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Access to oxytocin and misoprostol for management of post-partum haemorrhage in Kenya, Uganda and Zambia: a comparison of availability, prices and affordability.

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5 2 **Uganda and Zambia: a comparison of availability, prices and affordability.**

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52
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54 45 **Key words:** Access, Oxytocin, Misoprostol, Post-partum haemorrhage

Abstract**Objectives**

This paper assesses access to oxytocin and misoprostol at health facilities to improve prevention and management of postpartum haemorrhage by measuring the availability, prices and affordability of the medicines in Kenya, Uganda and Zambia.

Design

The assessment used a cross-sectional design adapted from the standardized WHO/HAI methodology on measuring availability, prices and affordability to medicines.

Setting

Data were collected in July and August 2017 from 376 health facilities from a target of 432 facilities across the three countries.

Participants

Health facility managers.

Primary and secondary outcome measures

Availability was calculated as the mean percentage of sampled medicine outlets where the medicine was found on the day of data collection. Medicine prices were compared to international reference prices (IRP) and expressed as median price ratios (MPRs). Affordability was calculated using the number of days required to pay for a standard treatment based on the daily income of the lowest-paid government worker.

Results

Availability of either oxytocin or misoprostol at health facilities was high; 81% in Kenya, 82% in Uganda, and 76% in Zambia. Oxytocin was more available than misoprostol, and it was most available in the public sector in the three countries. Availability of misoprostol was highest in the public sector in Uganda (88%). Oxytocin and misoprostol were purchased by patients at prices above IRP, but both medicines cost less than a day's wages and were therefore affordable. Availability of misoprostol was poor in rural settings where it would be more preferred due to lack of trained personnel and cold storage facilities required for oxytocin.

Conclusion

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2
3 74 Availability and affordability of either oxytocin or misoprostol at health facilities was optimal.
4
5 75 However, countries with limited resources should explore mechanisms to optimize
6
7 76 management of PPH by improving access to misoprostol especially in rural areas.
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9 77

10 78 **Strengths and limitations of the study**

- 12 79 • The WHO/HAI methodology that was used for this study is tested, reliable, standardized
13 80 and validated for the measurement of medicine prices and availability.
- 14 81 • The study provides details on availability, price, and affordability of individual medicines
15 82 across three sectors (public, private and mission).
- 16 83 • The methodology uses a cross-sectional design and therefore historical data trends were
17 84 not traced.
- 18 85 • The study only used two frontline medicines for PPH, while countries may have had
19 86 other alternative therapies including carbetocin which were not captured.
- 20 87 • Findings presented here may not be used to predict country pharmaceutical supply
21 88 chain but are intended to stimulate policy discussions on deliberate targeting and the
22 89 use of available technologies to improve access.

91 **Background**

92 The risk of women dying due to pregnancy and childbirth remains a major global health
93 challenge. In 2017 there were approximately 295,000 maternal deaths globally, of which 94%
94 occurred in low-and middle-income countries (LMICs). Sub-Saharan Africa contributed about
95 66% to these deaths [1]. The global leading cause of maternal mortality is haemorrhage,
96 accounting for 27% of all maternal deaths [2].

97 Postpartum haemorrhage (PPH) which occurs after childbirth accounts for most (72%) of the
98 three forms of haemorrhage. Antepartum haemorrhage which occurs during pregnancy
99 accounts for 24% while intrapartum haemorrhage (during childbirth) accounts for three percent
100 [2]. PPH is responsible for 34% of maternal deaths in Kenya, 25% in Uganda and 34% in Zambia
101 [3-5].

102 The World Health Organization (WHO) recommends oxytocin as the medicine of choice for
103 management of PPH, and misoprostol as the second line alternative when injection capability is
104 lacking and/or storage conditions for oxytocin are not met. Other uterotonics such as
105 ergometrine and carbetocin are also recommended when use of oxytocin is not feasible [1].

106 The relevance of oxytocin and misoprostol to health systems was further emphasised by the
107 United Nations Commission on Life-saving Commodities for women and children when they
108 were listed among the 13 lifesaving, low-cost medicines with greatest proven potential to avert
109 preventable deaths [6]. Both oxytocin and misoprostol are included in national essential
110 medicine lists in Kenya, Uganda and Zambia [7-9].

111
112 The quality, efficacy and safety of oxytocin and misoprostol have been widely studied [11-24].
113 Oxytocin is temperature sensitive and should therefore be stored under refrigeration at
114 temperatures between 2 and 8°C to prevent degradation expected at higher temperatures [11].
115 Degradation reduces potency and consequently the effectiveness of the medicine. Oxytocin
116 stability through the supply chain has proven a worry to policy makers and has been a subject

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2
3 117 of numerous investigations to ascertain quality and efficacy [12-14]. Some studies on the
4
5 118 quality of oxytocin found analyzed samples to contain less active pharmaceutical ingredients
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7 119 than was claimed on label, while some samples also failed sterility tests [15-17]. LMICs with low
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9 120 resources may also lack facilities required for adequate storage conditions for oxytocin to
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11 121 ensure integrity of the product, while they may also lack trained health workers for its
12
13 122 administration [18]. Women living among displaced populations, in conflict areas, hard to reach
14
15 123 areas, who deliver at home or with a traditional birth attendant seldom have access to a trained
16
17 124 health worker. Hence, they do not have access to oxytocin or if they do, it is not safely used
18
19 125 [10]. As a result of these challenges, prevention and treatment of PPH in low-resource settings
20
21 126 using oxytocin has not provided the desired impact [19, 20].
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23
24 128 Misoprostol, a prostaglandin, is an alternative to oxytocin in the management of PPH. It is
25
26 129 cheap, stable at room temperature and more convenient to administer. It can be administered
27
28 130 sublingually, orally and vaginally [20, 21, 25, 26]. It has been demonstrated through various
29
30 131 studies that use of misoprostol is feasible, improves uterotonic coverage, reduces incidence of
31
32 132 PPH and that it is effective for use at community and household level in low-resource settings
33
34 133 [21-23].

35
36 134 In 2015, the WHO expert committee on the selection and use of medicines recommended the
37
38 135 addition of misoprostol for the prevention and treatment of postpartum haemorrhage when
39
40 136 oxytocin is not available or cannot be used safely [24]. At different occasions the inclusion of
41
42 137 misoprostol in the list of WHO recommended medicines was debated for both efficacy and
43
44 138 safety reasons, but the 2015 decision to recommend misoprostol in addition to oxytocin for
45
46 139 prevention of PPH was reaffirmed in 2019 by a WHO expert committee [27]. Before 2015
47
48 140 misoprostol was indicated by WHO for use in induction of labour and management of
49
50 141 spontaneous and induced abortion [28]. The historical use of misoprostol for termination of
51
52 142 pregnancies may have affected its acceptability for routine use in prevention of PPH, despite
53
54 143 available convincing evidence of its therapeutic effect and relative safety in management of
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56 144 PPH. Another challenge is that the high doses of misoprostol required for post-partum
57
58 145 haemorrhage often result in troublesome side effects such as vomiting and shivering [29].

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3 146 Further, the longer half-life of the medicine means that it stays longer in the body and has
4
5 147 potential to cause complications [30].
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10 149 These two medicines could be used complementarily to overcome challenges and barriers in
11
12 150 policy, health sector infrastructure and health service delivery that at the moment inhibit the
13
14 151 optimal management of PPH [10, 31]. However, there is a knowledge gap on the accessibility of
15
16 152 both medicines in low-resource settings. This is a missed opportunity in closing the gap in the
17
18 153 reduction of maternal mortality in developing countries. This paper therefore assesses access to
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20 154 oxytocin and misoprostol in urban and rural health facilities in Kenya, Uganda and Zambia
21
22 155 through a comparison of availability, prices and affordability of the two medicines to facilitate
23
24 156 the optimal management of PPH.
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28 158 **Methods**

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31 159 An assessment of availability and prices of oxytocin and misoprostol was undertaken using data
32
33 160 from Health Action International (HAI) research on sexual and reproductive health commodities
34
35 161 (*SRHC: Measuring Prices, Availability & Affordability* [32]). The data was collected in Kenya,
36
37 162 Uganda and Zambia in July and August 2017 using a cross-sectional design with quantitative
38
39 163 methods adapted from the standardized WHO/HAI methodology [33], which has been validated
40
41 164 [34] and used extensively in several countries [35-37].
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165

44 166 *Patient and Public Involvement*

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46
47 167 The research agenda for this study was set by the multi-stakeholder platform Medicines
48
49 168 Transparency Alliance (MeTA) Councils in Kenya, Uganda and Zambia. The study protocols were
50
51 169 reviewed and approved by MeTA Councils. Data collectors were selected from the membership
52
53 170 of MeTA within the countries. Results were validated by stakeholders including civil society.
54
55 171 Dissemination plans were made by MeTA councils and results were disseminated to wide
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3 172 country and inter-country platforms including Ministries of Health, Parliamentarians, private
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5 173 sector as well as civil society members to inform policy.
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11 175 *Data collection*

12 176 For this study, the data on availability, price and affordability of the highest and lowest-priced
13
14 177 products of oxytocin 10IU, 1ml injections and misoprostol 200 µg tablets were extracted.
15

16 178 In each of the three countries, six geographical areas (districts, municipalities or counties) were
17
18 179 selected; the country's main urban centre and five other areas which were randomly selected.

19
20 180 All survey areas were reachable within one day's travel from the country's main urban centre
21
22 181 using a car or bus. Each survey area covered a population of between 100 000 and 250 000
23
24 182 people.

25 183 In each survey area, the main public hospital was selected first. Then, eight public health
26
27 184 facilities, four each from urban and rural areas, representing levels of care at which SRHCs
28
29 185 should be made available, were randomly selected [38]. Additionally, eight private (for profit)
30
31 186 and eight mission sector (not for profit) health facilities (four each from urban and rural areas)
32
33 187 that were within a three-hour drive radius of the main hospitals were selected. Thus, a total of
34
35 188 24 health facilities were sampled from each of the six survey areas in Kenya, Uganda and
36
37 189 Zambia, respectively, giving a total of 144 facilities per country. The final sample per country
38
39 190 ensured a minimum representation of 30 health facilities from the public, mission and private
40
41 191 sectors [33].
42

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44 193 Eight data collectors with experience of conducting medicine surveys worked in pairs of a
45
46 194 pharmacist and a social scientist under close supervision of a qualified survey manager. Prior to
47
48 195 data collection, the team was trained on the methodology. Data collectors used a semi-
49
50 196 structured questionnaire administered to facility managers while physically ascertaining the
51
52 197 availability of surveyed medicines. Availability was measured by the physical presence of a
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54 198 product in the outlet at the time of the survey. For each medicine surveyed, data collectors
55
56 199 recorded the product name for both the highest and lowest-priced medicines available, the
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3 200 manufacturer and unit price of the product. In the public sector in Uganda and Zambia where
4
5 201 medicines are free of charge to care seekers, prices were not recorded.

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7 202
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9 203 Once data collection was complete, survey data was entered into a pre-programmed Microsoft
10
11 204 Excel Workbook provided as part of the modified methodology. Data input was independently
12
13 205 checked for errors. Additional quality control measures were executed at various stages
14
15 206 throughout the study by a survey manager. The survey tools were pre-tested in Uganda in 2016
16
17 207 and a field test was conducted by all data collectors prior to data collection. Each data
18
19 208 collection team had a supervisor who cross checked the data on a daily basis for completeness,
20
21 209 legibility and consistency and reported to the survey manager. Prior to data entry all relayed
22
23 210 data was checked for completeness and consistency.

24 211
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26 212 *Data analysis*
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28
29 213 The availability of oxytocin and misoprostol was calculated as the percentage of sampled
30
31 214 medicine outlets where the medicine was found. Availability was also calculated for the
32
33 215 presence of either oxytocin or misoprostol at a facility. Data were reported in aggregate as
34
35 216 public, private or mission sector medicine outlets. Overall availability per sector was calculated
36
37 217 as mean of the two medicines surveyed.

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42 219 Patient prices were collected in local currency including Shillings in Uganda and Kenya, and
43
44 220 Kwacha in Zambia. The mean, minimum and maximum unit prices were calculated. To facilitate
45
46 221 cross-country comparisons, medicine prices obtained during the survey were expressed as
47
48 222 ratios relative to a standard set of international reference prices by dividing the mean unit
49
50 223 price (in dollars) by the Management Sciences for Health international buyers' reference unit
51
52 224 price derived on September 25th 2018 [39]. Mean price ratios (MPRs) were calculated only for
53
54 225 oxytocin and misoprostol products that had price data from at least four medicine outlets. The
55
56 226 exchange rate used to calculate MPRs was 1 USD = 102.67 Kenya Shillings (KES), 1 USD = 3667.9

227 Uganda Shillings (UGX), 1 USD = 8.85 Zambia Kwacha (ZMW) taken on 1st July, 2017 prior to the
228 first day of data collection [40, 41].

229
230 Affordability was calculated using the number of days' wages it requires to pay for standard
231 treatment or dose of treatment based on the daily income of the lowest-paid government
232 worker (LPGW) [33]. The daily wage of a LPGW is approximately KES 411 (USD 4) in Kenya, 6255
233 UGX (USD 1.78) in Uganda, and ZMW 96.7 (USD 10.92) in Zambia, as per public service salary
234 structures [42]. Treatments that required more than one day's wages to purchase were
235 considered unaffordable [33].

236

237 Results

238 A total of 376 health facilities, including 120, 124 and 132 health facilities in Kenya, Uganda and
239 Zambia, respectively, were surveyed as shown in table 1.

240 **Table 1: Number of facilities surveyed**

	Urban	Rural	Total
Kenya			
Public	22	22	44
Private	22	20	42
Mission	19	15	34
Total	63	57	120
Uganda			
Public	20	22	42
Private	22	20	42
Mission	20	20	40
Total	62	62	124
Zambia			
Public	30	42	72
Private	32	5	37
Mission	6	17	23
Total	68	64	132

241

242 *Availability across sectors*

243 Figure 1 shows the availability of either oxytocin or misoprostol at the surveyed health facilities
244 in the three countries. Overall availability of either oxytocin or misoprostol met the WHO
245 benchmark of 80% in Kenya (81%) and Uganda (82%) but was marginally lower in Zambia (76%).
246 Availability of oxytocin was higher than misoprostol except in Uganda. Availability of either
247 oxytocin or misoprostol was comparable between the public and mission sectors.

248

249 In the public sector, the three countries met the WHO benchmark for availability of oxytocin.
250 Misoprostol was only optimally available in the public sector in Uganda (88%), with availability
251 in Kenya and Zambia lower (36% and 21%, respectively). In the private sector, none of the
252 countries met the WHO recommended availability for misoprostol. Availability in Zambia was
253 especially low (24%).

254

255 *Availability in urban versus rural areas*

256 Figure 2 shows availability in urban versus rural areas. Oxytocin was available in over 80% of all
257 public urban and rural facilities across the three countries. Optimum availability of 80% was
258 further achieved for oxytocin in Kenya mission urban facilities (89%) and in Zambia's mission
259 sector for both urban and rural facilities (83% and 94%, respectively). Optimum availability of
260 misoprostol was only achieved in Ugandan public urban and rural facilities (90% and 86%,
261 respectively).

262

263 In Kenya, oxytocin had a higher availability than misoprostol across all urban and rural facilities
264 in the three sectors. Availability of misoprostol was lowest in the public sector: availability in

265 urban facilities was 45%, and 27% in rural facilities. In the private sector, there was a higher
266 availability in rural facilities than in urban facilities for both oxytocin and misoprostol.

267 In Uganda, the public sector was optimally stocked with both oxytocin and misoprostol across
268 urban and rural facilities. Rural public facilities had a higher availability of oxytocin than urban
269 public facilities. In the private sector, rural facilities also had a higher availability of oxytocin and
270 misoprostol compared to urban facilities.

271
272 Oxytocin had a high availability in Zambia's public and mission sectors across both urban and
273 rural facilities. Availability in the private sector was very low. Availability of misoprostol was low
274 across the sectors and areas, with highest availability found in urban mission facilities (50%).
275 Although both oxytocin and misoprostol were poorly available in the private sector, oxytocin
276 was more available in rural than urban facilities, while misoprostol had a higher availability in
277 urban facilities than in rural facilities.

278

279 *Prices and affordability*

280 Oxytocin and misoprostol were free for patients in the public and mission sectors in Zambia,
281 and in the public sector in Uganda. In Kenya's public sector, the lowest price was noted for
282 oxytocin, with a median price ratio (MPR) of USD 0.174 (Table 2). Both misoprostol and
283 oxytocin cost less than a day's wages for a LPGW across all countries and sectors, and can
284 therefore be considered affordable.

285

286 Notwithstanding the sectors in which the medicines were for free, the MPRs for oxytocin and
287 misoprostol were above one in the countries, ranging from 1.37 for misoprostol in Kenya's
288 public sector to 29.95 for misoprostol in the private sector in Zambia. This meant that both

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289 misoprostol and oxytocin were accessed by patients at prices that were more expensive
290 compared to international reference prices.

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Table 2: Prices and affordability of misoprostol and oxytocin across countries

		Public			Private			Mission		
		Price (USD)	Mean Price Ratio	Affordability of treatment (number of day's wages)	Price (USD)	Mean Price Ratio*	Affordability of treatment (number of day's wages)	Price (USD)	Mean Price Ratio	Affordability of treatment (number of day's wages)
Kenya	Oxytocin	0.029	0.17	0.01	1.354	8.14	0.34	0.672	4.04	0.30
	Misoprostol	0.273	1.37	0.07	1.967	9.84	0.49	1.217	6.09	0.17
Uganda	Oxytocin	0	NA	NA	0.998	5.99	0.57	0.408	2.45	0.23
	Misoprostol	0	NA	NA	0.589	2.95	0.34	0.39	1.95	0.22
Zambia	Oxytocin	0	NA	NA	0.678	4.08	0.06	NA	NA	NA
	Misoprostol	0	NA	NA	5.989	29.95	0.55	NA	NA	NA

NA=not applicable, USD=United States Dollar

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4 291 **Discussion**

5 292 This paper assesses access to oxytocin and misoprostol in urban and rural health facilities in
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7 293 Kenya, Uganda and Zambia through a comparison of availability, prices and affordability of the
8
9 294 two medicines to facilitate the optimal management of PPH.
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11 295

12 296 Overall, availability of uterotonics, expressed as the presence of either oxytocin or misoprostol,
13
14 297 was high in Kenya and Uganda, and just below the WHO benchmark of 80% in Zambia.
15
16 298 Misoprostol was markedly less available than oxytocin. Oxytocin and misoprostol were
17
18 299 accessed by patients in the private sector at prices that were more expensive than the
19
20 300 international reference prices. However, both medicines cost less than a day's wages, which is
21
22 301 considered affordable. The availability of misoprostol across urban and rural areas did not show
23
24 302 the expected pattern of having a higher availability of the medicine in rural areas, which are
25
26 303 more prone to health system barriers for use of oxytocin.
27

28 304

29 305 Oxytocin availability was high in the public and mission sectors but lower in the private sector,
30
31 306 particularly in Zambia. In the private sector, none of the countries met the WHO availability
32
33 307 benchmark of 80% for the two medicines. Besides the public sector in Uganda, misoprostol was
34
35 308 not optimally available in the other countries or sectors. Misoprostol had a low availability,
36
37 309 particularly in rural areas where the medicine ought to play a major role given that facilities in
38
39 310 these areas tend to lack adequately trained health workers and the health infrastructure
40
41 311 required to maintain cold chain to safeguard the quality of oxytocin [18]. Its poor availability in
42
43 312 Kenya and Zambia may be a result of slow diffusion of the intervention into the health system
44
45 313 [43, 44]. Moreover, misoprostol has been recommended by WHO for use in PPH since 2015
46
47 314 after several rounds of weighing the benefits and risks, but the debate about its role in PPH
48
49 315 prevention has continued over the years [24] [27]. The fear and stigma amongst health workers
50
51 316 about the use of misoprostol to induce abortions may also have contributed to the situation
52
53 317 [29]. In contrast, Uganda's efforts as an early adaptor [43, 44] to ensure availability of
54
55 318 misoprostol through government procurement and community level distribution strategies may
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3 319 explain why it has a higher availability of misoprostol, as well as lower PPH levels compared to
4
5 320 Kenya and Zambia (25% in Uganda versus 34% in both Kenya and Zambia) [3-5].
6

7 321
8
9 322 Urban facilities have better health infrastructure such as cold chain facilities, and also tend to
10
11 323 have more health workers compared to rural facilities [45-47]. It would therefore be expected
12
13 324 that these urban areas would have a higher availability of oxytocin and lower availability of
14
15 325 misoprostol than rural facilities. However, there were instances when rural facilities had a
16
17 326 higher availability of oxytocin and a lower availability of misoprostol. This may indicate that
18
19 327 stocking of oxytocin and misoprostol by health facilities does not take into consideration
20
21 328 challenges faced by the facilities to administer the medicines. It will require policy makers to
22
23 329 look into how to address context-specific barriers related to these medicines by ensuring that
24
25 330 they are deployed where they can have maximum impact [48, 49]. For example, efforts should
26
27 331 be made to deploy more misoprostol in rural areas where there is a lack of adequately trained
28
29 332 personnel and a lack of health infrastructure to properly use oxytocin, and to ensure that both
30
31 333 medicines are available to complement one another depending on circumstances.
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33 334
34 335 PPH levels across the countries are high despite health facilities having reached the WHO
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36 336 benchmark for availability of either oxytocin or misoprostol across the three countries. This
37
38 337 may confirm the finding from a study by Ononge et al that despite use of uterotonics, incidence
39
40 338 of PPH remains high [5]. It may be that some oxytocin found at health facilities may not have
41
42 339 the quality and efficacy for optimum management of PPH [15-17]. Countries should strive for
43
44 340 universal access as the 80% availability benchmark by WHO still leaves one in five facilities
45
46 341 without required medicine. However, availability of a medicine alone does not guarantee that it
47
48 342 is used, health worker beliefs and knowledge as well as necessary infrastructure such as
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50 343 electricity and equipment are needed to reduce PPH levels.
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52 344
53 345 Studies have shown that combinations of uterotonics have proven to be more effective. For
54
55 346 example, a misoprostol plus oxytocin combination was found to be more effective in preventing
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57 347 PPH than the currently used standard of oxytocin only [50]. This argument further emphasizes
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3 348 that having both oxytocin and misoprostol available at the health facility could help to improve
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5 349 PPH management.
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8 350 Although oxytocin and misoprostol were affordable to patients, the private sector prices were
9
10 351 varied and more expensive compared to IRPs. For example, the MPR of misoprostol ranged
11
12 352 from 1.37 in Kenya to 29.95 in Zambia. This suggests that countries need to explore pricing
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14 353 policies to improve affordability of the medicines.
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16 354
17 355 The WHO/HAI methodology that was used for this study is tested, reliable, standardized and
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19 356 validated for the measurement of medicine prices and availability [34]. The study provides
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21 357 details on availability, price, and affordability of individual medicines across three sectors
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23 358 (public, private and mission). The methodology uses a cross-sectional design and therefore
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25 359 historical data trends were not traced. The study only used two frontline medicines for PPH,
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27 360 while countries may have had other alternative therapies including carbetocin which were not
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29 361 captured. Findings presented here may not be used to predict country pharmaceutical supply
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31 362 chain but are intended to stimulate policy discussions on deliberate targeting and the use of
32
33 363 available technologies to improve access.
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35 364

36 365 **Conclusion**

37 366 Oxytocin and misoprostol had optimal availability in Kenya and Uganda, and was just below the
38
39 367 WHO benchmark in Zambia. In general, oxytocin was more available than misoprostol. Oxytocin
40
41 368 and misoprostol were purchased by patients at prices above international reference prices but
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43 369 both medicines cost less than a day's wages for a LPGW and were therefore considered
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45 370 affordable. However, there was no strategy in place that looked at which medicine could be
46
47 371 best utilized in which area. Countries with limited resources should explore mechanisms to
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49 372 balance access to both oxytocin and misoprostol between rural and urban areas to optimize
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51 373 management of PPH.
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3 376 **List of abbreviations**
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5 377 Post-partum haemorrhage (PPH); Median price ratio (MPR); Low- and middle-income countries
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7 378 (LMICs); Lowest-paid government worker (LPGW); sexual and reproductive health commodities
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9 379 (SRHC); Health Action International (HAI); World Health Organisation (WHO).
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14 381 **Declarations**

15
16 382 *Ethical approval and consent to participate*
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19 383 This study did not involve human subjects and did not involve direct interaction with patients
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21 384 and therefore ethical approval was not sought. However, Ministries of Health in Uganda and
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23 385 Zambia and Country Directors of Health in Kenya gave approval and provided introduction
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25 386 letters to health facilities.
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30 388 *Consent for publication*
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33 389 Not applicable
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39 391 *Data sharing statement*
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42 392 The datasets used and/or analysed during the current study are available from the
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44 393 corresponding author on request.
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49 395 *Competing interests*
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51 396 All authors declare no competing interests.
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13 403 *Authors' contribution*
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15

16 404 DK conceptualized the project, undertook data analysis and wrote the first draft of the
17
18 405 manuscript; GO, RDH, JSN, HTR, HL and AM revised the manuscript and critically reviewed its
19
20 406 contents. GO contributed to data analysis. AM critically reviewed the manuscript, provided
21
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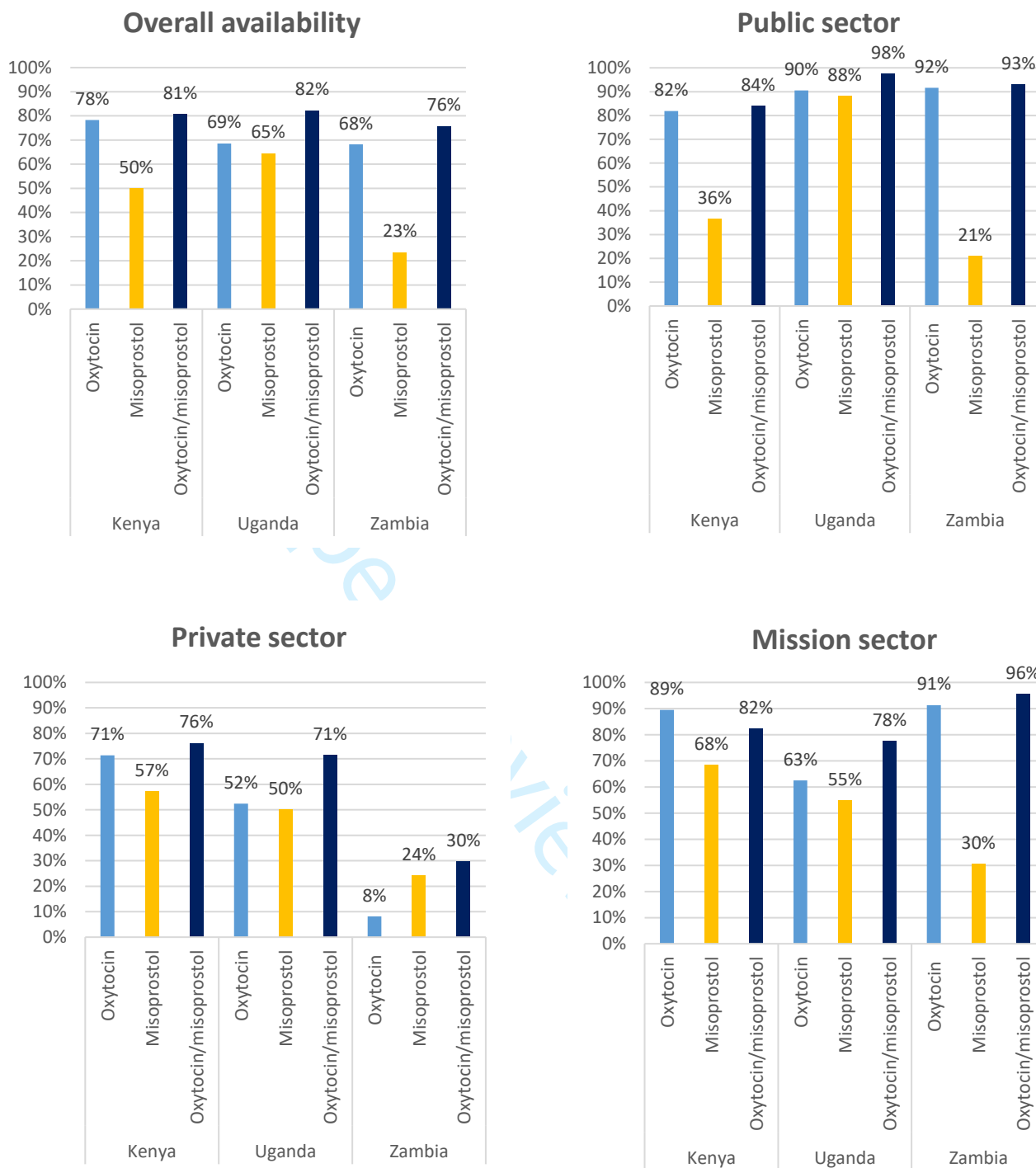


Fig 1: Availability of oxytocin and misoprostol across sectors in Kenya, Uganda and Zambia

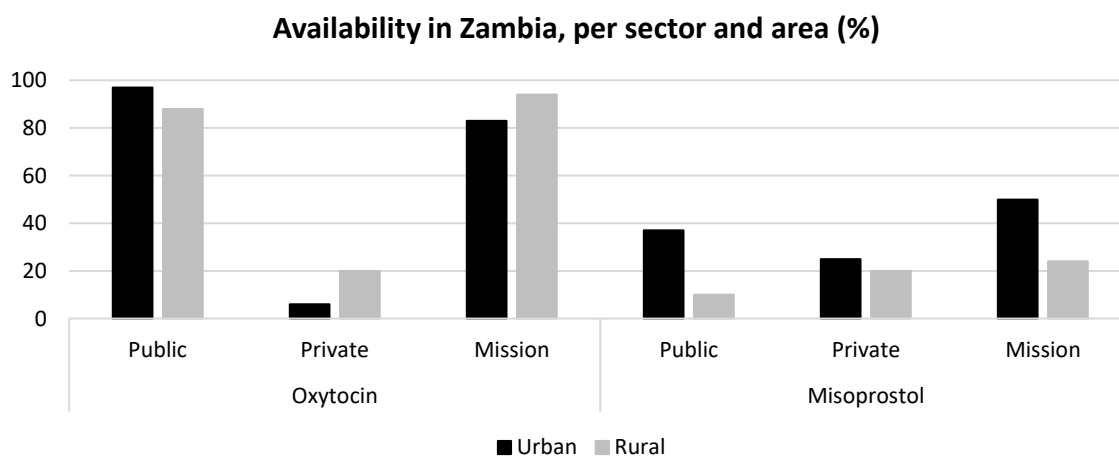
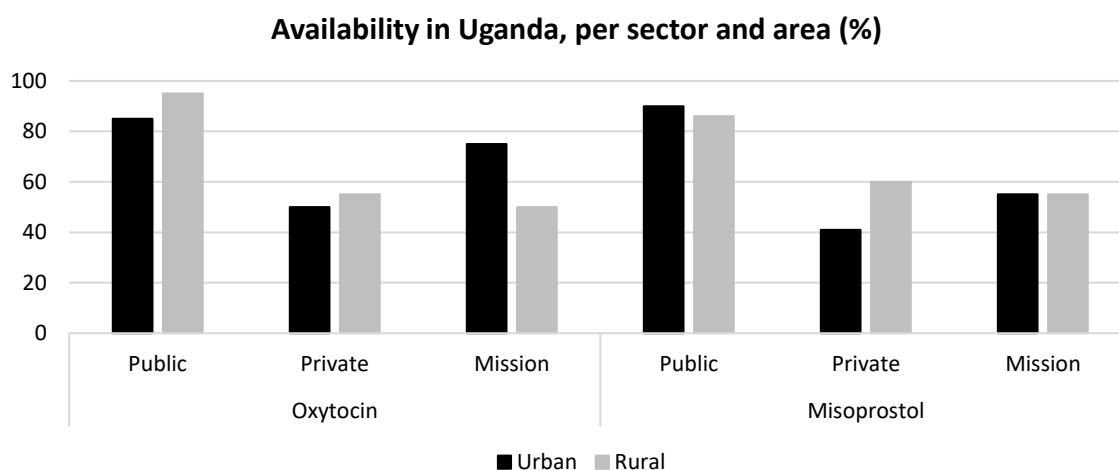
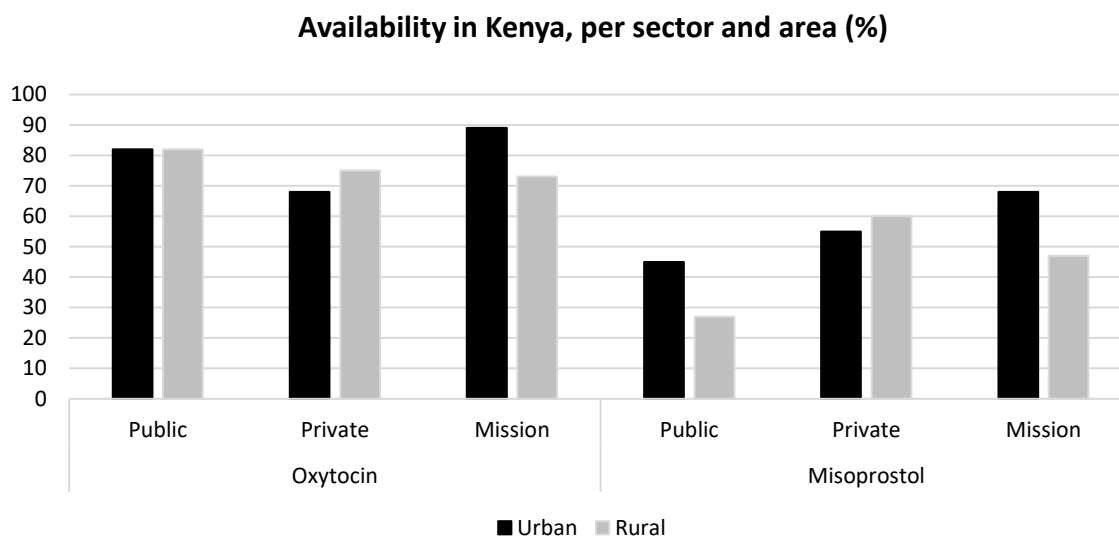


Figure 2: Availability of oxytocin and misoprostol in urban and rural facilities across countries

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4 1 **Access to oxytocin and misoprostol for management of post-partum haemorrhage in Kenya,**
5 2 **Uganda and Zambia. A cross-sectional assessment of availability, prices and affordability.**

6
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51
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53 44
54 45 **Key words:** Access, Oxytocin, Misoprostol, Post-partum haemorrhage

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3 46 **Abstract**

4
5 47 **Background**

6
7 48 The World Health Organisation (WHO) recommends use of oxytocin and misoprostol as the two
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9 49 frontline medicines for management of postpartum haemorrhage (PPH). This paper assesses
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11 50 access to oxytocin and misoprostol at health facilities to improve prevention and management
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13 51 of PPH by measuring their availability, prices and affordability in Kenya, Uganda and Zambia.
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16 52
17 53 **Methods**

18 54 An assessment was undertaken using data from Health Action International (HAI) research on
19
20 55 sexual and reproductive health commodities. Data was collected from 376 health facilities in
21
22 56 July and August 2017 using a cross-sectional design adapted from the standardized WHO/HAI
23
24 57 methodology.

25 58 Availability was calculated as mean percentage of sampled medicine outlets where medicine
26
27 59 was found on the day of data collection. Medicine prices were compared to international
28
29 60 reference prices (IRP) and expressed as median price ratios (MPRs). Affordability was calculated
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31 61 using number of days required to pay for a standard treatment based on the daily income of
32
33 62 the lowest-paid government worker.
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36 63
37 64 **Results**

38 65 Availability of either oxytocin or misoprostol at health facilities was high; 81% in Kenya, 82% in
39
40 66 Uganda, and 76% in Zambia. Oxytocin was more available than misoprostol, and it was most
41
42 67 available in the public sector in the three countries. Availability of misoprostol was highest in
43
44 68 the public sector in Uganda (88%). Oxytocin and misoprostol were purchased by patients at
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46 69 prices above IRP, but both medicines cost less than a day's wages and were therefore
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48 70 affordable. Availability of misoprostol was poor in rural settings where it would be more
49
50 71 preferred due to lack of trained personnel and cold storage facilities required for oxytocin.
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75 **Conclusion**

76 Availability and affordability of either oxytocin or misoprostol at health facilities met the WHO
77 benchmark of 80%. However, countries with limited resources should explore mechanisms to
78 optimize management of PPH by improving access to misoprostol especially in rural areas.

80 **Strengths and limitations of this study**

- 81 • The WHO/HAI methodology that was used for this study is tested, reliable, standardized
82 and validated for the measurement of medicine prices and availability.
- 83 • The study provides details on availability, price, and affordability of individual medicines
84 across three sectors (public, private and mission).
- 85 • The methodology uses a cross-sectional design and therefore historical data trends were
86 not traced.
- 87 • The study only used two frontline medicines for PPH, while countries may have had
88 other alternative therapies including carbetocin which were not captured.
- 89 • In Zambia we surveyed 23 mission facilities which was below the 30 facilities per sector
90 30 recommended by the methodology.

92 **Key questions**

93 *What is known?*

- 94 • The quality, efficacy and safety of oxytocin and misoprostol for management of post-
95 partum haemorrhage have been widely studied.
- 96 • There is a knowledge gap on the accessibility of oxytocin and misoprostol in low-resource
97 settings.

98 *What are the new findings?*

- 99 • Availability of either oxytocin or misoprostol was high in Kenya and Uganda and just below
100 the WHO benchmark of 80% in Zambia.
- 101 • Both medicines cost less than a day's wages, which is considered affordable.

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3 102 • The stocking of oxytocin and misoprostol by health facilities did not take into consideration
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5 103 challenges faced by the facilities to administer the medicines which may explain why
6
7 104 management of post-partum heamorrhage has remained a problem.
8

9 105 *What do the new findings imply?*
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12 106 • Policy makers should look into how to address context-specific barriers to ensure that
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14 107 medicines are adequately deployed for maximum benefit.
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16 108 • Countries with limited resources should explore mechanisms to balance access to both
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18 109 oxytocin and misoprostol between rural and urban areas to optimize management of PPH.
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111 **Background**

112 The risk of women dying due to pregnancy and childbirth remains a major global health
113 challenge. In 2017 there were approximately 295,000 maternal deaths globally, of which 94%
114 occurred in low-and middle-income countries (LMICs). Sub-Saharan Africa contributed about
115 66% to these deaths [1]. The global leading cause of maternal mortality is haemorrhage,
116 accounting for 27% of all maternal deaths [2].

117 Postpartum haemorrhage (PPH) which occurs after childbirth accounts for most (72%) of the
118 three forms of haemorrhage. Antepartum haemorrhage which occurs during pregnancy
119 accounts for 24% while intrapartum haemorrhage (during childbirth) accounts for three percent
120 [2]. PPH is responsible for 34% of maternal deaths in Kenya, 25% in Uganda and 34% in Zambia
121 [3-5].

122 The World Health Organization (WHO) recommends oxytocin as the medicine of choice for
123 management of PPH, and misoprostol as the second line alternative when injection capability is
124 lacking and/or storage conditions for oxytocin are not met. Other uterotonics such as
125 ergometrine and carbetocin are also recommended when use of oxytocin is not feasible [1].

126 The relevance of oxytocin and misoprostol to health systems was further emphasised by the
127 United Nations Commission on Life-saving Commodities for women and children when they
128 were listed among the 13 lifesaving, low-cost medicines with greatest proven potential to avert
129 preventable deaths [6]. Both oxytocin and misoprostol are included in national essential
130 medicine lists in Kenya, Uganda and Zambia [7-9].

131
132 The quality, efficacy and safety of oxytocin and misoprostol have been widely studied [10-23].
133 Oxytocin is temperature sensitive and should therefore be stored under refrigeration at
134 temperatures between 2 and 8°C to prevent degradation expected at higher temperatures[10].
135 Degradation reduces potency and consequently the effectiveness of the medicine. Oxytocin
136 stability through the supply chain has proven a worry to policy makers and has been a subject

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3 137 of numerous investigations to ascertain quality and efficacy [11-13]. Some studies on the
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5 138 quality of oxytocin found analyzed samples to contain less active pharmaceutical ingredients
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7 139 than was claimed in the label, while some samples also failed sterility tests [14-16]. LMICs with
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9 140 low resources may also lack facilities required for adequate storage conditions for oxytocin to
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11 141 ensure integrity of the product, while they may also lack trained health workers for its
12
13 142 administration [17]. Women living among displaced populations, in conflict areas, hard to reach
14
15 143 areas, who deliver at home or with a traditional birth attendant seldom have access to a trained
16
17 144 health worker. Hence, they do not have access to oxytocin or if they do, it is not safely used
18
19 145 [24]. As a result of these challenges, prevention and treatment of PPH in low-resource settings
20
21 146 using oxytocin has not provided the desired impact [18, 19].
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23
24 148 Misoprostol, a prostaglandin, is an alternative to oxytocin in the management of PPH. It is
25
26 149 cheap, stable at room temperature and more convenient to administer. It can be administered
27
28 150 sublingually, orally and vaginally [19, 20, 25, 26]. It has been demonstrated through various
29
30 151 studies that use of misoprostol is feasible, improves uterotonic coverage, reduces incidence of
31
32 152 PPH and that it is effective for use at community and household level in low-resource settings
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34 153 [20-22].

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36 154 In 2015, the WHO expert committee on the selection and use of medicines recommended the
37
38 155 addition of misoprostol for the prevention and treatment of postpartum haemorrhage when
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40 156 oxytocin is not available or cannot be used safely [23]. At different occasions the inclusion of
41
42 157 misoprostol in the list of WHO recommended medicines was debated for both efficacy and
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44 158 safety reasons, but the 2015 decision to recommend misoprostol in addition to oxytocin for
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46 159 prevention of PPH was reaffirmed in 2019 by a WHO expert committee [27]. Before 2015
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48 160 misoprostol was indicated by WHO for use in induction of labour and management of
49
50 161 spontaneous and induced abortion [28]. The historical use of misoprostol for termination of
51
52 162 pregnancies may have affected its acceptability for routine use in prevention of PPH, despite
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54 163 available convincing evidence of its therapeutic effect and relative safety in management of
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56 164 PPH. Another challenge is that the high doses of misoprostol required for post-partum
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58 165 haemorrhage often result in troublesome side effects such as vomiting and shivering [29].

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3 166 Further, the longer half-life of the medicine means that it stays longer in the body and has
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5 167 potential to cause complications [30].
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7 168 These two medicines could be used complementarily to overcome challenges and barriers in
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9 169 policy, health sector infrastructure and health service delivery that at the moment inhibit the
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11 170 optimal management of PPH [24, 31]. However, there is a knowledge gap on the accessibility of
12
13 171 both medicines in low-resource settings. This is a missed opportunity in closing the gap in the
14
15 172 reduction of maternal mortality in developing countries. This paper therefore assesses access to
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17 173 oxytocin and misoprostol in urban and rural health facilities in Kenya, Uganda and Zambia
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19 174 through a cross-sectional assessment of availability, prices and affordability at the patient level
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21 175 of the two medicines to facilitate the optimal management of PPH.
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24 25 177 **Methods**

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28 178 A secondary assessment of availability and prices of oxytocin and misoprostol was undertaken
29
30 179 using data from Health Action International (HAI) research on sexual and reproductive health
31
32 180 commodities (*SRHC: Measuring Prices, Availability & Affordability* [32]. The data was collected
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34 181 in Kenya, Uganda and Zambia in July and August 2017 using a cross-sectional design with
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36 182 quantitative methods adapted from the standardized WHO/HAI methodology [33], which has
37
38 183 been validated [34] and used extensively in several countries [35-37].
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41 42 185 *Patient and Public Involvement*

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44 186 The research agenda for this study was set by the multi-stakeholder platform Medicines
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46 187 Transparency Alliance (MeTA) Councils in Kenya, Uganda and Zambia. The study protocols were
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48 188 reviewed and approved by MeTA Councils. Data collectors were selected from the membership
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50 189 of MeTA within the countries. Results were validated by stakeholders including civil society.
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52 190 Dissemination plans were made by MeTA councils and results were disseminated to wide
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54 191 country and inter-country platforms including Ministries of Health, Parliamentarians, private
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56 192 sector as well as civil society members to inform policy.
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193

194 *Data collection*

195 For this study, the data on availability, price and affordability of the highest and lowest-priced
196 products of oxytocin 10IU, 1ml injections and misoprostol 200 µg tablets were extracted.

197 In each of the three countries, six geographical areas (districts, municipalities or counties) were
198 selected; the country's main urban centre and five other areas which were randomly selected.

199 All survey areas were reachable within one day's travel from the country's main urban centre
200 using a car or bus. Each survey area covered a population of between 100 000 and 250 000
201 people.

202
203 The WHO/HAI methodology prescribes a minimum of 30 health facilities from each of the
204 sectors, i.e. public, private and mission sectors, giving a minimum total of 90 facilities per
205 country [33]. In each survey area, the main public hospital was selected first. Then, eight public
206 health facilities, four each from urban and rural areas, representing levels of care at which
207 SRHCs should be made available, were randomly selected [38]. Additionally, eight private (for
208 profit) and eight mission sector (not for profit) health facilities (four each from urban and rural
209 areas) that were within a three-hour drive radius of the main hospitals were selected. Thus, a
210 total of 24 health facilities were sampled from each of the six survey areas in Kenya, Uganda
211 and Zambia, respectively, giving a total of 144 facilities per country.

212
213 Eight data collectors with experience of conducting medicine surveys worked in pairs of a
214 pharmacist and a social scientist under close supervision of a qualified survey manager. Prior to
215 data collection, the team was trained on the methodology. Data collectors used a semi-
216 structured questionnaire administered to facility managers while physically ascertaining the
217 availability of surveyed medicines. Availability was measured by the physical presence of a
218 product in the outlet at the time of the survey. For each medicine surveyed, data collectors
219 recorded the product name for both the highest and lowest-priced medicines available, the
220 manufacturer and unit price of the product. In the public sector in Uganda and Zambia where
221 medicines are free of charge to care seekers, prices were not recorded.

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5 223 Once data collection was complete, survey data was entered into a pre-programmed Microsoft
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7 224 Excel Workbook provided as part of the modified methodology. Data input was independently
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9 225 checked for errors. Additional quality control measures were executed at various stages
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11 226 throughout the study by a survey manager. The survey tools were pre-tested in Uganda in 2016
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13 227 and a field test was conducted by all data collectors prior to data collection. Each data
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15 228 collection team had a supervisor who cross checked the data on a daily basis for completeness,
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17 229 legibility and consistency and reported to the survey manager. Prior to data entry all relayed
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19 230 data was checked for completeness and consistency.
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21 231

22 232 *Data analysis*

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25 233 The availability of oxytocin and misoprostol was calculated as the percentage of sampled
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27 234 medicine outlets where the medicine was found. Availability was also calculated for the
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29 235 presence of either oxytocin or misoprostol at a facility. Data were reported in aggregate as
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31 236 public, private or mission sector medicine outlets. Overall availability per sector was calculated
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33 237 as mean of the two medicines surveyed.
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38 239 Patient prices were collected in local currency including Shillings in Uganda and Kenya, and
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40 240 Kwacha in Zambia. The mean, minimum and maximum unit prices were calculated. To facilitate
41
42 241 cross-country comparisons, medicine prices obtained during the survey were expressed as
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44 242 ratios relative to a standard set of international reference prices by dividing the mean unit
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46 243 price (in dollars) by the Management Sciences for Health international buyers' reference unit
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48 244 price derived on September 25th 2018 [39]. Mean price ratios (MPRs) were only calculated for
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50 245 oxytocin and misoprostol products that had price data from at least four medicine outlets per
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52 246 sector [33]. The exchange rate used to calculate MPRs was 1 USD = 102.67 Kenya Shillings (KES),
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54 247 1 USD = 3667.9 Uganda Shillings (UGX), 1 USD = 8.85 Zambia Kwacha (ZMW) taken on 1st July,
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56 248 2017 prior to the first day of data collection [40, 41].
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6 250 Affordability was calculated using the number of days' wages it requires to pay for standard
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8 251 treatment or dose of treatment based on the daily income of the lowest-paid government
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10 252 worker (LPGW) [33]. The daily wage of a LPGW is approximately KES 411 (USD 4) in Kenya, 6255
11 253 UGX (USD 1.78) in Uganda, and ZMW 96.7 (USD 10.92) in Zambia, as per public service salary
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13 254 structures [42]. Treatments that required more than one day's wages to purchase were
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15 255 considered unaffordable [33].
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21 257 **Results**

22
23 258 A total of 376 health facilities, including 120, 124 and 132 health facilities in Kenya, Uganda and
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25 259 Zambia, respectively, were surveyed as shown in figure 1 and 2.
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28 260 29 30 261 *Availability across sectors*

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33 262 Figure 1 shows the availability of either oxytocin or misoprostol at the surveyed health facilities
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35 263 in the three countries. Overall availability of either oxytocin or misoprostol met the WHO
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37 264 benchmark of 80% in Kenya (81%) and Uganda (82%) but was marginally lower in Zambia (76%).
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39 265 Availability of oxytocin was higher than misoprostol except in Uganda. Availability of either
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41 266 oxytocin or misoprostol was comparable between the public and mission sectors.
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45 267
46 268 In the public sector, the three countries met the WHO benchmark for availability of oxytocin.
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48 269 Misoprostol was only optimally available in the public sector in Uganda (88%), with availability
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50 270 in Kenya and Zambia lower (36% and 21%, respectively). In the private sector, none of the
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52 271 countries met the WHO recommended availability for misoprostol. Availability in Zambia was
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54 272 especially low (24%).
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6 275 *Availability in urban versus rural areas*
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9 276 Figure 2 shows availability in urban versus rural areas. Oxytocin was available in over 80% of all
10 277 public urban and rural facilities across the three countries. Optimum availability of 80% was
11 278 further achieved for oxytocin in Kenya mission urban facilities (89%) and in Zambia's mission
12 279 sector for both urban and rural facilities (83% and 94%, respectively). Optimum availability of
13 280 misoprostol was only achieved in Ugandan public urban and rural facilities (90% and 86%,
14 281 respectively).

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24 283 In Kenya, oxytocin had a higher availability than misoprostol across all urban and rural facilities
25 284 in the three sectors. Availability of misoprostol was lowest in the public sector: availability in
26 285 urban facilities was 45%, and 27% in rural facilities. In the private sector, there was a higher
27 286 availability in rural facilities than in urban facilities for both oxytocin and misoprostol.

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35 288 In Uganda, the public sector was optimally stocked with both oxytocin and misoprostol across
36 289 urban and rural facilities. Rural public facilities had a higher availability of oxytocin than urban
37 290 public facilities. In the private sector, rural facilities also had a higher availability of oxytocin and
38 291 misoprostol compared to urban facilities.

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46 293 Oxytocin had a high availability in Zambia's public and mission sectors across both urban and
47 294 rural facilities. Availability in the private sector was very low. Availability of misoprostol was low
48 295 across the sectors and areas, with highest availability found in urban mission facilities (50%).
49 296 Although both oxytocin and misoprostol were poorly available in the private sector, oxytocin
50 297 was more available in rural than urban facilities, while misoprostol had a higher availability in
51 298 urban facilities than in rural facilities.

299

300 *Prices and affordability*

301 Oxytocin and misoprostol were free for patients in the public and mission sectors in Zambia,
302 and in the public sector in Uganda. In Kenya's public sector, the lowest price was noted for
303 oxytocin, with a median price ratio (MPR) of USD 0.174 (Table 1). Both misoprostol and
304 oxytocin cost less than a day's wages for a LPGW across all countries and sectors, and can
305 therefore be considered affordable.

306

307 Notwithstanding the sectors in which the medicines were for free, the MPRs for oxytocin and
308 misoprostol were above one in the countries, ranging from 1.37 for misoprostol in Kenya's
309 public sector to 29.95 for misoprostol in the private sector in Zambia. This meant that both
310 misoprostol and oxytocin were accessed by patients at prices that were more expensive
311 compared to international reference prices.

Table 1: Prices and affordability of misoprostol and oxytocin across countries

		Public			Private			Mission		
		Price (USD)	Mean Price Ratio	Affordability of treatment (number of day's wages)	Price (USD)	Mean Price Ratio*	Affordability of treatment (number of day's wages)	Price (USD)	Mean Price Ratio	Affordability of treatment (number of day's wages)
Kenya	Oxytocin	0.029	0.17	0.01	1.354	8.14	0.34	0.672	4.04	0.30
	Misoprostol	0.273	1.37	0.07	1.967	9.84	0.49	1.217	6.09	0.17
Uganda	Oxytocin	0	NA	NA	0.998	5.99	0.57	0.408	2.45	0.23
	Misoprostol	0	NA	NA	0.589	2.95	0.34	0.39	1.95	0.22
Zambia	Oxytocin	0	NA	NA	0.678	4.08	0.06	NA	NA	NA
	Misoprostol	0	NA	NA	5.989	29.95	0.55	NA	NA	NA

NA=not applicable, USD=United States Dollar

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4 312 **Discussion**

5 313 This paper assesses access to oxytocin and misoprostol in urban and rural health facilities in
6 314 Kenya, Uganda and Zambia through a cross-sectional assessment of availability, prices and
7 315 affordability at the patient level of the two medicines to facilitate the optimal management of
8
9 316 PPH.
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14 318 Overall, availability of uterotonics, expressed as the presence of either oxytocin or misoprostol,
15 319 was high in Kenya and Uganda, and just below the WHO benchmark of 80% in Zambia.
16 320 Misoprostol was markedly less available than oxytocin. Oxytocin and misoprostol were
17 321 accessed by patients in the private sector at prices that were more expensive than the
18 322 international reference prices. However, both medicines cost less than a day's wages, which is
19 323 considered affordable. The availability of misoprostol across urban and rural areas did not show
20 324 the expected pattern of having a higher availability of the medicine in rural areas, which are
21 325 more prone to health system barriers for use of oxytocin.
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31 327 Oxytocin availability was high in the public and mission sectors but lower in the private sector,
32 328 particularly in Zambia. In the private sector, none of the countries met the WHO availability
33 329 benchmark of 80% for the two medicines. Besides the public sector in Uganda, misoprostol was
34 330 not optimally available in the other countries or sectors. Misoprostol had a low availability,
35 331 particularly in rural areas where the medicine ought to play a major role given that facilities in
36 332 these areas tend to lack adequately trained health workers and the health infrastructure
37 333 required to maintain cold chain to safeguard the quality of oxytocin [17]. Its poor availability in
38 334 Kenya and Zambia may be a result of slow diffusion of the intervention into the health system
39 335 [43, 44]. Moreover, misoprostol has been recommended by WHO for use in PPH since 2015
40 336 after several rounds of weighing the benefits and risks, but the debate about its role in PPH
41 337 prevention has continued over the years [23, 27]. The fear and stigma amongst health workers
42 338 about the use of misoprostol to induce abortions may also have contributed to the situation
43 339 [29]. In contrast, Uganda's efforts as an early adaptor [43, 44] to ensure availability of
44 340 misoprostol through government procurement and community level distribution strategies may
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3 341 explain why it has a higher availability of misoprostol, as well as lower PPH levels compared to
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5 342 Kenya and Zambia (25% in Uganda versus 34% in both Kenya and Zambia) [3-5].
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9 344 Urban facilities have better health infrastructure such as cold chain facilities, and also tend to
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11 345 have more health workers compared to rural facilities [45-47]. It would therefore be expected
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13 346 that these urban areas would have a higher availability of oxytocin and lower availability of
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15 347 misoprostol than rural facilities. However, there were instances when rural facilities had a
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17 348 higher availability of oxytocin and a lower availability of misoprostol. This may indicate that
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19 349 stocking of oxytocin and misoprostol by health facilities does not take into consideration
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21 350 challenges faced by the facilities to administer the medicines. It will require more research in
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23 351 this area to better understand the data and for policy makers to look into how to address
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25 352 context-specific barriers related to these medicines by ensuring that they are deployed where
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27 353 they can have maximum impact [48, 49]. For example, efforts should be made to deploy more
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29 354 misoprostol in rural areas where there is a lack of adequately trained personnel and a lack of
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31 355 health infrastructure to properly use oxytocin, and to ensure that both medicines are available
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33 356 to complement one another depending on circumstances.

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37 358 PPH levels across the countries are high despite health facilities having reached the WHO
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39 359 benchmark for availability of either oxytocin or misoprostol across the three countries. This
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41 360 may confirm the finding from a study by Ononge et al that despite use of uterotonics, incidence
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43 361 of PPH remains high [5]. It may be that some oxytocin found at health facilities may not have
44
45 362 the quality and efficacy for optimum management of PPH [14-16]. Countries should strive for
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47 363 universal access as the 80% availability benchmark by WHO still leaves one in five facilities
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49 364 without required medicine. However, availability of a medicine alone does not guarantee that it
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51 365 is used, health worker beliefs and knowledge as well as necessary infrastructure such as
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53 366 electricity and equipment are needed to reduce PPH levels.

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57 368 Studies have shown that combinations of uterotonics have proven to be more effective. For
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59 369 example, a misoprostol plus oxytocin combination was found to be more effective in preventing
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3 370 PPH than the currently used standard of oxytocin only [50]. This argument further emphasizes
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5 371 that having both oxytocin and misoprostol available at the health facility could help to improve
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7 372 PPH management.
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10 373 Although oxytocin and misoprostol were affordable to patients, the private sector prices were
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12 374 varied and more expensive compared to IRPs. For example, the MPR of misoprostol ranged
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14 375 from 1.37 in Kenya to 29.95 in Zambia. Therefore, even though availability met the WHO
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16 376 benchmark, individual patients may still be confronted with unavailability in the public sector,
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18 377 pushing them to seek care in the private sector where they may not be able to afford the prices
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20 378 of medicines. This suggests that countries need to explore pricing policies to improve
21
22 379 affordability of the medicines.
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24 380
25 381 The WHO/HAI methodology that was used for this study is tested, reliable, standardized and
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27 382 validated for the measurement of medicine prices and availability [34]. The study provides
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29 383 details on availability, price, and affordability of individual medicines across three sectors
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31 384 (public, private and mission). The methodology uses a cross-sectional design and therefore
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33 385 historical data trends were not traced. The study only used two frontline medicines for PPH,
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35 386 while countries may have had other alternative therapies including carbetocin which were not
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37 387 captured. The number of mission facilities surveyed in Zambia (23) was below the minimum
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39 388 (30) recommended for the methodology per sector [33]. The findings presented here may not
40
41 389 be used to predict country pharmaceutical supply chain but are intended to stimulate policy
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43 390 discussions on deliberate targeting and the use of available technologies to improve access.
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45 391

46 392 **Conclusion**

47 393 Availability of oxytocin and misoprostol met the WHO benchmark in Kenya and Uganda but was
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49 394 just below the WHO benchmark in Zambia. In general, oxytocin was more available than
50
51 395 misoprostol. Oxytocin and misoprostol were purchased by patients at prices above
52
53 396 international reference prices but both medicines cost less than a day's wages for a LPGW and
54
55 397 were therefore considered affordable. However, there was no strategy in place that looked at
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57 398 which medicine could be best utilized in which area. Countries with limited resources should

399 explore mechanisms to balance access to both oxytocin and misoprostol between rural and
400 urban areas to optimize management of PPH.

401 **List of abbreviations**

402 Post-partum haemorrhage (PPH); Median price ratio (MPR); Low- and middle-income countries
403 (LMICs); Lowest-paid government worker (LPGW); sexual and reproductive health commodities
404 (SRHC); Health Action International (HAI); World Health Organisation (WHO).

405

406 **Declarations**

407 *Ethical approval and consent to participate*

408 This study did not involve human subjects and did not involve direct interaction with patients
409 and therefore ethical approval was not sought. However, Ministries of Health in Uganda and
410 Zambia and Country Directors of Health in Kenya gave approval and provided introduction
411 letters to health facilities.

412

413 *Consent for publication*

414 Not applicable

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416 *Availability of data and materials*

417 The datasets used and/or analysed during the current study are available from the
418 corresponding author on request.

419

420 *Competing interests*

421 All authors declare no competing interests.

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7
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10 Partnership.
11 425
1213 426
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1516 427 *Authors' contribution*
17
1819 428 DK conceptualized the project, undertook data analysis and wrote the first draft of the
20 manuscript; GOI contributed to data analysis; GOI, HDH, JN, TR, HL and AM revised the
21 429 manuscript and critically reviewed its contents. GO contributed to data analysis. AM critically
22 430 reviewed the manuscript, provided comments and guidance on all drafts of manuscript.
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25
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28
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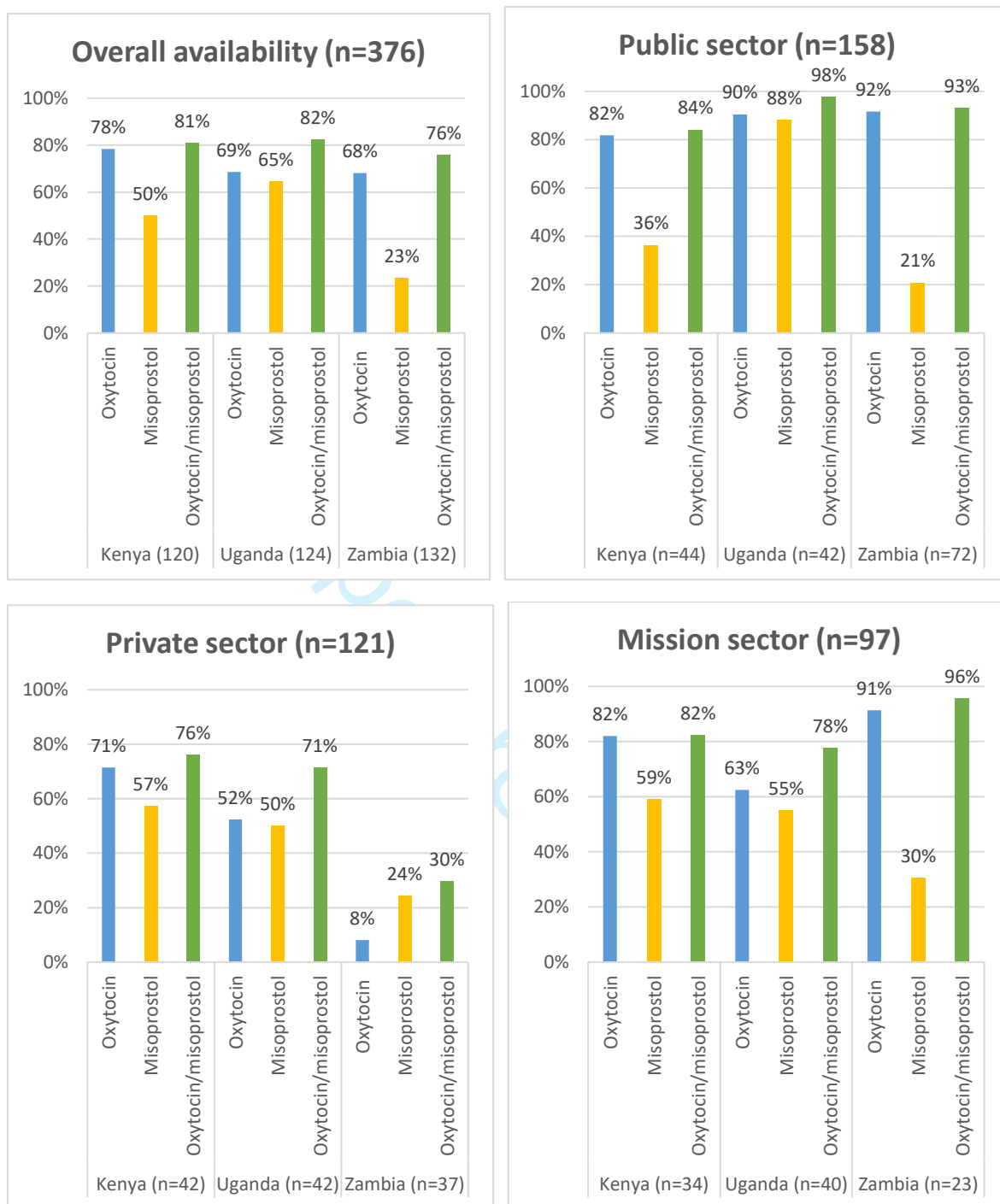


Fig 1: Availability of oxytocin and misoprostol across sectors in Kenya, Uganda and Zambia

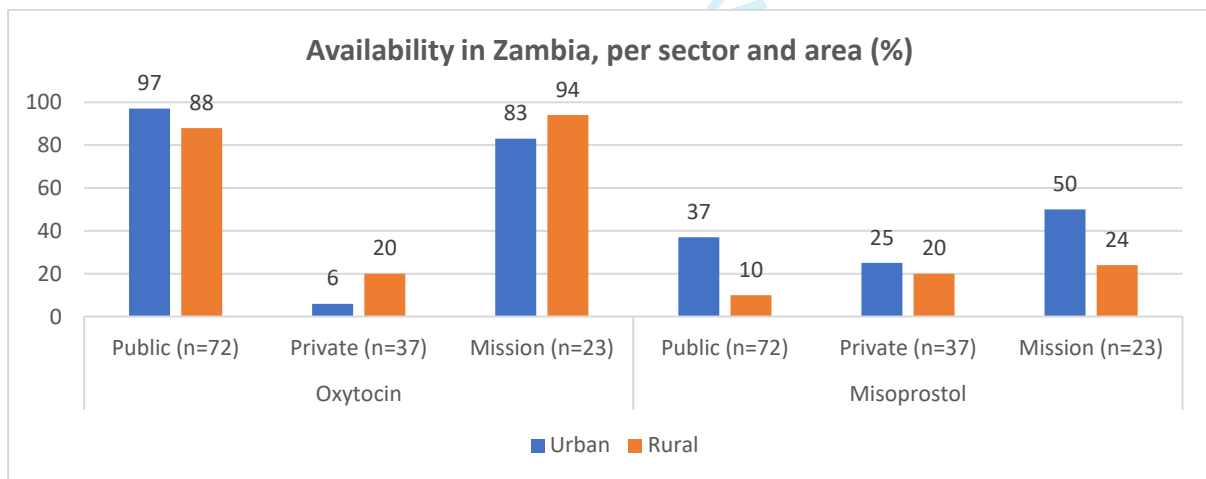
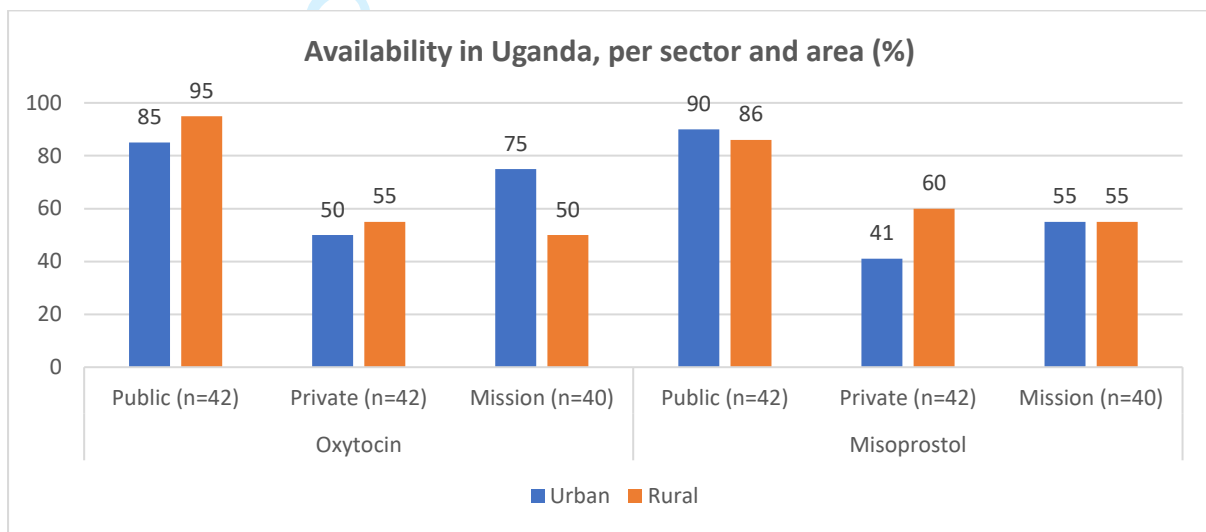
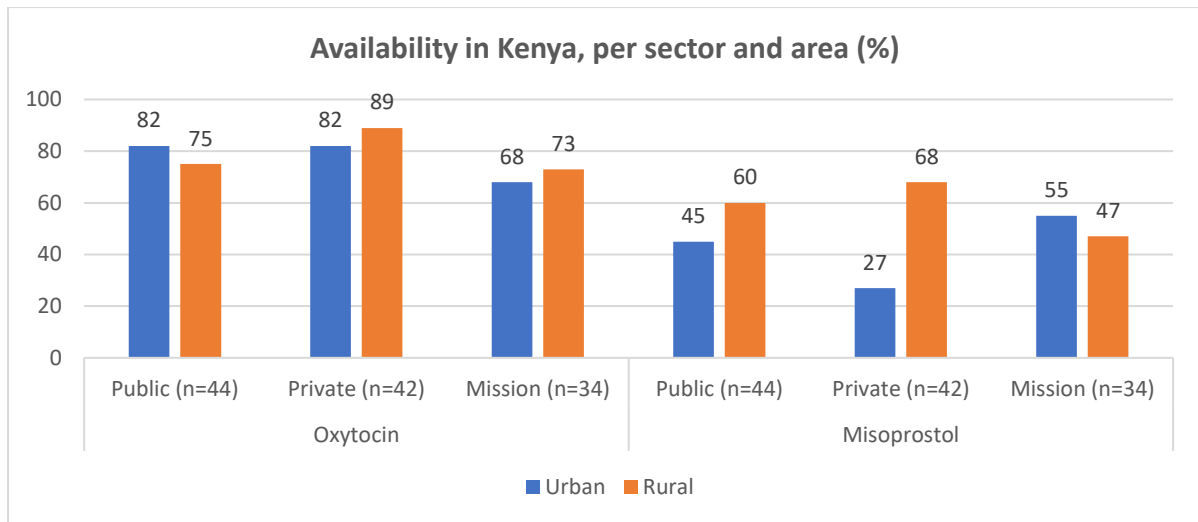


Figure 2: Availability of oxytocin and misoprostol in urban and rural facilities across countries

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4 1 **Access to oxytocin and misoprostol for management of post-partum haemorrhage in Kenya,**
5 2 **Uganda and Zambia. A cross-sectional assessment of availability, prices and affordability.**

6
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52 45 **Key words:** Access, Oxytocin, Misoprostol, Post-partum haemorrhage

1
2
3 46 **Abstract**

4
5 47 **Objective**

6
7 48 To assess access (availability and affordability) to oxytocin and misoprostol at health facilities in
8
9 49 Kenya, Uganda and Zambia to improve prevention and management of postpartum haemorrhage
10
11 50 (PPH).

12 51
13
14 52 **Design**

15
16 53 The assessment was undertaken using data from Health Action International (HAI) research on
17
18 54 sexual and reproductive health commodities based on a cross-sectional design adapted from the
19
20 55 standardized WHO/HAI methodology.

21 56
22
23 57 **Setting**

24
25 58 Data was collected from 376 health facilities in in Kenya, Uganda and Zambia in July and August
26
27 59 2017.

28
29 60
30
31 61 **Outcome measures**

32
33 62 Availability was calculated as mean percentage of sampled medicine outlets where medicine was
34
35 63 found on the day of data collection. Medicine prices were compared to international reference
36
37 64 prices (IRP) and expressed as median price ratios (MPRs). Affordability was calculated using
38
39 65 number of days required to pay for a standard treatment based on the daily income of the lowest-
40
41 66 paid government worker.

42 67
43
44 68 **Results**

45
46 69 Availability of either oxytocin or misoprostol at health facilities was high; 81% in Kenya, 82% in
47
48 70 Uganda, and 76% in Zambia. Oxytocin was more available than misoprostol, and it was most
49
50 71 available in the public sector in the three countries. Availability of misoprostol was highest in the
51
52 72 public sector in Uganda (88%). Oxytocin and misoprostol were purchased by patients at prices
53
54 73 above IRP, but both medicines cost less than a day's wages and were therefore affordable.

1
2
3 74 Availability of misoprostol was poor in rural settings where it would be more preferred due to
4
5 75 lack of trained personnel and cold storage facilities required for oxytocin.
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9
10 77 **Conclusion**

11
12 78 Availability and affordability of either oxytocin or misoprostol at health facilities met the WHO
13
14 79 benchmark of 80%. However, countries with limited resources should explore mechanisms to
15
16 80 optimize management of PPH by improving access to misoprostol especially in rural areas.
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18 81

19 82 **Strengths and limitations of this study**

- 20
21
22 83 • The WHO/HAI methodology that was used for this study is tested, reliable, standardized
23
24 84 and validated for the measurement of medicine prices and availability.
25
26 85 • The study provides details on availability, price, and affordability of individual medicines
27
28 86 across three sectors (public, private and mission).
29
30 87 • The methodology uses a cross-sectional design and therefore historical data trends were
31
32 88 not traced.
33
34 89 • The study only used two frontline medicines for PPH, while countries may have had
35
36 90 other alternative therapies including carbetocin which were not captured.
37
38 91 • In Zambia we surveyed 23 mission facilities which was below the 30 facilities per sector
39
40 92 30 recommended by the methodology.
41
42 93

95 **Background**

96 The risk of women dying due to pregnancy and childbirth remains a major global health challenge.
97 In 2017 there were approximately 295,000 maternal deaths globally, of which 94% occurred in
98 low-and middle-income countries (LMICs). Sub-Saharan Africa contributed about 66% to these
99 deaths [1]. The global leading cause of maternal mortality is haemorrhage, accounting for 27% of
100 all maternal deaths [2].

101 Postpartum haemorrhage (PPH) which occurs after childbirth accounts for most (72%) of the
102 three forms of haemorrhage. Antepartum haemorrhage which occurs during pregnancy accounts
103 for 24% while intrapartum haemorrhage (during childbirth) accounts for three percent [2]. PPH
104 is responsible for 34% of maternal deaths in Kenya, 25% in Uganda and 34% in Zambia [3-5].

105 The World Health Organization (WHO) recommends oxytocin as the medicine of choice for
106 management of PPH, and misoprostol as the second line alternative when injection capability is
107 lacking and/or storage conditions for oxytocin are not met. Other uterotonics such as
108 ergometrine and carbetocin are also recommended when use of oxytocin is not feasible [1].

109 The relevance of oxytocin and misoprostol to health systems was further emphasised by the
110 United Nations Commission on Life-saving Commodities for women and children when they were
111 listed among the 13 lifesaving, low-cost medicines with greatest proven potential to avert
112 preventable deaths [6]. Both oxytocin and misoprostol are included in national essential
113 medicine lists in Kenya, Uganda and Zambia [7-9].

114
115 The quality, efficacy and safety of oxytocin and misoprostol have been widely studied [10-23].
116 Oxytocin is temperature sensitive and should therefore be stored under refrigeration at
117 temperatures between 2 and 8°C to prevent degradation expected at higher temperatures[10].
118 Degradation reduces potency and consequently the effectiveness of the medicine. Oxytocin
119 stability through the supply chain has proven a worry to policy makers and has been a subject of
120 numerous investigations to ascertain quality and efficacy [11-13]. Some studies on the quality of

1
2
3 121 oxytocin found analyzed samples to contain less active pharmaceutical ingredients than was
4
5 122 claimed in the label, while some samples also failed sterility tests [14-16]. LMICs with low
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7 123 resources may also lack facilities required for adequate storage conditions for oxytocin to ensure
8
9 124 integrity of the product, while they may also lack trained health workers for its administration
10
11 125 [17]. Women living among displaced populations, in conflict areas, hard to reach areas, who
12
13 126 deliver at home or with a traditional birth attendant seldom have access to a trained health
14
15 127 worker. Hence, they do not have access to oxytocin or if they do, it is not safely used [24]. As a
16
17 128 result of these challenges, prevention and treatment of PPH in low-resource settings using
18
19 129 oxytocin has not provided the desired impact [18, 19].
20

21
22 131 Misoprostol, a prostaglandin, is an alternative to oxytocin in the management of PPH. It is cheap,
23
24 132 stable at room temperature and more convenient to administer. It can be administered
25
26 133 sublingually, orally and vaginally [19, 20, 25, 26]. It has been demonstrated through various
27
28 134 studies that use of misoprostol is feasible, improves uterotonic coverage, reduces incidence of
29
30 135 PPH and that it is effective for use at community and household level in low-resource settings
31
32 136 [20-22].
33

34 137 In 2015, the WHO expert committee on the selection and use of medicines recommended the
35
36 138 addition of misoprostol for the prevention and treatment of postpartum haemorrhage when
37
38 139 oxytocin is not available or cannot be used safely [23]. At different occasions the inclusion of
39
40 140 misoprostol in the list of WHO recommended medicines was debated for both efficacy and safety
41
42 141 reasons, but the 2015 decision to recommend misoprostol in addition to oxytocin for prevention
43
44 142 of PPH was reaffirmed in 2019 by a WHO expert committee [27]. Before 2015 misoprostol was
45
46 143 indicated by WHO for use in induction of labour and management of spontaneous and induced
47
48 144 abortion [28]. The historical use of misoprostol for termination of pregnancies may have affected
49
50 145 its acceptability for routine use in prevention of PPH, despite available convincing evidence of its
51
52 146 therapeutic effect and relative safety in management of PPH. Another challenge is that the high
53
54 147 doses of misoprostol required for post-partum haemorrhage often result in troublesome side
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56 148 effects such as vomiting and shivering [29]. Further, the longer half-life of the medicine means
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58 149 that it stays longer in the body and has potential to cause complications [30].
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3 150 These two medicines could be used complementarily to overcome challenges and barriers in
4
5 151 policy, health sector infrastructure and health service delivery that at the moment inhibit the
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7 152 optimal management of PPH [24, 31]. However, there is a knowledge gap on the accessibility of
8
9 153 both medicines in low-resource settings. This is a missed opportunity in closing the gap in the
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11 154 reduction of maternal mortality in developing countries. This paper therefore assesses access to
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13 155 oxytocin and misoprostol in urban and rural health facilities in Kenya, Uganda and Zambia
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15 156 through a cross-sectional assessment of availability, prices and affordability at the patient level
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17 157 of the two medicines to facilitate the optimal management of PPH.
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21 159 **Methods**

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23
24 160 A secondary assessment of availability and prices of oxytocin and misoprostol was undertaken
25
26 161 using data from Health Action International (HAI) research on sexual and reproductive health
27
28 162 commodities (*SRHC: Measuring Prices, Availability & Affordability* [32]. The data was collected
29
30 163 in Kenya, Uganda and Zambia in July and August 2017 using a cross-sectional design with
31
32 164 quantitative methods adapted from the standardized WHO/HAI methodology [33], which has
33
34 165 been validated [34] and used extensively in several countries [35-37].
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36 166

37 166 38 167 *Patient and Public Involvement*

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40
41 168 The research agenda for this study was set by the multi-stakeholder platform Medicines
42
43 169 Transparency Alliance (MeTA) Councils in Kenya, Uganda and Zambia. The study protocols were
44
45 170 reviewed and approved by MeTA Councils. Data collectors were selected from the membership
46
47 171 of MeTA within the countries. Results were validated by stakeholders including civil society.
48
49 172 Dissemination plans were made by MeTA councils and results were disseminated to wide country
50
51 173 and inter-country platforms including Ministries of Health, Parliamentarians, private sector as
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53 174 well as civil society members to inform policy.
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3 176 *Data collection*
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5 177 For this study, the data on availability, price and affordability of the highest and lowest-priced
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7 178 products of oxytocin 10IU, 1ml injections and misoprostol 200 µg tablets were extracted.

8
9 179 In each of the three countries, six geographical areas (districts, municipalities or counties) were
10
11 180 selected; the country's main urban centre and five other areas which were randomly selected.

12 181 All survey areas were reachable within one day's travel from the country's main urban centre
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14 182 using a car or bus. Each survey area covered a population of between 100 000 and 250 000
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16 183 people.
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19
20 185 The WHO/HAI methodology prescribes a minimum of 30 health facilities from each of the sectors,
21
22 186 i.e. public, private and mission sectors, giving a minimum total of 90 facilities per country [33]. In
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24 187 each survey area, the main public hospital was selected first. Then, eight public health facilities,
25
26 188 four each from urban and rural areas, representing levels of care at which SRHCs should be made
27
28 189 available, were randomly selected [38]. Additionally, eight private (for profit) and eight mission
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30 190 sector (not for profit) health facilities (four each from urban and rural areas) that were within a
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32 191 three-hour drive radius of the main hospitals were selected. Thus, a total of 24 health facilities
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34 192 were sampled from each of the six survey areas in Kenya, Uganda and Zambia, respectively, giving
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36 193 a total of 144 facilities per country.
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38 194
39 195 Eight data collectors with experience of conducting medicine surveys worked in pairs of a
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41 196 pharmacist and a social scientist under close supervision of a qualified survey manager. Prior to
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43 197 data collection, the team was trained on the methodology. Data collectors used a semi-
44
45 198 structured questionnaire administered to facility managers while physically ascertaining the
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47 199 availability of surveyed medicines. Availability was measured by the physical presence of a
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49 200 product in the outlet at the time of the survey. For each medicine surveyed, data collectors
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51 201 recorded the product name for both the highest and lowest-priced medicines available, the
52
53 202 manufacturer and unit price of the product. In the public sector in Uganda and Zambia where
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55 203 medicines are free of charge to care seekers, prices were not recorded.
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3 205 Once data collection was complete, survey data was entered into a pre-programmed Microsoft
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5 206 Excel Workbook provided as part of the modified methodology. Data input was independently
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7 207 checked for errors. Additional quality control measures were executed at various stages
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9 208 throughout the study by a survey manager. The survey tools were pre-tested in Uganda in 2016
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11 209 and a field test was conducted by all data collectors prior to data collection. Each data collection
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13 210 team had a supervisor who cross checked the data on a daily basis for completeness, legibility
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15 211 and consistency and reported to the survey manager. Prior to data entry all relayed data was
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17 212 checked for completeness and consistency.
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20 214 *Data analysis*

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22
23 215 The availability of oxytocin and misoprostol was calculated as the percentage of sampled
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25 216 medicine outlets where the medicine was found. Availability was also calculated for the presence
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27 217 of either oxytocin or misoprostol at a facility. Data were reported in aggregate as public, private
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29 218 or mission sector medicine outlets. Overall availability per sector was calculated as mean of the
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31 219 two medicines surveyed.
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36 221 Patient prices were collected in local currency including Shillings in Uganda and Kenya, and
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38 222 Kwacha in Zambia. The mean, minimum and maximum unit prices were calculated. To facilitate
39
40 223 cross-country comparisons, medicine prices obtained during the survey were expressed as ratios
41
42 224 relative to a standard set of international reference prices by dividing the mean unit price (in
43
44 225 dollars) by the Management Sciences for Health international buyers' reference unit price
45
46 226 derived on September 25th 2018 [39]. Mean price ratios (MPRs) were only calculated for oxytocin
47
48 227 and misoprostol products that had price data from at least four medicine outlets per sector [33].
49
50 228 The exchange rate used to calculate MPRs was 1 USD = 102.67 Kenya Shillings (KES), 1 USD =
51
52 229 3667.9 Uganda Shillings (UGX), 1 USD = 8.85 Zambia Kwacha (ZMW) taken on 1st July, 2017 prior
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54 230 to the first day of data collection [40, 41].
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3 232 Affordability was calculated using the number of days' wages it requires to pay for standard
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5 233 treatment or dose of treatment based on the daily income of the lowest-paid government worker
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7 234 (LPGW) [33]. The daily wage of a LPGW is approximately KES 411 (USD 4) in Kenya, 6255 UGX
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9 235 (USD 1.78) in Uganda, and ZMW 96.7 (USD 10.92) in Zambia, as per public service salary
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11 236 structures [42]. Treatments that required more than one day's wages to purchase were
12
13 237 considered unaffordable [33].
14

15 238

18 239 **Results**

20 240 A total of 376 health facilities, including 120, 124 and 132 health facilities in Kenya, Uganda and
21
22 241 Zambia, respectively, were surveyed as shown in figure 1 and 2.
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24

25 242

28 243 *Availability across sectors*

30 244 Figure 1 shows the availability of either oxytocin or misoprostol at the surveyed health facilities
31
32 245 in the three countries. Overall availability of either oxytocin or misoprostol met the WHO
33
34 246 benchmark of 80% in Kenya (81%) and Uganda (82%) but was marginally lower in Zambia (76%).
35
36 247 Availability of oxytocin was higher than misoprostol except in Uganda. Availability of either
37
38 248 oxytocin or misoprostol was comparable between the public and mission sectors.
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42 250 In the public sector, the three countries met the WHO benchmark for availability of oxytocin.
43
44 251 Misoprostol was only optimally available in the public sector in Uganda (88%), with availability in
45
46 252 Kenya and Zambia lower (36% and 21%, respectively). In the private sector, none of the countries
47
48 253 met the WHO recommended availability for misoprostol. Availability in Zambia was especially
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50 254 low (24%).
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3 257 *Availability in urban versus rural areas*
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6 258 Figure 2 shows availability in urban versus rural areas. Oxytocin was available in over 80% of all
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8 259 public urban and rural facilities across the three countries. Optimum availability of 80% was
9
10 260 further achieved for oxytocin in Kenya mission urban facilities (89%) and in Zambia's mission
11
12 261 sector for both urban and rural facilities (83% and 94%, respectively). Optimum availability of
13
14 262 misoprostol was only achieved in Ugandan public urban and rural facilities (90% and 86%,
15
16 263 respectively).
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21 265 In Kenya, oxytocin had a higher availability than misoprostol across all urban and rural facilities
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23 266 in the three sectors. Availability of misoprostol was lowest in the public sector: availability in
24
25 267 urban facilities was 45%, and 27% in rural facilities. In the private sector, there was a higher
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27 268 availability in rural facilities than in urban facilities for both oxytocin and misoprostol.
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32 270 In Uganda, the public sector was optimally stocked with both oxytocin and misoprostol across
33
34 271 urban and rural facilities. Rural public facilities had a higher availability of oxytocin than urban
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36 272 public facilities. In the private sector, rural facilities also had a higher availability of oxytocin and
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38 273 misoprostol compared to urban facilities.
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43 275 Oxytocin had a high availability in Zambia's public and mission sectors across both urban and
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45 276 rural facilities. Availability in the private sector was very low. Availability of misoprostol was low
46
47 277 across the sectors and areas, with highest availability found in urban mission facilities (50%).
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49 278 Although both oxytocin and misoprostol were poorly available in the private sector, oxytocin was
50
51 279 more available in rural than urban facilities, while misoprostol had a higher availability in urban
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53 280 facilities than in rural facilities.
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3 282 *Prices and affordability*
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6 283 Oxytocin and misoprostol were free for patients in the public and mission sectors in Zambia, and
7
8 284 in the public sector in Uganda. In Kenya's public sector, the lowest price was noted for oxytocin,
9
10 285 with a median price ratio (MPR) of USD 0.174 (Table 1). Both misoprostol and oxytocin cost less
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12 286 than a day's wages for a LPGW across all countries and sectors, and can therefore be considered
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14 287 affordable.
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19 289 Notwithstanding the sectors in which the medicines were for free, the MPRs for oxytocin and
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21 290 misoprostol were above one in the countries, ranging from 1.37 for misoprostol in Kenya's public
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23 291 sector to 29.95 for misoprostol in the private sector in Zambia. This meant that both misoprostol
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25 292 and oxytocin were accessed by patients at prices that were more expensive compared to
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27 293 international reference prices.
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Table 1: Prices and affordability of misoprostol and oxytocin across countries

		Public			Private			Mission		
		Price (USD)	Mean Price Ratio	Affordability of treatment (number of day's wages)	Price (USD)	Mean Price Ratio*	Affordability of treatment (number of day's wages)	Price (USD)	Mean Price Ratio	Affordability of treatment (number of day's wages)
Kenya	Oxytocin	0.029	0.17	0.01	1.354	8.14	0.34	0.672	4.04	0.30
	Misoprostol	0.273	1.37	0.07	1.967	9.84	0.49	1.217	6.09	0.17
Uganda	Oxytocin	0	NA	NA	0.998	5.99	0.57	0.408	2.45	0.23
	Misoprostol	0	NA	NA	0.589	2.95	0.34	0.39	1.95	0.22
Zambia	Oxytocin	0	NA	NA	0.678	4.08	0.06	NA	NA	NA
	Misoprostol	0	NA	NA	5.989	29.95	0.55	NA	NA	NA

NA=not applicable, USD=United States Dollar

294 Discussion

295 This paper assesses access to oxytocin and misoprostol in urban and rural health facilities in
296 Kenya, Uganda and Zambia through a cross-sectional assessment of availability, prices and
297 affordability at the patient level of the two medicines to facilitate the optimal management of
298 PPH.

299
300 Overall, availability of uterotonics, expressed as the presence of either oxytocin or misoprostol,
301 was high in Kenya and Uganda, and just below the WHO benchmark of 80% in Zambia.
302 Misoprostol was markedly less available than oxytocin. Oxytocin and misoprostol were accessed
303 by patients in the private sector at prices that were more expensive than the international
304 reference prices. However, both medicines cost less than a day's wages, which is considered
305 affordable. The availability of misoprostol across urban and rural areas did not show the expected
306 pattern of having a higher availability of the medicine in rural areas, which are more prone to
307 health system barriers for use of oxytocin.

308
309 Oxytocin availability was high in the public and mission sectors but lower in the private sector,
310 particularly in Zambia. In the private sector, none of the countries met the WHO availability
311 benchmark of 80% for the two medicines. Besides the public sector in Uganda, misoprostol was
312 not optimally available in the other countries or sectors. Misoprostol had a low availability,
313 particularly in rural areas where the medicine ought to play a major role given that facilities in
314 these areas tend to lack adequately trained health workers and the health infrastructure required
315 to maintain cold chain to safeguard the quality of oxytocin [17]. Its poor availability in Kenya and
316 Zambia may be a result of slow diffusion of the intervention into the health system [43, 44].
317 Moreover, misoprostol has been recommended by WHO for use in PPH since 2015 after several
318 rounds of weighing the benefits and risks, but the debate about its role in PPH prevention has
319 continued over the years [23, 27]. The fear and stigma amongst health workers about the use of
320 misoprostol to induce abortions may also have contributed to the situation [29]. In contrast,
321 Uganda's efforts as an early adaptor [43, 44] to ensure availability of misoprostol through
322 government procurement and community level distribution strategies may explain why it has a

323 higher availability of misoprostol, as well as lower PPH levels compared to Kenya and Zambia
324 (25% in Uganda versus 34% in both Kenya and Zambia) [3-5].

325
326 Urban facilities have better health infrastructure such as cold chain facilities, and also tend to
327 have more health workers compared to rural facilities [45-47]. It would therefore be expected
328 that these urban areas would have a higher availability of oxytocin and lower availability of
329 misoprostol than rural facilities. However, there were instances when rural facilities had a higher
330 availability of oxytocin and a lower availability of misoprostol. This may indicate that stocking of
331 oxytocin and misoprostol by health facilities does not take into consideration challenges faced
332 by the facilities to administer the medicines. It will require more research in this area to better
333 understand the data and for policy makers to look into how to address context-specific barriers
334 related to these medicines by ensuring that they are deployed where they can have maximum
335 impact [48, 49]. For example, efforts should be made to deploy more misoprostol in rural areas
336 where there is a lack of adequately trained personnel and a lack of health infrastructure to
337 properly use oxytocin, and to ensure that both medicines are available to complement one
338 another depending on circumstances.

339
340 PPH levels across the countries are high despite health facilities having reached the WHO
341 benchmark for availability of either oxytocin or misoprostol across the three countries. This may
342 confirm the finding from a study by Ononge et al that despite use of uterotonics, incidence of
343 PPH remains high [5]. It may be that some oxytocin found at health facilities may not have the
344 quality and efficacy for optimum management of PPH [14-16]. Countries should strive for
345 universal access as the 80% availability benchmark by WHO still leaves one in five facilities
346 without required medicine. However, availability of a medicine alone does not guarantee that it
347 is used, health worker beliefs and knowledge as well as necessary infrastructure such as
348 electricity and equipment are needed to reduce PPH levels.

349
350 Studies have shown that combinations of uterotonics have proven to be more effective. For
351 example, a misoprostol plus oxytocin combination was found to be more effective in preventing

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3 352 PPH than the currently used standard of oxytocin only [50]. This argument further emphasizes
4
5 353 that having both oxytocin and misoprostol available at the health facility could help to improve
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7 354 PPH management.
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10 355 Although oxytocin and misoprostol were affordable to patients, the private sector prices were
11
12 356 varied and more expensive compared to IRPs. For example, the MPR of misoprostol ranged from
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14 357 1.37 in Kenya to 29.95 in Zambia. Therefore, even though availability met the WHO benchmark,
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16 358 individual patients may still be confronted with unavailability in the public sector, pushing them
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18 359 to seek care in the private sector where they may not be able to afford the prices of medicines.
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20 360 This suggests that countries need to explore pricing policies to improve affordability of the
21
22 361 medicines.
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24 362
25 363 The WHO/HAI methodology that was used for this study is tested, reliable, standardized and
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27 364 validated for the measurement of medicine prices and availability [34]. The study provides details
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29 365 on availability, price, and affordability of individual medicines across three sectors (public, private
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31 366 and mission). The methodology uses a cross-sectional design and therefore historical data trends
32
33 367 were not traced. The study only used two frontline medicines for PPH, while countries may have
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35 368 had other alternative therapies including carbetocin which were not captured. The number of
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37 369 mission facilities surveyed in Zambia (23) was below the minimum (30) recommended for the
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39 370 methodology per sector [33]. The findings presented here may not be used to predict country
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41 371 pharmaceutical supply chain but are intended to stimulate policy discussions on deliberate
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43 372 targeting and the use of available technologies to improve access.
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45 373

46 374 **Conclusion**

47 375 Availability of oxytocin and misoprostol met the WHO benchmark in Kenya and Uganda but was
48
49 376 just below the WHO benchmark in Zambia. In general, oxytocin was more available than
50
51 377 misoprostol. Oxytocin and misoprostol were purchased by patients at prices above international
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53 378 reference prices but both medicines cost less than a day's wages for a LPGW and were therefore
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55 379 considered affordable. However, there was no strategy in place that looked at which medicine
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57 380 could be best utilized in which area. Countries with limited resources should explore mechanisms

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3 381 to balance access to both oxytocin and misoprostol between rural and urban areas to optimize
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5 382 management of PPH.
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8 383 **List of abbreviations**

9
10 384 Post-partum haemorrhage (PPH); Median price ratio (MPR); Low- and middle-income countries
11
12 385 (LMICs); Lowest-paid government worker (LPGW); sexual and reproductive health commodities
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14 386 (SRHC); Health Action International (HAI); World Health Organisation (WHO).
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16 387

17
18 388 **Declarations**

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21 389 *Ethical approval and consent to participate*

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24 390 This study did not involve human subjects and did not involve direct interaction with patients and
25
26 391 therefore ethical approval was not sought. However, Ministries of Health in Uganda and Zambia
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28 392 and Country Directors of Health in Kenya gave approval and provided introduction letters to
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30 393 health facilities.
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35 395 *Consent for publication*

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44 398 *Availability of data and materials*

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46 399 The datasets used and/or analysed during the current study are available from the corresponding
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48 400 author on request.
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54 402 *Competing interests*

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56 403 All authors declare no competing interests.
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11 407 Partnership.
1213
14 408
1516 409 *Authors' contribution*
1718
19 410 DK conceptualized the project, undertook data analysis and wrote the first draft of the
20
21 411 manuscript; GOI contributed to data analysis; GOI, HDH, JN, TR, HL and AM revised the
22
23 412 manuscript and critically reviewed its contents. GO contributed to data analysis. AM critically
24
25 413 reviewed the manuscript, provided comments and guidance on all drafts of manuscript.
2627
28 414
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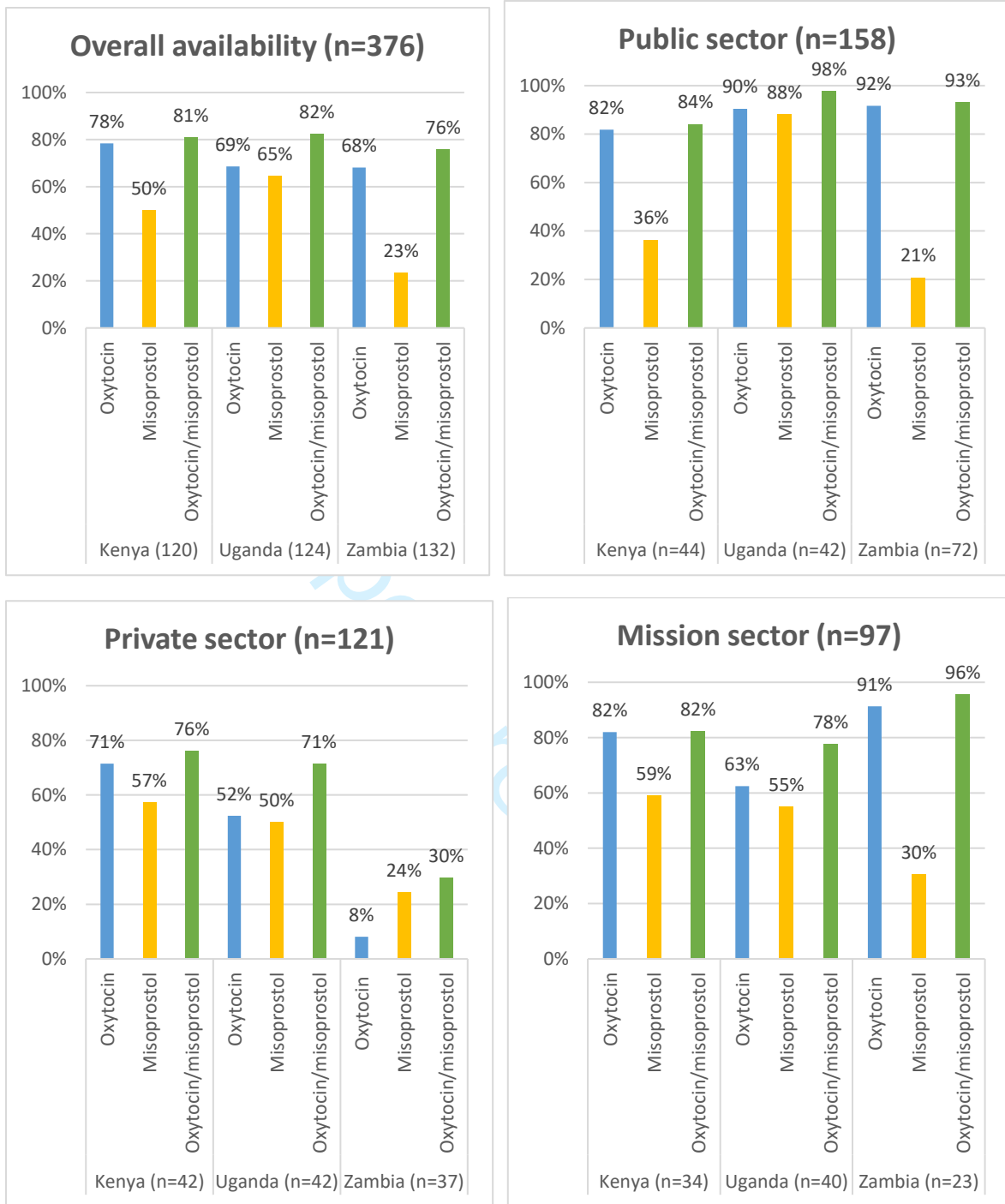


Fig 1: Availability of oxytocin and misoprostol across sectors in Kenya, Uganda and Zambia

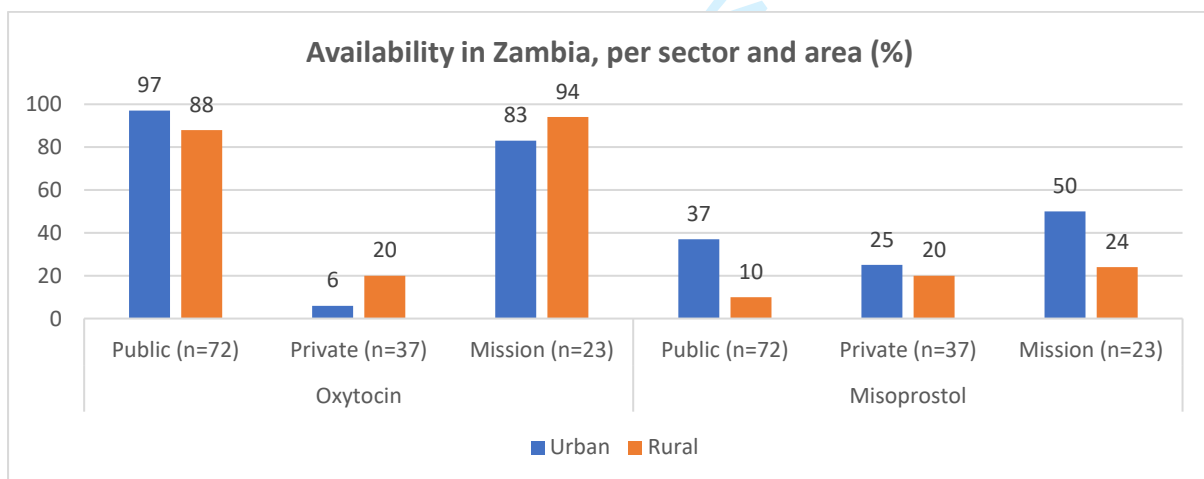
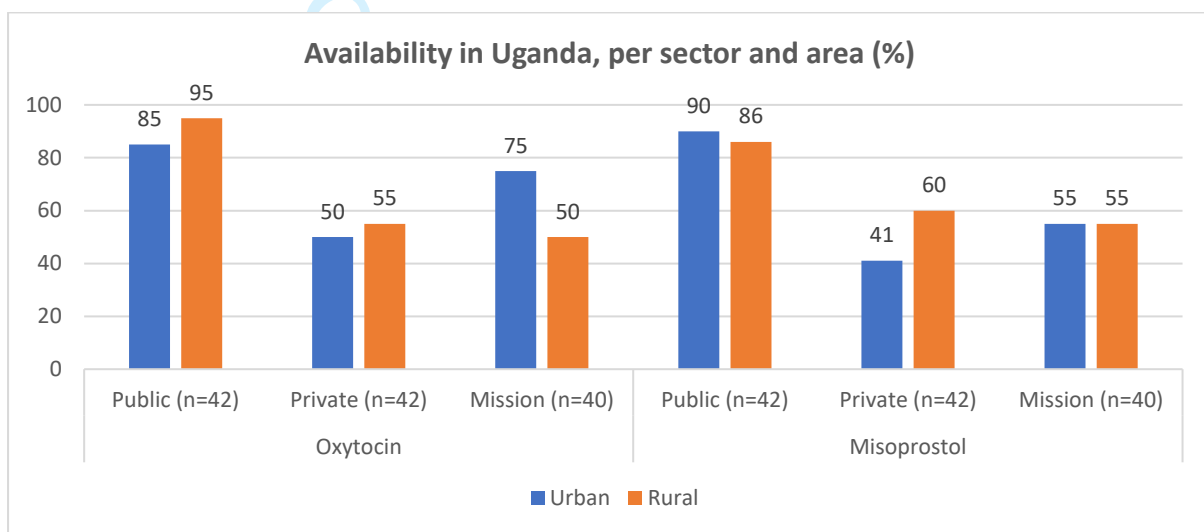
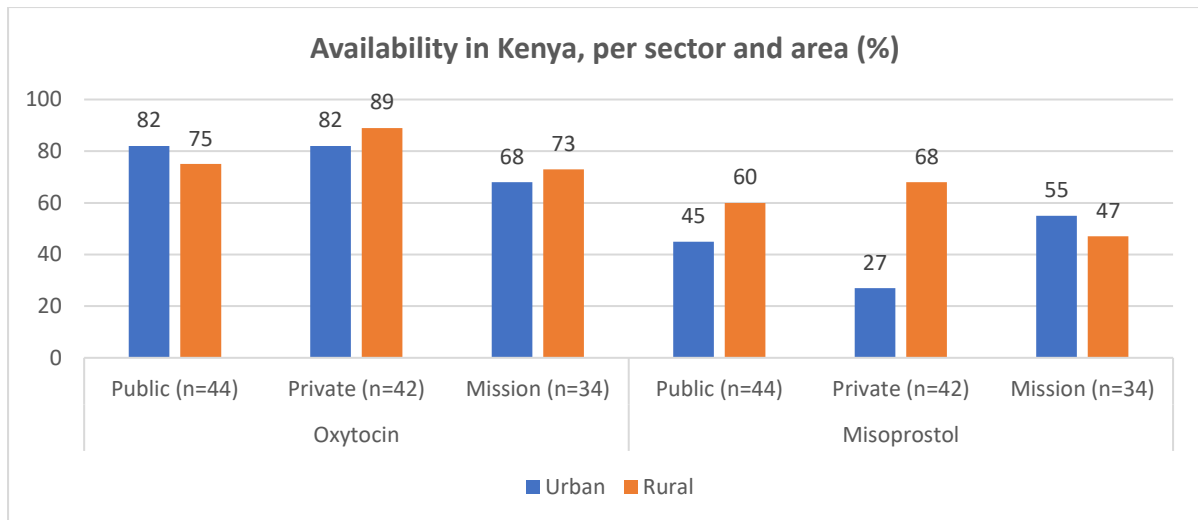


Figure 2: Availability of oxytocin and misoprostol in urban and rural facilities across countries

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Available	Recommendation	Page No.
Title and abstract	1	Yes	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
			(b) Provide in the abstract is an informative and balanced summary of what was done and what was found	2
Introduction				
Background/rationale	2	Yes	Explain the scientific background and rationale for the investigation being reported	5-7
Objectives	3	Yes	State specific objectives, including any prespecified hypotheses	7
Methods				
Study design	4	Yes	Present key elements of study design early in the paper	7
Setting	5	Yes	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8
Participants	6	Yes	(a) Give the eligibility criteria, and the sources and methods of selection of participants	8
Variables	7	Yes	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9
Data sources/ measurement	8*	Yes	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-9
Bias	9	N/A	Describe any efforts to address potential sources of bias	N/A
Study size	10	Yes	Explain how the study size was arrived at	8
Quantitative variables	11	Yes	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-10
Statistical methods	12	N/A	(a) Describe all statistical methods, including those used to control for confounding	-
			(b) Describe any methods used to examine subgroups and interactions	
			(c) Explain how missing data were addressed	
			(d) If applicable, describe analytical methods taking account of sampling strategy	
			(e) Describe any sensitivity analyses	
Results				
Participants	13*	N/A	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	-
			(b) Give reasons for non-participation at each stage	
			(c) Consider use of a flow diagram	
Descriptive data	14*	Yes	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
			(b) Indicate number of participants with missing data for each	-

			variable of interest	
Outcome data	15*	Yes	Report numbers of outcome events or summary measures	10-13
Main results	16	N/A	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	-
			(b) Report category boundaries when continuous variables were categorized	-
			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	N/A	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion				
Key results	18	Yes	Summarises key results with reference to study objectives	14
Limitations	19	Yes	Discusses limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Yes	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-15
Generalisability	21	No	Discuss the generalisability (external validity) of the study results	-
Other information				
Funding	22	Yes	Gives the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for exposed and unexposed groups.

N/A- Not applicable

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.