Making Deliveries Safer

Smiles for Mothers

# ESTABLISHING A SUSTAINABLE SUPPLY CHAIN MECHANISM FOR QUALITY UTEROTONICS IN KANO, LAGOS, AND NIGER STATES

## Authors

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## About Smiles for Mothers

The Smiles for Mothers program builds on the efforts of the Nigerian government to reduce maternal death due to postpartum haemorrhage (PPH) in Kano, Lagos, and Niger States. The program supported the 3 states to apply human-centred Design (HCD) principles to develop and implement costed roadmaps for the adoption and roll-out of medicines aligned with WHO recommendations on the use of uterotonics to prevent postpartum haemorrhage, including introducing a new uterotonic, heat-stable Carbetocin.

The Smiles for Mothers program is committed to improving the quality of care for the prevention of PPH in public health facilities and reducing mortality due to PPH using a system-strengthening approach that covers patient literacy and community awareness, supply chain management, and service delivery.

## About the Organisation

The Smiles for Mothers program, through a consortium made up of the Solina Center for International Development and Research (SCIDaR), Clinton Health Access Initiative (CHAI), and Co-Creation Hub (CCHUB) supports the Federal Ministry of Health and the state governments of Kano, Niger and Lagos to reduce maternal mortality due to postpartum haemorrhage (PPH). This program is supported by funding from MSD, through MSD for Mothers, the company's global initiative to help create a world where no woman has to die while giving life. MSD for Mothers is an initiative of Merck & Co., Inc., Rahway, NJ, USA.

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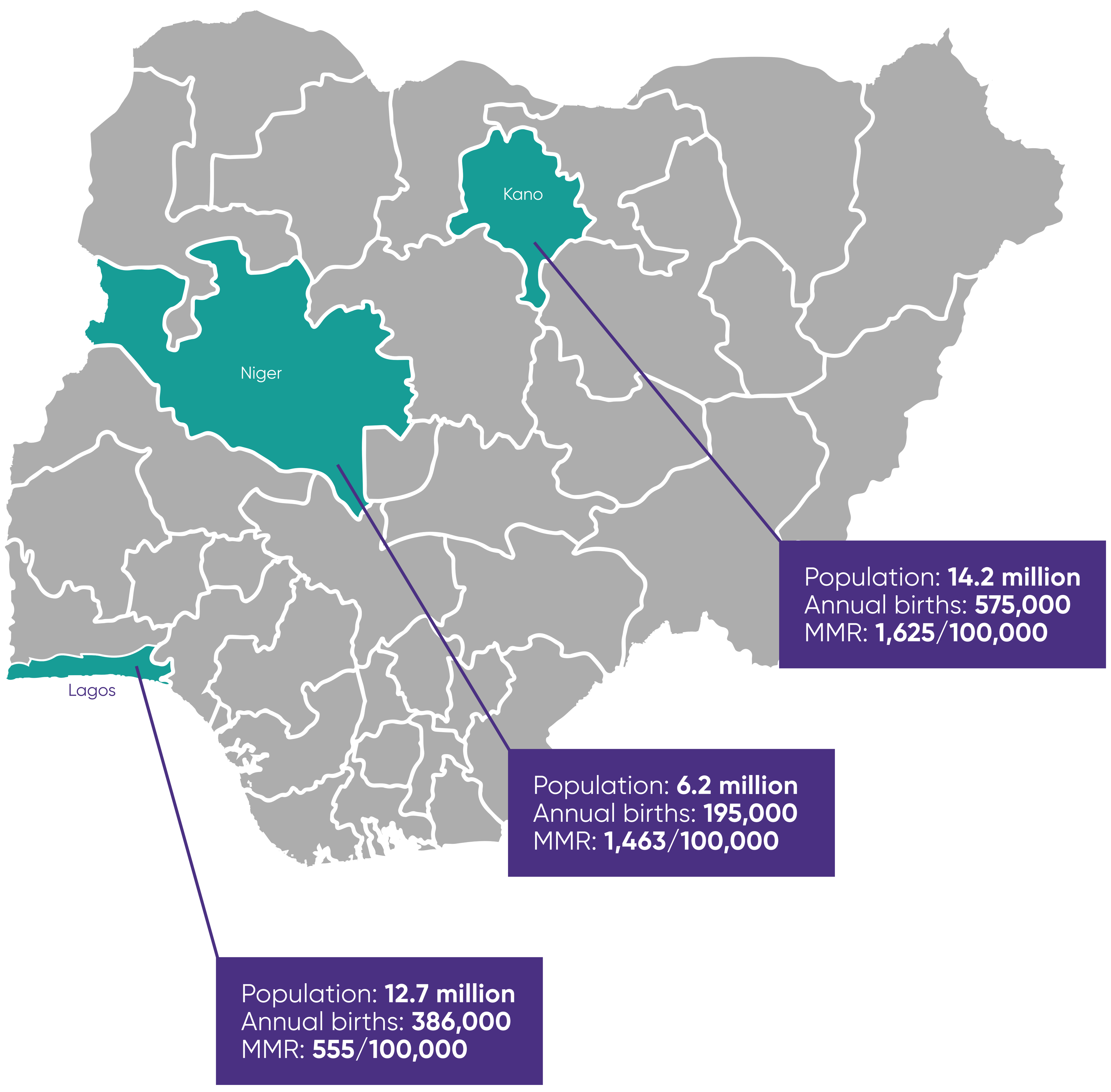
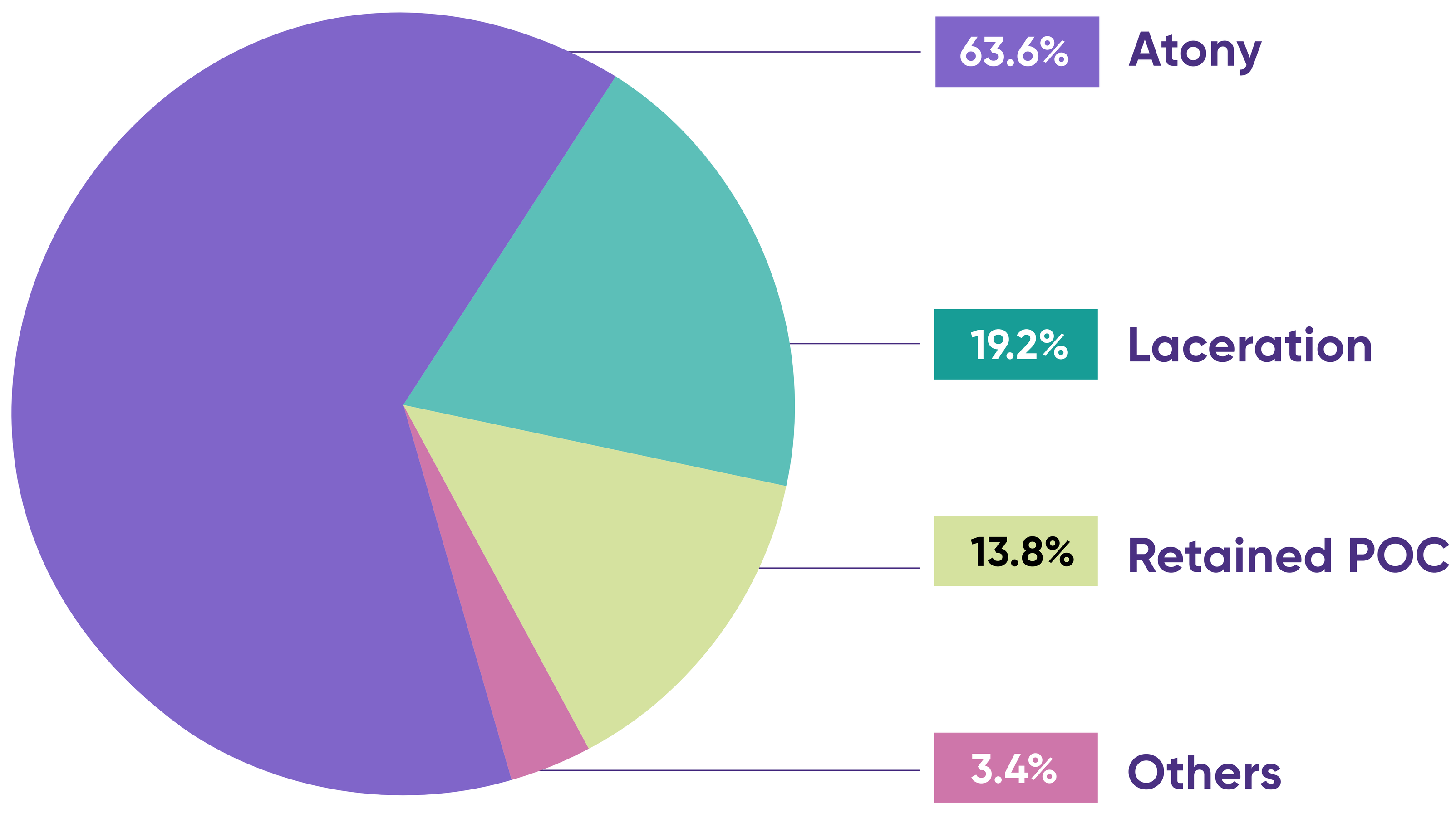
# Introduction

Maternal mortality poses a major global health challenge, especially in Low- and Middle-income countries (LMICs) such as Nigeria. Nigeria bears one of the highest burdens of maternal deaths worldwide, with nearly 20% of global maternal deaths occurring in the country every year[3]. Nigeria is one of the countries with a very high rate of maternal deaths globally, with a maternal mortality ratio of 512 per 100,000 live births.[1] This masks regional disparities within the country--which operates a federal system of government with states that are autonomous and responsible for funding and implementation of primary and secondary health care—which reveal even higher mortality rates in some states[4,5].




Post-partum hemorrhage is one of the leading causes of maternal mortality in the country. The results of a study carried out in the Southern part of the country attributed 27.7% of the maternal deaths recorded to post-partum hemorrhage. In another study in Northern Nigeria, post-partum hemorrhage accounted for 26% of maternal deaths in the area. Routine active management of the third stage of Labor with Uterotonics such as Oxytocin and Misoprostol is the most effective strategy to prevent post-partum hemorrhage due to uterine atony[11]

### Commonest causes of PPH in Nigeria



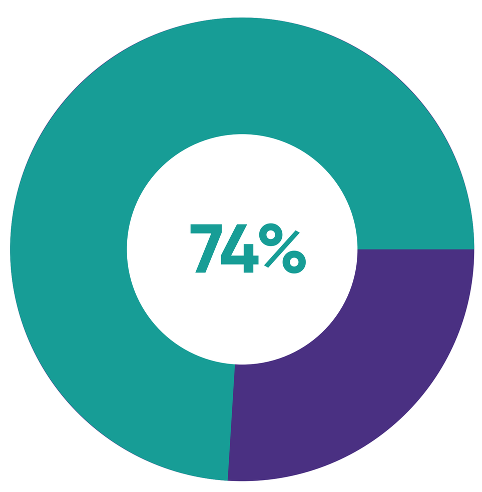

Uterine atony is the most common cause of postpartum hemorrhage in Nigeria

While Oxytocin remains the gold standard for the management of PPH in Nigeria, challenges with maintaining its cold chain significantly impact its potency at service delivery points. This poor quality of Oxytocin was evident in a 2017 survey of quality medicines in maternal health conducted in Nigeria, which showed that 74% of oxytocin injection samples obtained from wholesale and retail pharmacies failed an assay test[12]. Similarly, 34% of sampled products did not meet the specifications for concentration of Misoprostol tablets despite all samples passing visual inspection[12].

### Use of Oxytocin among health workers and Uterotonics quality concerns

A recent study of clinicians in Nigeria showed that 78% of them used oxytocin for PPH management. Oxytocin is the gold standard for PPH prevention

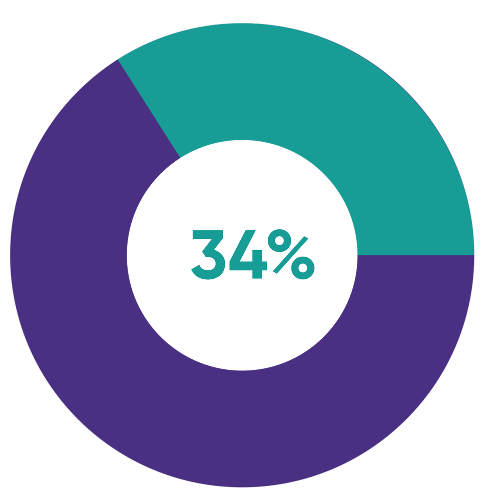

### Survey of quality of Oxytocin in Nigeria




Failed quality assay
Passed quality assay

Quality audit of oxytocin injections in circulation in Nigeria showed an alarming failure rate, up to 74% of samples failed quality test

### Quality of Misoprostol in health facilities




Does not meet specifications
Meets specifications

Although all samples passed a visual inspection, 34% did not meet specification for recommended concentration of Misoprostol

In addition to inadequate storage facilities, lack of knowledge of the appropriate storage conditions for heat-sensitive Uterotonics and improper use of Uterotonics by health workers contribute to the low quality and inefficacy of Uterotonics. In a research on the clinical experiences with the use of oxytocin injection by healthcare providers, only 52% of the respondents knew Oxytocin should be stored at 2°C to 8°C. 41% used 20IU and as much as 10% used 30IU to 60IU for management of PPH[13].

### Supply Chain Challenges contributing to Maternal Mortality

#### Quantification and procurement

Poor forecasting and supply planning[1] as well as weak tendering and procurement processes[2] leading to unavailability of quality products

#### Warehousing and distribution

Incorrect storage of heat sensitive Uterotonics due to poor infrastructure maintenance[4] and lack of cold-chain equipment[3]

#### Data management

Poor data visibility due to inadequate collection, collation and computation practices in facilities and central stores[5]

#### Inventory management

Non uniform inventory management strategies across nodes in the supply chain leading to losses, stock outs and expiries

Challenges across different aspects of the essential medicines supply chain contribute to high maternal mortality and negatively impact new product introduction.

# The Opportunity - Introduction of heat-stable Carbetocin in PPH Management

In 2018, the WHO updated its recommendations on Uterotonics for the prevention of post-partum hemorrhage to include Carbetocin as a Uterotonic option for PPH prevention, especially in settings where Oxytocin is unavailable or its quality cannot be guaranteed[14]. The guidelines update followed the CHAMPION trials, a randomized clinical trial conducted to research the non-inferiority of Carbetocin (heat-stable Carbetocin), a heat-stable analogue of Oxytocin, for the prevention of post-partum hemorrhage during the third stage of labor.

### Updated WHO recommendations


#### Recommendation 1.1

The use of oxytocin (10 IU, IM/IV) is recommended for the prevention of PPH for all births[1]

#### Recommendation 1.2

The use of carbetocin (100 mcg, IM/IV) is recommended for the prevention of PPH for all births in contexts where its cost is comparable to other effective uterotonics[1]

#### Recommendation 1.3

In settings where oxytocin is unavailable (or its quality cannot be guaranteed), the use of other injectable uterotonics (carbetocin, or if appropriate ergometrine/methylergometrine, or oxytocin and ergometrine fixed-dose combination) or oral misoprostol is recommended for the prevention of PPH[1]

Additionally, a network meta-analysis conducted in 2018 by Gallos, et al[15] demonstrated that Heat-stable Carbetocin (HSC) is the highest-ranked single Uterotonic agent for the prevention of blood loss ≥ 500m, HSC may also reduce the use of additional Uterotonics and HSC and Oxytocin have the most favourable side effect profiles among Uterotonics to prevent PPH[15].

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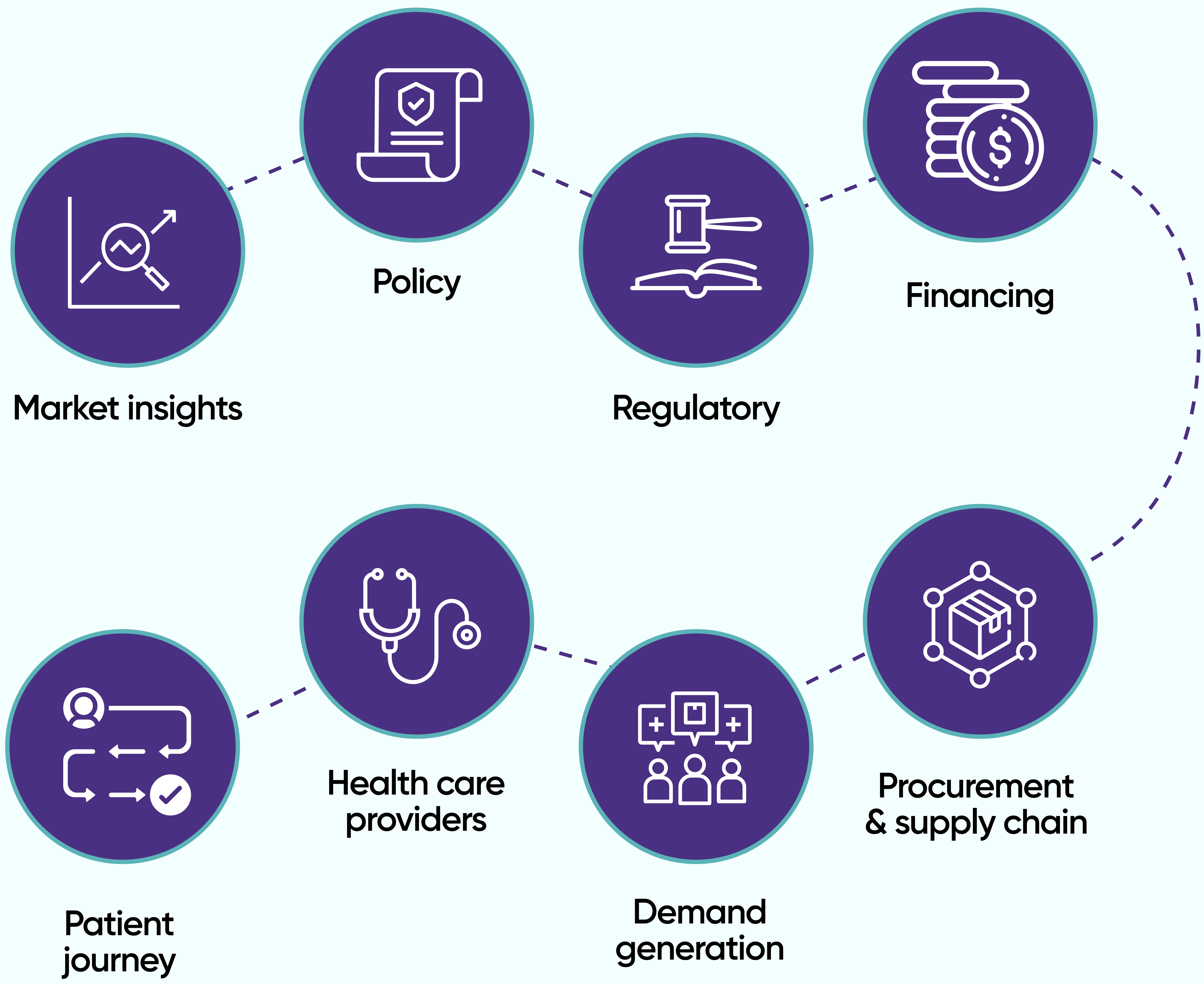
The Smiles for Mothers program supported the Federal Ministry of Health (FMoH) and state governments of Kano, Lagos, and Niger to design and implement innovations to address PPH-related maternal mortality, including the problem of unavailability of quality uterotonics at service points. These innovations included the rollout of the 2018 updated WHO recommendations on Uterotonics to prevent PPH and systems-strengthening interventions to improve the supply chain of essential medicines and Pharmacovigilance in the states.

Smiles for Mothers utilized human-centered design to map the adoption journey for the WHO recommendations on Uterotonics across the market-shaping value chain. Human Centred Design workshops were conducted over 3 phases to identify and map interventions for the successful rollout of the 2018 WHO recommendations.

**Applying Human Centered Design to map interventions to successfully rollout the WHO recommendations on PPH prevention across the market shaping and health system strengthening value chain**

| Phase | Co-research | Co-design | Co-refinement |
|---|---|---|---|
| Process | Collaborated with stakeholders to collect, analyze and synthesize data to identify opportunities | Collaborated with stakeholders to collect, analyze and synthesize data to identify opportunities | Collaborated with stakeholders to collect, analyze and synthesize data to identify opportunities |
| Output | 3 Co-research workshops across 3 states | 9 working sessions for co- design | 2 virtual training sessions in 2 states |
| | 33 Health facilities visited & 221 stakeholders, policy makers, health workers & pregnant women interviewed | 300 separate ideas generated to answer challenge statement | Costed road maps developed (including prototypes of promising solutions) |




The value chain - Building blocks for market shaping & health system strengthening

# Achievements and Successes

We supported the Nigerian government to design and implement critical interventions across the value chain to improve the availability of quality Uterotonics and to rollout the new product heat stable Carbetocin. The program recorded successes across the market shaping value chain leading to improvements in the supply chain for uterotonics and successful rollout of HSC

### Achievements and Successes of the Smiles for Mothers program

Policies

**Supported advocacy for inclusion of heat stable Carbetocin in the National Essential Medicines List (NEML) and dissemination of the document to states**

- Provided the foundation for state level adoption of the updated guidelines in Kano Lagos and Niger

**Supported the FMOH of Nigeria to review and update the Life Saving Skills Manual**

- Laid the foundation for an updated training curriculum and capacity building for health workers in line with the updated WHO recommendations


## Regulatory, financing and procurement

- Collaborated with IDA Foundation and Ferring Pharmaceuticals to obtain NAFDAC approval and secured the required approval for further shipments of Carbetocin Ferring
- Provided **23,000 doses of HSC** for clinical training of health care workers and 6 months of implementation research across 18 secondary health facilities in the 3 focus states
- Distributed **over 46,000 ampoules of HSC** to the focus states to be seeded to the drug revolving fund to drive scalability of HSC and generate funds for subsequent procurement


INDEX NO: 193437
NAFDAC REGISTRATION NO: C4-1721
SERIAL NO: 0000160878
APPLICANT TIN NO: NGO

NATIONAL AGENCY FOR FOOD AND DRUG ADMINISTRATION AND CONTROL (NAFDAC)

Certificate of Registration is hereby granted in respect of:
CARBETOCIN FERRING INJ

*Name & Address of Applicant:*
IDA FOUNDATION
[illegible]

*Name & Address of Manufacturer:*
FERRING PHARMACEUTICAL (CHINA) CO., LTD
[illegible]

*Additional Manufacturing Sites:*

*Additional Details*

| S/N | ITEM | DETAILS |
|---|---|---|
| 1 | HS CODE | [illegible] |
| 2 | PRODUCT CATEGORY | DRUGS |
| 3 | PRODUCT OR PHARMA CLASS | OBSTETRIC AND GYNAECOLOGICAL MEDICATIONS |
| 4 | COMPOSITION/ACTIVE INGREDIENTS & STRENGTH, EXCIPIENTS | [illegible] |
| 5 | DOSAGE FORM/PRESENTATION | [illegible] |
| 6 | PACK SIZES | [illegible] |
| 7 | DATE OF APPROVAL | [illegible] |
| 8 | EXPIRY DATE | [illegible] |

Director-General (NAFDAC)

## Health worker training

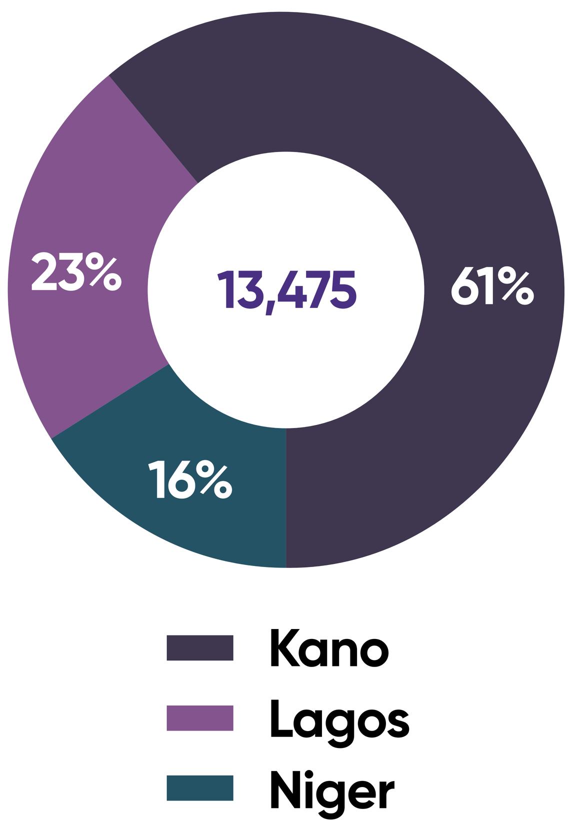
- Trained 770 clinicians (Doctors, Nurses and Midwives on AMTSL
- Trained 136 Pharmacists and Pharmacy Technicians on supply chain best practices, including Pharmacovigilance
- 18 implementation research sites receiving peer-led mentoring on basic emergency obstetric and newborn care (BEMONC)
- 86 implementation facilities (77 SHFs and 9 PHCs) receiving mentoring on supply chain management

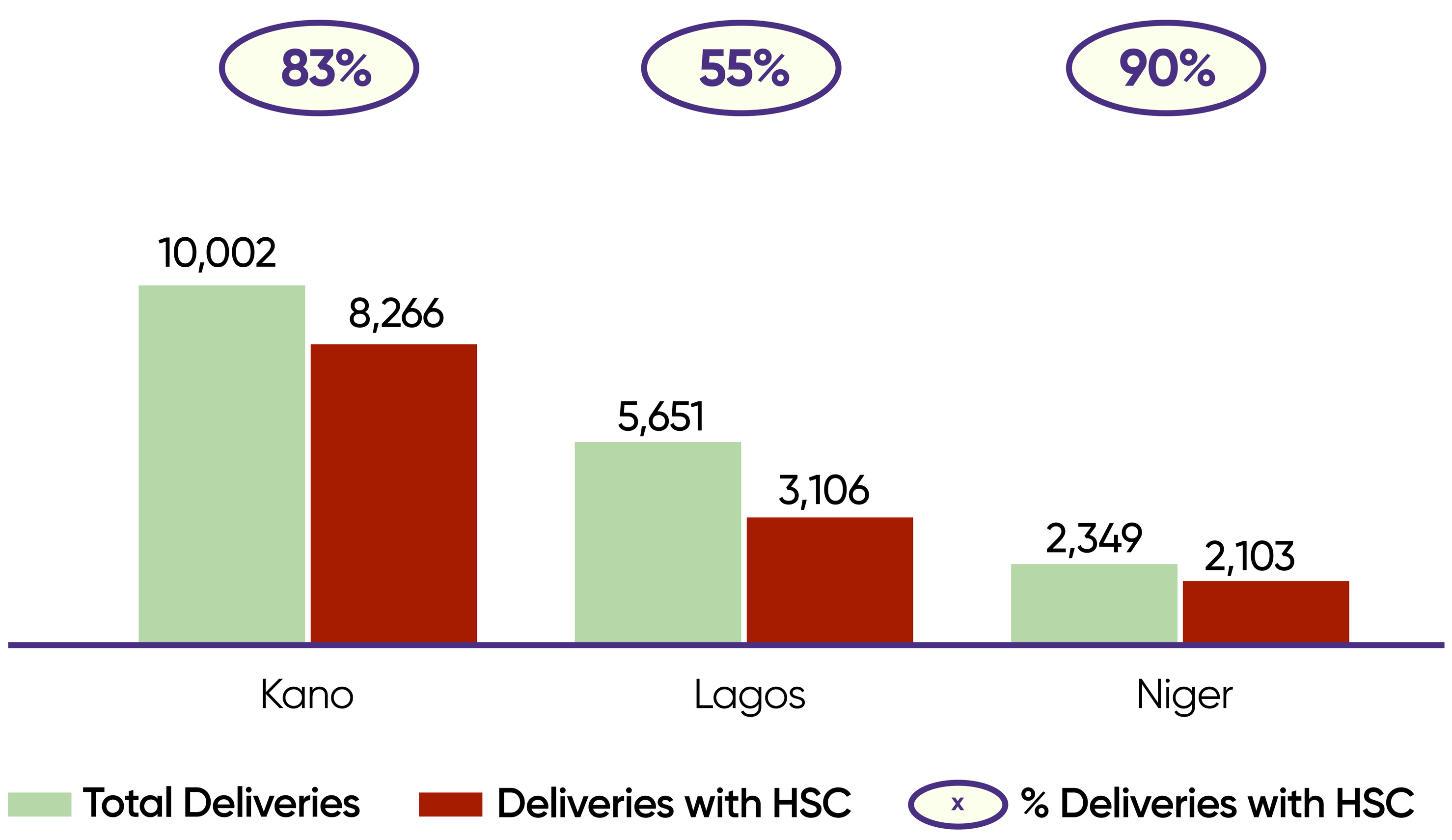
## HSC utilization in facilities

### Heat Stable Carbetocin utilization across 18 program health facilities for the prevention of post partum hemorrhage over 6 months

Over 13,000 doses administered

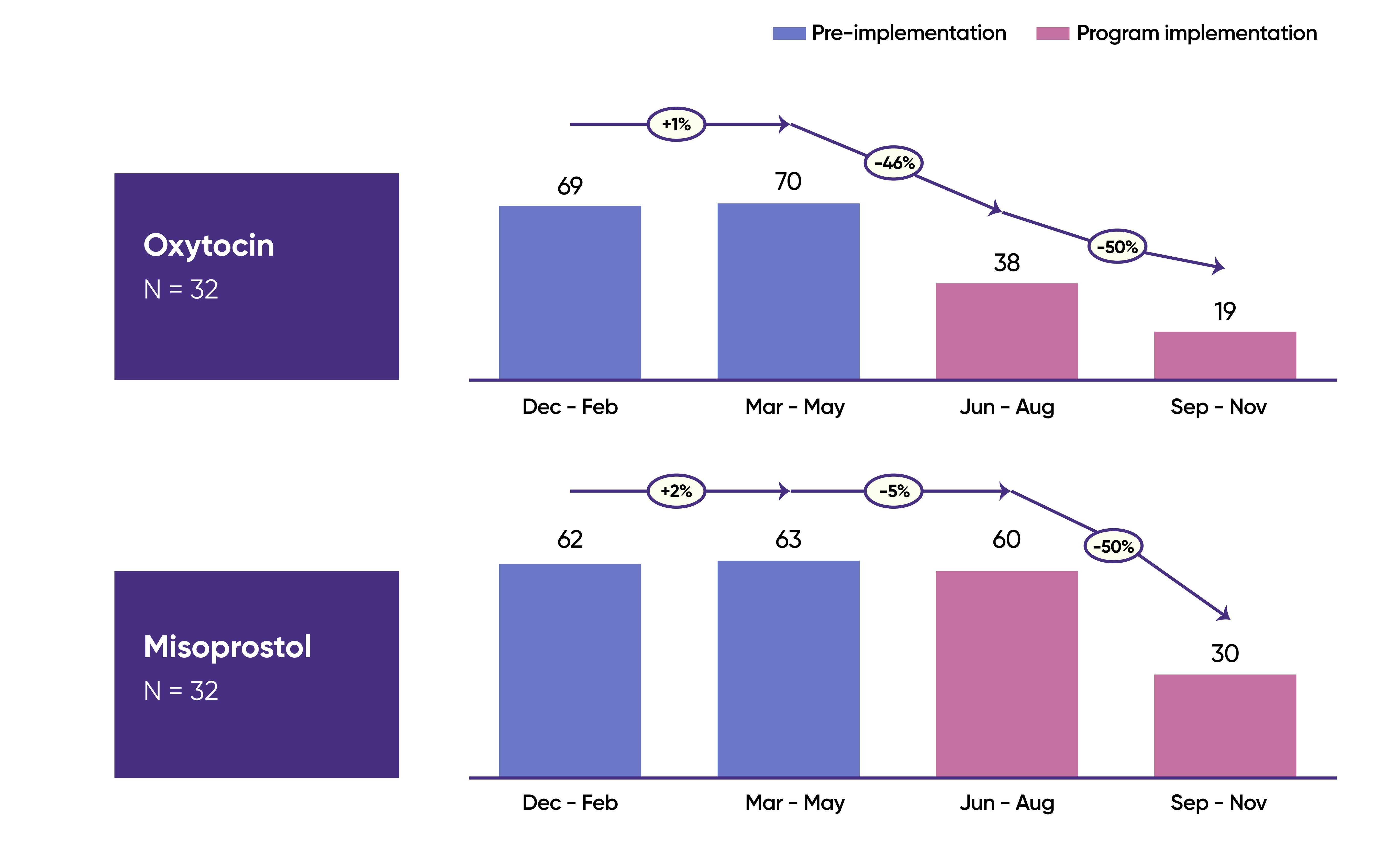
70 program facilities purchasing through DRF



Improvements in Uterotonic stock availability

**Comparison of Uterotonic stockout rate across health facilities in Kano 6 months before program implementation and during the program intervention (% of health facilities reporting stockouts)**




## Wider Health Systems Improvements Recorded

Smiles for Mothers interventions have facilitated wider health system improvements to reduce PPH across the focus states and potentially across Nigeria

**Advocacy for procurement of Quality Uterotonics through the Drug Management agencies**
- DMCSA in Kano procuring better quality brands of Oxytocin

**Supply Chain Integration**
- Supporting integration of Oxytocin and other heat sensitive Uterotonics into the vaccine supply chain

**Cold Chain Maintenance**
- Reducing the burden on cold chain infrastructure through HSC introduction

**Pharmacovigilance strengthening**
- Strengthening Pharmacovigilance for essential medicines using HSC introduction as a touch point

Successful adoption and rollout of the 2018 WHO recommendations across Nigeria will lead to overall improvements in the quality of maternal and child health care in services in Nigeria and also enhanced effort of the Nigerian government towards Sustainable Development Goal 3.1; to reduce maternal mortality ratio to less than 70 deaths of100,000 live births by 2030.

## Recommendations for Action

- Obtain multisector collaboration and early buy-in of government, donors, implementing partners and the private sector to ensure successful rollout of new guidelines and early adoption of innovations
- Utilize adult learning techniques like on-the-job coaching in addition to didactic training approaches for effective capacity transfer and behaviour modification among health workers
- Identify sustainable financing options to drive procurement of life-saving commodities and reduce waste by understanding the total commodity requirements through effective quantification
- Plan for potential delays in the supply chain processes that may extend the lead time for delivery of supplies, including unforeseen geopolitical events such as wars and pandemics like COVID19; as well as bureaucratic processes which often cause significant delays in activities like product registration despite the best efforts of regulatory agencies
- Prioritize Pharmacovigilance and ADR reporting as a cornerstone for program interventions and commit resources to equip health workers with the capacity and tools to implement effectively

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