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

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Ice-breaker

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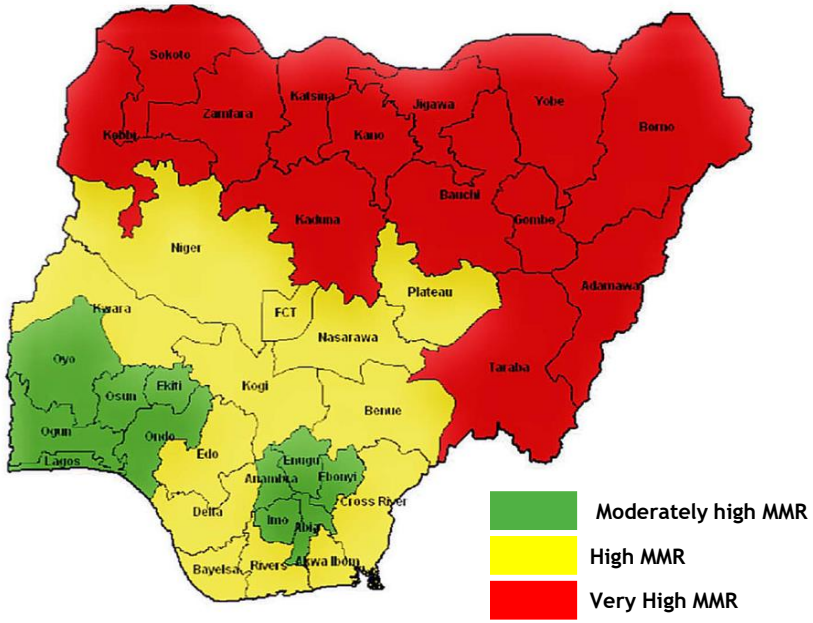
Introducing Heat-stable Carbetocin as a cost-effective maternal health care commodity to improve health systems resilience in Nigeria

- Olatunde Amode, Clinton Health Access initiative

Presentation outline

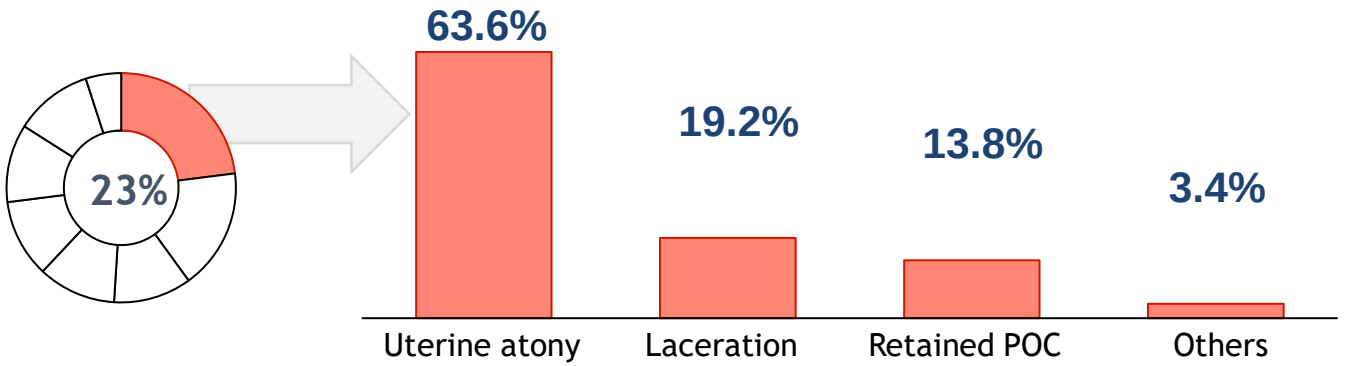
- Background and Context
- Postpartum hemorrhage burden in Nigeria
- Heat stable carbetocin introduction in Nigeria
- Predictive analysis of cost-effectiveness of heat stable carbetocin
- Conclusion

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



82,0000
Maternal deaths per annum

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[1].



213,401,323
Population

53,350,330
Women of Reproductive Age

7,900,000
Births per annum

- Administration of a uterotonic after birth is the most effective tool for prevention and treatment of PPH.
- A quality audit uterotonics from health facilities and pharmacies found that up to 74% of oxytocin and 34% of misoprostol samples failed quality test[2].
- Skilled birth attendance rate is 51% with variations across different states of the country[3].

#RHSUPPLIES2023

1. Trends in maternal mortality 2000 to 2020: estimates by WHO, UNICEF, UNFPA, World Bank Group and UNDESA/Population Division. Geneva: World Health Organization; 2023. 9789240068759-eng.pdf (who.int)
2. Anyakora C et al. Quality medicines in maternal health: results of oxytocin, misoprostol, magnesium sulfate and calcium gluconate quality audits. BMC Pregnancy Childbirth. 2018 Jan 30;18(1):44.
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

2020 — Heat stable carbetocin added to the national essential medicine list

2021 — Heat stable carbetocin added to essential medicine lists in Kano and Niger states

2022 — Postpartum management algorithm in the life-saving skills manual updated to include heat-stable carbetocin and tranexamic acid

2023 — Heat stable carbetocin added to the essential medicine list of Lagos state

87 — **Facilities engaged**

(3 Tertiary HFs, 75 secondary HFs, 9 PHCs)

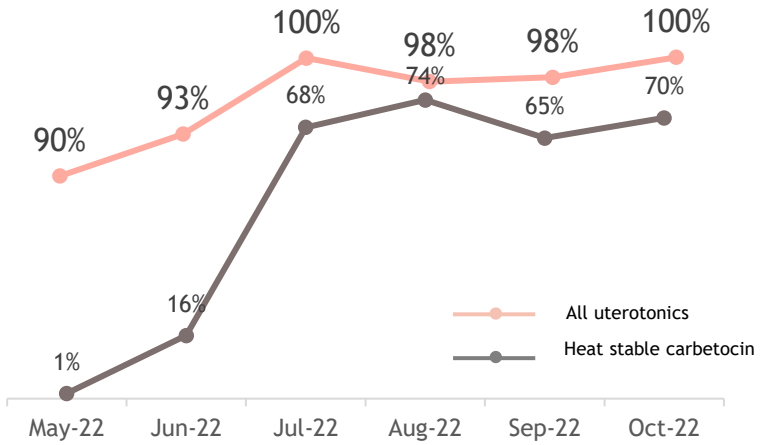
907 — **Health workers trained**

(770 doctors, nurses or midwives, 137 pharmacists)

5% — **Women reached**

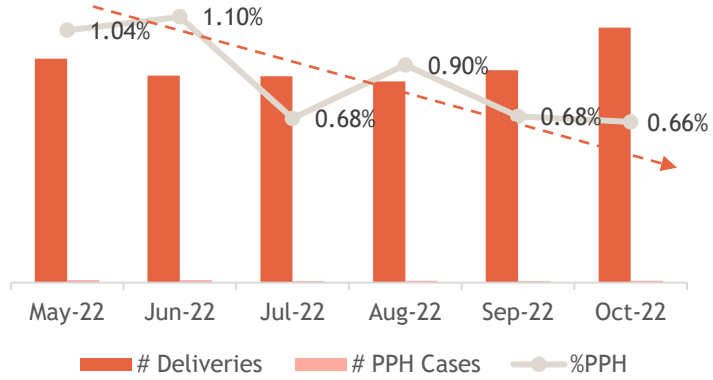
101,531 of 2,032,828

Uterotonic Administration *(n=18)*



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

PPH Incidence *(n=18)*



Downward trend in PPH incidence with a 36.5% decrease recorded in all deliveries

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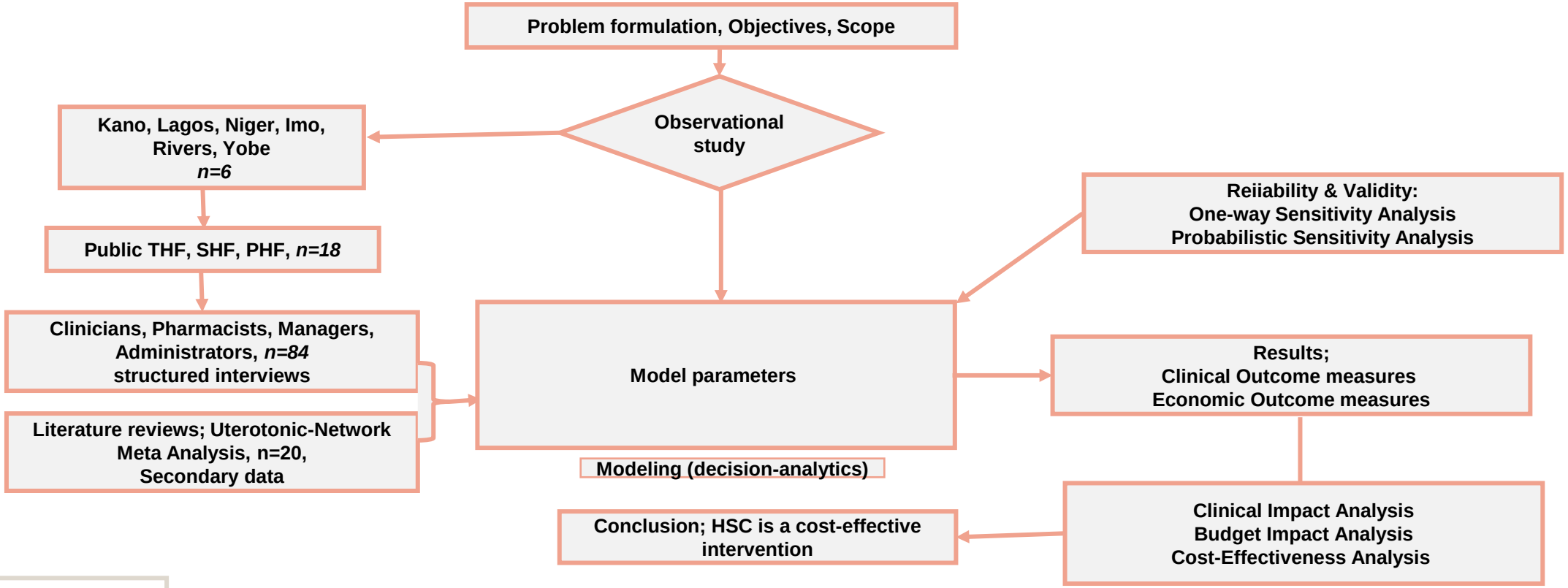
SfM Nigeria conducted a cost-effectiveness analysis from November 2020 to December 2021 using a predictive analytic model

Aim

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

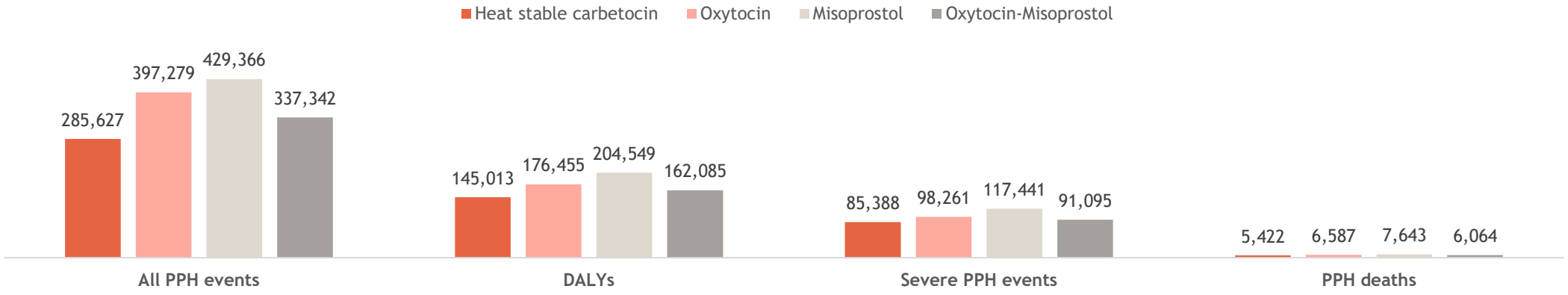
Objectives

1. To assess the cost-effectiveness of heat-stable carbetocin for the prevention of PPH compared to oxytocin, misoprostol, and oxytocin-misoprostol combination.
2. Support the development of an investment case for new uterotonic introduction in Kano, Lagos, Niger states, Nigeria and other low and middle-income settings.

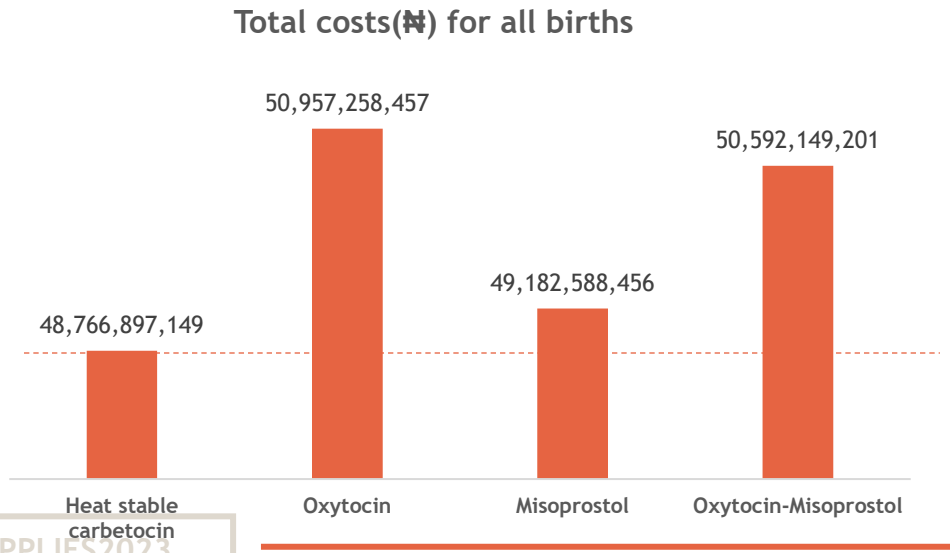


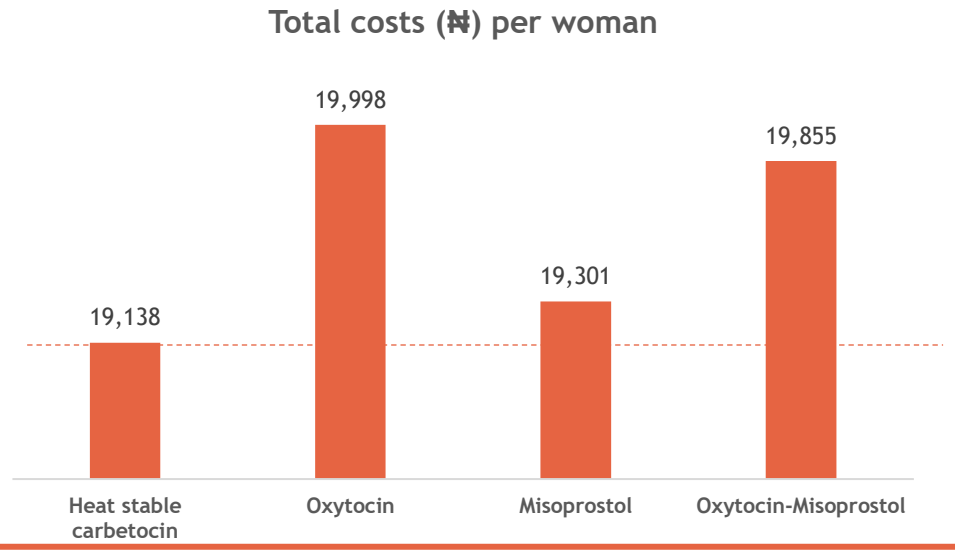
Heat-stable Carbetocin is found to be more cost-effective compared to oxytocin, misoprostol and oxytocin-misoprostol combination for PPH prevention

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

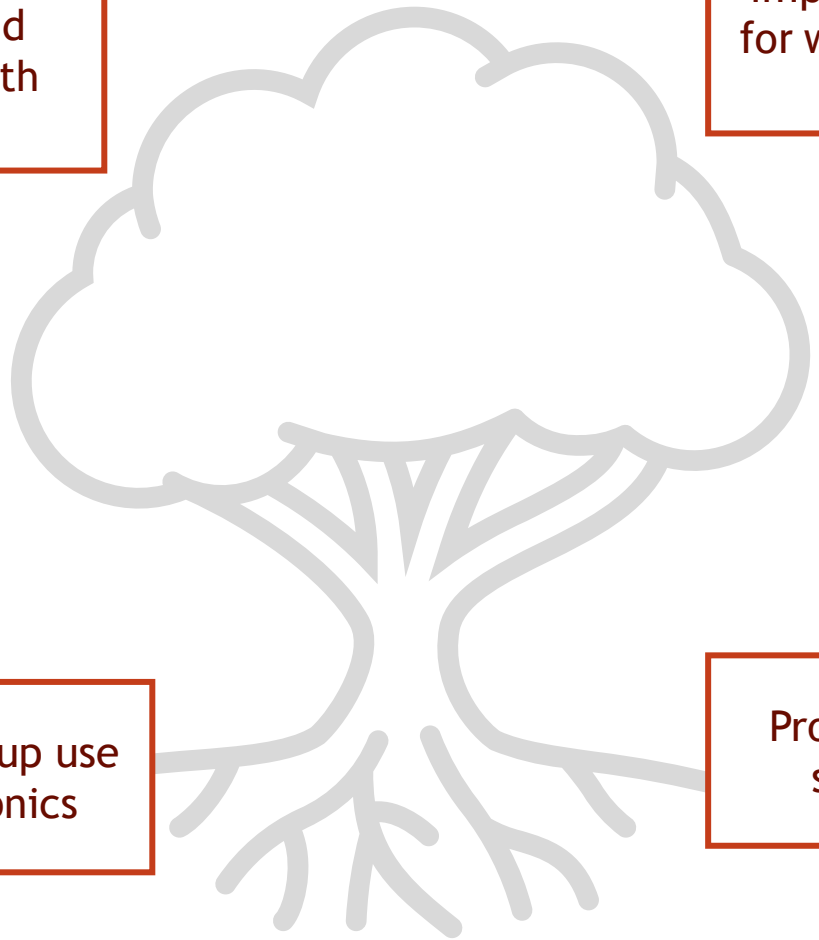
Improve quality of health care for women delivering at health facilities

Increasing access to high quality uterotonics

Drive demand for in-facility births

Introducing and scaling up use of heat stable uterotonics

Provide community-oriented skilled birth attendance



THANK YOU

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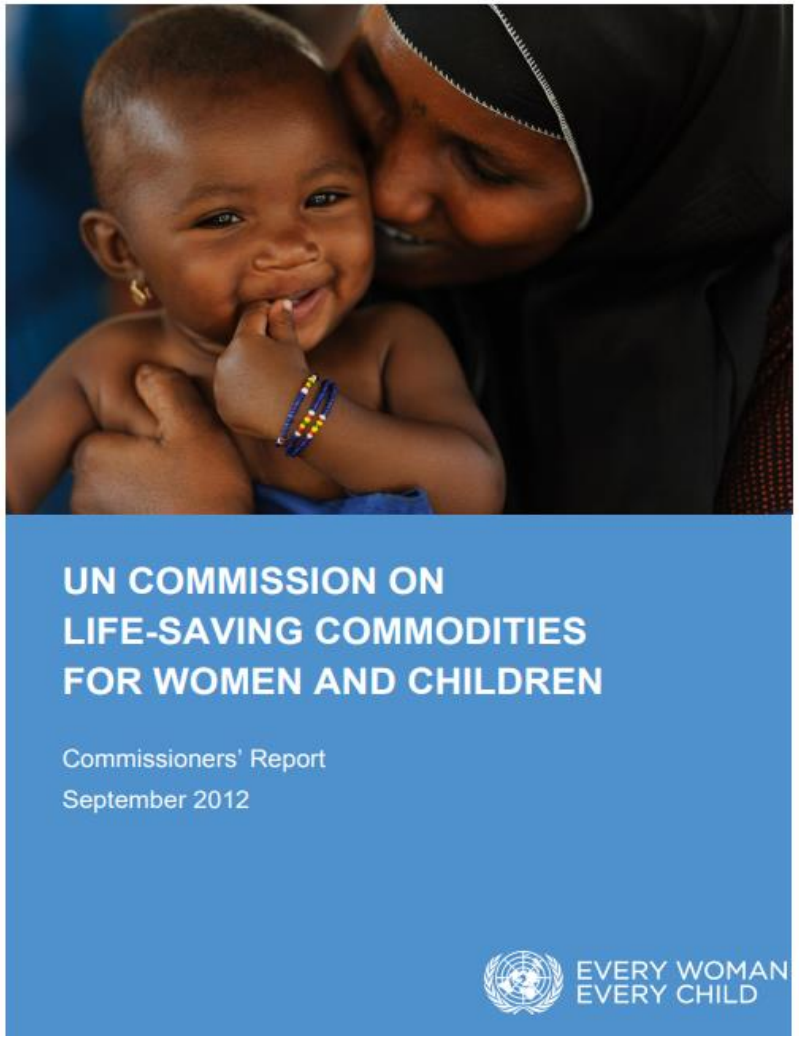
A Private Public collaboration model to accelerate introduction of a maternal health drug on the EML in public health sector

- 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 uterotonic quality problems, among 13 RMNCH medicines, across LMICs[1]

- Specific recommendations proposed to address the issue:
  - *Too expensive (via pilots):*
    - Thermo-stable oxytocin formulation
    - Temperature monitoring devices for oxytocin packaging
    - Oxytocin pre-loaded, single use injection devices for lower cadres
  - *Low Probability of Success to formulate; too slow go-to-market*
    - 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

[1] WHO. Survey of the quality of medicines identified by the United Nations Commission on life-saving Commodities for Women and Children. Geneva: World Health Organization; 2015. Available from: http://apps.who.int/medicinedocs/documents/s23209en/s23209en.pdf

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

Critical scientific & technological advances for sustainable global development

Thermo-stabilizing mechanisms for preserving vaccines & other temperature sensitive, lifesaving pharmaceuticals so that they do not require refrigeration

…the long-term solution is to obviate the need for refrigeration altogether.

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

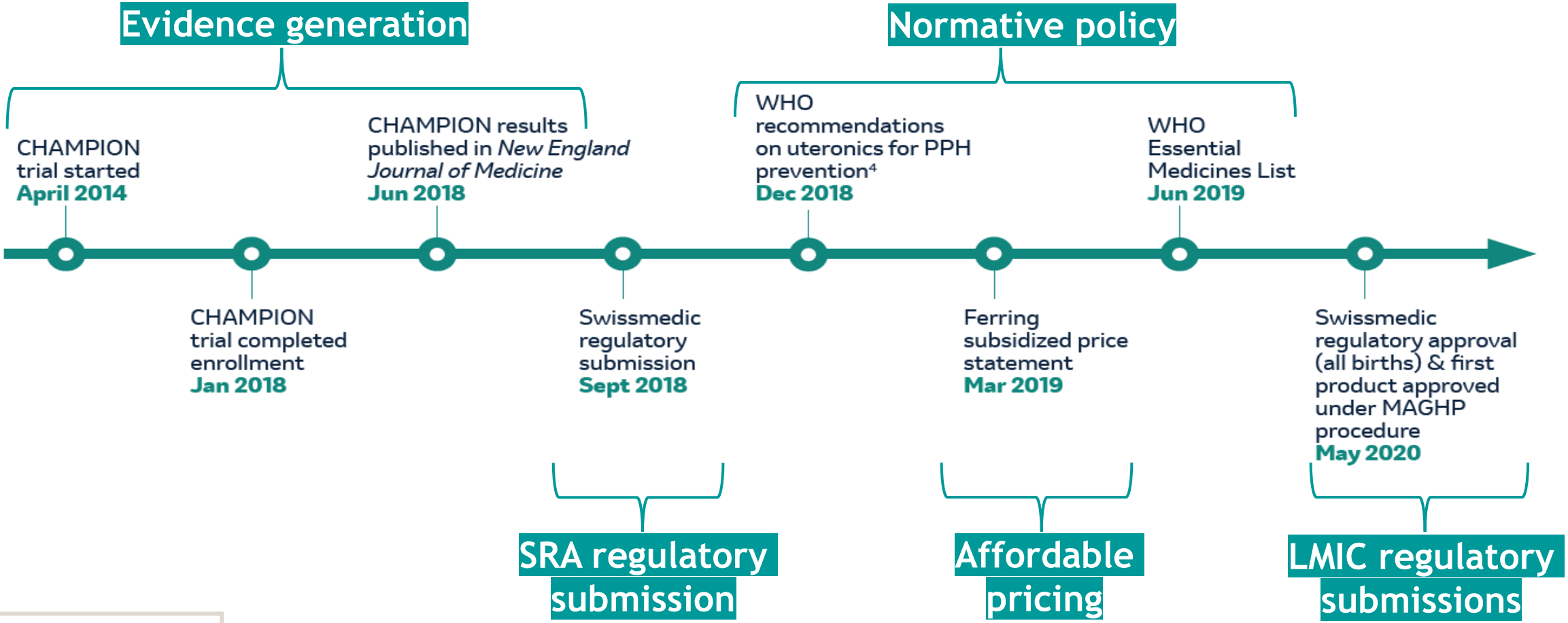
➢ Prioritized carbetocin thermo-stable formulation

- *15+ years of safe & efficacious use preventing PPH in C-section births in HIC/UMICs*

Source: *"50 Breakthroughs: Critical scientific and technological advances for sustainable global development"*, Lawrence Berkely National Lab, 2014; https://ligtt.org/50-breakthroughs

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)*



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

Status: Heat-stable carbetocin inclusion into:

	Country	EML	National guideline
1	Burkina Faso		
2	Côte d'Ivoire		
3	DRC		
4	Ethiopia		
5	Ghana		
6	Kenya		
7	Liberia		
8	Nigeria		*LSS updated*
9	Rwanda		
10	Senegal		
11	Sierra Leone		
12	South Sudan		
13	Uganda		
14	Zambia		

Updated

Drafting

Update pending

Implementation Research
(publications pending)

Feasibility, acceptability & appropriate use of heat-stable carbetocin studies conducted in at least nine (8 SSA & India) countries

Multi-country analyses show heat-stable carbetocin is cost-effective compared to oxytocin, misoprostol & oxytocin+/-misoprostol for the prevention of PPH

Administering heat-stable carbetocin for PPH prevention:

Countries modeled*

- India *(published)*
- Nigeria *(publication pending)*
- Uganda *(preliminary results)*

	Saves direct medical costs of	Reduces all PPH events by	Reduces severe PPH events by
vs. Oxytocin	1% - 4%	28% - 40%	13% - 15%
vs. Misoprostol	1% - 4%	33% - 51%	27% - 38%
vs. Oxytocin+/- Misoprostol	1% - 4%	18% - 30%	7% - 12%

* 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).

Anita with her baby (Nigeria)

Photo: Paul Joseph Brown

THANK YOU