Health Economic Modelling to Support Decision-Making

Assessing a Novel Uterotonic for the Prevention of Postpartum Haemorrhage

Jeffrey L. Jacobs - Director, Product Innovation & Market Access, Merck for Mothers
Kunal Saxena, PhD - Director, Center for Observational Research & Real World Evidence, Merck

PPH Community of Practice Annual Meeting
July 21–23, 2020
Intractable unmet need in PPH prevention

“For many years, we have been looking for a heat stable uterotonic that can prevent postpartum haemorrhage in women in those parts of the world that do not have access to reliable refrigeration and where the quality of non-heat stable uterotonics cannot be ensured.”

- Dr Tedros Adhanom Ghebreyesus, Director-General, World Health Organization, June 2020
Responding to unmet need

A novel alternative for PPH prevention - Heat-stable Carbetocin

Heat-stability characteristics @ 30°C, 40°C, 50°C

Comparative efficacy & safety analysis

WHO / Country Recognition

World Health Organization Model List of Essential Medicines

WHO recommendations
Uterotonic for the prevention of postpartum haemorrhage
December 2018

Stringent Regulatory Approval
Institut suisse des produits thérapeutiques
Swiss Agency for Therapeutic Products

May 2020 --- Swissmedic has authorised Carbetocin Ferring, injectable solution, for the prevention of uterine haemorrhage due to postpartum uterine atony.
Novel innovation

How are novel innovations assessed for potential adoption?

- What is the clinical impact of the new intervention?
- How much does it cost?

Health outcomes & Price
Janet's mother and sister hold a treasured photo
Janet, a mother of three, fell victim to PPH

Health Economic Modelling to Support Decision-Making

Background

Kunal Saxena, PhD
Director, Center for Observational Research & Real World Evidence
Merck
Potential adoption of a novel innovation demands a holistic assessment

Cost-Effectiveness Analysis

Good value for my money?

Health outcomes & Costs
Cost-effectiveness analysis: a combination of inputs

General inputs

Clinical inputs

Economic inputs

285 parameters

Decision tree

Outcome
Cost-effectiveness
Janet’s mother and sister hold a treasured photo of Janet, a mother of three, who fell victim to Postpartum Hemorrhage (PPH).

Strengthening Postpartum Hemorrhage

Health Economic Modelling to Support Decision-Making

Utero-tonics for the Prevention of PPH

The Model

Photo: Paul Joseph Brown
Health economic model for uterotonics in the prevention of PPH

Objective:
• inform decision-makers on potential integration of a novel uterotonic into country programming

Allows for:
• integration of different treatments, health outcomes & costs associated with PPH due to uterine atony;

• cost-effectiveness analyses of heat-stable carbetocin compared to other uterotonics* for PPH prevention
  • heat-stable carbetocin is the newest recognized uterotonic for PPH prevention^

• exploration of different hypothetical scenarios

* ergometrine was not included in the assessment despite being included in the WHO Recommendations. Country-level Guidelines are inconsistent to its utility
^ WHO Recommendations on uterotonics for the prevention of PPH, 2018; WHO EML, 2019
Janet’s mother and sister hold a treasured photo of Janet, a mother of three, who fell victim to PPH.

**Strengthening Postpartum Hemorrhage**

**Health Economic Modelling to Support Decision-Making**

**Uterotonics for the Prevention of PPH**

**Structure**

*India as use-case*
At each section of the decision tree, inputs are applied. These inputs are sourced via literature review or, where not available, key opinion leader guidance is captured.

Key: C-section, caesarean section; mL, millilitre; PPH, postpartum haemorrhage. No PPH = blood loss of less than 500mL within 24 hours after birth; Mild-to-moderate PPH = blood loss of 500 mL or more within 24 hours after birth. Severe PPH = blood loss of 1,000mL or more within 24 hours after birth.
Health Economic Model - Structure

Perspective & Population

- The public healthcare system
  - central or state governments
  - hospital administrators

- India as the use-case
  - readily adaptable to other low- & middle-income countries

- Considers direct costs to the healthcare system only
  - Costs: drugs, administration, healthcare resource utilization, follow-up & cold-chain
  - Adverse events associated with uterotonics were not modelled

- Considers pregnant women in the 3rd stage of labour while undergoing delivery in public health facilities (caesarian and vaginal deliveries; subgroup for women who have anaemia)

- Considers quality concerns with oxytocin
Health Economic Model - Structure

Intervention vs Comparator: prevention of PPH

**Heat-stable Carbetocin**

**Intervention:**
Heat-stable Carbetocin 100µg IM or IV injection

**Comparators**

*Comparators:*
- Oxytocin 10IU IM or IV injection**, or
- Misoprostol 600 mcg (oral) , or
- Oxytocin 10IU IM/IV + Misoprostol 600mcg (oral)^

*Ergometrine is not included in the model
** 1st choice, as per Indian Guidelines
^ Estimated at 20% in the model (80% of women receive oxytocin 10 IU & 20% of women receive oxytocin 10IU + misoprostol 600µg)
Janet’s mother and sister hold a treasured photo
Janet, a mother of three, fell victim to PPH

Strengthening Postpartum Hemorrhage

Cost-effectiveness Analysis
(India as use-case)

Inputs
Health Economic Model

Inputs

General
- Population
- Health care setting

Clinical
- Uterotonic dosing
- Efficacy
- PPH Management
- Disability
- Mortality

Economic
- Drug & drug administration costs
- Healthcare resource use (PPH-related)
- Cold-chain costs
Health Economic Model - Inputs

Key Inputs – examples

**General**

Proportion of C-section births*:

| Source | 11.9% National Family Health Survey, Government of India (2017) |

**Clinical**

Risk of Mortality as per location of Healthcare Setting*:

<table>
<thead>
<tr>
<th>Healthcare Setting</th>
<th>Risk of mortality: odds ratio</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>2.16</td>
<td>Tort et al. (2015)</td>
</tr>
<tr>
<td>Secondary</td>
<td>1.49</td>
<td></td>
</tr>
<tr>
<td>Tertiary</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

**Economic (Indian rupees [USD])**

Blood Transfusion per Unit of Blood*#:

<table>
<thead>
<tr>
<th>Healthcare Setting</th>
<th>Cost of Blood Transfusion per Unit of Blood</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>1,126 [14.94]</td>
<td>KOL opinion</td>
</tr>
<tr>
<td>Secondary</td>
<td>1,126 [14.94]</td>
<td></td>
</tr>
<tr>
<td>Tertiary</td>
<td>1,689 [22.41]</td>
<td></td>
</tr>
</tbody>
</table>

* Above data inputs are readily modifiable within the model by changing the source
* Exchange rate of US $ 1 = 75.23 Indian rupees (www.oanda.com/currency/converter, Accessed June 9, 2020)
Strengthening Postpartum Hemorrhage

Cost-effectiveness Analysis
(India as use-case)

Results

Janet’s mother and sister hold a treasured photo
Janet, a mother of three, fell victim to PPH
Cost-effectiveness Analysis

Results

Based on a set cohort size of women, the assumptions as per the model structure, and the inputs provided, the following types of cost-effectiveness results will be generated:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Total costs</th>
<th>Incremental Cost</th>
<th>Effectiveness</th>
<th>Incremental Effectiveness</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heat-stable Carbetocin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxytocin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxy/Miso@</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Misoprostol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Key: ICER = incremental cost-effectiveness ratio
@ Oxy/Miso = oxytocin +/- misoprostol (assumption: 80% of women receive only oxytocin & 20% of women receive oxytocin + misoprostol)
Cost-effectiveness Analysis

Heat-stable carbetocin is cost-effective compared to oxytocin, oxy/miso & misoprostol for PPH prevention

Incremental Cost-Effectiveness Ratio (ICER) – All PPH Events Avoided

Base case results for the cohort of 1,000,000 women*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>ICER All PPH Events Avoided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heat-stable Carbetocin</td>
<td></td>
</tr>
<tr>
<td>Oxytocin</td>
<td>Heat-stable Carbetocin is dominant</td>
</tr>
<tr>
<td>Oxy/Miso@</td>
<td>Heat-stable Carbetocin is dominant</td>
</tr>
<tr>
<td>Misoprostol</td>
<td>Heat-stable Carbetocin is dominant</td>
</tr>
</tbody>
</table>

"Dominant" = intervention is less costly with better health outcomes

Key: * Cohort size is readily modifiable
@ Oxy/Miso = oxytocin +/- misoprostol (assumption: 80% of women receive only oxytocin & 20% of women receive oxytocin + misoprostol)
**Key Take Aways**

- Effective PPH prevention is the first-line of defense, at a population level, to improve health outcomes & reduce costs

- Heat-stable carbetocin is a cost-effective uterotonic for PPH prevention, associated with lower total treatment costs and better health outcomes

- Sensitivity analysis results found the risk of mortality and duration of hospital stay to have the greatest impact on cost-effectiveness

- After testing different scenarios, heat-stable carbetocin is the most cost-effective uterotonic for PPH prevention in all but one analysis

- Heat-stable carbetocin warrants inclusion into country programming because it makes the health system more efficient and less burdensome

- Heat-stable carbetocin, as shown by this cost-effectiveness analysis, can strengthen country responses to PPH and support achievement of country SDG* & UHC* goals

---

* SDG = Sustainable Development Goals; UHC = Universal Health Coverage
Janet’s mother and sister hold a treasured photo of Janet, a mother of three, who fell victim to PPH.

Strengthening Postpartum Hemorrhage

Health Economic Modelling to Support Decision-Making

Assessing a Novel Uterotonic for the Prevention of Postpartum Haemorrhage

Thank you!

For follow-up, please write: Jeffrey_Jacobs@merck.com