OiU, the analysis focuses on determining, on a country-by-country basis, the minimum increase in oxytocin coverage that would be necessary for Uniject to be a cost-effective intervention according to local cost-effectiveness thresholds. Base case results scenarios incorporating the most likely magnitude of benefit estimation, according to a regional expert panel, are included.

Methods

MEASURES OF EFFECTIVENESS AND ANALYTICAL METHODS

One of the main limitations in accurately estimating the cost-effectiveness of OiU versus oxytocin in ampoules is that there is no high-quality evidence about the relative effectiveness of Uniject (i.e., rate of change of use of oxytocin when using Uniject instead of standard oxytocin ampoules). This issue was approached in two ways:

1. Threshold analysis: The threshold analysis allowed for the estimation of the minimum increase in the rate of oxytocin use that would be necessary for OiU to be cost-effective. In other words, since accurate information about the relative effectiveness of OiU does not exist, the following question was examined: How much should OiU increase the rate of oxytocin use to be considered a cost-effective intervention? With this information, a decision-maker can judge whether this required increase in the use of oxytocin is realistic and can be obtained in her/his context by switching to Uniject.

For the derivation of the cost-effective increase in oxytocin use we set a desired incremental cost per quality-adjusted life year (QALY) gained for each country as equal to the per capita gross domestic product (GDP), and used the threshold analysis to derive this "cost-effective effect" (minimum increase in oxytocin use at which Uniject would be cost-effective). The value of one GDP per capita (GDPPC) has been suggested by the WHO as a threshold below which health care interventions can be considered cost-effective, and it is usually referenced in Latin America *(33)*. For example, a threshold of one GDPPC is explicitly considered in Mexico when deciding on the inclusion of a technology in the public health care system *(34)*.

2. Cost-effectiveness analysis: Second, a standard cost-effectiveness analysis was performed, using an estimate of the relative effectiveness of Uniject obtained from a regional expert panel as part of this study. Due to the lack of published scientific evidence to quantify the expected increase in oxytocin coverage rates as a consequence of making Uniject available, a consensus panel of experts in Latin-American maternal health was convened through a modified Delphi panel methodology (35).

Four hypothetical scenarios were built:

1. A comprehensive emergency obstetric and newborn care (CEmONC) facility with a baseline use of oxytocin of 50%
2. A CEmONC facility with a baseline use of oxytocin of 80%
3. A basic emergency obstetric and newborn care (BEmONC) facility with a baseline use of oxytocin of 50%
4. A BEmONC facility with a baseline use of oxytocin of 80%

The expert panel estimated the expected increase in oxytocin coverage rates if oxytocin in ampoules were replaced with Uniject in each of these scenarios (without any other intervention or educational measure tending to increase the use of oxytocin). The experts estimated a mean expected effect and a minimum and maximum effect to be explored in the sensitivity analysis. A second round was conducted in which the experts were able to see (anonymously) the results of the first round and were given the opportunity to modify their responses given in the first round. Finally, we obtained an average value from all the responses given at the second round.

Cost-effectiveness was evaluated using the incremental cost-effectiveness ratio (ICER). ICERs are calculated as the ratio the difference in costs (Δ costs) and the difference in benefits (Δ consequences) of two interventions. Costs include the costs of implementing the strategy (i.e., differential cost of Uniject) minus any medical costs averted (i.e., episodes of PPH). The change in consequences is the difference in health outcomes between the Uniject and the ampoule arm

(expressed as life years [LYs] or QALYs gained). Thus, the ICER reflects the additional cost for each additional unit of outcome obtained as a result of using Uniject.

It is important to note that there are other potential benefits of Uniject that were not included in this analysis. It has been postulated that Uniject may reduce infections caused by contaminated needles, decrease accidental needle injuries, and reduce sharps disposal volume. These potential benefits may have an effect on both clinical and cost outcomes. However, the results reported in this document account only for the benefits related to the eventual increase in oxytocin coverage rates due to the availability of OiU.

MODEL DESCRIPTION

As the study addresses an acute and static health problem and intervention, an epidemiological model that could capture the most relevant events and costs of the two interventions was designed. An epidemiological model was built to estimate the impact of replacing oxytocin in ampoules with Uniject oxytocin on the incidence of PPH, on the associated health consequences of PPH episodes, and on health care costs. Excel (Microsoft® Professional Edition 2010) with Visual Basic® Macros (Microsoft® Visual Basic 7.0) was selected as the model platform.

The International Society for Pharmacoeconomics and Outcomes Research criteria for model development and reporting were applied *(36)*. The model is based on the assumption that the baseline risk of PPH (i.e., the risk of PPH without mediating any preventive intervention) is similar for all deliveries in all countries *(37)*; and that this risk is modified by current rates of oxytocin use in each country. So, the current risk of PPH was estimated as:

R_PPH_country = P_Ox_country *R_PPH_basal * RR_Ox_protec + (1- P_Ox_country)* R_PPH_basal

[Formula 1]

Where *R_PPH_country* is the risk of PPH at the country level; *P_Ox_country* is the current oxytocin coverage rate; *R_PPH_basal* is the baseline risk of PPH (risk of PPH without mediating any preventive intervention); and *RR_Ox_protec* is the relative risk (RR) of PPH if oxytocin is administered before delivery of the placenta.

The methodology for the information source selection and parameter incorporation is available in the Outcomes and Parameters section.

As previously mentioned, we assumed that, if used at the same rate, oxytocin was equally efficacious in the Uniject injection system and in ampoules. This assumption is based on the fact that both strategies use the same drug and route of administration.

To achieve more accurate estimates, deliveries at three different facility levels were stratified: CEmONC, BEmONC (including other non-CEmONC health facilities such as health posts), and home. The current proportion of deliveries receiving oxytocin in each type of facility was estimated as:

P_Ox_CEMONC = P_Ox_country / (P_CEMONC + RR_Ox_BEMONC * P_BEMONC)

P_Ox_BEMONC = P_Ox_CEMONC * RR_Ox_BEMONC

[Formula 2]

Where *P_Ox_CEMONC* is the proportion of deliveries receiving oxytocin in CEmONC facilities; *P_Ox_country* is the current oxytocin coverage rate at the country level; *P_CEMONC* is the proportion of deliveries at CEmONC facilities; *RR_Ox_BEMONC* is the relative risk of oxytocin use at BEmONC facilities compared to CEmONC facilities; *P_BEMONC* is the proportion of

deliveries at BEmONC facilities; and *P_Ox_BEMONC* is the current oxytocin coverage rate in BEmONC facilities. The proportion of home deliveries receiving oxytocin is assumed to be 0% because in most cases in LAC these are deliveries occurring outside the health system.

The case fatality rate at the country level was estimated as:

R_death_PPH = R_death_delivery*P_Death_PPH

CF_country = R_death_PPH / R_PPH_country

[Formula 3]

Where *CF_country* is the case fatality rate at the country level; *R_death_PPH* is the current death rate from PPH (according to local statistics); *R_death_delivery* is the maternal mortality rate at the country level (according to local statistics); *P_Death_PPH* is the proportion of death due to PPH; and *R_PPH_country* is the risk of PPH at the country level (from Formula 1).

The specific case fatality rate for each health facility level was estimated as:

CF_CEMONC = CF_country /(P_CEMONC + P_BEMONC * RR_CF_BEMONC + P_Home* RR_CF_Home)

CF_BEMONC = CF_CEMONC * RR_CF_BEMONC

CF_Home = CF_CEMONC * RR_CF_Home

[Formula 4]

Where *CF_CEMONC* is the case fatality rate at CEmONC facilities, *CF_country* is the case fatality rate at the country level (from Formula 3); *P_CEMONC* is the proportion of deliveries at CEmONC facilities; *P_BEMONC* is the proportion of deliveries at BEmONC facilities; *RR_CF_BEMONC* is the relative risk of death from PPH at BEmONC facilities compared to CEmONC facilities; *P_Home* is the proportion of home deliveries; *RR_CF_Home* is the relative risk of death from PPH for home deliveries compared to CEmONC facilities; *CF_BEMONC* is the case fatality rate at BEmONC facilities; and *CF_Home* is the case fatality rate for home deliveries.

To estimate the effect of different scenarios of oxytocin use, the risk of PPH was estimated for each setting according to:

R_PPH_new = P_Ox_new * R_PPH_basal * RR_Ox_protec + (1- P_Ox_new) * R_PPH_basal

[Formula 5]

Where *R_PPH_new* is the new risk of PPH after the increase in the proportion of deliveries receiving oxytocin; *P_Ox_new* is the new proportion of deliveries receiving oxytocin; *R_PPH_basal* is the baseline risk of PPH (risk of PPH without mediating any preventive intervention); and *RR_Ox_protec* is the relative risk of PPH when receiving oxytocin.

And the new death rates from PPH were estimated as:

R_death_PPH_new = R_PPH_new * CF_sector

[Formula 6]

Where *R_death_PPH_new* is the expected new death rate from PPH after the increase in the oxytocin coverage rate; *R_PPH_new* is the new risk of PPH after the increase in the oxytocin coverage rate (from Formula 5); and *CF_sector* is the specific case fatality rate of PPH for each type of facility (from Formula 4) as the model assumes that the case fatality rate remains unchanged after

the intervention (the effect of increasing the proportion of deliveries receiving oxytocin is a reduction in the risk of PPH, but once a PPH occurs the case fatality of the episode is the same).

The expected effect of replacing oxytocin in ampoules with Uniject oxytocin was obtained from comparing the estimated risks of PPH (incidence) and death from PPH associated with the two interventions.

To estimate the minimum increase in oxytocin use that would be needed for Uniject to become a cost-effective intervention based on local cost-effectiveness thresholds we initially estimated the number of PPH episodes that would need to be prevented as:
PPH_avoid = Cost_intervention / (Cost_PPH + QALY_lost * CE_Thr)

[Formula 7]

Where *PPH_avoid* is the number of PPH episodes that would need to be prevented; *Cost_intervention* is the total incremental cost of replacing oxytocin in ampoules with Uniject in the places where the intervention is planned; *Cost_PPH* is the mean cost of each PPH episode; *QALY_lost* is the mean number of QALY lost for each PPH episode (these last two values obtained from the calibrated model for each country); and *CE_Thr* is the cost-effectiveness threshold (assumed to be one GDP per capita per QALY in the base case).

Then the new risk of PPH that would be necessary to achieve was estimated as:

R_PPH_objective = R_PPH_country – (PPH_avoid/total_deliveries)

[Formula 8]

Where *R_PPH_objective* is the risk of PPH that would be necessary to achieve for Uniject to be cost-effective; *R_PPH_country* is the risk of PPH at the country level (obtained from Formula 1); *PPH_avoid* is the number of PPH episodes that would be needed to be prevented (from Formula 7); and *total_deliveries* is the total number of deliveries.

And finally, the new oxytocin coverage rate at the country level that would be necessary to obtain was estimated as:

Objective_Ox_country = (R_PPH_objective - R_PPH_basal) / (R_PPH_basal*(RR_Ox_protec – 1)

[Formula 9]

Where *Objective_Ox_country* is the new oxytocin coverage rate at the country level that would be necessary to achieve for Uniject to be cost-effective; *R_PPH_objective* is the risk of PPH that would be necessary to achieve (from Formula 8); *R_PPH_basal* is the baseline risk of PPH (risk of PPH without mediating any preventive intervention); and *RR_Ox_protec* is the relative risk of PPH when receiving oxytocin.

TARGET POPULATION AND SUBGROUPS

The target population is composed of all women giving birth in a calendar year in each of the LAC countries. The initial age of women in the model varies according to the mean age at first birth in LACcountries.

SETTING AND LOCATION

All births in each country were included. Birth settings were categorized as CEmONC facilities, BEmONC facilities (including other non-CEmONC health facilities such as health posts), and home birth deliveries. The components of EmONC were delineated by WHO, UNICEF, and UNFPA at the beginning of 1990s *(38)*. EmONC facilities should be able to manage common maternal and newborn complications in order to decrease need for referral. In BEmONC facilities, providers can supply parenteral antibiotics, anticonvulsants, oxytocics, manual removal of placenta, manual vacuum aspiration for retained products, assisted instrumental delivery by vacuum extractor, and newborn resuscitation with mask. CEmONC should provide the same services as BEmONC plus have capability for surgery (for cesarean sections) and blood transfusions (some definitions of CEmONC also include advanced newborn resuscitation) *(39)*.

STUDY PERSPECTIVE

The study was carried out from the perspective of each country's healthcare sector. . Intervention startup costs (e.g., costs of research and development of intervention materials for physician prescription) are excluded such that all interventions are evaluated and compared as if operating under steady-state conditions.

COMPARATORS

We compared two alternatives: 1) current level of use of oxytocin in ampoules administered in "syringe + needles" for AMSTL, as it is the current main recommendation of most guidelines; and 2) switching to Uniject as the way to administer oxytocin.

Both of these interventions are part of a package of suggested interventions to prevent PPH:

- Standard use of oxytocin: oxytocin 10 IU IM/5 IU IV
- Uniject: 10 IU per dose IM

TIME HORIZON

We compared the progress of a hypothetical cohort of women giving birth in each LAC country in different birth settings. Women are followed throughout their lifetime.

DISCOUNT RATE

The analysis was carried out from the perspective of each country´s health care system. Expected future costs and benefits were converted into a present value amount through discounting. Following recommendations of most LAC guidelines *(40)*, costs and effects were discounted at a rate of 5% per annum (range 0%–10% for the sensitivity analysis).

OUTCOMES AND PARAMETERS

The health outcomes of each intervention, and their differences, are evaluated in terms of PPH, hysterectomies, deaths, LYs, and QALYs.

All the retrieved data were divided into two groups: global parameters (where due to the nature of the issue, we assume null or minimal differences among the countries); and country-specific data (which vary due to sociodemographic and health system differences between the countries).

Global parameters:

- Probability of PPH without oxytocin for prevention
- Conditional probability of severe PPH (given PPH)
- Hysterectomy due to severe PPH
- RR of PPH with oxytocin

- Case fatality ratio at CEmONC facilities
- Case fatality ratio at BEmONC facilities
- Case fatality ratio at home

Country-specific data:

- Average age at delivery
- Life expectancy *(41)*
- Annual deliveries
- Maternal mortality ratio (per 100,000 live-births)
- Use of oxytocin
- Case fatality rate (proportion of death on all PPH)
- Proportion of maternal death due to PPH (PPH/death)
- Proportion of CEmONC, BEmONC, and home deliveries
- RR of use of oxytocin

SEARCH STRATEGY

In order to make a direct comparison between OiU and oxytocin in ampoules, as well as for the rest of the parameters required for the model, a rapid review, with a limit of the last 15 years was conducted in general and specialized databases: MEDLINE, CENTRAL, Cochrane Pregnancy and Childbirth Group's Trials Register, Latin American and Caribbean Health Science Information, WHO and PAHO databases, nongovernmental organizations (NGOs), and other organizations known to be active in the maternal health field to find datasets not captured by bibliographic searches. In addition, ministerial databases of LAC countries were reviewed. The search strategy included the following MeSH and free-text terms for postpartum hemorrhage and its causes : 'postpartum hemorrhage', 'hemorrhage/and (pregnant* or postpartum* or postpartum or post partal)', 'epidemiological data', 'Maternal Health Services', 'hospital information system', 'medical information system', 'facility', 'maternal mortality', 'maternal death', 'oxytocin', 'third stage of labor'.

INFORMATION SOURCE SELECTION AND PARAMETER INCORPORATION

A decision rule that would establish a priority order among the possible data sources to populate the model was defined to include: 1) use good-quality local (country-specific) sources when available *(42–44)*; 2) use international sources when local data were unavailable or incomplete, and when the parameter was considered transferable from other settings; and 3) derive or estimate the parameter from the best available local data when international sources were considered "non-transferable." An evidence hierarchy was used in order to select the most appropriate sources to populate the model (i.e., population-based observational studies for epidemiological or resource use data, experimental/RCT evidence for comparative effects). Selection of studies to decide the value of base case, the inferior value, and the superior value were based on studies that assessed PPH using objective measures (i.e., weighing blood). Prospective designs were prioritized. Data on oxytocin efficacy were obtained from a Cochrane systematic review.

The average age at delivery for each country was obtained from Gomez et al. and from the Demographic and Health Surveys *(45, 46)*. For those countries for which no information was available, the average of the values obtained in the rest of the countries of the region was used. Data about annual deliveries was obtained from United Nations databases 2010 *(47)*.

COSTS

Cost Differential for Using Oxytocin in Uniject Instead of Oxytocin in Ampoules

The model requires data on the expected incremental cost of using OiU. This increment is assumed to be the difference between the price of 10 IU of oxytocin in the Uniject injection system and 10 IU of oxytocin in ampoules plus the costs of disposable syringes and needles. The price of OiU is not extensively available yet in LAC. According to the studies found and local available data sources the cost of oxytocin ampoules shows a great variability between countries. In Guatemala, for example, a study used US$ 0.30 as the cost of ampoules plus syringes and needles in one scenario and US$ 0.87 in another; and US$ 1.2 for OiU. This means an incremental cost (considering only these items) ranging between 38% and 300% *(48)*. In another study, performed in Vietnam, ampoules were US$ 0.40, OiU was US$ 0.50, and the incremental cost for OiU was 25% *(32)*. The report of Abt Associates based its estimation on a cost of US$ 0.20 per dose for ampoules and supposed an incremental cost of US$ 0.10 if OiU were used instead. This translates to a 50% increment *(31)*. So, in a context of great variability and uncertainty on prices, three different scenarios for incremental cost were considered: US$ 0.50; US$ 1.00; and US$ 1.50.

Additional costs for transportation, training, or salaries are not included as these costs did not appear to be significant in other studies *(31, 48)*. We included an adjustment for the wastage rate of ampoules and the costs due to the increase in space required for storage of OiU. However, as both adjustments are considered to be equal in incremental terms and benefit both arms equally, they balance themselves out and do not generate any impact on differential estimations. All costs are expressed in 2013 US dollars according to the current exchange rates published by the International Monetary Fund (IMF) *(49)*.

Cost of Events

Two clinical events were included in the model: non-severe PPH (blood loss more than 500 mL but less than 1,000 mL) and severe PPH (blood loss of 1,000 mL or more). Both were estimated following a micro-costing approach, using a list of resources and utilization rates identified by experts in the field. The same list of resources and utilization rates are assumed for all countries. See tables A-1, A-2 and A-3 in the annex.

There is no accurate information available on unit costs for all countries, unit costs were estimated using two different approaches and focusing on maximizing the information available. Specifically, for the cost of hospital stays, the main driver of total costs, we used the methodology proposed by WHO-CHOICE *(50)*. Using the coefficients showed in Annex Table A-2, the model was replicated with 2013 data instead of the 2008 data originally used. This exercise was repeated for each country to provide for estimations of inpatient costs. In the case of Brazil, we prioritized another source; the inpatient costs were obtained from Longo et al. *(51)* and actualized to 2013 using the local consumer price index *(49)*.

For the rest of the inputs, a similar approach to that proposed by Goldie et al. with the incorporation of recommendations from Johns et al were followed *(48, 49, 52)*. First, an international scenario of unit costs based on the best available information of different countries and published sources was created. All data were initially expressed in 2013 international dollars (I$) to calculate unit costs. To transform local currency units (LCUs) to international dollars, we assumed an exchange rate of US$ 1 = I$ 1 for tradable goods and the purchasing power parity (PPP) between countries published by the World Bank and IMF for non-tradable goods (*49, 53)* . As needed, consumer price index adjustments with local data were carried out to reflect the base case year of costs. Data on prices were obtained from the World Outlook Database of the IMF *(49)*. See the list of unit costs in Annex Table A-1.

After this international scenario was created, all values were expressed in LCUs using the exchange rate for tradable goods and the PPP for non-tradable. Then all values were re-expressed in 2013 current dollars using the current exchange rate published by the IMF *(49)*.

The model did not include other clinical events beyond non-severe and severe PPH, both of which occur in the first year and have no long-term implications. Thus discount for health care costs was not necessary and applied only for health effects.

INTERNAL VALIDATION

Internal testing and debugging were performed to ensure that the mathematical calculations were accurate and consistent with the specifications of the model. The model was checked and tested during the modeling process to identify any errors relating to data incorporation and modeling syntax. Null and extreme input values were used and the test of replication using equivalent input values was applied. Inconsistencies were detected and programming errors corrected.

The model structure and the parameters' calculation approach were calibrated for each country. Calibration was performed to ensure that the model could reproduce the results of the sources used to run the model and adequately reflect the current situation in each country. PPH death rates predicted by the model were compared with local health statistics. The case fatality rates of PPH episodes were estimated for each country (see Formula 3) in order to obtain PPH death rates consistent with local statistics.

SENSITIVITY ANALYSIS

A deterministic sensitivity analyses was performed to estimate the impact of uncertainty on results by varying each parameter separately within a specific range of values (see ranges in Tables 1 and 2).The most influential parameters in the deterministic sensitivity analysis were included in a probabilistic sensitivity analysis (PSA) in which all inputs were varied simultaneously across 10,000 Monte Carlo simulations, according to specific probability distributions (see distribution descriptions in Tables 1 and 2).

Table 1. Country-specific parameters: Base case values, ranges used in sensitivity analysis, and source of data

Country	Annual deliveries		Age at delivery		Skilled birth attendance (%)		Proportion CEmONC (%)		Oxytocin use (%)		Maternal mortality rate (p/100,000)		Proportion of deaths due to PPH (%)		Life expectancy		PPH episode cost (non-severe) US$ 2013		PPH episode cost (severe) US$ 2013		Exch. rate (US$ 1)	GDP (thousands US$ 2013)
Argentina	694,000	1	25.5 (23.0-28.1)	2	99	4	80	B 4,5	71.1 (57.7-88.4)	6,7,8	77.0 (67.0-87.)	9	10.00 (5.6-14.9)	10,11,16	81.0 (77.0–85.0)	19	$76.8 (57.6-96.0)	C	$978.6 (733.9-1,223.2)	C	$ 5.2 [21]	$ 12.0 [21]
Bahamas	1,500	1	21.6 (19.5-23.8)	A	99	4	80	B 4,5	71.6 (57.6-89.1)	6,7,8	47.0 (28.0-75.)	9	16.05 (12.0-20.1)	A	79.0 (75.0–83.0)	19	$151.6 (113.7-189.5)	C	$2,103.7 (1,577.8-2,629.6)	C	$ 1.0 [21]	$ 23.5 [21]
Barbados	3,000	1	21.6 (19.5-23.8)	A	99	4	80	B 4,5	71.6 (57.6-89.1)	6,7,8	51.0 (19.0-140.)	9	9.70 (7.3-12.1)	20	82.0 (78.0–86.0)	19	$108.7 (81.5-135.8)	C	$1,450.5 (1,087.9-1,813.1)	C	$ 2.0 [21]	$ 16.8 [21]
Belize	8,000	1	21.6 (19.5-23.8)	A	95	4	80	B 4,5	68.7 (55.3-85.5)	6,7,8	53.0 (33.0-88.)	9	16.05 (12.0-20.1)	A	80.0 (76.0–84.0)	19	$36.1 (27.1-45.1)	C	$357.9 (268.4-447.4)	C	$ 2.0 [21]	$ 4.6 [21]
Bolivia	263,000	1	21.1 (19.0-23.2)	2	71	4	30	B 4,5	51.4 (41.3-63.9)	6,7,8	190.0 (130.0-290.)	9	15.40 (11.6-19.3)	17	74.0 (70.0–78.0)	19	$26.4 (19.8-33.0)	C	$211.3 (158.4-264.1)	C	$ 6.7 [21]	$ 2.7 [21]
Brazil	3,023,000	1	21.6 (19.5-23.8)	2	97	4	80	B 4,5	74.2 (59.6-92.2)	6,7,8	56.0 (36.0-85.)	9	10.90 (8.2-13.6)	11	79.0 (75.0–83.0)	19	$41.8 (31.4-52.3)	C	$459.3 (344.5-574.1)	C	$ 1.7 [21]	$ 12.3 [21]
Chile	241,500	1	21.6 (19.5-23.8)	2	99	4	80	B 4,5	71.6 (57.6-89.1)	6,7,8	25.0 (21.0-29.)	9	6.53 (4.9-8.2)	18	84.0 (80.0–88.0)	19	$96.6 (72.5-120.8)	C	$1,273.6 (955.2-1,591.9)	C	$ 516.0 [21]	$ 16.3 [21]
Colombia	914,000	1	21.6 (19.4-23.8)	2	96	4	80	B 4,5	69.5 (55.9-86.4)	6,7,8	92.0 (80.0-100.)	9	17.70 (13.3-22.1)	17	84.0 (80.0–88.0)	19	$51.2 (38.4-64.0)	C	$588.7 (441.5-735.9)	C	$ 1,954.0 [21]	$ 8.2 [21]
Costa Rica	73,000	1	21.6 (19.5-23.8)	A	99	4	80	B 4,5	71.6 (57.6-89.1)	6,7,8	40.0 (15.0-31.)	9	15.70 (11.8-19.6)	11	82.0 (78.0–86.0)	19	$63.6 (47.7-79.4)	C	$776.7 (582.5-970.8)	C	$ 532.3 [21]	$ 10.4 [21]
Cuba	112,000	1	21.6 (19.5-23.8)	A	99	4	80	B 4,5	71.6 (57.6-89.1)	6,7,8	73.0 (60.0-87.)	9	4.40 (3.3-5.5)	11	81.0 (77.0–85.0)	19	$40.9 (30.7-51.2)	C	$427.0 (320.3-533.8)	C	$ 1.0 [21]	$ 5.4 [21]
Dominican Rep.	216,000	1	21.6 (19.5-23.8)	A	98	4	80	B 4,5	70.9 (57.0-88.2)	6,7,8	115.0 (100.0-210.)	9	12.65 (9.5-15.8)	11	80.0 (76.0–84.0)	19	$41.4 (31.0-51.7)	C	$438.6 (328.9-548.2)	C	$ 41.8 [21]	$ 5.8 [21]
Ecuador	299,000	1	21.6 (19.5-23.8)	A	99	4	80	B 4,5	66.6 (53.6-82.9)	6,7,8	110.0 (62.0-180.)	9	29.40 (22.1-36.8)	11	78.0 (74.0–82.0)	19	$41.5 (31.1-51.9)	C	$439.1 (329.3-548.8)	C	$ 1.0 [21]	$ 5.6 [21]
El Salvador	126,000	1	21.6 (19.5-23.8)	A	84	4	50	B 4,5	60.8 (48.9-75.6)	6,7,8	81.0 (55.0-120.)	9	16.05 (12.0-20.1)	12	79.0 (75.0–83.0)	19	$32.5 (24.4-40.6)	C	$303.0 (227.3-378.8)	C	$ 1.0 [21]	$ 3.9 [21]
Grenada	2,000	1	21.6 (19.5-23.8)	A	99	4	80	B 4,5	71.6 (57.6-89.1)	6,7,8	24.0 (15.0-38.)	9	16.05 (12.0-20.1)	A	78.0 (74.0–82.0)	19	$53.6 (40.2-67.1)	C	$623.0 (467.3-778.8)	C	$ 2.7 [21]	$ 7.8 [21]
Guatemala	467,000	1	19.9 (17.9-21.9)	3	51	4	30	B 4,5	36.9 (29.7-45.9)	6,7,8	120.0 (110.0-140.)	9	58.10 (43.6-72.6)	13	70.0 (66.0–74.0)	19	$28.4 (21.3-35.6)	C	$246.3 (184.7-307.9)	C	$ 8.4 [21]	$ 3.4 [21]
Guyana	14,000	1	20.7 (18.6-22.8)	A	83	4	50	B 4,5	60.1 (48.3-74.7)	6,7,8	280.0 (180.0-430.)	9	16.05 (12.0-20.1)	A	70.0 (66.0–74.0)	19	$32.5 (24.4-40.6)	C	$300.9 (225.7-376.2)	C	$ 209.6 [21]	$ 3.9 [21]
Haiti	266,000	1	20.1 (18.1-22.1)	A	26	4	30	B 4,5	18.8 (15.1-23.4)	6,7,8	315.0 (210.0-610.)	9	16.05 (12.0-20.1)	A	79.0 (75.0–83.0)	19	$17.9 (13.4-22.4)	C	$87.4 (65.6-109.3)	C	$ 40.8 [21]	$ 0.8 [21]
Honduras	203,000	1	22.2 (20.0-24.4)	2	67	4	30	B 4,5	48.5 (39.0-60.3)	6,7,8	100.0 (64.0-160.)	9	47.06 (35.3-58.8)	14	79.0 (75.0–83.0)	19	$24.5 (18.4-30.6)	C	$182.6 (136.9-228.2)	C	$ 20.1 [21]	$ 2.3 [21]
Jamaica	51,000	1	21.6 (19.5-23.8)	A	96	4	80	B 4,5	69.5 (55.9-86.4)	6,7,8	110.0 (77.0-170.)	9	16.05 (12.0-20.1)	A	80.0 (76.0–84.0)	19	$41.3 (31.0-51.6)	C	$437.7 (328.3-547.1)	C	$ 91.9 [21]	$ 5.6 [21]

Country	Annual deliveries		Age at delivery		Skilled birth attendance (%)		Proportion CEmONC (%)		Oxytocin use (%)		Maternal mortality rate (p/100,000)		Proportion of deaths due to PPH (%)		Life expectancy		PPH episode cost (non-severe) US$ 2013		PPH episode cost (severe) US$ 2013		Exch. rate (US$ 1)	GDP (thousands US$ 2013)
Mexico	2,217,000	1	21.6 (19.5-23.8)	2	94	4	50	B 4,5	71.6 (57.6-89.1)	6,7,8	50.0 (44.0-56.)	9	24.30 (18.2-30.4)	11	78.0 (74.0–82.0)	19	$74.7 (56.0-93.3)	C	$941.3 (705.9-1,176.6)	C	$ 12.3 [21]	$ 11.0 [21]
Nicaragua	138,000	1	21.6 (19.5-23.8)	3	74	4	30	B 4,5	54.1 (43.5-67.3)	6,7,8	95.0 (54.0-170.)	9	16.05 (12.0-20.1)	15	82.0 (78.0–86.0)	19	$22.5 (16.9-28.1)	C	$148.7 (111.6-185.9)	C	$ 24.7 [21]	$ 1.8 [21]
Panama	70,000	1	21.6 (19.5-23.8)	2	91	4	50	B 4,5	65.9 (52.9-81.9)	6,7,8	92.0 (75.0-110.)	9	16.40 (12.3-20.5)	11	80.0 (76.0–84.0)	19	$72.4 (54.3-90.5)	C	$904.7 (678.6-1,130.9)	C	$ 1.0 [21]	$ 11.1 [21]
Paraguay	156,000	1	21.6 (19.5-23.8)	2	97	4	80	B 4,5	71.1 (57.2-88.5)	6,7,8	99.0 (60.0-160.)	9	25.40 (19.1-31.8)	11	80.0 (76.0–84.0)	19	$35.6 (26.7-44.5)	C	$355.7 (266.8-444.6)	C	$ 4,043.7 [21]	$ 4.5 [21]
Peru	154,000	1	21.9 (20.0-22.9)	2	83	4	50	B 4,5	65.6 (52.7-81.6)	6,7,8	67.0 (42.0-110.)	9	50.00 (37.5-62.5)	11	80.0 (76.0–84.0)	19	$45.7 (34.3-57.2)	C	$502.8 (377.1-628.5)	C	$ 2.9 [21]	$ 7.1 [21]
Saint Lucia	3,000	1	21.6 (19.5-23.8)	A	99	4	80	B 4,5	71.6 (57.6-89.1)	6,7,8	35.0 (22.0-54.)	9	16.05 (12.0-20.1)	A	80.0 (76.0–84.0)	19	$52.5 (39.4-65.6)	C	$616.9 (462.7-771.2)	C	$ 2.7 [21]	$ 7.6 [21]
St. Vincent & Grenadines	2,000	1	21.6 (19.5-23.8)	A	99	4	80	B 4,5	71.6 (57.6-89.1)	6,7,8	48.0 (30.0-78.)	9	16.05 (12.0-20.1)	A	78.0 (74.0–82.0)	19	$47.2 (35.4-59.0)	C	$537.9 (403.4-672.4)	C	$ 2.7 [21]	$ 6.7 [21]
Suriname	10,000	1	21.6 (19.5-23.8)	2	90	4	50	B 4,5	65.1 (52.4-81.0)	6,7,8	130.0 (89.0-190.)	9	36.00 (27.0-45.0)	11	81.0 (77.0–85.0)	19	$61.5 (46.1-76.9)	C	$749.1 (561.8-936.3)	C	$ 3.3 [21]	$ 9.5 [21]
Trinidad & Tobago	20,000	1	21.6 (19.5-23.8)	2	98	4	80	B 4,5	70.9 (57.0-88.2)	6,7,8	46.0 (26.0-84.)	9	2.80 (2.1-3.5)	11	76.0 (72.0–80.0)	19	$122.3 (91.7-152.8)	C	$1,660.7 (1,245.5-2,075.8)	C	$ 6.4 [21]	$ 20.1 [21]
Uruguay	15,000	1	21.6 (19.5-23.8)	2	99	4	80	B 4,5	71.6 (57.6-89.1)	6,7,8	29.0 (21.0-39.)	9	4.40 (3.3-5.5)	11	82.0 (78.0–86.0)	19	$99.1 (74.3-123.9)	C	$1,315.2 (986.4-1,643.9)	C	$ 20.0 [21]	$ 15.3 [21]
Venezuela	158,000	1	21.6 (19.5-23.8)	2	95	4	80	B 4,5	68.7 (55.3-85.5)	6,7,8	92.0 (78.0-110.)	9	17.01 (12.8-21.3)	11,17,18	81.0 (77.0–85.0)	19	$69.0 (51.8-86.3)	C	$858.9 (644.2-1,073.7)	C	$ 6.5 [21]	$ 11.5 [21]

Notes:

Abbreviations: CEmONC: comprehensive emergency obstetric and newborn care; PPH: postpartum hemorrhage; A: average from other countries (see text); B: estimation based on data from Argentina, Bolivia, El Salvador, and Honduras and references 4 and 5 (see text); C: see methods in manuscript (cost section).

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Probability distributions: To run the probabilistic sensitivity analysis (PSA) both the maternal mortality rate and the proportion of deaths due to PPH were assumed to follow a truncated normal distribution with a medium equal to the base case value and a standard deviation that keeps all simulations between the maximum and minimum values of the deterministic ranges. The costs of severe, non-severe PPH and the incremental cost of Uniject were assumed to follow a Uniform distribution varying between the maximum and minimum value of the deterministic ranges. The rest of the variables were not included in the PSA as they showed to be not relevant for it in the deterministic sensitivity analysis.

Table 2. Global parameters: Base case values, ranges used for the deterministic sensitivity analysis and data sources

Parameters	Value & range	Source
Probability of PPH without oxytocin	0.12 (0.10 - 0.14)	Althabe 2008, Carroli 2008, and Gulmezoglu 2001
Conditional probability of severe PPH (given PPH)	0.18 (0.15 - 0.21)	Althabe 2008, Calvert 2012, and Gulmezoglu 2001
Hysterectomy due to severe PPH	0.03 (0.02 - 0.05)	Gulmezoglu 2001, Souza 2013
Case fatality ratio, HOME	2.26 (1.66 - 7.19)	WHO bulletin, Aguirre 1997
Case fatality ratio, BEMONC	1.88 (1.25 - 2.28)	WHO bulletin
Relative risk of PPH when receiving oxytocin	0.50 (0.43 - 0.57)	Cotter 2001
Discount rate	5% (0% - 10%)	Augustovski, 2010
QALY hysterectomy	0.99 (0.95 - 1.00)	O´Sullivan 2009
Incremental cost of Uniject (US dollars of 2013)	$1.00 ($0.50 - $1.50)	Assumption
Oxytocin effectiveness (% gap reduction)	30.23% (12.03%-53.75%)	DELPHI Panel

Notes:

For the probabilistic sensitivity analysis (PSA), both the "probability of PPH without oxytocin" and the "conditional probability of severe PPH (given PPH)" were assumed to follow a uniform distribution varying between the maximum and minimum values of the deterministic ranges. The "% or increment of oxytocin use (CEMON-BEMONC)" was assumed to follow a truncated normal distribution with a media equal to the base case value and a standard deviation that keeps all simulations between the maximum and minimum values of the deterministic ranges. The rest of the variables were not included in the PSA as they showed to be not relevant for it in the deterministic sensitivity analysis.

Results

STUDY PARAMETERS AND CALIBRATION

Global parameters and country-specific parameters are summarized in Tables 1 and 2, including base case values, ranges, and distributions used for the sensitivity analysis and data sources.

Maternal mortality ratios were retrieved from the WHO report, "Women and Health: Maternal Mortality Ratio by Country" (data from year 2010) *(54)*. The proportion of deaths due to PPH among all maternal deaths was retrieved from several sources to obtain data for all the included countries *(19–23, 55, 56)*. In those cases where country-specific data were not available we used the median value obtained from the countries for which information was available.

The precise incidence of PPH is difficult to establish, in part because of the lack of consensus on its definition and on the way it should be measured. Therefore, there is a wide variation in the incidence reported in different published studies *(3)*. There is evidence that incidence is usually underestimated, partly because of the inaccurate strategies used to measure the bleeding. On the one hand, this variability depended on how the bleeding amount was measured (mainly, some did it objectively and some did it subjectively); on the other hand, not all the papers mentioned the proportion of patients that received uterotonic drugs. Based on Althabe 2008, Carroli 2008, and Gulmezoglu 2001, three potential scenarios using values of 10%, 12%, and 14% *(7, 18, 57)* were constructed. As variability in the proportion of severe PPH was also found, three scenarios based on Althabe 2008, Calvert 2012, and Gulmezoglu 2001, assuming values of 15%, 18%, and 21% *(3, 18, 57)* were constructed.

Based on Begley et al, it was assumed that AMTSL reduced the rate of PPH by 50%.*(10)*. The most recent WHO recommendations for preventing PPH stress that administration of a uterotonic drug, such as oxytocin, is the most important component of AMTSL, thus it was assumed that the effects of AMTSL were due to the use of oxytocin *(12)*.

Data on oxytocin coverage in each country was obtained from a study published by Souza et al. and from several reports from the Prevention of Postpartum Hemorrhage Initiative (POPPHI) *(19–23)*. We assumed that data on oxytocin use, which were obtained from Souza et al., could overestimate the actual coverage rates for each country, because the data come from a biased sample of selected tertiary care facilities *(20)*. This assumption was supported by a register published by Karolinski et al. (Panamerican Health Organization in Argentina) regarding all births in the province of Buenos Aires, Argentina, which showed a lower oxytocin coverage rate in that country *(58, 59)*. This difference is most likely due to the fact that one was a prospective study in which compliance is usually more frequent than usual (because participants were told that were participating in a trial) and the other (the register) was a record of interventions performed and therefore had a much greater likelihood of reflecting actual coverage rates. That is why the data from Souza et al. were used as the maximal value in the countries that were reported on in that paper. For countries that were not reported on by Souza et al., a maximum oxytocin use of 90% was assumed (the average value in Souza et al.). In order to obtain the base case value, data from Karolinski et al. was used to adjust country data, assuming that the relative difference between Souza and Karolinski for the case of Argentina was extrapolated to the other countries. As the relation between these two figures was 0.72, that correction factor was applied to the figures found in the other reports from the other countries. We acknowledge that this could also overestimate the real oxytocin coverage rate, but we assume it better reflects the real country value. For the minimum oxytocin use value estimation, we assumed that it was equal to the difference between the maximum and the base case value. Finally, assuming that the proportion of births attended by skilled birth attendants (SBAs) represented the institutional deliveries, we further multiplied the obtained values by the proportion of SBAs in each country to obtain the oxytocin coverage rate for each country *(60)*.

Evidence about the use of oxytocin in CEmONC and BEmONC is contradictory and scarce. Based on sources and supported by expert opinions, it was assumed that the use of oxytocin in CEmONC and BEmONC hospitals is similar *(19, 21–23)*.

Data on the proportion of births occurring in CEmONC and BEmONC facilities for each country were unavailable. To estimate these values it was assumed that the proportion of births attended by SBAs correlates with the proportion of births attended in CEmONC facilities. The countries were grouped into three strata based on WHO data (2011) on the proportion of births attended by SBAs *(60)* and on data on the proportion of births occurring in CEmONC facilities from Argentina, Bolivia, El Salvador, and Honduras: a) those countries that had more than 95% of births attended by an SBA and had 80% of those births in CEmONC facilities; b) those countries that had between 80% and 94% of births attended by an SBA and had 50% of those births in CEmONC facilities; and c) those countries that had less than 80% of births attended by an SBA and had 30% of those births in CEmONC facilities *(61–63)*.

Life Years (LYs) and Quality-Adjusted Life Years (QALYs)

LYs were estimated for each cohort in each country. Women surviving birth were assumed to have the life expectancy for women in their respective country, and those dying from PPH were assumed to die at the mean age of delivery in each country.

In order to derive QALYs, we reviewed studies that reported quality of life after surviving a hysterectomy during a woman´s lifetime. A value of 0.985 was used in order to incorporate the long-term quality of life decrements due to hysterectomy *(64)*.

Measure of Effectiveness of Uniject: Expert Panel Results

Eight recognized experts in maternal and child health with extensive experience in Latin America participated in the Delphi panel and completed the two rounds of consultations.

Expert panel members:

Alicia Aleman, MD (Uruguay)
José Belizan, MD, PhD (Argentina)
Pierre Buekens, MD, PhD (EE.UU)
Guilherme Cecatti, MD, MSc, PhD (Brazil)
Agustín Conde-Agudelo, MD, PhD (Colombia)
Edgar Kestler, MD, PhD (Guatemala)
Jeffrey Smith, MD, MPH (EE.UU)
Giselle Tomasso, MD (Uruguay)

The expert panel estimated that OiU might increase oxytocin use up to 64.1%, in settings with a baseline use of 50% and up to 86.5% in settings with a baseline use of 80%. Estimates for CEmONC and BEmONC facilities were very similar. In order to obtain a measure of effectiveness of Uniject that could be applicable to all countries, based on the results of the expert panel we assumed that the replacement of oxytocin in ampoules with OiU would be able to save 30.23% of the current gap in the oxytocin coverage rate (mean value obtained from the expert panel). This would mean, for example, that in a country where 75% of women are receiving oxytocin for prevention of PPH (gap 25%), the provision of OiU might increase this proportion to 82.6%.

In addition to this average measure of effectiveness (30.23%), and based on the uncertainty ranges estimated by the expert panel, the range to be used in the sensitivity analysis was defined to be between 12.03% and 53.75%.

Calibration

Calibration of the model was successful and adequately reflected the national statistics on maternal mortality rates in each country and the proportion of maternal deaths due to PPH, using the sources previously described.

INCREMENTAL COSTS AND OUTCOMES

In the 30 Latin American and Caribbean countries included, the impact of replacing oxytocin in ampoules with OiU in terms of health benefits and costs was evaluated.

In the threshold analysis, assuming that an intervention is cost-effective if its ICER is equal to or less than one GDP per capita per QALY, the minimum required increment in the facility oxytocin coverage rates to make OiU a cost-effective strategy ranged from 1.3% in Suriname to 15.8% in Haiti. In more than 60% of the countries, the required increment was below 5%. This means that in a country where 70% of women giving birth in institutions currently receive oxytocin, replacing oxytocin in ampoules with OiU would be cost-effective if it can increase oxytocin use to 75%. In only three of the 30 countries analyzed the absolute increment in oxytocin use needed to be cost-effective at threshold of 1 GDPPC per QALY was over 10%. Detailed results of the threshold analysis for each country are shown in the second column of Table 3. Base case threshold values as well as the summary results of the sensitivity analysis (95% CI) are reported in the table.

In the deterministic sensitivity analysis the most influential variables were the discount rate, the Uniject magnitude of benefit, and the baseline level of oxytocin use. Less influential variables were oxytocin effectiveness to prevent PPH, proportion of maternal deaths due to PPH, and cost of Uniject. These findings were consistent among countries. In the annex examples of the deterministic sensitivity analysis (tornado diagrams) of Argentina, Brazil, Colombia, and Peru (Annex Figures A-1 to A-4) are shown. In the PSA, in addition to the aforementioned parameters we incorporated maternal mortality, PPH baseline risk without oxytocin, probability of severe PPH, and unit cost of events. Probability distributions are shown in the footnotes to Tables 1 and 2.

In Table 3 the 95% CI of the 10,000 results generated in the PSA are reported. Even after considering global parameter uncertainty, the threshold value for the required increment in oxytocin use remained below 10% in two-thirds of the countries, a value that was considered highly attainable by the expert panel, as was described in the panel results section.

In the cost-effectiveness analysis, in all 30 countries the OiU strategy showed a reduction in PPH episodes and deaths and an increase in QALYS. OiU could prevent more than 40,000 PPH episodes annually, accounting for more than 4,000 LYs saved in LAC countries. The incremental QALYs per 1,000 institutional deliveries ranged from 0.02 to 0.71 (see fourth column of Table 3 for base case values and 95% CI of the PSA).

Switching to OiU represented both an increment in oxytocin-related costs, due to the higher unit cost of the Uniject injection system, as well as a reduction in the health care cost of PPH and its complications. In 27% of the countries the savings in health care costs outweighed the additional cost of OiU, showing OiU as a cost-saving strategy. In the remaining 22 countries OiU was associated with a net cost increment that ranged from US$ 0.005 to US$ 0.847 per delivery (see third column of Table 3 for countries base case values per 1,000 deliveries and PSA 95% CI).

Cost-effectiveness ratios were estimated as the ratio between the difference in costs (Δ costs) and the difference in benefits (Δ consequences). The Uniject strategy ranged from being dominant (i.e., cost saving and health beneficial) to having an ICER of $ 8,990 per QALY gained. In the great majority of the countries these ICERs were below one GDP per capita, showing Uniject as a highly cost-effective strategy.

In the last columns of Table 3 the results of the PSA are shown, expressed as the likelihood of considering OiU efficient using three decreasingly stringent criteria (cost saving, cost-effective at a one GDP per capita threshold, and cost-effective at a three GDP per capita threshold). With the three-GDP threshold, OiU would be universally cost-effective in the 30 countries analyzed.

Table 3. Base case results and 95% confidence intervals from probabilistic sensitivity analysis, 2013US dollars, 5% discount rate

Country	Threshold Analysis	Cost-Effectiveness Analysis					
	Absolute increment in oxytocin use needed to be cost-effective at threshold of 1 GDPPC per QALY	Cost difference per 1,000 institutional deliveries	Incremental QALYs per 1,000 institutional deliveries	Incremental cost-effectiveness ratio ($ per QALY)	Prob. of being cost saving	Prob. of being cost-effective at a threshold of 1 GDPPC[a]	Prob. of being cost-effective at a threshold of 3 GDPPC[b]
Argentina	3.38% (1.7% to 6.2%)	-$ 223.2 (-$ 1,329 to $ 723)	0.11 (0.05 to 0.18)	Cost Saving (-9,760 to 10,954)	62%	98%	100%
Bahamas	1.68% (0.9% to 3.1%)	-$ 1,521.8 (-$ 3,664 to $ 117)	0.10 (0.04 to 0.19)	Cost Saving (-33,897 to 2,215)	97%	100%	100%
Barbados	2.81% (1.3% to 5.8%)	-$ 755.7 (-$ 2,422 to $ 391)	0.07 (0.01 to 0.15)	Cost Saving (-89,318 to 9,513)	89%	99%	100%
Belice	8.32% (4.4% to 15.4%)	$ 528.5 (-$ 14 to $ 1,152)	0.12 (0.05 to 0.20)	4,585 (-107 to 19,165)	3%	47%	94%
Bolivia	7.11% (3.8% to 12.9%)	$ 700.7 ($ 165 to $ 916)	0.33 (0.10 to 0.43)	2,141 (517 to 6,916)	0%	64%	99%
Brasil	5.01% (2.6% to 9.1%)	$ 500.6 (-$ 152 to $ 1,142)	0.07 (0.03 to 0.14)	6,676 (-1,307 to 31,343)	8%	73%	99%
Chile	4.12% (2.0% to 7.7%)	-$ 546.5 (-$ 2,076 to $ 508)	0.03 (0.01 to 0.05)	Cost Saving (-52,973 to 27,468)	82%	94%	99%
Colombia	3.31% (1.7% to 6.0%)	$ 258.3 (-$ 511 to $ 1,004)	0.22 (0.11 to 0.36)	1,192 (-1,873 to 7,077)	23%	99%	100%
Costa Rica	4.42% (2.3% to 8.0%)	$ 37.8 (-$ 904 to $ 785)	0.09 (0.04 to 0.15)	422 (-8,187 to 14,386)	44%	95%	100%
Cuba	10.18% (5.3% to 18.5%)	$ 446.4 (-$ 163 to $ 1,078)	0.05 (0.02 to 0.08)	8,990 (-2,385 to 34,339)	8%	32%	79%
Rep. Dominicana	4.94% (2.5% to 9.3%)	$ 434.0 (-$ 212 to $ 1,037)	0.19 (0.08 to 0.36)	2,233 (-894 to 9,612)	9%	88%	100%
Ecuador	2.91% (1.4% to 5.9%)	$ 329.3 (-$ 353 to $ 934)	0.48 (0.22 to 0.82)	681 (-614 to 3,224)	17%	100%	100%
El Salvador	8.02% (4.1% to 14.0%)	$ 593.1 ($ 56 to $ 967)	0.16 (0.06 to 0.25)	3,673 (336 to 12,088)	1%	53%	97%
Granada	6.79% (3.4% to 11.8%)	$ 217.2 (-$ 663 to $ 935)	0.06 (0.03 to 0.10)	3,773 (-8,811 to 24,760)	27%	67%	97%
Guatemala	3.01% (1.6% to 5.0%)	$ 660.8 ($ 63 to $ 614)	0.71 (0.16 to 0.61)	925 (140 to 2,855)	1%	99%	100%
Guyana	3.45% (1.7% to 6.6%)	$ 594.8 ($ 20 to $ 995)	0.52 (0.18 to 0.76)	1,143 (50 to 4,171)	2%	97%	100%
Haití	15.81% (7.9% to 32.1%)	$ 847.5 ($ 105 to $ 373)	0.45 (0.04 to 0.23)	1,864 (676 to 6,625)	0%	6%	65%
Honduras	5.78% (2.8% to 11.1%)	$ 734.6 ($ 166 to $ 867)	0.52 (0.13 to 0.66)	1,415 (363 to 4,677)	0%	77%	99%
Jamaica	4.50% (2.2% to 8.2%)	$ 435.2 (-$ 242 to $ 1,030)	0.23 (0.10 to 0.41)	1,884 (-758 to 7,026)	9%	92%	100%
México	2.82% (1.5% to 4.9%)	$ 5.1 (-$ 1,083 to $ 830)	0.14 (0.06 to 0.24)	36 (-5,489 to 11,657)	46%	97%	100%
Nicaragua	15.02% (7.7% to 28.4%)	$ 780.0 ($ 248 to $ 1,001)	0.17 (0.05 to 0.25)	4,468 (1,444 to 13,712)	0%	6%	60%
Panamá	2.54% (1.3% to 4.4%)	-$ 114.1 (-$ 1,074 to $ 715)	0.20 (0.08 to 0.30)	Cost Saving (-4,840 to 7,404)	56%	99%	100%
Paraguay	4.24% (2.1% to 8.2%)	$ 548.9 (-$ 43 to $ 1,154)	0.32 (0.13 to 0.56)	1,720 (-105 to 6,747)	3%	91%	100%
Perú	2.30% (1.1% to 4.7%)	$ 513.2 (-$ 141 to $ 956)	0.32 (0.07 to 0.53)	1,612 (-418 to 9,194)	7%	95%	99%
Santa Lucía	6.03% (3.0% to 11.0%)	$ 227.4 (-$ 622 to $ 900)	0.08 (0.03 to 0.14)	2,825 (-6,357 to 20,598)	26%	76%	99%
San Vicente y las Granadinas	6.00% (3.0% to 11.1%)	$ 320.4 (-$ 480 to $ 1,079)	0.11 (0.04 to 0.19)	3,003 (-3,123 to 15,909)	18%	77%	99%
Suriname	1.29% (0.6% to 2.5%)	$ 71.2 (-$ 836 to $ 789)	0.58 (0.24 to 0.98)	122 (-1,193 to 2,304)	40%	100%	100%
Trinidad y Tabago	3.36% (1.7% to 6.0%)	-$ 1,001.2 (-$ 2,874 to $ 340)	0.02 (0.01 to 0.04)	Cost Saving (-105,629 to 25,080)	90%	96%	100%
Uruguay	4.24% (2.2% to 7.8%)	-$ 594.3 (-$ 2,102 to $ 506)	0.02 (0.01 to 0.04)	Cost Saving (-65,429 to 36,916)	82%	92%	98%
Venezuela	2.43% (1.2% to 4.2%)	-$ 58.9 (-$ 1,132 to $ 767)	0.21 (0.09 to 0.34)	Cost Saving (-4,170 to 6,998)	52%	100%	100%

CE: cost-effective; GDPPC: gross domestic product per capita; QALY: quality-adjusted life years; Prob.: probability.
[a]Refers to a threshold of 1 GDPPC per QALY; [b]Refers to a threshold of 3 GDPPC per QALY.

Note: All negative ICERS are cost saving.

To better inform decision-makers, undiscounted results are included for Table 3 (Table A-1) as well as six additional tables (Tables A-2 to A-7) where, in addition to presenting discounted and undiscounted scenarios, the analysis excludes the uncertainty related to Uniject cost and presents it in three different cost scenarios (US$ 0.50; US$ 1.00, and US$ 1.50 incremental Uniject cost as compared to oxytocin in ampoules).

A web version of the economic model is available at http://www.iecs.org.ar/iecs-visor.php?cod_producto=811. It is intended to serve several purposes: 1) as a user-friendly platform, where decision-makers, researchers, and other stakeholders can find and use the model results to help with local decision-making; 2) as a regional dissemination tool for the current project; and 3) as a tool to enable researchers and health policymakers in each country to fine-tune the model to their specific setting, with the possibility of selecting the values of the different parameters and obtaining new results tailored to the local reality in their country/region. Although we made an effort to incorporate the best available set of parameters for all countries in the region, local realities may differ and parameters may change in the future. Therefore, this web adaptation will allow decision-makers to adapt results according their needs or local specifications.

Conclusions

Uniject was cost-saving or very cost-effective in almost all countries in LAC. Even if countries can achieve only small increases in oxytocin use by incorporating Uniject, this strategy could be considered an efficient use of resources. These results were shown to be robust in the sensitivity analysis under a wide range of assumptions and scenarios.

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Annex

Table A-1. Micro-costing exercise, list of resources, quantities, and percentage for PPH and severe PPH

PPH	Description	Quantity	%
Oxytocin (mono-dose vial)	10 UI ampoules x 100 x 1 ml	4	100%
Ergometrine	Ampoules x 0.5mg (1 mg doses)	2	70%
Balloon tamponade	Unit	1	5%
Oxygen	Unit	1	10%
Crystalloid solution	Sol. 500 ml	2	100%
Extended hospital stay	-	1	20%
Referral to hospital	1 transport	1	0%
Carbetocin	Ampoules 10 mcg	1	2%
Misoprostol	Tablets 200 mcg	4	20%
SEVERE PPH	**Description**	**Quantity**	**%**
Oxytocin (mono-dose vial)	10 UI ampoules x 100 x 1 ml	4	100%
Ergometrine	Ampoules x 0.5mg (1 mg doses)	2	70%
Balloon tamponade	Unit	1	10%
Anti-shock garment	-	1	10%
Oxygen	Unit	1	50%
Crystalloid solution	Sol. 500 ml	4	100%
Blood transfusion	1 unit	4	30%
Extended hospital stay	Common	3	100%
Surgery	Hysterectomy	1	1%
Referral to hospital	1 transport	1	23%
Carbetocin	Ampoules 10 mcg	1	2%
Misoprostol	Tablets 200 mcg	4	20%

Table A-2. WHO CHOICE model parameters to estimate facility unit costs

Variable	Regression Coefficient	95% Confidence Interval
Natural log of GDP per capita (PPP)	1.192***	[1.111, 1.272]
Natural log of occupancy rate	-0.0201**	[-0.0340, -0.00623]
Natural logarithm of total inpatient admissions	-.0.600***	[-0.649, -0.550]
Dummy variable for level 3 facilities	0.0252*	[0.00471, 0.0457]
Dummy variable for teaching hospitals	-0.204***	[-0.275, -0.132]
Dummy variable for public level hospitals	0.257***	[0.163, 0.351]
Dummy variable for private level hospitals	-0.144***	[-0.182, -0.107]
Dummy variable for observations in Brazil	-1.638***	[0.0710, 0.148]
Constant	-4.277***	[-1.694, -1.583]
Observations	3407	[-5.035, -3.519]
R^2	0.76	
Adjusted R^2	0.76	

p<0.05, **p<0.01, ***p<0.001

Source: WHO-CHOICE

Table A-3. Micro-costing exercise, unitary costs in 2013 international dollars

Inputs		I$ 2013
Oxytocin ampoule	Trad	1,08
Disposable syringes	Trad	0,09
Disposable needles	Trad	-
Uniject	Trad	0,56
Ergometrine	Trad	0,48
Balloon tamponade	Trad	5,42
Oxygen	Trad	7,95
Crystalloid solution	Trad	4,52
Hospital Stay	No Trad	WHO-CHOICE (Country-specific)*
Referral to hospital	No Trad	79,89
Carbetocin	Trad	0,00
Misoprostol	Trad	0,05
Anti-shock garment	Trad	3,61
Blood transfusion	No Trad	4,52
Surgery (Hysterectomy)	No Trad	442,65

* See costs section methodology in text

Table A-4. Base case results and 95% confidence intervals from probabilistic sensitivity analysis, 2013 US dollars, undiscounted values

Country	Threshold Analysis	Cost-Effectiveness Analysis					
	Absolute increment in oxytocin use needed to be cost-effective at threshold of 1 GDPPC per QALY	Cost difference per 1,000 institutional deliveries	Incremental QALYs per 1,000 institutional deliveries	Incremental cost-effectiveness ratio ($ per QALY)	Prob. of being cost saving	Prob. of being cost-effective at a threshold of 1 GDPPC[a]	Prob. of being cost-effective at a threshold of 3 GDPPC[b]
Argentina	1.74% (0.9% to 3.2%)	-$ 223.2 (-$ 1,329 to $ 723)	0.31 (0.15 to 0.52)	Cost Saving (-3,447 to 3,863)	62%	100%	100%
Bahamas	0.86% (0.4% to 1.7%)	-$ 1,521.8 (-$ 3,664 to $ 117)	0.31 (0.13 to 0.56)	Cost Saving (-11,652 to 762)	97%	100%	100%
Barbados	1.54% (0.7% to 4.1%)	-$ 755.7 (-$ 2,422 to $ 391)	0.22 (0.02 to 0.46)	Cost Saving (-29,434 to 3,145)	89%	100%	100%
Belice	4.09% (2.1% to 7.8%)	$ 528.5 (-$ 14 to $ 1,152)	0.34 (0.14 to 0.58)	1,554 (-36 to 6,495)	3%	94%	100%
Bolivia	3.11% (1.6% to 5.9%)	$ 700.7 ($ 165 to $ 916)	0.89 (0.27 to 1.16)	786 (190 to 2,539)	0%	98%	100%
Brasil	2.24% (1.1% to 4.2%)	$ 500.6 (-$ 152 to $ 1,142)	0.22 (0.08 to 0.40)	2,295 (-449 to 10,777)	8%	99%	100%
Chile	2.75% (1.4% to 4.9%)	-$ 546.5 (-$ 2,076 to $ 508)	0.09 (0.04 to 0.15)	Cost Saving (-16,984 to 8,815)	82%	100%	100%
Colombia	1.32% (0.7% to 2.4%)	$ 258.3 (-$ 511 to $ 1,004)	0.68 (0.34 to 1.11)	382 (-600 to 2,270)	23%	100%	100%
Costa Rica	2.21% (1.2% to 3.9%)	$ 37.8 (-$ 904 to $ 785)	0.27 (0.13 to 0.44)	139 (-2,698 to 4,742)	44%	100%	100%
Cuba	6.17% (3.3% to 10.8%)	$ 446.4 (-$ 163 to $ 1,078)	0.15 (0.07 to 0.25)	3,004 (-797 to 11,476)	8%	79%	100%
Rep. Dominicana	2.15% (1.1% to 4.2%)	$ 434.0 (-$ 212 to $ 1,037)	0.57 (0.23 to 1.06)	757 (-303 to 3,259)	9%	100%	100%
Ecuador	1.14% (0.5% to 2.4%)	$ 329.3 (-$ 353 to $ 934)	1.43 (0.66 to 2.43)	231 (-208 to 1,093)	17%	100%	100%
El Salvador	3.75% (1.9% to 6.8%)	$ 593.1 ($ 56 to $ 967)	0.46 (0.18 to 0.71)	1,281 (117 to 4,216)	1%	96%	100%
Granada	4.00% (2.1% to 7.2%)	$ 217.2 (-$ 663 to $ 935)	0.17 (0.08 to 0.30)	1,297 (-3,029 to 8,515)	27%	97%	100%
Guatemala	1.11% (0.6% to 1.8%)	$ 660.8 ($ 63 to $ 614)	2.10 (0.47 to 1.79)	315 (48 to 972)	1%	100%	100%
Guyana	1.49% (0.7% to 2.9%)	$ 594.8 ($ 20 to $ 995)	1.34 (0.45 to 1.97)	443 (19 to 1,617)	2%	100%	100%
Haití	7.38% (3.5% to 16.6%)	$ 847.5 ($ 105 to $ 373)	1.18 (0.11 to 0.60)	716 (260 to 2,545)	0%	58%	97%
Honduras	2.28% (1.1% to 4.6%)	$ 734.6 ($ 166 to $ 867)	1.50 (0.38 to 1.90)	491 (126 to 1,621)	0%	99%	100%
Jamaica	1.93% (0.9% to 3.6%)	$ 435.2 (-$ 242 to $ 1,030)	0.67 (0.30 to 1.19)	648 (-260 to 2,417)	9%	100%	100%
México	1.29% (0.7% to 2.2%)	$ 5.1 (-$ 1,083 to $ 830)	0.42 (0.17 to 0.71)	12 (-1,860 to 3,951)	46%	100%	100%
Nicaragua	7.13% (3.5% to 14.2%)	$ 780.0 ($ 248 to $ 1,001)	0.50 (0.14 to 0.71)	1,558 (504 to 4,782)	0%	57%	99%
Panamá	1.08% (0.6% to 1.9%)	-$ 114.1 (-$ 1,074 to $ 715)	0.59 (0.23 to 0.92)	Cost Saving (-1,595 to 2,418)	56%	100%	100%
Paraguay	1.71% (0.8% to 3.4%)	$ 548.9 (-$ 43 to $ 1,154)	0.94 (0.38 to 1.64)	583 (-35 to 2,287)	3%	100%	100%
Perú	0.88% (0.4% to 1.9%)	$ 513.2 (-$ 141 to $ 956)	0.94 (0.22 to 1.57)	548 (-142 to 3,128)	7%	99%	100%
Santa Lucía	3.24% (1.5% to 5.9%)	$ 227.4 (-$ 622 to $ 900)	0.24 (0.10 to 0.42)	957 (-2,154 to 6,984)	26%	98%	100%
San Vicente y las Granadinas	3.07% (1.5% to 5.8%)	$ 320.4 (-$ 480 to $ 1,079)	0.31 (0.13 to 0.55)	1,047 (-1,089 to 5,551)	18%	99%	100%
Suriname	0.48% (0.2% to 0.9%)	$ 71.2 (-$ 836 to $ 789)	1.75 (0.71 to 2.93)	41 (-399 to 771)	40%	100%	100%
Trinidad y Tabago	2.49% (1.3% to 4.4%)	-$ 1,001.2 (-$ 2,874 to $ 340)	0.07 (0.03 to 0.12)	Cost Saving (-37,921 to 9,018)	90%	100%	100%
Uruguay	3.05% (1.6% to 5.4%)	-$ 594.3 (-$ 2,102 to $ 506)	0.07 (0.03 to 0.13)	Cost Saving (-21,562 to 12,168)	82%	98%	100%
Venezuela	1.02% (0.5% to 1.8%)	-$ 58.9 (-$ 1,132 to $ 767)	0.62 (0.28 to 1.01)	Cost Saving (-1,393 to 2,339)	52%	100%	100%

CE: cost-effective; GDPPC: gross domestic product per capita; QALY: quality-adjusted life years; Prob.: probability.

[a]Refers to a threshold of 1 GDPPC per QALY; [b]Refers to a threshold of 3 GDPPC per QALY.

Note: All negative ICERS are cost saving

Table A-5. Scenario analysis: Incremental cost of Uniject of US$=0.5. Results of the threshold and cost-effectiveness analysis and 95% confidence intervals from probabilistic sensitivity analysis, 2013 US dollars, 5% discount rate

Country	Threshold Analysis	Cost-Effectiveness Analysis					
	Absolute increment in oxytocin use needed to be cost-effective at threshold of 1 GDPPC per QALY	Cost difference per 1,000 institutional deliveries	Incremental QALYs per 1,000 institutional deliveries	Incremental cost-effectiveness ratio ($ per QALY)	Prob. of being cost saving	Prob. of being cost-effective at a threshold of 1 GDPPC[a]	Prob. of being cost-effective at a threshold of 3 GDPPC[b]
Argentina	1.69% (1.2% to 2.5%)	-$ 723.2 (-$ 1,873 to -$ 36)	0.11 (0.06 to 0.17)	Cost Saving (-13,757 to -627)	98%	100%	100%
Bahamas	0.84% (0.6% to 1.3%)	-$ 2,021.8 (-$ 4,289 to -$ 557)	0.10 (0.05 to 0.19)	Cost Saving (-35,879 to -7,220)	100%	100%	100%
Barbados	1.41% (0.9% to 2.5%)	-$ 1,255.7 (-$ 2,894 to -$ 270)	0.07 (0.01 to 0.16)	Cost Saving (-184,893 to -4,135)	100%	100%	100%
Belice	4.16% (3.0% to 6.2%)	$ 28.5 (-$ 344 to $ 271)	0.12 (0.05 to 0.19)	248 (-2,772 to 4,628)	37%	97%	100%
Bolivia	3.56% (2.6% to 5.6%)	$ 200.7 (-$ 15 to $ 278)	0.33 (0.10 to 0.43)	613 (-47 to 2,428)	4%	98%	100%
Brasil	2.50% (1.7% to 3.9%)	$ 0.6 (-$ 494 to $ 314)	0.07 (0.03 to 0.14)	09 (-4,494 to 10,733)	41%	98%	100%
Chile	2.06% (1.5% to 3.2%)	-$ 1,046.5 (-$ 2,502 to -$ 89)	0.03 (0.01 to 0.05)	Cost Saving (-60,857 to -5,605)	99%	100%	100%
Colombia	1.65% (1.2% to 2.3%)	-$ 241.7 (-$ 818 to $ 185)	0.22 (0.10 to 0.34)	Cost Saving (-3,053 to 1,529)	80%	100%	100%
Costa Rica	2.21% (1.6% to 3.2%)	-$ 462.2 (-$ 1,389 to $ 87)	0.09 (0.04 to 0.15)	Cost Saving (-12,260 to 1,746)	93%	100%	100%
Cuba	5.09% (3.5% to 7.9%)	-$ 53.6 (-$ 489 to $ 264)	0.05 (0.02 to 0.08)	Cost Saving (-7,450 to 10,734)	54%	89%	99%
Rep. Dominicana	2.47% (1.7% to 3.8%)	-$ 66.0 (-$ 570 to $ 237)	0.19 (0.09 to 0.32)	Cost Saving (-2,279 to 2,209)	58%	100%	100%
Ecuador	1.46% (0.9% to 2.5%)	-$ 170.7 (-$ 679 to $ 170)	0.48 (0.21 to 0.89)	Cost Saving (-1,304 to 644)	78%	100%	100%
El Salvador	4.01% (2.8% to 6.1%)	$ 93.1 (-$ 211 to $ 283)	0.16 (0.06 to 0.24)	576 (-1,218 to 4,536)	23%	96%	100%
Granada	3.39% (2.4% to 5.0%)	-$ 282.8 (-$ 997 to $ 175)	0.06 (0.03 to 0.11)	Cost Saving (-14,115 to 5,054)	84%	99%	100%
Guatemala	1.50% (1.1% to 2.0%)	$ 160.8 (-$ 78 to $ 179)	0.71 (0.18 to 0.60)	225 (-144 to 955)	11%	100%	100%
Guyana	1.73% (1.1% to 2.8%)	$ 94.8 (-$ 238 to $ 277)	0.52 (0.20 to 0.75)	182 (-436 to 1,213)	24%	100%	100%
Haití	7.90% (5.1% to 13.5%)	$ 347.5 ($ 54 to $ 115)	0.45 (0.05 to 0.23)	764 (279 to 2,310)	0%	51%	98%
Honduras	2.89% (1.9% to 4.8%)	$ 234.6 ($ 14 to $ 259)	0.52 (0.15 to 0.67)	452 (25 to 1,510)	2%	99%	100%
Jamaica	2.25% (1.5% to 3.5%)	-$ 64.8 (-$ 511 to $ 247)	0.23 (0.10 to 0.40)	Cost Saving (-1,805 to 2,119)	56%	100%	100%
México	1.41% (1.0% to 2.0%)	-$ 494.9 (-$ 1,385 to $ 166)	0.14 (0.06 to 0.22)	Cost Saving (-7,645 to 2,788)	88%	100%	100%
Nicaragua	7.51% (5.1% to 11.7%)	$ 280.0 ($ 79 to $ 301)	0.17 (0.05 to 0.25)	1,604 (357 to 5,792)	0%	55%	97%
Panamá	1.27% (0.9% to 1.7%)	-$ 614.1 (-$ 1,404 to $ 36)	0.20 (0.08 to 0.30)	Cost Saving (-6,666 to 304)	96%	100%	100%
Paraguay	2.12% (1.4% to 3.6%)	$ 48.9 (-$ 395 to $ 301)	0.32 (0.12 to 0.55)	153 (-1,055 to 2,120)	32%	100%	100%
Perú	1.15% (0.7% to 2.0%)	$ 13.2 (-$ 420 to $ 326)	0.32 (0.05 to 0.55)	41 (-1,397 to 4,592)	47%	98%	99%
Santa Lucía	3.01% (2.1% to 4.5%)	-$ 272.6 (-$ 948 to $ 167)	0.08 (0.04 to 0.14)	Cost Saving (-9,588 to 4,090)	81%	100%	100%
San Vicente y las Granadinas	3.00% (2.1% to 4.6%)	-$ 179.6 (-$ 803 to $ 199)	0.11 (0.05 to 0.19)	Cost Saving (-6,165 to 3,785)	72%	99%	100%
Suriname	0.65% (0.4% to 1.0%)	-$ 428.8 (-$ 1,113 to $ 104)	0.58 (0.24 to 0.90)	Cost Saving (-1,925 to 298)	91%	100%	100%
Trinidad y Tabago	1.68% (1.1% to 2.7%)	-$ 1,501.2 (-$ 3,147 to -$ 358)	0.02 (0.01 to 0.05)	Cost Saving (-123,406 to -21,027)	100%	100%	100%
Uruguay	2.12% (1.4% to 3.2%)	-$ 1,094.3 (-$ 2,447 to -$ 218)	0.02 (0.01 to 0.04)	Cost Saving (-80,637 to -13,058)	100%	100%	100%
Venezuela	1.22% (0.9% to 1.8%)	-$ 558.9 (-$ 1,487 to $ 76)	0.21 (0.09 to 0.33)	Cost Saving (-6,330 to 740)	95%	100%	100%

CE: cost-effective; GDPPC: gross domestic product per capita; QALY: quality-adjusted life years; Prob.: probability.
[a]Refers to a threshold of 1 GDPPC per QALY; [b]Refers to a threshold of 3 GDPPC per QALY.
Note: All negative ICERS are cost saving

Table A-6. Scenario analysis: Incremental cost of Uniject of US$=1.5. Results of the threshold and cost-effectiveness analysis and 95% confidence intervals from probabilistic sensitivity analysis, 2013 US dollars, 5% discount rate

Country	Threshold Analysis	Cost-Effectiveness Analysis					
	Absolute increment in oxytocin use needed to be cost-effective at threshold of 1 GDPPC per QALY	Cost difference per 1,000 institutional deliveries	Incremental QALYs per 1,000 institutional deliveries	Incremental cost-effectiveness ratio ($ per QALY)	Prob. of being cost saving	Prob. of being cost-effective at a threshold of 1 GDPPC[a]	Prob. of being cost-effective at a threshold of 3 GDPPC[b]
Argentina	5.07% (4.0% to 6.7%)	$ 276.8 (-$ 843 to $ 1,099)	0.11 (0.03 to 0.19)	2,562 (-5,041 to 29,401)	26%	85%	98%
Bahamas	2.51% (2.0% to 3.6%)	-$ 1,021.8 (-$ 3,845 to $ 669)	0.10 (0.03 to 0.22)	Cost Saving (-26,939 to 18,782)	83%	98%	100%
Barbados	4.22% (2.9% to 6.9%)	-$ 255.7 (-$ 2,011 to $ 865)	0.07 (0.01 to 0.17)	Cost Saving (-34,968 to 45,689)	55%	89%	98%
Belice	12.48% (9.7% to 17.9%)	$ 1,028.5 ($ 450 to $ 1,271)	0.12 (0.04 to 0.24)	8,923 (1,923 to 31,926)	0%	17%	70%
Bolivia	10.67% (8.3% to 15.2%)	$ 1,200.7 ($ 677 to $ 991)	0.33 (0.08 to 0.45)	3,669 (1,613 to 13,009)	0%	20%	90%
Brasil	7.51% (5.9% to 10.3%)	$ 1,000.6 ($ 480 to $ 1,307)	0.07 (0.02 to 0.15)	13,343 (3,523 to 55,989)	0%	42%	90%
Chile	6.18% (4.8% to 7.8%)	-$ 46.5 (-$ 1,654 to $ 960)	0.03 (0.01 to 0.05)	Cost Saving (-33,141 to 102,495)	54%	75%	92%
Colombia	4.96% (4.2% to 6.1%)	$ 758.3 (-$ 6 to $ 1,196)	0.22 (0.07 to 0.39)	3,499 (-20 to 17,477)	3%	84%	100%
Costa Rica	6.63% (5.6% to 8.3%)	$ 537.8 (-$ 334 to $ 1,123)	0.09 (0.04 to 0.16)	6,007 (-2,197 to 29,396)	10%	60%	98%
Cuba	15.27% (12.6% to 19.1%)	$ 946.4 ($ 437 to $ 1,290)	0.05 (0.02 to 0.09)	19,060 (5,248 to 63,777)	0%	3%	34%
Rep. Dominicana	7.41% (5.5% to 10.5%)	$ 934.0 ($ 393 to $ 1,278)	0.19 (0.07 to 0.36)	4,805 (1,266 to 18,753)	0%	49%	95%
Ecuador	4.37% (3.1% to 6.8%)	$ 829.3 ($ 190 to $ 1,256)	0.48 (0.17 to 0.94)	1,714 (256 to 6,329)	1%	95%	100%
El Salvador	12.02% (9.3% to 17.3%)	$ 1,093.1 ($ 552 to $ 1,147)	0.16 (0.05 to 0.27)	6,769 (2,105 to 23,995)	0%	12%	78%
Granada	10.18% (8.1% to 13.1%)	$ 717.2 (-$ 105 to $ 1,170)	0.06 (0.02 to 0.11)	12,458 (-1,314 to 55,452)	4%	28%	74%
Guatemala	4.51% (3.7% to 5.8%)	$ 1,160.8 ($ 400 to $ 699)	0.71 (0.14 to 0.71)	1,625 (610 to 4,920)	0%	89%	100%
Guyana	5.18% (3.8% to 7.8%)	$ 1,094.8 ($ 634 to $ 1,146)	0.52 (0.13 to 0.76)	2,103 (788 to 8,705)	0%	80%	100%
Haití	23.71% (16.9% to 39.1%)	$ 1,347.5 ($ 313 to $ 376)	0.45 (0.04 to 0.24)	2,964 (1,264 to 10,023)	0%	0%	29%
Honduras	8.68% (6.3% to 13.8%)	$ 1,234.6 ($ 651 to $ 940)	0.52 (0.11 to 0.73)	2,379 (991 to 8,671)	0%	44%	95%
Jamaica	6.74% (5.1% to 9.2%)	$ 935.2 ($ 437 to $ 1,216)	0.23 (0.08 to 0.44)	4,048 (929 to 15,398)	0%	64%	98%
México	4.23% (3.6% to 5.2%)	$ 505.1 (-$ 392 to $ 1,162)	0.14 (0.04 to 0.24)	3,566 (-1,938 to 31,519)	13%	82%	98%
Nicaragua	22.53% (17.2% to 32.3%)	$ 1,280.0 ($ 797 to $ 1,063)	0.17 (0.03 to 0.28)	7,332 (3,172 to 34,053)	0%	0%	20%
Panamá	3.81% (3.2% to 4.8%)	$ 385.9 (-$ 526 to $ 1,042)	0.20 (0.06 to 0.32)	1,977 (-1,865 to 16,100)	19%	92%	100%
Paraguay	6.36% (4.8% to 9.7%)	$ 1,048.9 ($ 543 to $ 1,310)	0.32 (0.10 to 0.61)	3,287 (965 to 13,464)	0%	64%	97%
Perú	3.45% (2.3% to 5.5%)	$ 1,013.2 ($ 364 to $ 1,147)	0.32 (0.06 to 0.53)	3,182 (712 to 19,068)	0%	78%	98%
Santa Lucía	9.04% (6.9% to 12.1%)	$ 727.4 ($ 19 to $ 1,206)	0.08 (0.03 to 0.16)	9,038 (114 to 41,301)	2%	34%	86%
San Vicente y las Granadinas	9.01% (7.1% to 12.2%)	$ 820.4 ($ 129 to $ 1,241)	0.11 (0.04 to 0.20)	7,690 (624 to 33,402)	0%	40%	86%
Suriname	1.94% (1.4% to 2.8%)	$ 571.2 (-$ 224 to $ 1,058)	0.58 (0.18 to 0.97)	979 (-336 to 5,549)	10%	99%	100%
Trinidad y Tabago	5.04% (3.9% to 6.8%)	-$ 501.2 (-$ 2,307 to $ 802)	0.02 (0.01 to 0.04)	Cost Saving (-70,533 to 100,967)	63%	78%	91%
Uruguay	6.36% (5.0% to 8.5%)	-$ 94.3 (-$ 1,366 to $ 952)	0.02 (0.01 to 0.04)	Cost Saving (-40,588 to 92,259)	46%	66%	86%
Venezuela	3.65% (3.0% to 4.7%)	$ 441.1 (-$ 715 to $ 1,122)	0.21 (0.06 to 0.37)	2,143 (-1,800 to 18,958)	19%	92%	100%

CE: cost-effective; GDPPC: gross domestic product per capita; QALY: quality-adjusted life years; Prob.: probability.

[a]Refers to a threshold of 1 GDPPC per QALY; [b]Refers to a threshold of 3 GDPPC per QALY.

Note: All negative ICERS are cost saving

Table A-7. Scenario analysis: Incremental cost of Uniject of US$=1.0. Results of the threshold and cost-effectiveness analysis and 95% confidence intervals from probabilistic sensitivity analysis, 2013 US dollars, 5% discount rate

Country	Threshold Analysis	Cost-Effectiveness Analysis					
	Absolute increment in oxytocin use needed to be cost-effective at threshold of 1 GDPPC per QALY	Cost difference per 1,000 institutional deliveries	Incremental QALYs per 1,000 institutional deliveries	Incremental cost-effectiveness ratio ($ per QALY)	Prob. of being cost saving	Prob. of being cost-effective at a threshold of 1 GDPPC[a]	Prob. of being cost-effective at a threshold of 3 GDPPC[b]
Argentina	3.38% (2.7% to 4.3%)	-$ 223.2 (-$ 1,612 to $ 555)	0.11 (0.04 to 0.19)	Cost Saving (-9,688 to 12,238)	58%	97%	100%
Bahamas	1.68% (1.3% to 2.3%)	-$ 1,521.8 (-$ 4,123 to -$ 85)	0.10 (0.04 to 0.21)	Cost Saving (-28,193 to -2,006)	98%	100%	100%
Barbados	2.81% (2.0% to 4.8%)	-$ 755.7 (-$ 2,942 to $ 319)	0.07 (0.00 to 0.17)	Cost Saving (-58,453 to 32,434)	85%	97%	99%
Belice	8.32% (6.4% to 11.5%)	$ 528.5 ($ 27 to $ 798)	0.12 (0.04 to 0.21)	4,585 (140 to 20,589)	2%	44%	88%
Bolivia	7.11% (5.5% to 10.2%)	$ 700.7 ($ 319 to $ 631)	0.33 (0.08 to 0.48)	2,141 (767 to 7,591)	0%	55%	98%
Brasil	5.01% (3.9% to 6.6%)	$ 500.6 ($ 72 to $ 838)	0.07 (0.02 to 0.14)	6,676 (594 to 42,860)	2%	72%	97%
Chile	4.12% (3.3% to 5.4%)	-$ 546.5 (-$ 2,009 to $ 401)	0.03 (0.01 to 0.05)	Cost Saving (-43,102 to 36,211)	76%	91%	98%
Colombia	3.31% (2.8% to 4.1%)	$ 258.3 (-$ 363 to $ 721)	0.22 (0.07 to 0.36)	1,192 (-1,267 to 9,572)	21%	95%	100%
Costa Rica	4.42% (3.6% to 5.5%)	$ 37.8 (-$ 947 to $ 625)	0.09 (0.03 to 0.16)	422 (-6,648 to 19,414)	39%	91%	100%
Cuba	10.18% (8.1% to 13.3%)	$ 446.4 (-$ 149 to $ 808)	0.05 (0.02 to 0.09)	8,990 (-1,712 to 44,201)	7%	28%	71%
Rep. Dominicana	4.94% (3.7% to 6.9%)	$ 434.0 (-$ 179 to $ 786)	0.19 (0.06 to 0.38)	2,233 (-491 to 11,611)	5%	79%	100%
Ecuador	2.91% (2.1% to 4.8%)	$ 329.3 (-$ 269 to $ 737)	0.48 (0.16 to 0.98)	681 (-432 to 4,148)	10%	98%	100%
El Salvador	8.02% (6.3% to 10.9%)	$ 593.1 ($ 181 to $ 729)	0.16 (0.04 to 0.26)	3,673 (827 to 16,629)	0%	48%	93%
Granada	6.79% (5.5% to 8.7%)	$ 217.2 (-$ 647 to $ 686)	0.06 (0.02 to 0.11)	3,773 (-6,744 to 31,798)	26%	59%	91%
Guatemala	3.01% (2.5% to 3.7%)	$ 660.8 ($ 166 to $ 446)	0.71 (0.13 to 0.67)	925 (261 to 3,314)	0%	98%	100%
Guyana	3.45% (2.5% to 5.5%)	$ 594.8 ($ 103 to $ 708)	0.52 (0.14 to 0.82)	1,143 (200 to 4,718)	0%	95%	100%
Haití	15.81% (11.3% to 25.5%)	$ 847.5 ($ 179 to $ 247)	0.45 (0.03 to 0.23)	1,864 (812 to 7,218)	0%	4%	56%
Honduras	5.78% (4.2% to 9.2%)	$ 734.6 ($ 328 to $ 605)	0.52 (0.11 to 0.68)	1,415 (530 to 5,657)	0%	69%	100%
Jamaica	4.50% (3.4% to 6.2%)	$ 435.2 (-$ 208 to $ 784)	0.23 (0.08 to 0.43)	1,884 (-586 to 9,906)	8%	83%	100%
México	2.82% (2.3% to 3.4%)	$ 5.1 (-$ 801 to $ 629)	0.14 (0.04 to 0.23)	36 (-4,252 to 14,795)	44%	96%	100%
Nicaragua	15.02% (10.8% to 22.5%)	$ 780.0 ($ 398 to $ 685)	0.17 (0.04 to 0.26)	4,468 (1,702 to 18,681)	0%	3%	64%
Panamá	2.54% (2.1% to 3.1%)	-$ 114.1 (-$ 949 to $ 548)	0.20 (0.07 to 0.32)	Cost Saving (-3,503 to 7,659)	53%	100%	100%
Paraguay	4.24% (3.1% to 6.6%)	$ 548.9 ($ 72 to $ 824)	0.32 (0.09 to 0.61)	1,720 (84 to 8,544)	2%	84%	100%
Perú	2.30% (1.6% to 3.7%)	$ 513.2 (-$ 30 to $ 713)	0.32 (0.07 to 0.60)	1,612 (-46 to 9,690)	5%	92%	100%
Santa Lucía	6.03% (4.8% to 8.3%)	$ 227.4 (-$ 469 to $ 755)	0.08 (0.03 to 0.16)	2,825 (-4,274 to 27,455)	20%	67%	96%
San Vicente y las Granadinas	6.00% (4.8% to 8.1%)	$ 320.4 (-$ 492 to $ 730)	0.11 (0.04 to 0.22)	3,003 (-3,059 to 19,270)	20%	76%	98%
Suriname	1.29% (1.0% to 1.9%)	$ 71.2 (-$ 736 to $ 643)	0.58 (0.15 to 0.98)	122 (-940 to 4,177)	36%	100%	100%
Trinidad y Tabago	3.36% (2.6% to 4.5%)	-$ 1,001.2 (-$ 3,177 to $ 278)	0.02 (0.01 to 0.05)	Cost Saving (-81,478 to 25,326)	90%	97%	100%
Uruguay	4.24% (3.3% to 5.5%)	-$ 594.3 (-$ 2,459 to $ 496)	0.02 (0.01 to 0.05)	Cost Saving (-57,553 to 59,832)	78%	90%	96%
Venezuela	2.43% (2.0% to 3.0%)	-$ 58.9 (-$ 1,067 to $ 643)	0.21 (0.07 to 0.36)	Cost Saving (-3,380 to 8,844)	52%	100%	100%

CE: cost-effective; GDPPC: gross domestic product per capita; QALY: quality-adjusted life years; Prob.: probability.
[a]Refers to a threshold of 1 GDPPC per QALY; [b]Refers to a threshold of 3 GDPPC per QALY.
Note: All negative ICERS are cost saving

Figure A-1. Deterministic sensitivity analysis: Net benefit each 1,000 deliveries expressed in terms of GDPPC considering a cost-effectiveness threshold of 1 GDPPC, Argentina

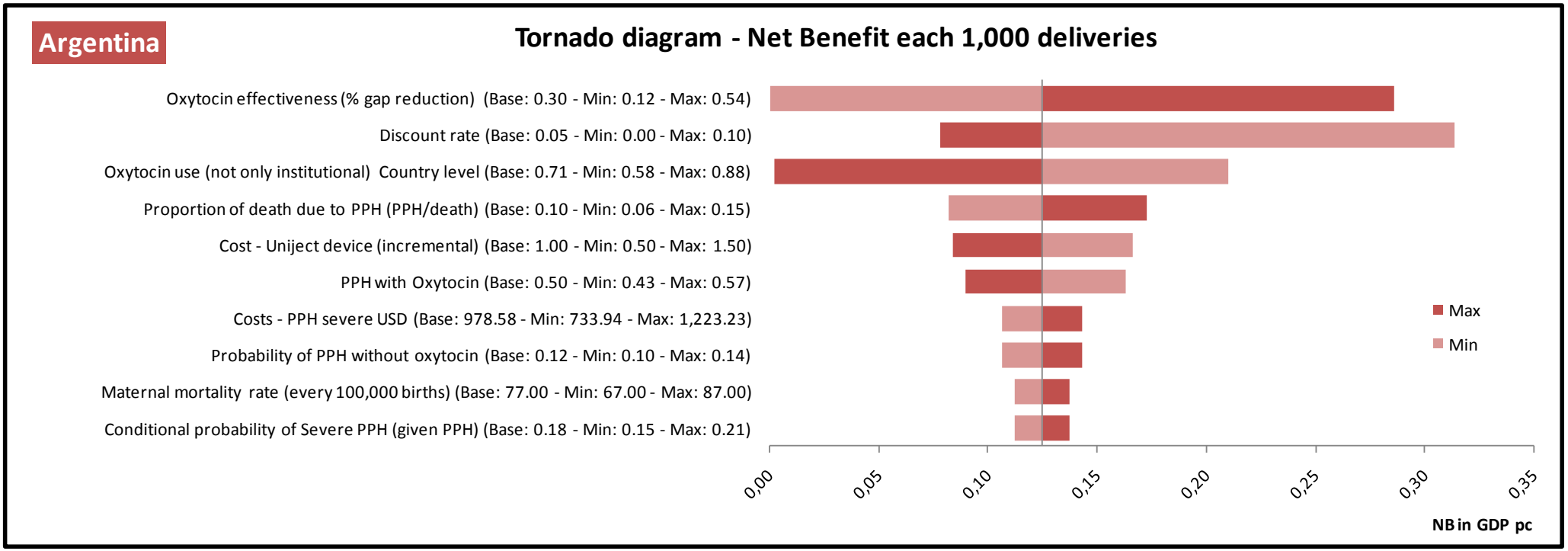

Figure A-2. Deterministic sensitivity analysis: Net benefit each 1,000 deliveries expressed in terms of GDPPC considering a cost-effectiveness threshold of 1 GDPPC, Colombia

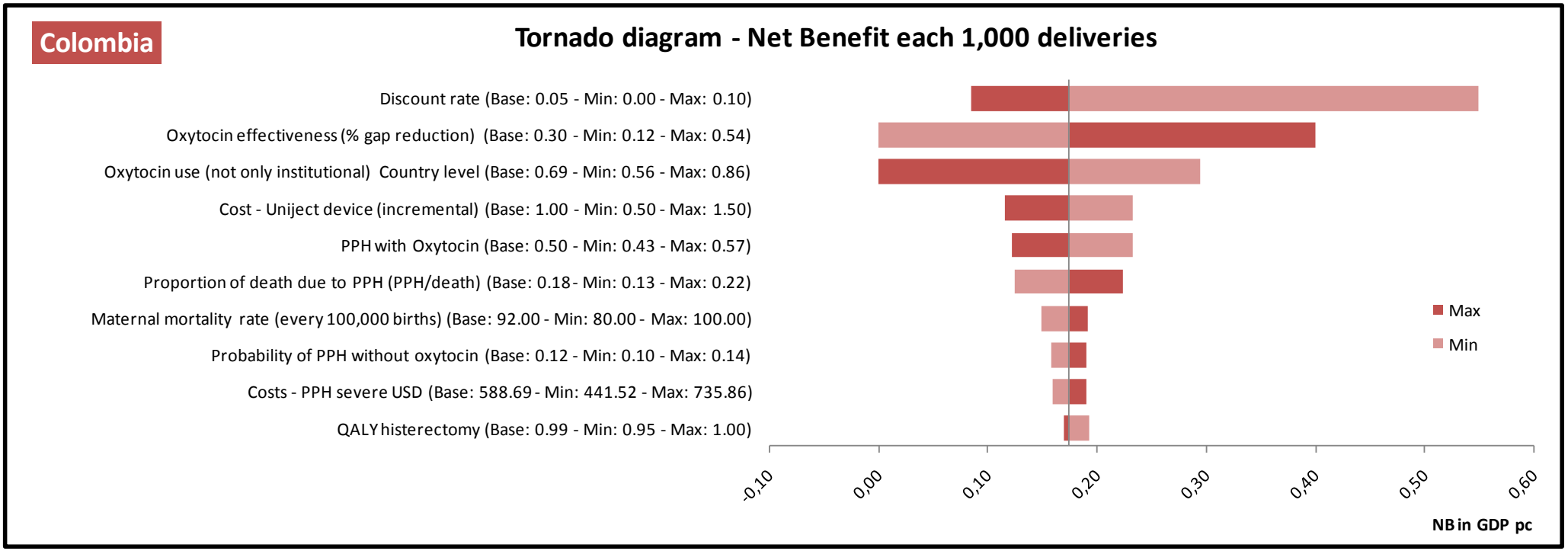

Figure A-3. Deterministic sensitivity analysis: Net benefit each 1,000 deliveries expressed in terms of GDPPC considering a cost-effectiveness threshold of 1 GDPPC, Brazil

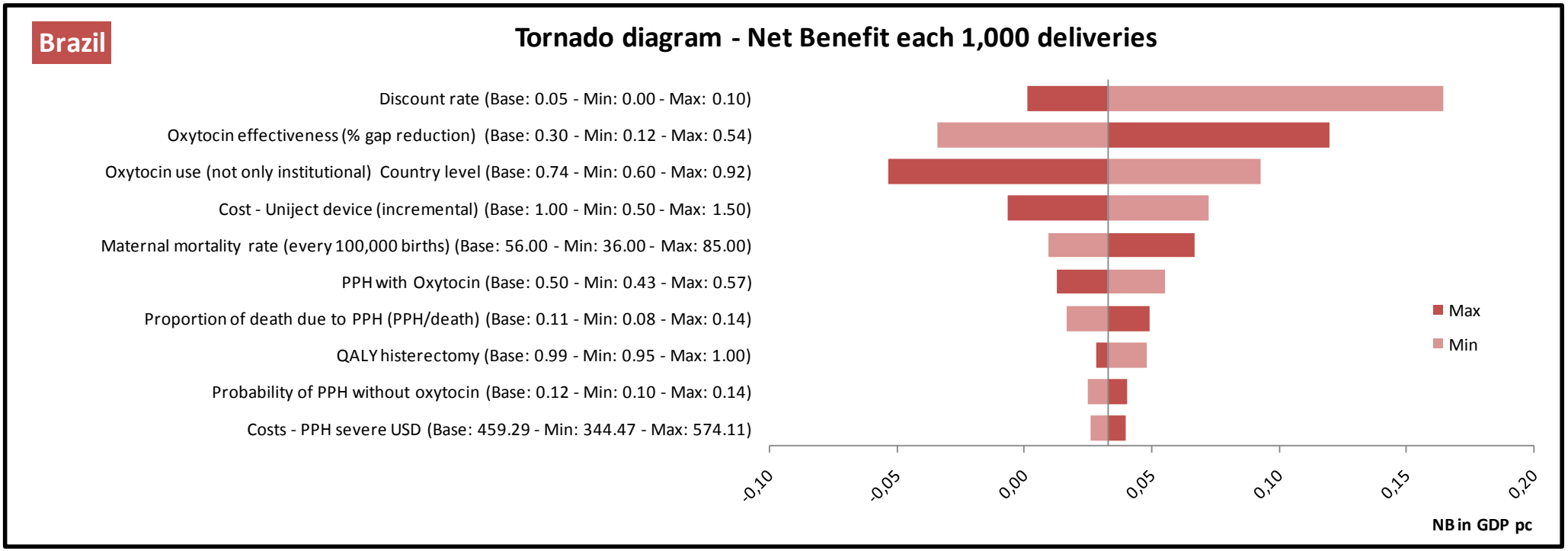

Figure A-4. Deterministic sensitivity analysis: Net benefit each 1,000 deliveries expressed in terms of GDPPC considering a cost-effectiveness threshold of 1 GDPPC, Peru