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Access and use of oxytocin for post-partum hemorrhage prevention: targeting the poorest in six Mesoamerican countries

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Manuscripts

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3 1 Access and use of oxytocin for post-partum hemorrhage prevention: targeting the poorest in six
4 2 Mesoamerican countries

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27 ABSTRACT

28 **Introduction:** Hemorrhage remains the leading cause of maternal mortality both worldwide and in
29 Mesoamerica. Active management of third stage of labor and oxytocin use to reduce postpartum
30 hemorrhage mortality are not optimally applied in Mesoamerica. The Salud Mesoamérica Initiative
31 aims to reduce maternal mortality in Mesoamerica.

32 **Methods:** We compared the availability and administration of oxytocin for the prevention of
33 postpartum hemorrhage in the poorest Mesoamerican communities. 166 basic-level and
34 comprehensive-level health facilities in Belize, Guatemala, Honduras, Mexico, Nicaragua, and
35 Panama were included in the study. Medical records were sampled at random using a systematic
36 sampling method for uncomplicated full-term deliveries (n = 2,470) at baseline (2011–2013) and at
37 first-phase follow-up (2013–2014). Multivariable logistic regression analysis was used.

38 **Results:** Availability of oxytocin increased from 82.9% to 97.6%. Oxytocin administration increased
39 from 83.6% to 88.4%. Significant improvements were seen for availability of oxytocin (aOR = 8.41,
40 95% CI = 1.50–47.30). Administration of oxytocin was found to be significantly higher in Honduras
41 (aOR = 2.96; 95% CI = 1.00–8.76) in reference to Guatemala at follow-up.

42 **Conclusion:** After interventions to increase health facility supplies, the study showed a significant
43 improvement in availability but not administration of oxytocin in poor communities within
44 Mesoamerica. Efforts are needed to improve the use of oxytocin.

45 STRENGTHS AND LIMITATIONS OF THIS STUDY

- 46 • To our knowledge, this study is the first multinational study of oxytocin coverage amongst
47 this targeted poor population and region. We provide a current assessment of the evidence-
48 to-practice gap for post-partum hemorrhage prevention in Mesoamerica for the most
49 underserved populations.

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3 50 • Challenges to this study involve logistic limitations in collecting data on some of the facility
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5 51 inputs.
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9 52 **INTRODUCTION**
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13 53 Hemorrhage remains the leading cause of maternal mortality both worldwide and in
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15 54 Mesoamerica, accounting for 31.4% of total maternal deaths globally(1) and ranging from 38.0% of
16
17 55 total maternal deaths in Nicaragua to 17.9% in Belize based on recent estimates.(2) While maternal
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19 56 mortality has declined in the last two decades, Millennium Development Goal 5, of reducing
20
21 57 maternal mortality by three-fourths, was not achieved globally in 2015.(3,4) A new target has been
22
23 58 set for the Sustainable Development Goals to reduce the global maternal mortality ratio to less than
24
25 59 70 per 100,000 live births by 2030.(5) Currently, most of the Mesoamerican countries in this study
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27 60 fall short of or near this target, with the highest maternal mortality ratio, of 109.6 per 100,000 live
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29 61 births, occurring in Honduras.(6)
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34 62 International guidelines for postpartum hemorrhage, from the World Health Organization
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36 63 (WHO), International Federation of Gynecology and Obstetrics (FIGO), and the International
37
38 64 Confederation of Midwives (ICM), recommend active management of third stage of labor (AMTSL)
39
40 65 with emphasis on administering oxytocin, the drug of choice for prevention and treatment of uterine
41
42 66 atony.(7,8) Oxytocin is the cornerstone of AMTSL due to its efficacy in reducing postpartum
43
44 67 hemorrhage risk by 40–60%.(9–11) Despite such evidence, translating these best practices into a
45
46 68 real-world clinical standard of care is not optimally applied in Mesoamerica, with the proper use of
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48 69 uterotonics as low as 10–20% in some studies.(12,13)
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52 70 With efforts to close the evidence-to-practice gap, the Salud Mesoamérica Initiative (SMI)
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54 71 aims to reduce maternal and child mortality for the poorest quintile in Mesoamerica.(14) SMI is a
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56 72 public-private partnership between the Ministries of Health in participating Mesoamerican countries
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58 73 and donors that focuses on improving preventive child health, family planning, antenatal care,
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3 74 peripartum care, and Essential Obstetric and Newborn Care (EONC).(15) SMI follows a results-based
4
5 75 financing model (16,17) in which Ministries of Health commit to achieve negotiated targets for eight
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7 76 to twelve performance indicators. To receive the performance payment incentive, countries need to
8
9 77 achieve at least eighty percent of targets. At the beginning of each phase, donors contribute
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11 78 approximately half the funding, with the rest from domestic sources.
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15 79 The first phase of SMI interventions, presented in this study, aims to improve system
16
17 80 readiness by increasing availability of inputs and improving norms. The second phase targets
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19 81 improvements in coverage and quality of care. Specifically, performance indicators for postpartum
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21 82 hemorrhage prevention involve increasing availability of oxytocin in this first phase and ensuring
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23 83 administration of oxytocin postpartum in the second phase.
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27 84 In this study, a multinational analysis of oxytocin use for this targeted population and region,
28
29 85 we examine the availability and administration of oxytocin for the prevention of postpartum
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31 86 hemorrhage at the first follow-up of the SMI intervention. In doing so, we assess the extent to which
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33 87 international guidelines are adhered to on the patient level for one aspect of essential obstetric care
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35 88 in Mesoamerica.
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39 89 **METHODS**

40 90 **Study setting and design**

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45 91 As part of the Salud Mesoamérica Initiative, 2,470 uncomplicated deliveries from 166 health
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47 92 facilities were included in this analysis to assess the availability and administration of oxytocin for
48
49 93 the prevention of postpartum hemorrhage in the poorest Mesoamerican communities. These
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51 94 poorest communities were identified by the Initiative administrators based on census data, using as
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53 95 criteria to have the highest concentration of population in the lowest quintile of income. Data
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3 96 collection was conducted at the baseline (2011–2013) and the first-phase follow-up (2013–2014)
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5 97 time periods.
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8 98 The first phase, a year of intervention implementation prior to follow-up data collection,
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10 99 focused on system readiness and supply-side performance indicators. For postpartum hemorrhage
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12 100 prevention, the performance indicator involved increasing the availability of oxytocin, through
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14 101 interventions such as strengthening supply chains; improving procurement processes, warehouse
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16 102 and pharmacy storage practices; traffic light systems to monitor expiry dates; inventory
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18 103 management processes; improving norms and protocols of care to adhere to international
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20 104 guidelines; creating decision flow-charts and checklists.
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24 105 Facilities were classified into different levels of Essential Obstetric and Neonatal Care
25
26 106 (EONC):(15) basic-level facilities have the capacity to manage uncomplicated vaginal deliveries and
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28 107 stabilize patients with complications prior to transfer to higher level of care; and comprehensive-
29
30 108 level facilities attend both uncomplicated and complicated births, with capacity to accept referral
31
32 109 patients and perform surgical and emergency care. While the project and its evaluation includes all
33
34 110 countries in Mesoamerica, due to availability of data for this specific analysis we used data from
35
36 111 Ministry of Health facilities serving the poorest areas in Belize, Guatemala, Honduras, Mexico (state
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38 112 of Chiapas), Nicaragua, and Panama. Basic- and comprehensive-level health facilities were selected
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40 113 with certainty due to a small number of these hospitals. Because of this, the same facilities were
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42 114 visited in the baseline and follow-up measurements.
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47 115 A three-part health facility survey was administered at these facilities for both rounds of
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49 116 data collection. The survey included an interview questionnaire to the facility directors on the facility
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51 117 infrastructure and resources; an observation checklist of pharmaceutical inventory and medical and
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53 118 laboratory equipment; and a retrospective review of medical records to examine treatment
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55 119 practices. Medical records of uncomplicated deliveries per international classification of diseases
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57 120 (ICD) coding during the specified timeframes were sampled at random using a systematic sampling
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3 121 method, until the required quota for each facility level was met. For the systematic sampling, using
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5 122 the listing of deliveries attended in each facility, a random starting point was selected in time over
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7 123 the period of study (about 18 months), and from there cases were selected with an interval equal to
8
9 124 the size of the sampling fraction. Sampling quotas varied by facility type, round, and country. Sample
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11 125 size of records to be reviewed was calculated due to availability of resources. Expected sample sizes
12
13 126 had enough power to detect differences in evaluation indicators, including treatment to deliveries
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15 127 according to the national norms. Due to availability of resources, it was possible to increase the
16
17 128 number of cases in the sample in the follow-up to increase power, especially in the countries with a
18
19 129 reduced number of cases in the baseline (Belize). Overall, we had a power over 80% to detect
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21 130 differences of 10 percentage points between baseline and follow-up for oxytocin availability in all
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23 131 countries excepting Belize and Nicaragua. Further details of the methodology are available
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25 132 elsewhere.(14,17–19)

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30 133 Quality of data in medical records varied by facility and country. To measure standardized,
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32 134 replicable, and comparable metrics from varying medical record sources, indicators that were linked
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34 135 to discharge diagnosis and ICD coding were constructed by the Ministries of Health based on the
35
36 136 protocols and guidelines of each country. Criteria checklists for each indicator differed by EONC
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38 137 facility level. These criteria checklists were then transformed into data points and conditional
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40 138 algorithms for data collection. During field visits, medical record data availability and measurability
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42 139 of criteria were assessed.(20) Data collection was conducted by trained physicians and nurses from
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44 140 the region, and data were submitted electronically using the survey software DatStat Illume.

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49 141
50 142 Availability of oxytocin was defined as supply on the day of survey visit; and administration
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52 143 of oxytocin was defined as given intravenously or intramuscularly for postpartum hemorrhage
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54 144 prevention (excluding postpartum hemorrhage treatment).(20) Uncomplicated delivery records
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56 145 selected for review included full-term (>37 weeks) gestational age at participating health facilities,
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58 146 including cesarean sections without complications per ICD coding. Deliveries with adverse outcomes

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3 147 per ICD coding that required hemorrhage treatment were excluded, due to collection under a
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5 148 separate survey module.
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8 149 Approval for this study involved the institutional review board from the University of
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10 150 Washington (exemption as a non-human-subject research determination), partnering data-collection
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12 151 agencies, and the Ministry of Health in each country. Prior to data collection, informed consent was
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14 152 obtained from each health facility administrator. During the data extraction process, medical records
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16 153 were anonymized.
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20 154 **Statistical analysis**

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24 155 We used multivariable logistic regression analysis to evaluate possible facility-level factors
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26 156 associated with the primary outcomes of oxytocin availability and administration. Covariates
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28 157 included in the analysis were timing of data collection (baseline versus first-phase follow-up),
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30 158 country, and EONC facility type (basic versus comprehensive). Additionally for oxytocin
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32 159 administration, we examined relevant training within the last year (routine labor care, basic
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34 160 emergency obstetrical care, or maternal complications care); and oxytocin availability (day of survey
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36 161 visit), and skilled personnel (doctor, nurse). When fitting the regression models, skilled personnel
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38 162 was dropped from the model due to predicting success perfectly, meaning a skilled personnel was
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40 163 always present for the administration of oxytocin. The rate of missing data was 4.4% for oxytocin
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42 164 availability and 0.7% for oxytocin administration for the regression analysis. P values <0.05 were
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44 165 considered significant. Stata 14.2 (StataCorp LP, College Station, TX, USA) was used for all analysis.
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166 RESULTS

167 Sample characteristics

168 Table 1 presents the medical records, patient, facility, and personnel characteristics. The
 169 majority of deliveries were in basic-level health facilities (64.3%). We sampled the most medical
 170 records from Guatemala (27.5%), followed by Chiapas (Mexico) (20.8%), Honduras (19.6%), Panama
 171 (16.0%), Nicaragua (11.9%), and Belize (4.2%), based on the quota for records within each facility,
 172 prevalence of records of interest, and sampling interval. Mean maternal age was 24.3 years and
 173 ranged from 11 to 48 years. Of these women, 55.2% were single, 44.8% were married or in a social
 174 partnership, and 72.7% had less than a secondary education. Nearly all patients (99.7%) had a single
 175 gestational pregnancy, and only 0.3% had a multiple gestational pregnancy. Most of these patients
 176 delivered vaginally (97.7%) as opposed to by cesarean section (2.3%). Supply (on the day of survey
 177 visit) for oxytocin at baseline was 82.9%, which increased to near complete availability (97.6%) at
 178 first-phase follow-up. Personnel on staff – that is, skilled birth attendants employed by the facility –
 179 at baseline was 96.2% for physicians and 91.0% for nurses and increased to 100% and 93.2%,
 180 respectively, at follow-up. Relevant training – that is, instruction on routine labor care, basic
 181 emergency obstetrical care, or maternal complications care – provided within the last year increased
 182 from 74.0% at baseline to 92.0% at first-phase follow-up.

183 **Table 1. Medical records, patient, and facility characteristics by first-phase**
 184 **follow-up**

185 Medical records characteristics				
		n (%)		
		Baseline 922 (37.3)	Follow-up 1,548 (62.7)	Total 2,470 ^a (100)
	EONC ^b facility type			
	Basic-level	616 (66.8)	971 (62.7)	1,587 (64.3)
	Comprehensive-level	306 (33.2)	577 (37.3)	883 (35.8)
	Country			

	Belize	14 (1.5)	90 (5.8)	104 (4.2)
	Guatemala	247 (26.8)	432 (27.9)	679 (27.5)
	Honduras	234 (25.4)	249 (16.1)	483 (19.6)
	Mexico	180 (19.5)	334 (21.6)	514 (20.8)
	Nicaragua	90 (9.8)	205 (13.2)	295 (11.9)
	Panama	157 (17.0)	238 (15.4)	395 (16.0)
Patient characteristics				
	Maternal age ^c	24.3 (6.7)	24.3 (6.6)	24.3 (6.6)
	Marital status			
	Single	409 (61.8)	656 (51.8)	1,065 (55.2)
	Partnership	253 (38.2)	610 (48.1)	863 (44.8)
	Education			
	Less than secondary	392 (70.5)	772 (73.9)	1,164 (72.7)
	Secondary or higher	164 (29.5)	273 (26.1)	437 (27.3)
	Pregnancy type			
	Single gestational	154 (98.7)	917 (99.9)	1,071 (99.7)
	Multiple gestational	2 (1.3)	1 (0.1)	3 (0.3)
	Delivery type			
	Vaginal	409 (98.6)	1,091 (97.3)	1,500 (97.7)
	Cesarean section	6 (1.5)	30 (2.7)	36 (2.3)
Facility and personnel characteristics				
		n (%)		
		Baseline 78 (47.0)	Follow-up 88 (53.0)	Total 166 (100)
	Oxytocin supply ^d	58 (82.9)	83 (97.6)	141 (91.0)
	Personnel on staff ^e			
	Physician	75 (96.2)	88 (100)	163 (98.2)
	Nurse	71 (91.0)	82 (93.2)	153 (92.2)
	Relevant training ^f	57 (74.0)	81 (92.0)	138 (83.6)

186 a n may vary for each variable due to missingness

187 b Essential Obstetric and Newborn Care

188 c mean ± SD

189 d day of survey visit

190 e skilled birth attendants employed by the facility. Midwife excluded due to varying skill level amongst countries.

191 f within last year, includes routine labor care, basic emergency obstetrical care, maternal complications

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193 Availability and administration of oxytocin for postpartum hemorrhage

194 prevention

195 Overall, availability of oxytocin (on the day of the survey) increased from 82.9% to 97.7%

196 and administration of oxytocin increased from 83.6% to 88.4% from baseline to first-phase follow-

197 up. Notably, all countries achieved 100% availability of oxytocin at first-phase follow-up, except for

198 Guatemala (91.7). Comprehensive level facilities achieved 100% availability, compared to basic level

199 facilities (96.8%) at first-phase follow-up. Administration of oxytocin at first-phase follow-up ranged
 200 from 80.0% in Belize to 94.8% in Honduras. Oxytocin administration was nearly the same at basic
 201 (88.4%) and comprehensive level (88.5%) facilities at first-phase follow-up. (Table 2).

202 **Table 2. Oxytocin availability and administration by facility type, country, and**
 203 **first-phase follow-up**

Oxytocin Availability		n (%)		
		Baseline 58 (82.9)	Follow-up 83 (97.6)	Total ^a 141 (91.0)
EONC facility type ^b				
	Basic-level	43 (84.3)	61 (96.8)	104 (91.2)
	Comprehensive-level	15 (78.9)	22 (100.0)	37 (90.2)
Country				
	Belize	4 (100.0)	4 (100.0)	8 (100.0)
	Guatemala	15 (88.2)	22 (91.7)	37 (90.2)
	Honduras	13 (92.9)	12 (100.0)	25 (96.2)
	Mexico	7 (100.0)	14 (100.0)	21 (75.0)
	Nicaragua	6 (85.7)	14 (100.0)	20 (95.2)
	Panama	13 (92.9)	17 (100.0)	30 (96.8)
Oxytocin Administration for prevention of post-partum hemorrhage		n (%)		
		Baseline 771 (83.6)	Follow-up 1,353 (88.4)	Total 2,124 (86.6)
EONC facility type				
	Basic-level	521 (84.6)	852 (88.4)	1,373 (86.9)
	Comprehensive-level	250 (81.7)	501 (88.5)	751 (86.1)
Country				
	Belize	9 (64.3)	72 (80.0)	81 (77.9)
	Guatemala	198 (80.2)	393 (91.0)	591 (87.0)
	Honduras	224 (95.7)	221 (94.8)	445 (95.3)
	Mexico	129 (71.7)	277 (82.9)	406 (79.0)
	Nicaragua	87 (96.7)	168 (82.8)	255 (87.0)
	Panama	124 (79.0)	222 (93.3)	346 (87.6)

204 ^a n may vary for each variable due to missingness

205 ^b Essential Obstetric and Newborn Care

207 Table 3 shows possible first-phase follow-up and facility determinants of the main outcomes:
 208 the availability and administration of oxytocin. Odds of availability were significantly higher at first-
 209 phase follow-up compared to baseline (aOR = 8.41, 95% CI = 1.50–47.30), while odds of
 210 administration increased in magnitude but were not significant at first-phase follow-up (aOR = 1.63,
 211 95% CI 0.83–3.21). Additionally, administration of oxytocin was found to be significantly higher in
 212 Honduras (aOR = 2.96; 95% CI = 1.00–8.76) in reference to Guatemala. Other covariates examined,

213 such as comprehensive-level facility, relevant training, and oxytocin availability, showed a positive
 214 but not significant correlation to the primary outcomes.

215 **Table 3. Factors associated with availability and administration of oxytocin**

	Oxytocin availability		Oxytocin administration for prevention of post-partum hemorrhage	
	Crude OR (95% CI) (n= 2,257)	Adjusted OR ^a (95% CI) (n= 2,257)	Crude OR (95% CI) (n =2,343)	Adjusted OR (95% CI) (n =2,343)
First-phase follow-up	7.29 (1.48–35.84)	8.41 (1.50–47.30)	1.43 (0.79–2.62)	1.63 (0.83–3.21)
Country				
Belize	<i>Predicts success perfectly^b</i>	<i>Predicts success perfectly</i>	0.52 (0.13–2.12)	0.44 (0.11–1.71)
Guatemala	1	1	1	1
Honduras	1.70 (0.18–16.46)	2.24 (0.27–18.24)	2.71 (1.02–7.22)	2.96 (1.00–8.76)
Mexico	0.67 (0.14–3.10)	0.51 (0.11–2.46)	0.57 (0.25–1.31)	0.57 (0.24–1.37)
Nicaragua	2.22 (0.23–21.71)	2.01 (0.19–20.92)	1.00 (0.38–2.62)	0.95 (0.35–2.54)
Panama	3.43 (0.36–33.05)	3.83 (0.36–41.22)	1.04 (0.41–2.66)	1.03 (0.40–2.61)
Comprehensive-level facility	1.00 (0.24–4.15)	1.29 (0.31–5.31)	0.92 (0.47–1.81)	0.96 (0.46–2.00)
Relevant training ^c	--	--	1.49 (0.71–3.13)	1.08 (0.44–2.67)
Oxytocin availability ^d	--	--	2.01 (0.92–4.39)	1.45 (0.66–3.19)

216 a adjusted for first-phase follow-up, country, and comprehensive-level facility. Relevant training and oxytocin availability not included (not applicable).

217 b Belize attained availability of oxytocin at all times (regression for this binary variable not possible)

218 c within last year, includes routine labor care, basic emergency obstetrical care, maternal complications

219 d day of survey visit

220 All models clustered at health facility level

221 DISCUSSION

222 Main findings

223 To our knowledge, this study is the first multinational analysis of oxytocin use among the
 224 poorest population within Mesoamerica. We provide an updated, regional evaluation of postpartum
 225 hemorrhage prevention practices that may guide clinical management and policy priorities for this

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3 226 targeted population. Our study showed that the availability of oxytocin improved significantly after
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5 227 system readiness interventions. Administration of oxytocin increased but not in the same proportion
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8 228 as availability, which suggests that increasing the availability of inputs is necessary but not sufficient
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10 229 to improve quality of care.
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13 230 **Interpretation**

16 231 There remains a paucity of studies with regard to oxytocin availability and use in
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18 232 Mesoamerica (13,21–25) or in low-resource countries in general.(12,27–32) In Mesoamerica,
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20 233 previous studies have evaluated hospitals within a single country(13,21,22) rather than through a
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22 234 multinational analysis, compared global regions without sub-analysis by country in each region,(26)
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24 235 or indirectly evaluated oxytocin use with relevant training being the primary outcome.(23–25) On a
25
26 236 broader level, other studies compare oxytocin to other uterotonics worldwide,(31–35) and
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28 237 international guidelines have been revised.(36) However, oxytocin remains the first-line drug for
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30 238 postpartum hemorrhage prevention in health facilities. Thus, this study is of value in providing a
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32 239 current assessment of the implementation of active management of third stage of labor practices in
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34 240 Mesoamerica for the most underserved populations.
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39 241 Our study attests that clinical standards of care could be achieved in Mesoamerica with
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41 242 proper monitoring and management of oxytocin supplies. As expected from the implementation
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43 243 timeline, the first stage of the Salud Mesoamérica Initiative focused on improving system readiness,
44
45 244 namely strengthening facility infrastructure, supply chains, availability and stock monitoring for
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47 245 drugs and equipment, and referral networks; while the second stage is primarily focused on
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49 246 increasing health care coverage and quality of care through interventions such as training, service
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51 247 delivery reorganization, and quality improvement.(14,37) Consequently, increasing the availability of
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53 248 oxytocin, a goal of the first phase of the initiative, was achieved. Increasing the availability of inputs
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55 249 is necessary but not sufficient to improve quality of care. Comprehensive quality improvement
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57 250 strategies would be needed that involve not only increasing availability of equipment and supplies,
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251 but also improving skills and abilities of personnel, and establishing mechanisms to improve
252 processes, identify causes, and lift barriers to ensure proper practices of care in the next phase.

253 Limitations

254 This study has some limitations. First, oxytocin availability was defined based on the day of
255 the visit to health facilities, which may not match the day of delivery in a medical record. Due to
256 logistic limitations, it was not possible to assess stock-outs of oxytocin over a longer period of time.
257 Therefore, we must consider oxytocin availability the day of the visit as a proxy for availability over a
258 longer period of time. Quality of available oxytocin cannot be included when defining oxytocin
259 availability, as data was not collected on expiration or storage of oxytocin. Second, this study
260 focused on uncomplicated full-term deliveries and did not include patients resulting in hemorrhage
261 due to two separate survey modules for data collection. In the module with adverse outcomes from
262 hemorrhage, uterotonics were often administered more than once without distinction of whether
263 for prevention or treatment. Third, sample sizes also vary by country, and in some cases like Belize,
264 the reduced sample size limited our capacity to have country-specific precise estimates and to
265 detect significant differences between baseline and follow-up measurements. Fourth, quality of
266 record keeping may affect the information used in this study and may vary by country. Nonetheless,
267 we used a standard methodology across countries, automated data collection, and used quality
268 control measures that ensure comparability between countries.

269 CONCLUSION

270 The study showed a significant improvement in availability of oxytocin at facilities that
271 provide care to poor communities within Mesoamerica, but not optimal administration, as expected
272 after emphasis on supply-side interventions. Continued monitoring and evaluation, beyond input
273 availability, are essential to better understand how to improve processes and clinical practices. Our

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3 274 study provides valuable information to close the evidence-to-practice gap and to reduce maternal
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5 275 mortality in Mesoamerica.
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9 276 LIST OF ABBREVIATIONS

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13 277 Active management of third stage of labor (AMTSL)
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15 278 Essential Obstetric and Newborn Care (EONC)
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17 279 International Confederation of Midwives (ICM)
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19 280 International Federation of Gynecology and Obstetrics (FIGO)
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21 281 Salud Mesoamérica Initiative (SMI)
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23 282 World Health Organization (WHO)
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28 283 DECLARATIONS

29 284 Ethics approval

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33 285 University of Washington Institutional Review Board. No patient consent required.
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36 286 Patient and Public Involvement

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39 287 Patients or the public were not involved in the design, conduct, reporting, or dissemination of our
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41 288 research.
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44 289 Data Sharing

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48 290 Data are owned by the Inter-American Development Bank. SMI baseline survey data, which
49
50 291 comprise the minimal dataset, are publicly available on the SMI website. SMI follow-up survey data
51
52 292 are currently available upon written request from the Inter-American Development Bank, whose
53
54 293 contact information is listed below. Javier Lesaca, Communications Officer, Salud Mesoamerica
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296 **Competing interests**

297 The authors declare that they have no competing interests

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305 **Authors' contributions**

306 AMK conceived the study and prepared data analysis, interpretation of data, initial draft, and final
307 manuscript. AMS, EBP, and CKJ contributed to and reviewed data analysis. AGM, MDM, KS, PZB,
308 DRZ, and EI contributed to the acquisition of the data. BH and AHM supervised the study and data
309 compilation and contributed to interpretation of data. All authors critically reviewed the draft and
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Access and use of oxytocin for post-partum hemorrhage prevention: a pre-post study targeting the poorest in six Mesoamerican countries

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27 ABSTRACT

28 **Objectives:** Hemorrhage remains the leading cause of maternal mortality in Central America. The
29 Salud Mesoamerica Initiative aims to reduce such mortality via performance indicators. Our
30 objective was to assess the availability and administration of oxytocin, before and after applying
31 Salud Mesoamerica Initiative interventions in the poorest health facilities across Central America.

32 **Design:** pre-post study.

33 **Setting:** 166 basic-level and comprehensive-level health facilities in Belize, Guatemala, Honduras,
34 Mexico, Nicaragua, and Panama.

35 **Participants:** A random sample of medical records for uncomplicated full-term deliveries (n = 2,470)
36 per international classification of diseases coding at baseline (July 2011–August 2013) and at first-
37 phase follow-up (January 2014–October 2014).

38 **Interventions:** A year of intervention implementation prior to first-phase follow-up data collection
39 focused on improving access to oxytocin by strengthening supply chains, procurement, storage
40 practices, and pharmacy inventory monitoring, using a results-based financing model.

41 **Primary and secondary outcome measures:** Oxytocin availability (primary outcome) and
42 administration (secondary outcome) for post-partum hemorrhage prevention.

43 **Results:** Availability of oxytocin increased from 82.9% to 97.6%. Oxytocin administration increased
44 from 83.6% to 88.4%. Significant improvements were seen for availability of oxytocin (aOR = 8.41,
45 95% CI = 1.50–47.30). Administration of oxytocin was found to be significantly higher in Honduras
46 (aOR = 2.96; 95% CI = 1.00–8.76) in reference to Guatemala at follow-up.

47 **Conclusion:** After interventions to increase health facility supplies, the study showed a significant
48 improvement in availability but not administration of oxytocin in poor communities within
49 Mesoamerica. Efforts are needed to improve the use of oxytocin.

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3 50 **Trial registration:** not applicable
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7 51 **STRENGTHS AND LIMITATIONS OF THIS STUDY**

- 9 52 • Using a results-based financing model, interventions focused on improving access to
10 53 oxytocin by strengthening supply chains, procurement, storage practices, and pharmacy
11 54 inventory monitoring,
- 12 55 • Based on a random sampling method of medical records, a multinational dataset containing
13 56 2,470 deliveries was utilized for the pre-post evaluation of post-partum hemorrhage
14 57 prevention in the poorest populations of Mesoamerica.
- 15 58 • To measure comparable metrics from varying medical record sources, indicators linked to
16 59 ICD coding were constructed by the Ministries of Health based on protocols and guidelines
17 60 of each country.
- 18 61 • We used multivariable logistic regression analysis to evaluate possible factors associated
19 62 with the primary outcome of oxytocin availability and the secondary outcome of oxytocin
20 63 administration.
- 21 64 • Challenges to this study involve logistic limitations in collecting data on some of the facility
22 65 inputs, sample size variation by country, and quality of record keeping.

23 66 **INTRODUCTION**

24 67 Hemorrhage remains the leading cause of maternal mortality both worldwide and in
25 68 Mesoamerica, accounting for 31.4% of total maternal deaths globally(1) and ranging from 38.0% of
26 69 total maternal deaths in Nicaragua and Guatemala to 17.9% in Belize based on 2016 Global Burden
27 70 of Disease Study estimates.(2) While maternal mortality has declined in the last two decades,
28 71 Millennium Development Goal 5, of reducing maternal mortality by three-fourths, was not achieved
29 72 globally in 2015.(3,4) A new target has been set for the Sustainable Development Goals to reduce
30 73 the global maternal mortality ratio to less than 70 per 100,000 live births by 2030.(5) Currently, most

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3 74 of the Mesoamerican countries in this study fall short of or near this target, with the highest
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5 75 maternal mortality ratio, of 109.6 per 100,000 live births, occurring in Honduras.(6)
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8 76 International guidelines for postpartum hemorrhage, from the World Health Organization
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10 77 (WHO), International Federation of Gynecology and Obstetrics (FIGO), and the International
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12 78 Confederation of Midwives (ICM), recommend active management of third stage of labor (AMTSL)
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14 79 with emphasis on administering oxytocin, the drug of choice for prevention and treatment of uterine
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16 80 atony.(7,8) Oxytocin is the cornerstone of AMTSL due to its efficacy in reducing postpartum
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18 81 hemorrhage risk by 40–60%.(9–11) Despite such evidence, translating these best practices into a
19
20 82 real-world clinical standard of care is not optimally applied in Mesoamerica, with the proper use of
21
22 83 uterotonics as low as 10–20% in some studies.(12,13)
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27 84 With efforts to close the evidence-to-practice gap, the Salud Mesoamérica Initiative (SMI)
28
29 85 aims to reduce maternal and child mortality for the poorest quintile in Mesoamerica.(14) SMI is a
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31 86 public-private partnership between the Ministries of Health in participating Mesoamerican countries
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33 87 and donors that focuses on improving four major domains of maternal and child health: preventive
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35 88 child health and vaccines; family planning; antenatal care and postpartum care; and Essential
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37 89 Obstetric and Newborn Care (EONC).(15) SMI follows a results-based financing model (16,17) in
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39 90 which Ministries of Health commit to achieve negotiated targets for eight to twelve performance
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41 91 indicators. Within the EONC domain, health facility performance indicators focused on the
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43 92 availability of equipment (i.e. resuscitation equipment, cesarean section kits, stethoscopes),
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45 93 essential medications (i.e. antibiotics, antihypertensives), and laboratory inputs (i.e. glucometer, cell
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47 94 counter). To receive the performance payment incentive, countries need to achieve at least eighty
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49 95 percent of targets. At the beginning of each phase, donors contribute approximately half the
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51 96 funding, with the rest from domestic sources.
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56 97 The first phase of SMI interventions, presented in this study, focused on system readiness by
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58 98 increasing availability of inputs and improving norms. The second upcoming phase directs efforts
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3 99 towards coverage and quality of care. Performance indicators for postpartum hemorrhage
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5 100 prevention involve increasing availability of oxytocin in this first phase and ensuring administration
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7 101 of oxytocin postpartum in the second phase.
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10 102 In this analysis, we examine foremost the availability, and to a lesser extent the
11
12 103 administration, of oxytocin for the prevention of postpartum hemorrhage at the first follow-up of
13
14 104 the SMI intervention. As such, we assess the extent to which international guidelines are adhered to
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16 105 on the patient level for one aspect of essential obstetric care in poor Mesoamerica.
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21 106 **METHODS**

22 23 24 25 107 **Study setting and design**

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29 108 As part of the Salud Mesoamérica Initiative, 2,470 uncomplicated deliveries from 166 health
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31 109 facilities were included in this analysis to assess the availability and administration of oxytocin for
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33 110 the prevention of postpartum hemorrhage in the poorest Mesoamerican communities. These
34
35 111 poorest communities were identified by the Initiative administrators based on census data, using as
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37 112 criteria to have the highest concentration of population in the lowest quintile of income. Data
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39 113 collection was conducted at the baseline (July 2011–August 2013) and the first-phase follow-up
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41 114 (January 2014–October 2014) time periods.
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45 115 The first phase, a year of intervention implementation prior to follow-up data collection,
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47 116 focused on supply-side performance indicators. For postpartum hemorrhage prevention, the
48
49 117 performance indicator involved increasing the availability of oxytocin, through interventions such as
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51 118 strengthening supply chains (i.e. develop efficient distribution routes; optimize supply patterns and
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53 119 frequency of stocking facilities); improving procurement processes (i.e. review stock estimates for
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55 120 stockouts and emergency supplies; establish hospital policies to purchase life-saving medicines),
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57 121 warehouse and pharmacy storage practices (i.e. monitor continuously temperature and electricity
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3 122 for cold chains); traffic light systems to monitor expiry dates (i.e. color code expiration dates on a
4
5 123 monthly basis); and inventory management processes (i.e first-in first-out utilization of medicines;
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7 124 and anticipate emergency stock with each reorder cycle).
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10 125 Facilities were classified into different levels of Essential Obstetric and Neonatal Care
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12 126 (EONC):(15) basic-level facilities manage uncomplicated vaginal deliveries and stabilize patients with
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14 127 complications prior to transfer to higher level of care; and comprehensive-level facilities oversee
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16 128 uncomplicated and complicated births, accept referral patients, and perform surgical and emergency
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18 129 care. While the project and its evaluation includes all countries in Mesoamerica, due to availability of
19
20 130 data for this specific analysis we used data from Ministry of Health facilities serving the poorest
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22 131 areas in Belize, Guatemala, Honduras, Mexico (state of Chiapas), Nicaragua, and Panama. Basic- and
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24 132 comprehensive-level health facilities were selected with certainty due to a small number of these
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26 133 hospitals.
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31 134 A three-part health facility survey was administered at these facilities for both rounds of
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33 135 data collection. The survey included an interview questionnaire to the facility directors on the facility
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35 136 infrastructure and resources; an observation checklist of pharmaceutical inventory and medical and
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37 137 laboratory equipment; and a review of medical records to examine care practices. Medical records
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39 138 of uncomplicated deliveries per international classification of diseases (ICD) coding during the
40
41 139 specified timeframes were sampled at random. Following a systematic sampling method, records
42
43 140 were extracted until the required quota for each facility level was met.
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47 141 With the list of deliveries attended in each facility available, a random starting point was
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49 142 selected in time over the period of study (about 18 months). Cases were then selected with an
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51 143 interval equivalent to the sampling fraction. Sample size of records to be reviewed was calculated
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53 144 due to availability of resources, varying by round, facility, and country. Therefore, a larger overall
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55 145 sample size was assigned to countries with a larger operation (Honduras, Guatemala and Mexico),
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57 146 and was distributed across the facilities to be surveyed depending on their EONC level. Expected
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3 147 sample sizes had enough power to detect differences in evaluation indicators, including treatment to
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5 148 deliveries according to the national norms. Due to availability of resources, it was possible to
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7 149 increase the number of cases in the sample in the follow-up to increase power, especially in the
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9 150 countries with a reduced number of cases in the baseline (Belize). Overall, we had a power over 80%
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11 151 to detect differences of 10 percentage points between baseline and follow-up for oxytocin
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13 152 availability in all countries excepting Belize and Nicaragua. Additional information of the
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15 153 methodology is available elsewhere.(14,17–19)
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19 154 To measure standardized, replicable, and comparable metrics from varying medical record
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21 155 sources, indicators that were linked to discharge diagnosis and ICD coding were constructed by the
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23 156 Ministries of Health based on the protocols and guidelines of each country. Criteria checklists for
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25 157 each indicator differed by EONC facility level. These criteria checklists were then transformed into
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27 158 data points and conditional algorithms for data collection. During field visits, medical record data
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29 159 availability and measurability of criteria were assessed.(20) Data collection was conducted by
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31 160 trained physicians and nurses from the region, and data were submitted electronically using the
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33 161 survey software DatStat Illume.
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38 162 Availability of oxytocin was defined as supply on the day of survey visit; and administration
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40 163 of oxytocin was defined as given intravenously or intramuscularly for postpartum hemorrhage
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42 164 prevention (excluding postpartum hemorrhage treatment). Uncomplicated delivery records selected
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44 165 for review included full-term (>37 weeks) gestational age at participating health facilities, including
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46 166 cesarean sections without complications per ICD coding. Deliveries with adverse outcomes per ICD
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48 167 coding that required hemorrhage treatment were excluded, due to collection under a separate
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50 168 survey module.
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169 **Statistical analysis**

170 We used multivariable logistic regression analysis to evaluate possible facility-level factors
171 associated with the primary outcome of oxytocin availability and the secondary outcome of oxytocin
172 administration. Covariates evaluated in this study were timing of data collection (baseline versus
173 first-phase follow-up), country, and EONC facility type (basic versus comprehensive). Additionally for
174 oxytocin administration, we examined relevant training within the last year (routine labor care, basic
175 emergency obstetrical care, or maternal complications care); and oxytocin availability (day of survey
176 visit), and skilled personnel (doctor, nurse). When fitting the regression models, skilled personnel
177 was dropped from the model due to predicting success perfectly, meaning a skilled personnel was
178 always present for the administration of oxytocin. The rate of missing data was 4.4% for oxytocin
179 availability and 0.7% for oxytocin administration for the regression analysis. P values <0.05 were
180 considered significant. We used Stata 14.2 (StataCorp LP, College Station, TX, USA) for the analysis.

181 **Patient and Public Involvement**

182 Patients or the public were not involved in the design, conduct, reporting, or dissemination of our
183 research.

184 **RESULTS**

185 **Sample characteristics**

186 Table 1 presents the medical records, patient, facility, and personnel characteristics. The
187 majority of deliveries were in basic-level health facilities (64.3%). We sampled the most medical
188 records from Guatemala (27.5%), followed by Chiapas (Mexico) (20.8%), Honduras (19.6%), Panama
189 (16.0%), Nicaragua (11.9%), and Belize (4.2%), based on the quota for records within each facility,
190 prevalence of records of interest, and sampling interval. With a range from 11 to 48 years, the mean

191 maternal age was 24.3 years. Of these patients, 55.2% were single (no social partnership), and 72.7%
 192 attained less than a secondary education. Nearly all patients (99.7%) had a single gestational
 193 pregnancy, and only 0.3% had a multiple gestational pregnancy. Most of these patients delivered
 194 vaginally (97.7%) as opposed to by cesarean section (2.3%). Supply (on the day of survey visit) for
 195 oxytocin at baseline was 82.9%, which increased to near complete availability (97.6%) at first-phase
 196 follow-up. Personnel on staff – that is, skilled birth attendants employed by the facility – at baseline
 197 was 96.2% for physicians and 91.0% for nurses and increased to 100% and 93.2%, respectively, at
 198 follow-up. Relevant training – that is, instruction on routine labor care, basic emergency obstetrical
 199 care, or maternal complications care – provided within the last year increased from 74.0% at
 200 baseline to 92.0% at first-phase follow-up.

201 **Table 1. Medical records, patient, and facility characteristics by first-phase**
 202 **follow-up**

Medical records characteristics				
		n (%)		
		Baseline 922 (37.3)	Follow-up 1,548 (62.7)	Total 2,470 ^a (100)
	EONC ^b facility type			
	Basic-level	616 (66.8)	971 (62.7)	1,587 (64.3)
	Comprehensive-level	306 (33.2)	577 (37.3)	883 (35.8)
	Country			
	Belize	14 (1.5)	90 (5.8)	104 (4.2)
	Guatemala	247 (26.8)	432 (27.9)	679 (27.5)
	Honduras	234 (25.4)	249 (16.1)	483 (19.6)
	Mexico	180 (19.5)	334 (21.6)	514 (20.8)
	Nicaragua	90 (9.8)	205 (13.2)	295 (11.9)
	Panama	157 (17.0)	238 (15.4)	395 (16.0)
Patient characteristics				
	Maternal age ^c	24.3 (6.7)	24.3 (6.6)	24.3 (6.6)
	Marital status			
	Single	409 (61.8)	656 (51.8)	1,065 (55.2)
	Partnership	253 (38.2)	610 (48.1)	863 (44.8)
	Education			
	Less than secondary	392 (70.5)	772 (73.9)	1,164 (72.7)
	Secondary or higher	164 (29.5)	273 (26.1)	437 (27.3)
	Pregnancy type			
	Single gestational	154 (98.7)	917 (99.9)	1,071 (99.7)
	Multiple gestational	2 (1.3)	1 (0.1)	3 (0.3)
	Delivery type			

	Vaginal	409 (98.6)	1,091 (97.3)	1,500 (97.7)
	Cesarean section	6 (1.5)	30 (2.7)	36 (2.3)
Facility and personnel characteristics				
		n (%)		
		Baseline 78 (47.0)	Follow-up 88 (53.0)	Total 166 (100)
	Oxytocin supply ^d	58 (82.9)	83 (97.6)	141 (91.0)
	Personnel on staff ^e			
	Physician	75 (96.2)	88 (100)	163 (98.2)
	Nurse	71 (91.0)	82 (93.2)	153 (92.2)
	Relevant training ^f	57 (74.0)	81 (92.0)	138 (83.6)

204 a n may vary for each variable due to missingness

205 b Essential Obstetric and Newborn Care

206 c mean \pm SD

207 d day of survey visit

208 e skilled birth attendants employed by the facility. Midwife excluded due to varying skill level amongst countries.

209 f within last year, includes routine labor care, basic emergency obstetrical care, maternal complications

210

211 Availability and administration of oxytocin for postpartum hemorrhage

212 prevention

213 Availability of oxytocin (on the day of the survey) increased from 82.9% to 97.7% and
 214 administration of oxytocin increased from 83.6% to 88.4% from baseline to first-phase follow-up.
 215 Notably, all countries achieved 100% availability of oxytocin at first-phase follow-up, except for
 216 Guatemala (91.7). Comprehensive level facilities achieved 100% availability, compared to basic level
 217 facilities (96.8%) at first-phase follow-up. Administration of oxytocin at first-phase follow-up ranged
 218 from 80.0% in Belize to 94.8% in Honduras. Oxytocin administration was nearly the same at basic
 219 (88.4%) and comprehensive level (88.5%) facilities at first-phase follow-up. (Table 2).

220 **Table 2. Oxytocin availability and administration by facility type, country, and**
 221 **first-phase follow-up**

Oxytocin Availability		n (%)		
		Baseline 58 (82.9)	Follow-up 83 (97.6)	Total^a 141 (91.0)
	EONC facility type ^b			
	Basic-level	43 (84.3)	61 (96.8)	104 (91.2)
	Comprehensive-level	15 (78.9)	22 (100.0)	37 (90.2)
	Country			
	Belize	4 (100.0)	4 (100.0)	8 (100.0)

	Guatemala	15 (88.2)	22 (91.7)	37 (90.2)
	Honduras	13 (92.9)	12 (100.0)	25 (96.2)
	Mexico	7 (100.0)	14 (100.0)	21 (75.0)
	Nicaragua	6 (85.7)	14 (100.0)	20 (95.2)
	Panama	13 (92.9)	17 (100.0)	30 (96.8)
Oxytocin Administration for prevention of post-partum hemorrhage		n (%)		
		Baseline 771 (83.6)	Follow-up 1,353 (88.4)	Total 2,124 (86.6)
EONC facility type				
Basic-level		521 (84.6)	852 (88.4)	1,373 (86.9)
Comprehensive-level		250 (81.7)	501 (88.5)	751 (86.1)
Country				
Belize		9 (64.3)	72 (80.0)	81 (77.9)
Guatemala		198 (80.2)	393 (91.0)	591 (87.0)
Honduras		224 (95.7)	221 (94.8)	445 (95.3)
Mexico		129 (71.7)	277 (82.9)	406 (79.0)
Nicaragua		87 (96.7)	168 (82.8)	255 (87.0)
Panama		124 (79.0)	222 (93.3)	346 (87.6)

222 a n may vary for each variable due to missingness

223 b Essential Obstetric and Newborn Care

224

225 Table 3 shows possible first-phase follow-up and facility determinants of the availability
 226 (primary outcome) and administration of oxytocin (secondary outcome). Odds of availability were
 227 significantly higher at first-phase follow-up compared to baseline (aOR = 8.41, 95% CI = 1.50–47.30),
 228 while odds of administration increased in magnitude but were not significant at first-phase follow-up
 229 (aOR = 1.63, 95% CI 0.83–3.21). Additionally, administration of oxytocin was found to be significantly
 230 higher in Honduras (aOR = 2.96; 95% CI = 1.00–8.76) in reference to Guatemala. Other covariates
 231 examined, such as comprehensive-level facility, relevant training, and oxytocin availability, showed a
 232 positive but not significant correlation to the outcomes.

233 **Table 3. Factors associated with availability (primary outcome) and**
 234 **administration of oxytocin (secondary outcome)**

	Oxytocin availability		Oxytocin administration for prevention of post-partum hemorrhage	
	Crude OR (95% CI) (n = 2,257)	Adjusted OR ^a (95% CI) (n = 2,257)	Crude OR (95% CI) (n = 2,343)	Adjusted OR (95% CI) (n = 2,343)
First-phase follow-up	7.29 (1.48–35.84)	8.41 (1.50–47.30)	1.43 (0.79–2.62)	1.63 (0.83–3.21)
Country				

Belize	<i>Predicts success perfectly^b</i>	<i>Predicts success perfectly</i>	0.52 (0.13–2.12)	0.44 (0.11–1.71)
Guatemala	1	1	1	1
Honduras	1.70 (0.18–16.46)	2.24 (0.27–18.24)	2.71 (1.02–7.22)	2.96 (1.00–8.76)
Mexico	0.67 (0.14–3.10)	0.51 (0.11–2.46)	0.57 (0.25–1.31)	0.57 (0.24–1.37)
Nicaragua	2.22 (0.23–21.71)	2.01 (0.19–20.92)	1.00 (0.38–2.62)	0.95 (0.35–2.54)
Panama	3.43 (0.36–33.05)	3.83 (0.36–41.22)	1.04 (0.41–2.66)	1.03 (0.40–2.61)
Comprehensive-level facility	1.00 (0.24–4.15)	1.29 (0.31–5.31)	0.92 (0.47–1.81)	0.96 (0.46–2.00)
Relevant training ^c	--	--	1.49 (0.71–3.13)	1.08 (0.44–2.67)
Oxytocin availability ^d	--	--	2.01 (0.92–4.39)	1.45 (0.66–3.19)

235 a adjusted for first-phase follow-up, country, and comprehensive-level facility. Relevant training and oxytocin availability not included (not applicable).

236 b Belize attained availability of oxytocin at all times (regression for this binary variable not possible)

237 c within last year, includes routine labor care, basic emergency obstetrical care, maternal complications

238 d day of survey visit

239 All models clustered at health facility level

240 DISCUSSION

241 There remains a paucity of studies with regard to oxytocin access and use in Mesoamerica
 242 (13,21–23) or in low-resource countries in general.(12,24–30) In Mesoamerica, García-Elorrio et al
 243 2014 and Low et al 2012 conducted pre-post evaluations at health facilities within a single country,
 244 rather than a multinational analysis. These studies focused on oxytocin administration interventions,
 245 such as multifaceted provider skills in Nicaragua and AMTSL training in Honduras respectively,
 246 without attention to improving oxytocin availability, the primary outcome of this study. Therefore,
 247 we provide an updated, regional evaluation of postpartum hemorrhage prevention practices that
 248 may guide clinical management and policy priorities for this targeted population. Our study showed
 249 that the availability of oxytocin improved significantly after system readiness interventions, among
 250 the poorest population within Mesoamerica.

251 This analysis attests that clinical standards of care could be achieved in Mesoamerica with
 252 proper monitoring and management of oxytocin supplies. As expected from the implementation

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3 253 timeline, the first stage of the Salud Mesoamérica Initiative focused on improving system readiness,
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5 254 namely strengthening facility infrastructure, supply chains, procurement processes, storage
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7 255 practices, and inventory monitoring of drugs and equipment.(14,16) Consequently, increasing the
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9 256 availability of oxytocin, the primary goal of the first phase of the initiative, was achieved. While,
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11 257 administration of oxytocin, a lesser goal, increased but not in the same proportion as availability,
12
13 258 which suggests that increasing the availability of inputs is necessary but not sufficient to improve
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15 259 quality of care. Comprehensive quality improvement strategies would be needed that involve not
16
17 260 only increasing availability of equipment and supplies, but also improving skills and abilities of
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19 261 personnel, and establishing mechanisms to improve processes, identify causes, and lift barriers to
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21 262 ensure proper practices of care in the next phase.

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26 263 This study has some limitations. First, oxytocin availability was defined based on the day of
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28 264 the visit to health facilities, which may not match the day of delivery in a medical record. Due to
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30 265 logistic limitations, it was not possible to assess stock-outs of oxytocin over a longer period of time.
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32 266 Therefore, we must consider oxytocin availability the day of the visit as a proxy for availability over a
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34 267 longer period of time. Quality of available oxytocin cannot be included when defining oxytocin
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36 268 availability, as data was not collected on expiration or storage of oxytocin. Second, this study
37
38 269 focused on uncomplicated full-term deliveries and did not include patients resulting in hemorrhage
39
40 270 due to two separate survey modules for data collection. In the module with adverse outcomes from
41
42 271 hemorrhage, uterotonics were often administered more than once without distinction of whether
43
44 272 for prevention or treatment. Third, sample sizes also vary by country, and in some cases like Belize,
45
46 273 the reduced sample size limited our capacity to have country-specific precise estimates and to
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48 274 detect significant differences between baseline and follow-up measurements. Fourth, quality of
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50 275 record keeping may affect the information used in this study and may vary by country. Nonetheless,
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52 276 we used a standard methodology across countries, automated data collection, and used quality
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54 277 control measures that ensure comparability between countries.
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278 CONCLUSION

279 The study showed a significant improvement in availability of oxytocin at facilities that
280 provide care to poor communities within Mesoamerica, but not optimal administration, as expected
281 after emphasis on supply-side interventions. Continued monitoring and evaluation, beyond input
282 availability, are essential to better understand how to improve processes and clinical practices. Our
283 study provides valuable information to close the evidence-to-practice gap and to reduce maternal
284 mortality in Mesoamerica.

285 LIST OF ABBREVIATIONS

- 286 Active management of third stage of labor (AMTSL)
287 Essential Obstetric and Newborn Care (EONC)
288 International Confederation of Midwives (ICM)
289 International Federation of Gynecology and Obstetrics (FIGO)
290 Salud Mesoamérica Initiative (SMI)
291 World Health Organization (WHO)

292 DECLARATIONS

293 Ethics approval

294 Approval for this study involved the institutional review board from the University of
295 Washington (exemption as a non-human-subject research determination), partnering data-collection
296 agencies (El Colegio de la Frontera Sur-Mexico), the Ministry of Health in each country (Belize,
297 Guatemala, Honduras, Mexico, Nicaragua, Panama), and the indigenous communities in Panama and
298 Mexico. Prior to data collection, informed consent was obtained from each health facility

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3 299 administrator. During the data extraction process, medical records were anonymized. No patient
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5 300 consent required.
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8 9 301 **Data Sharing**

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11 302 Data are owned by the Inter-American Development Bank. SMI baseline survey data, which
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13 303 comprise the minimal dataset, are publicly available on the SMI website. SMI follow-up survey data
14
15 304 are currently available upon written request from the Inter-American Development Bank, whose
16
17 305 contact information is listed below. Javier Lesaca, Communications Officer, Salud Mesoamerica
18
19 306 Initiative, Inter-American Development Bank, 1300 New York Ave. NW, Washington, DC 20577.
20
21 307 contact@saludmesoamerica.org.
22
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26 308 **Competing interests**

27
28
29
30 309 The authors declare that they have no competing interests
31
32

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44
45 316 interpretation, or preparation of the manuscript.
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49 317 **Authors' contributions**

50
51 318 AMK conceived the study and prepared data analysis, interpretation of data, initial draft, and final
52
53 319 manuscript. AMS, EBP, and CKJ contributed to and reviewed data analysis. AGM, MDM, KS, PZB,
54
55 320 DRZ, and EI contributed to the acquisition of the data. BH and AHM supervised the study and data
56
57 321 compilation and contributed to interpretation of data. All authors critically reviewed the draft and
58
59 322 approved the final manuscript.
60

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract p.1/line 1; p.2/line 32 (b) Provide in the abstract an informative and balanced summary of what was done and what was found p.2/line 38-40; p.3/line 53-56 .
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported p.3-5/lines 69-103 .
Objectives	3	State specific objectives, including any prespecified hypotheses p.5/lines 104-106 .
Methods		
Study design	4	Present key elements of study design early in the paper p.5-6/lines 118-127 .
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection p.5/lines 111-117; p.6/lines 129-138 .
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants p.6-7/lines 139-153 . (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable p.7/lines 169-173
Data sources/ measurement	8*	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 p.7/lines 160-167
Bias	9	Describe any efforts to address potential sources of bias p. 14/lines 293-302
Study size	10	Explain how the study size was arrived at p.7/lines 153-159 .
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why p.6/lines 129-138; p.7-8/lines 169-175 .
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding p.8/lines 182-193 . (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed p.8line 191 (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy p.5/lines 111-117, p.6-7/lines 146-159 . (e) Describe any sensitivity analyses not applicable

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Results		
Participants	13*	(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 p.9/line 213 (Table 1) (b) Give reasons for non-participation at each stage not applicable (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders p.9/line 213 (Table 1) (b) Indicate number of participants with missing data for each variable of interest p.9/line 213 (Table 1) ; p.8/lines 190-192 . (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount) not applicable
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures p.10/line 230 (Table 2)
Main results	16	(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 p.11/line 243 (Table 3) (b) Report category boundaries when continuous variables were categorized not applicable (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses not applicable
Discussion		
Key results	18	Summarise key results with reference to study objectives p. 12/lines 260-262 .
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias p.14/lines 293-307 .
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence p.13-14/lines 276-291
Generalisability	21	Discuss the generalisability (external validity) of the study results p.14/lines 309-311 .
Other information		
Funding	22	Give 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 p.16/lines 344-349

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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.