PPH: Opportunities for improved health outcomes and cost-savings - Heat-stable Carbetocin as a use-case in product introduction

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Jeffrey Jacobs, MSD for Mothers
Ice-breaker

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Or use QR code
Introducing Heat-stable Carbetocin as a cost-effective maternal health care commodity to improve health systems resilience in Nigeria

• Olatunde Amode, Clinton Health Access initiative
• Background and Context

• Postpartum hemorrhage burden in Nigeria

• Heat stable carbetocin introduction in Nigeria

• Predictive analysis of cost-effectiveness of heat stable carbetocin

• Conclusion
Obstetric Hemorrhage is a leading cause of maternal death contributing about 23%. Uterine atony is the commonest cause of PPH.

Nigeria has a maternal mortality ratio of 1,047 per 100,000 live births, with a women standing a 1 in 19 life-time risk of maternal death.

- Administration of a uterotonic after birth is the most effective tool for prevention and treatment of PPH.
- A quality audit uterotonic from health facilities and pharmacies found that up to 74% of oxytocin and 34% of misoprostol samples failed quality test.
- Skilled birth attendance rate is 51% with variations across different states of the country.

3. UNICEF. Nigeria Country Office Annual Report 2022. RAM3 COAR.rdl (unicef.org)
The Smiles for Mothers project (2020 - 2023) piloted the use of heat stable carbetocin for PPH prevention in 3 states in Nigeria

Heat stable carbetocin added to the national essential medicine list

Heat stable carbetocin added to essential medicine lists in Kano and Niger states

Postpartum management algorithm in the life-saving skills manual updated to include heat-stable carbetocin and tranexamic acid

Heat stable carbetocin added to the essential medicine list of Lagos state

Facilities engaged (3 Tertiary HFs, 75 secondary HFs, 9 PHCs) 87

Health workers trained (770 doctors, nurses or midwives, 137 pharmacists) 907

Women reached 101,531 of 2,032,828 5%

Uterotonic Administration (n=18)

PPH Incidence (n=18)

Total uterotonic administration increased as HSC utilization increased from 16% at introduction to 70% at the end of the study period

Downward trend in PPH incidence with a 36.5% decrease recorded in all deliveries
SfM Nigeria conducted a cost-effectiveness analysis from November 2020 to December 2021 using a predictive analytic model.

**Aim**

To determine the relative cost-effectiveness of Heat-Stable Carbetocin compared with the current standard of care for PPH prevention in Nigeria.

**Objectives**

1. To assess the cost-effectiveness of heat-stable carbetocin for the prevention of PPH compared to oxytocin, misoprostol, and oxytocin-misoprostol combination.


**Problem formulation, Objectives, Scope**

- Kano, Lagos, Niger, Imo, Rivers, Yobe, n=6
- Public THF, SHF, PHF, n=18
- Clinicians, Pharmacists, Managers, Administrators, n=84, structured interviews
- Literature reviews; Uterotonic-Network Meta Analysis, n=20, Secondary data

**Observational study**

**Model parameters**

Modeling (decision-analytics)

**Results:**

- Clinical Outcome measures
- Economic Outcome measures

**Reliability & Validity:**

- One-way Sensitivity Analysis
- Probabilistic Sensitivity Analysis

**Conclusion:**

HSC is a cost-effective intervention
Heat-stable Carbetocin is found to be more cost-effective compared to oxytocin, misoprostol and oxytocin-misoprostol combination for PPH prevention.

Using HSC for PPH prevention is associated with less PPH deaths and less DALYs when compared to oxytocin, misoprostol and oxytocin-misoprostol combination.

The use of heat stable carbetocin for PPH prevention comes at a lesser cost to the healthcare system, with lower PPH events driving this cost differential.
Adopting context-specific design-thinking approaches to tackle challenges in the PPH care will improve maternal care delivery and health outcomes

- Sustainable financing and funding of maternal health care commodities
- Increasing access to high quality uterotonics
- Introducing and scaling up use of heat stable uterotonics
- Improve quality of health care for women delivering at health facilities
- Drive demand for in-facility births
- Provide community-oriented skilled birth attendance
THANK YOU

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A Private Public collaboration model to accelerate introduction of a maternal health drug on the EML in public health sector

• Jeffrey Jacobs, MSD for Mothers
UN Commission on Life Saving Medicines highlights serious quality problems in uterotonics across low- & middle-income countries with limited tangible solutions

- 2012 report identified serious uterotonics quality problems, among 13 RMNCH medicines, across LMICs

- Specific recommendations proposed to address the issue:
  - Thermo-stable oxytocin formulation
  - Temperature monitoring devices for oxytocin packaging
  - Oxytocin in pre-loaded, single-use injection devices for lower cadres
  - Non-parenteral inhalation/intranasal spray-dried (dry powder)

- Remaining recommendation: highest probability of success to formulate and with reasonable go-to-market timeline
  - Thermo-stable oxytocin formulation

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Collaborating to accelerate introduction of a thermo-stable uterotonic on the EML into the public health sector

- **Problem Statement:**
  - Sub-optimal outcomes of uterotonics in preventing PPH

- **Prioritized carbetocin thermo-stable formulation**
  - 15+ years of safe & efficacious use preventing PPH in C-section births in HIC/UMICs

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Collaboration on heat-stable carbetocin led to new evidence, WHO normative policy inclusion, affordable pricing and SRA & LMIC NRA approval.

- Objective: advance a proprietary formulation of carbetocin to prevent PPH designed to be stable..., even in hot and tropical climates (ICH climatic zone IV)

Evidence generation:
- CHAMPION trial started: April 2014
- CHAMPION trial completed enrollment: Jan 2018
- CHAMPION results published in New England Journal of Medicine: Jun 2018

Normative policy:
- WHO recommendations on uterotonics for PPH prevention: Dec 2018
- WHO Essential Medicines List: Jun 2019
- Swissmedic regulatory submission: Sept 2018
- Ferring subsidized price statement: Mar 2019
- Swissmedic regulatory approval (all births) & first product approved under MAGHP procedure: May 2020

SRA regulatory submission
Affordable pricing
LMIC regulatory submissions

SRA = Stringent Regulatory Authority; NRA = National Regulatory Authority
Collaboration on country translation of global normative PPH policy led to inclusion of heat-stable carbetocin on the Essential Medicines List of at least 12 LMICs

<table>
<thead>
<tr>
<th>Country</th>
<th>EML</th>
<th>National guideline</th>
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<tbody>
<tr>
<td>Burkina Faso</td>
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<td>Côte d’Ivoire</td>
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Feasibility, acceptability & appropriate use of heat-stable carbetocin studies conducted in at least nine (8 SSA & India) countries (publications pending)
Multi-country analyses show heat-stable carbetocin is cost-effective compared to oxytocin, misoprostol & oxytocin+/-misoprostol for the prevention of PPH

<table>
<thead>
<tr>
<th>Countries modeled*</th>
<th>Saves direct medical costs of all PPH events by</th>
<th>Reduces severe PPH events by</th>
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<tbody>
<tr>
<td>vs. Oxytocin</td>
<td>1% - 4%</td>
<td>28% - 40%</td>
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<tr>
<td>vs. Misoprostol</td>
<td>1% - 4%</td>
<td>33% - 51%</td>
</tr>
<tr>
<td>vs. Oxytocin+/-Misoprostol</td>
<td>1% - 4%</td>
<td>18% - 30%</td>
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*Kenya (under-development)
**Carbetocin Ferring** (heat-stable formulation of Carbetocin) for the prevention of PPH

- is specifically designed to address limitations in refrigeration in cold-chain transport and storage in the public sector of low- & lower-middle income countries, where more than 90% of PPH-related deaths occur.

- is cost-effective compared to oxytocin and misoprostol for the prevention of PPH, as a result of fewer PPH events and reduced use of additional uterotonics, blood transfusions and healthcare resources, such as cold chain. **Carbetocin Ferring** can save not only women’s lives, but also millions of public healthcare dollars.

- **Carbetocin Ferring** is available at a not-for-profit, accessible price for public-sector & not-for-profit healthcare facilities in low- & lower-middle income countries.

- is WHO Prequalified, is included in the WHO Essential Medicines List and the UNFPA Product Catalogue and is manufactured following globally-recognized quality standards (GMP - Good Manufacturing Practice).
THANK YOU