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## SPECIAL COLLECTION

### ORIGINAL ARTICLE HEAT-STABLE CARBETOCIN

## An Implementation Research Study on Uterotonics Use Patterns and Heat-stable Carbetocin Acceptability and Safety for Prevention of Postpartum Hemorrhage in Nigeria

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### ABSTRACT

**Background and Objective:** The burden of maternal mortality attributable to postpartum hemorrhage (PPH) remains high in Nigeria. Currently, oxytocin, and misoprostol, which are largely of suboptimal quality, are used for PPH prevention and treatment. Heat-stable carbetocin (HSC) is a viable uterotonic option for PPH prevention in a setting like Nigeria where compromised supply and cold chain systems result in the preponderance of poor-quality oxytocin and suboptimal PPH management. It is crucial to understand how healthcare providers (HCPs) accept and use HSC for PPH prevention, and what factors encourage correct uterotonic usage in health facilities, given PPH's ongoing public health challenge. This study aims to elucidate the current prophylactic use of HSC, oxytocin, and misoprostol in secondary and tertiary public health facilities while assessing HSC acceptability to clinicians and establishing factors that enable the appropriate use of uterotonics in health facilities.

**Methods:** Descriptive analysis conducted on quantitative data from patient chart reviews, HCP interviews and assessment, and facility assessment using Stata 15 and Microsoft Excel are presented as counts and percentages, while qualitative data from key informant interviews and in-depth interviews are coded and analyzed using NVivo. The findings from 18 publicly owned secondary and tertiary healthcare facilities across Kano, Lagos, and Niger states in Nigeria were interpreted according to thematic areas. Health facilities selection criteria were high volume of deliveries ( $\geq 30$  deliveries per month), accessible location, availability of trained HCPs (specifically doctors, nurses, and midwives), and willingness to participate in the study.

**Results:** HSC was administered prophylactically in 10,284 (56%) of 18,364 deliveries, with a total of 148 (0.8%) women developing PPH. Approximately 76% of HCPs preferred HSC for PPH prevention compared to other available uterotonics, with clinical guidance from senior HCPs (76%), in-service training (76%), mentoring (84%), and supportive supervision (75%) contributing significantly to the choice and practice of uterotonics use by HCPs.

**Conclusion and Global Health Implications:** HSC, a thermostable analog of oxytocin, holds the potential to prevent PPH without the added cost of administering additional uterotonics and interventions. The introduction

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of HSC requires concerted procurement and capacity-building efforts to create an enabling environment for scale-up. HSC is non-inferior to oxytocin in preventing PPH, has few side effects compared to misoprostol or oxytocin-misoprostol combination, and more cost-effective when compared with the other three uterotonics. Although the geographical scope of our study is only three states in Nigeria, the preponderance of suboptimal uterotonics across the country makes our findings applicable to the whole country and other low- and middle-income countries with similar challenges.

**Keywords:** Thermostable Uterotonics, Postpartum Hemorrhage, Heat-Stable Carbetocin, Maternal Mortality, Training and Mentoring, Supportive Supervision, Supply Chain

Quick Response Code



## INTRODUCTION

### *Background of the Study*

Globally, approximately 800 women die every minute from preventable causes related to pregnancy and childbirth.<sup>[1]</sup> Despite the maternal mortality ratio (MMR) decreasing by 34% between 2000 and 2020, maternal mortality in sub-Saharan Africa remains unacceptably high, contributing 68% of the global burden.<sup>[2]</sup>

In Nigeria, postpartum hemorrhage (PPH) contributes to 20% of maternal deaths.<sup>[2]</sup> Administration of a uterotonic after delivery is recognized as the most effective measure to prevent PPH. About 61% of deliveries in Nigeria occur outside healthcare facilities, with only 43% of deliveries attended by a skilled birth attendant. Public health facilities, particularly those providing primary healthcare and located in the rural areas, provide the majority of maternity services and access to uterotonics immediately after delivery. World Health Organization (WHO) reports that 48.9% of uterotonic samples tested in samples collected from low- and middle-income countries (LMIC) failed quality assessment tests.<sup>[3]</sup> The high prevalence of substandard and falsified uterotonics, particularly oxytocin, misoprostol, and ergometrine correlates with the high incidence of PPH and maternal deaths. Substandard uterotonics are attributable to defects during manufacturing, transporting, and storing. In addition, the incidence of PPH is increased by the use of expired drugs and falsified uterotonics.

Oxytocin, the principal uterotonic for PPH prevention and treatment in Nigeria, has had persistent cold storage challenges. Degradation and other supply chain-related issues result in the nonavailability of good-quality oxytocin at the point of care.<sup>[4,5]</sup> Assay tests on samples from Nigerian health facilities and pharmacies reveal that oxytocin and misoprostol often have reduced potency and efficacy. This issue stems from manufacturing quality and improper storage conditions, which are crucial for maintaining the effectiveness of these uterotonics.<sup>[6]</sup> Due to the low efficacy of available oxytocin, clinicians administer misoprostol alongside oxytocin to improve uterine contraction and reduce PPH events.<sup>[7]</sup> Unlike oxytocin, misoprostol does not require

cold storage conditions and is stable at room temperature. Misoprostol, however, degrades when exposed to humidity and must be stored in double aluminum blisters to avoid degradation. The oxytocin-misoprostol combination, though not a recommendation of the WHO, has gained traction in the prevention and treatment of PPH in recent years. The combination has shown more efficacy than oxytocin or misoprostol administered singly to prevent PPH; however, it is associated with more side effects.

Recognizing the challenges with the quality of uterotonics, WHO in 2018 recommended heat-stable carbetocin (HSC) as a prophylactic uterotonic option in settings where the quality of oxytocin cannot be guaranteed.<sup>[8]</sup> HSC, an oxytocin analog does not require cold storage and retains its efficacy for at least three years stored at 30°C and six months at 40°C.<sup>[9]</sup> The addition of HSC to the WHO Essential Medicines List following its recommendation means that countries like Nigeria can benefit from the wide-scale use of HSC for PPH prevention.<sup>[10]</sup>

With the addition of HSC to the available uterotonics for PPH prevention in Nigeria, it is important to not only provide evidence of its efficacy and effectiveness in preventing PPH, but also necessary to document the necessary conditions for its safe introduction as well as provide the perspective of HCPs with use case experience. Thus, to provide context-specific evidence for HSC use for PPH prevention, we assessed the introduction of HSC in three Nigerian states, and the complementary system strengthening activities such as providing on-the-job training, mentoring HCPs, and facilitating availability and access to quality maternal care important for its safe and appropriate use.

The innovatory introduction of HSC at an affordable public access price makes its cost comparable to that of other uterotonics in the field. This unique opportunity to add to the body of knowledge on HSC use and applicability for PPH prevention in Nigeria, given the appalling reports on oxytocin and misoprostol efficacy, also provides relevant information generalizable to similar countries. Elucidation of HCPs perceptions and promoting factors for rational use of uterotonics is also important to inform intentional scale-up interventions across the country.

### **Objectives of the Study**

The study aimed to generate context-specific research evidence for the safe and effective use of uterotonics to prevent and manage PPH, including the scale-up of relevant new innovations in Nigeria. The specific objectives were to (1) assess the current clinical practices for three prophylactic uterotonics—HSC, oxytocin, and misoprostol—in use in secondary and tertiary public health facilities; (2) investigate the acceptability of HSC to providers for prophylactic use; and (3) understand the factors that enable the appropriate use of uterotonics in health facilities.

### **Specific Aims and Hypothesis**

Our null hypothesis states that the addition of HSC to the current uterotonic mix for PPH prevention will not be associated with a significant change in clinical practice relating to PPH prevention and management, as HSC may not be acceptable to clinicians for PPH prevention and that there are no enabling factors for the appropriate use of uterotonics for PPH management.

### **METHODS**

This study utilized a mixed-methods research design to obtain information about the clinical use of three prophylactic uterotonics in secondary and tertiary healthcare facilities across three states with a high burden of maternal mortality from PPH (Kano [Northern Nigeria]; Lagos [Western Nigeria], and Niger [Middle Belt Nigeria]) in Nigeria. Combining elements of quantitative and qualitative data was necessary to provide a more comprehensive context to our study, increase its generalizability, and with triangulation, increase the credibility of our findings.

Eighteen publicly owned maternal healthcare facilities (six per state) were purposefully selected for the study, which spanned five months between June and October 2022. Selection criteria of health facilities included a high volume of deliveries ( $\geq 30$  deliveries per month), easily accessible location, presence of trained HCPs (specifically doctors, nurses, and midwives), and willingness to participate in the study.

For standardization, HCPs were retrained on Comprehensive Emergency Obstetric Newborn Care (CEmONC) and trained on the safe and appropriate use of HSC during Active Management of the Third Stage of Labor (AMTSL), followed by a ten-week clinical mentoring program to strengthen clinical skills through mentor-supported, on-the-job training activities. Additional interventions included enhancing the supply chain for consistent availability of HSC and other maternal health products, revitalizing the pharmacovigilance system, distributing updated PPH management guidelines

and tools, and implementing a supportive supervision system to improve supply chain operations, particularly for uterotonics.

### **Study Variables**

In this study, the acceptability of HSC as a dependent variable is defined as the percentage of HCPs administering HSC for PPH prevention during AMTSL. Acceptability is determined to be dependent on the percentage of HCPs reporting their willingness to use HSC for AMTSL, the percentage of HCPs reporting HSC as their preferred uterotonic of choice for AMTSL HSC with covariables as their perception of the ease of administration, quality, effectiveness in preventing blood loss and cost of HSC, oxytocin, and misoprostol. The percentage of HCPs reporting on the perceived safety of the three uterotonics as a dependent variable has the percentage reporting on the risk of occurrence of side effects and their perception of the ease of managing side effects associated with each uterotonic. Appropriate use of uterotonic is defined as its use for recommended/approved indications (HSC-PPH prevention; oxytocin and misoprostol-PPH prevention and treatment), with the percentage of cases in which HSC was administered for PPH prevention dependent on the administration of appropriate doses of a given uterotonic.

### **Statistical Analysis**

Descriptive analysis was conducted, with results presented as counts and percentages for categorical variables. Data cleaning and analyses were conducted in Stata 15<sup>[11]</sup> and Microsoft Excel.<sup>[12]</sup> Entries with missing values and duplicates were deleted. Inconsistency and errors were corrected where possible and checks were carried out to ensure consistency of the data formats. Following qualitative data collection, all transcripts were coded, data analyzed using NVivo,<sup>[13]</sup> and findings interpreted according to thematic areas. Qualitative data collection was processed by converting text to a consistent format, removing irrelevant text, stemming words where necessary, correcting spelling errors, and extracting previously named entities. Combining quantitative and qualitative data improved our understanding of uterotonic use across facilities; however, we recognize the possibility of subjective bias that may occur due to the novel nature of HSC and dissatisfaction with oxytocin and misoprostol.

### **Ethical Approval**

Approval was obtained from the National Health Research Ethical Committee (NHREC) with approval number NHREC/01/01/2007-15/03/2022 and the State Institutional Review Boards in Kano, Lagos, and Niger.

## RESULTS

### Sociodemographic Characteristics

All HCPs that participated in this study were full-time employees who had been working in their facilities for not less than a year. As shown in Table 1, the HCPs comprised 50 doctors, 24 nurses, 49 midwives, and 54 nurse-midwives, with nurses and midwives making up a greater percentage of HCPs participating in the study.

### Main Outcome Results

#### HSC use for PPH prevention

All of the HCPs interviewed had administered uterotonics in the last delivery they assisted, with 83% stating that HSC was administered compared to 30% for oxytocin and 30% for misoprostol. Seventy-four percent indicated that patients were counseled prior to the administration of uterotonics. The indication for HSC use was for PPH

prevention during AMTSL in 99% of cases, with only one respondent reported giving HSC for PPH treatment. Oxytocin was reported given for PPH prevention 92% of the time and misoprostol 96%.

The pattern and trend of uterotonic use by HCPs, from 1024 patient charts reviewed over a five-month period, were approximately 10 per facility per month. Uterotonics were administered in 943 in-facility deliveries and 81 home deliveries presented with complications. Of the in-facility deliveries, 93% of charts showed at least one uterotonic drug being administered, while 31% of women received two or more uterotonics. As shown in Table 2, among the 540 that received only one uterotonic, 60% had HSC, 36% oxytocin, and 4% misoprostol. Oxytocin was given mostly at a dose of 10 units (20 units maximum) misoprostol and HSC was given at 600 µg and 100 µg per patient, respectively. In summary, the availability of HSC resulted in its administration to a greater

Distribution of healthcare providers			
Cadre	Quantity (n)	Percentage (%)	
Doctors	50	28%	
Nurses	24	14%	
Midwives	49	27%	
Nurse-Midwives	54	31%	
Total	177	100%	
Acceptance and safety of HSC			
	HSC	Misoprostol	Oxytocin
	N = 177	N = 177	N = 177
Acceptance of HSC			
Uterotonic preference	135 (76%)	7 (4%)	34 (20%)
Willingness to use	167 (94%)	Not asked	Not asked
Ease of administration	175 (99%)	176 (99%)	175 (99%)
Effectiveness in preventing blood loss	167 (94%)	175 (99%)	171 (97%)
Quality of drug	158 (90%)	161 (92%)	152 (87%)
Cost of Uterotonic	32 (18%)	27 (15%)	16 (9%)
Safety of HSC			
Safe for use during AMTSL	170 (96%)	151 (85%)	174 (98%)
High risk of side effects	6 (3%)	66 (37%)	31 (18%)
Ease of managing side effects	102 (58%)	157 (89%)	141 (80%)

HSC: Heat-stable carbetocin, AMTSL: Active management of third stage of labor.

**Table 2:** Cost factors influencing the use of uterotonics from the clinician's perspective and distribution pattern of use of a single uterotonic for postpartum hemorrhage (PPH) prevention.

Cost factors influencing the use of uterotonics from the clinician's perspective		
<b>Awareness of cost to patient (N = 177)</b>		
HSC		38 (22%)
Oxytocin		106 (60%)
Misoprostol		111 (63%)
<b>Cost as a determinant of uterotonic choice</b>		
Not at all important		75 (43%)
Slightly important		21 (12%)
Medium importance		13 (7%)
Important		43 (24%)
Very important		25 (14%)
<b>Importance of cost when considering which uterotonic to use</b>		
Not at all important		62 (35%)
Slightly important		22 (12%)
Medium importance		8 (5%)
Important		58 (33%)
Very important		27 (15%)
Distribution pattern of use of a single uterotonic for postpartum hemorrhage (PPH) prevention		
Uterotonic type	Quantity (n)	Percentage (%)
Heat-stable carbetocin	324	60%
Oxytocin	193	36%
Misoprostol	23	4%
Total	540	100%

HSC: Heat-stable carbetocin.

percentage of women for PPH prevention when compared to oxytocin and misoprostol.

### Acceptance and Safety of HSC for Prophylactic Use

Structured in-depth informant interviews with 177 HCPs were conducted to assess their acceptance of HSC for PPH prevention and uncover the factors that informed their preference. The 177 respondents had a median of 10 years of experience; 96% of the respondents had assisted in at least 10 deliveries and 63% reported using HSC (along with other uterotonics). As summarized in Table 3, 76% of the HCPs preferred HSC for PPH prevention compared to other available uterotonics, with 85% stating the effectiveness of HSC as the reason for their preference. Ninety-seven percent of HCPs welcomed the introduction of HSC for the prevention of PPH, while 94% informed their willingness to use HSC routinely and consistently for AMTSL.

As shown in Table 1, of almost all HCPs interviewed, 99% stated that HSC, like oxytocin and misoprostol, had a good safety profile and was easy to administer. In terms of efficacy, 94% of HCPs stated that HSC is effective at preventing blood loss. Our null hypothesis is rejected, considering that a significant percentage of HCPs welcomed and expressed their willingness to administer HSC for PPH prevention immediately after delivery.

### Factors enabling the use of uterotonics in health facilities

To understand factors enabling choice and use of uterotonics and facility assessments conducted at the 18 facilities, 100% reported HCPs had access to administer HSC and other uterotonics within one minute of delivery. Although 31% of HCPs reported that HSC was stored under lock and key, 98% stated that it was available at all times of the day, all days of the week. In 14 of the 18 facilities, HSC was available in the labor room. Only 9% of HCPs (8 of 18 facilities) were

**Table 3:** HSC acceptability and contributory factors to acceptance.

Acceptability	Quantity (n)	Percentage (%)
Preference of HSC for PPH prevention	134	76%
HSC welcomed as an addition to uterotonic mix	171	97%
Willingness to use HSC for PPH prevention	168	94%
<b>Factors</b>		
High safety profile	175	99%
Efficacy in preventing PPH	168	94%

HSC: Heat-stable carbetocin, PPH: Postpartum hemorrhage.

**Table 4:** Factors affecting HCP decision-making in selecting a uterotonic for PPH prevention.

Determining factor	Quantity (n)	Percentage (%)
Guidance by senior colleagues	134	76%
In-service training workshops	134	76%
Structured mentoring sessions	147	84%
Supportive supervision visits	133	75%
Job aids	177	100%

HCP: Healthcare provider, PPH: Postpartum hemorrhage.

aware of HSC stockout in the preceding 30 days, with no facility stocked out of either oxytocin or misoprostol in the same interval. From key informant interviews and in-depth interviews, respondents reported that training via seminars, workshops, and step-down training on the appropriate use of uterotonics, including HSC, contributed to their knowledge. On their level of knowledge on the appropriate use case for both oxytocin and misoprostol, 80% of clinicians confirmed knowing that both drugs can be used for induction and augmentation of labor, prevention of PPH, and treatment of PPH. As shown in Table 4, approximately 76% of HCPs stated that their uterotonic administration practices were shaped by specific guidance from senior providers in their facility on the appropriate use of uterotonics. About 76% of clinicians related their uterotonic use pattern to knowledge obtained during in-service training sessions, 84% to mentoring, and 75% to supportive supervision visits. All clinicians (100%) had access to educational materials on PPH prevention and management, such as guidelines, protocols, algorithms, or treatment flowcharts.

More clinicians were knowledgeable about the cost of oxytocin and misoprostol (60% and 63%, respectively) compared to 22% for HSC. However, 43% of clinicians indicated that cost did not significantly influence their choice of uterotonic medication. About 14% affirmed that cost was an important determinant in selecting a uterotonic. The results are shown in Table 2. While the availability and access are basic to determining the choice of uterotonics, knowledge, particularly imparted during mentorship, appears to have a great influence on the choices of HCPs.

## DISCUSSION

This implementation research study was conducted to provide insight into the current clinical use of three uterotonics—HSC, oxytocin, and misoprostol—in secondary and tertiary public health facilities, to delineate HSC acceptance for prophylactic use and variables that contribute to this acceptance by clinicians, and finally to understand how selected factors enable the appropriate use of uterotonics by HCPs.

At the completion of our study, HSC had been used for PPH prevention in about 60% of deliveries. During the study period, 18,480 deliveries occurred in the implementation facilities: 14,135 vaginal deliveries and 4,345 cesarean sections (CS). HSC was used for PPH prevention in 10,284 (56%) of deliveries. One hundred and forty-eight (0.8%) women with documented uterotonic use developed PPH, with 98 (66%) occurring during vaginal deliveries and 50 (34%) occurring during CS. In all PPH cases observed, additional uterotonics were administered as treatment.

As high as 97% of HCPs welcomed HSC inclusion as a uterotonic for PPH prophylaxis. This high level of acceptance was further emphasized by 94% of HCPs stating their willingness to continue using it and 76% declaring their preference for HSC for PPH prevention when compared to oxytocin and misoprostol. Identified variables to promote acceptance include effectiveness, safety profile, and affordability, while factors that contributed to HCP's choice of uterotonic for PPH prevention were found to include knowledge and clinical competence in its administration, cost, and accessibility to the medication at the point of care.

During the study period, 148 (0.8%) women with documented uterotonic use developed PPH, with 98 (66%) occurring in vaginal deliveries and 50 (34%) CS. Records in our implementation facilities indicated that 93% of women delivering had at least one uterotonic administered for PPH prevention, while 7% of case notes reviewed had no entry or record of uterotonic use. The PPH rate of 0.8% in our study is less than reported by Akhter *et al.* in their randomized control trial, which assessed HSC versus oxytocin administration for PPH prevention. PPH developed in 23 (15.3%) and 31 (20.7%) patients in HSC and oxytocin groups, respectively.<sup>[14]</sup> Accurate quantification of blood loss during delivery affects reported PPH rates and methods used for quantification significantly correlate with the level of accuracy and timely commencement of appropriate management protocol. Findings from the EMOTIVE trial showed that the use of calibrated drapes for collection and quantification of blood loss volume identified PPH in 93.1% in intervention facilities versus 51.1% detection rate in control sites.<sup>[7]</sup> All PPH cases in our study had administration of additional uterotonic for treatment.

The majority of HCPs in our study affirmed their acceptance of HSC use for PPH prevention. Likewise, 97% welcomed its introduction, and 94% expressed willingness to use it consistently. HSC acceptance among HCPs was attributed to its perceived high efficacy, safety profile, high quality, and relative comparative cost to oxytocin and misoprostol, similar to findings in other studies.<sup>[15]</sup> Although findings by Anyakora *et al.*, Ammendorffer *et al.*, and Torloni *et al.*

revealed low-quality uterotonics in Nigeria,<sup>[3,6,15]</sup> HCPs in our study perceived oxytocin and misoprostol as equally effective in preventing PPH. The safety profile of uterotonics also contributed to their preference for HSC, with responses showing that HSC was perceived as easy to administer, with fewer side effects as noted in other studies.<sup>[7,16]</sup>

Our findings showed that 45% of clinicians considered the cost of HSC to be a significant determinant of their decision to use it for PPH prophylaxis. However, only 22% of clinicians were aware of the cost of HSC. This suggests that greater efforts are needed to increase awareness of HSC's subsidized price in LMIC. Uterotonics are sometimes combined or higher doses of oxytocin given to achieve the desired uterine contraction, and HCPs highlighted that this is primarily due to quality issues. This finding is similar to that found by Ejekam *et al.* in a qualitative study on uterotonics where 23% of respondents reported experiencing oxytocin failure in PPH prevention, of whom 54.3% changed to another uterotonic and 37.1% doubled the dose of oxytocin for their patients.<sup>[17]</sup> In our study, 93% of women had at least one uterotonic drug being administered while 31% of women received two or more uterotonics, a situation similar to the near-universal prophylactic coverage found in the Every Newborn (EN)-Birth multicountry validation study.<sup>[18]</sup> Due to the novelty of HSC, robustness in-country data on prophylaxis coverage rate and use are unavailable. However, records from our study facilities show it was consistently administered at the WHO recommended dose of 100  $\mu$ g and for indication of PPH prevention. In the analysis of oxytocin use, we found that administered dose varied between 10 units (the WHO recommendation) and 20 units, with more women receiving the 20-unit dose. This practice of administering above the WHO dose is similar to reports by Ejekam *et al.*, where clinicians affirmed increasing oxytocin dose on account of perceived low quality of available oxytocin,<sup>[17]</sup> and by Ruysen *et al.*, where findings of use of up to 40 units were reported, especially during cesarean deliveries.<sup>[18]</sup>

### Strengths and Limitations of the Study

The objectives of our study were clearly stated and served as a guide to developing the findings and results of this study. The collection and analysis of quantitative and qualitative data provided a greater understanding of the uterotonic use pattern found in this study. Adopting a mixed-methods design also increases the generalizability, validity, and credibility of our study.

Despite improvements observed over the period of our study, documentation remains a major challenge in a large proportion of facilities, with incomplete entries, inadequate use of monitoring tools, and nonspecific records of diagnosis

or patient management decisions by HCPs affecting the quality of study data. This increased the length of time spent in collecting data as more charts had to be reviewed. The high rate of staff turnover, including new hires and transfers within and between facilities, created significant knowledge gaps that posed challenges for the study, as participating HCPs could not be randomly selected.

Responses on availability and access to uterotonics in some instances were affected by bureaucratic processes and issues with accountability. Storage of uterotonics in pharmacies, until patients were in advanced labor, had to be interpreted as access and availability at point-of-care. Since a major contributor to HSC acceptability relates to issues on cold chain defects, HCPs in facilities with poor cold chain equipment may automatically interpret this to mean that available oxytocin was of poor quality due to degradation and this HSC comparative advantage may be a confounder in its high use rate.

## CONCLUSION AND GLOBAL HEALTH IMPLICATIONS

There are great benefits to large-scale uptake of HSC use for PPH prevention in LMIC where conditions of limited cold chain infrastructure contribute to other factors responsible for the high prevalence of PPH. Our findings indicate that HSC, being both cost-effective and high quality, is a viable and preferred option among HCPs for PPH prevention. This positions HSC as a key solution in overcoming challenges associated with low-quality uterotonics in LMICs. Local manufacturing of high-quality uterotonics in Nigeria and other LMICs based on acceptability and expected increased demand will reduce the cost of these medicines, thus increasing affordability by women and their families. The initial cost to health systems in LMICs of scaling up the use of HSC could be significant, as the training on HSC use protocol is mandatory due to the possibility of its misuse for induction and augmentation of labor—two contraindications of HSC.

Currently, HSC is approved for use in PPH prevention. Its efficacy and effectiveness in preventing PPH provide an opportunity for its application in the treatment of PPH.

Finally, as the use of HSC for PPH prevention increases across different geographies, the rate of PPH and consequently its attributed maternal mortalities and morbidities is expected to reduce with the improvement of maternal care indicators in these countries. The addition of other targeted interventions like the improvement of cold chain systems and consistent capacity building of HCPs will drive the renewed march toward achieving SDG 3.1 of reducing the global MMR to less than 70 per 100,000 live births.

## Key Messages

- Heat-stable carbetocin (HSC) as a uterotonic for postpartum hemorrhage (PPH) prevention is acceptable to healthcare providers (HCPs) as it has been found to be effective, with a high safety profile, while not burdened by issues around cold storage like oxytocin.
- Quality-assured HSC is not only cost-effective but also priced comparably to high-quality oxytocin, making it a financially viable option for healthcare systems.
- Establishing a structured system of regular on-the-job training and mentorship of HCPs on PPH prevention and management, and other areas of maternal care ensures the appropriate use of uterotonics and improves the maternity experience.

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## COMPLIANCE WITH ETHICAL STANDARDS

### Conflicts of Interest

The authors have no conflicts of interest.

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None.

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### Ethics Approval

Approval was obtained from the National Health Research Ethical Committee (NHREC) with approval number NHREC/01/01/2007-15/03/2022 and the State Institutional Review Boards in Kano, Lagos, and Niger.

### Declaration of Patient Consent

Patient consent is not required as there are no patients in this study.

### Use of Artificial Intelligence (AI)-Assisted Technology for Manuscript Preparation

The authors confirm that there was no use of AI-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

## Disclaimer

The Authors declare that this is an original paper; it is not currently submitted wholly or partly to any other journal for publication. All sources quoted have been indicated by in-text citations and details given in the reference section.

## Special Collection

This article is published as part of the special collection on prevention and treatment of postpartum hemorrhage in high-burden low- and middle-income countries: building cross-national evidence through implementation research.

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