An integrated approach to improve maternal and perinatal outcomes in rural Guatemala: a stepped-wedge cluster randomized trial

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Abstract

***Objective**:* To evaluate the impact on maternal and newborn health indicators of an intervention package.

***Methods**:* A random stepped-wedge design across six sub-districts within two districts in Guatemala from January-2014 to January-2017. Data on outcomes were collected on all births in all 33-health centers from nine months. The intervention package included: distribution of promotional materials encouraging health center birth; education for traditional birth attendants about the importance of health center-birth and; provider capacity building using simulation training. Main outcomes were number of health center births, maternal morbidity, and perinatal morbidity and mortality. Women, providers and data collectors were unblinded to the intervention.

***Results**:* There were 24,412 deliveries. Health center births per 1,000 live births showed an overall increase, although the adjusted (for secular trends and clustering) relative risk (aRR) for the treatment effect was not statistically significant (aRR 1.04, [CI: 0.97 - 1.17, p = 0.24]). Furthermore, maternal morbidity decreased (aRR 0.78 [CI: 0.60 – 1.02, p = 0.07]), as well as perinatal morbidity (aRR 0.84 [CI: 0.68 - 1.05, p = 0.13]).

***Conclusion**:* This study represents one of the few randomized evaluations of an integrated approach to improve birth outcomes in a low-income setting.

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Introduction

Despite significant global declines in maternal and perinatal morbidity and mortality since 1990, many low-income countries lag behind in reaching global targets, often in geographies where fewer births take place in facilities and where the use of routine evidence-based practices and quality emergency response are not standard [1]. Within Guatemala, districts where indigenous populations comprise a high proportion of the total population experience higher maternal mortality (e.g. 177 per 100,000 live births and 150 per 100,000 live births for Huehuetenango and Alta Verapaz, respectively) and perinatal mortality rates (43 per 1,000 live births for Huehuetenango, 35 per 1000 births for Alta Verapaz) [2-4]. These high rates are partially due to a low proportion of deliveries attended by skilled labor [5]. This is driven by both demand side (i.e. perception of quality of care and access to facilities) and supply side (i.e quality of clinical care, treatment during birth, and cultural sensitivity) factors [6-8].

Study rationale

Our intervention included (1) a social marketing campaign to increase the demand for health center births; (2) outreach activities by professional midwives to improve the link between traditional birth attendants (TBAs) and the formal healthcare system and (3) a

simulation and team training program to improve clinical skills and team function among providers.

Social marketing has been used in a broad number of public health programs as a vehicle to encourage healthy behaviors or behavior change [9,10]. Has also been used successfully for the promotion of family planning methods, smoking cessation campaigns and youth weight loss programs [11-13].

Qualitative studies in Guatemala suggest that patient lack of trust in the quality of care is one of the determinants that deter women from giving birth in health centers [14]. Following promising results from a pilot project that built interest among local stakeholders, we launched the current study, aiming to implement and evaluate the impact of an intervention package at scale, across the 2 rural districts of Huehuetenango and Alta Verapaz [15]. Given the nature of the intervention package, we chose health centers and the municipalities as clusters and they serve as the unit of delivery of the intervention and randomization to assess the impact of the intervention on the outcomes of births occurring at the health center level. A stepped-wedge design was chosen because there were limited resources to roll-out the intervention to all health centers simultaneously.

Methods

We conducted a cluster randomized stepped-wedge trial to evaluate a package of three interventions on health center birth volume and maternal and perinatal morbidity and mortality in the districts of Huehuetenango and Alta Verapaz, Guatemala, from January 2014 to January 2017. A 2015 national survey showed that 60.6% of births in

Huehuetenango and 43.2% in Alta Verapaz were registered as having occurred at home [16]. The study was registered at ClinicalTrials.gov, NCT03151070.

The intervention package was implemented in 33 health centers (15 were located in Alta Verapaz and 18 in Huehuetenango) and their surrounding municipalities, representing 100% of the secondary level healthcare centers in these geographies. The eligibility criteria for health centers included: is open 24 hours, 7 days a week, has medical personnel and basic supplies, capable of providing basic emergency obstetric and neonatal care and does not perform cesarean sections, vacuum, forceps assisted delivery or blood transfusions. In general, these facilities have at least one skilled provider who is able to identify and provide immediate care for obstetric hemorrhage, eclampsia, preeclampsia and infection [17].

The study included 3 populations: 1) mothers with pregnancies ≥ 28 weeks of gestational age who delivered during the trial period and their infants (including stillbirths and newborns who died prior to discharge for whom outcomes were available); 2) TBAs and community members who live in the proximity of the health center where the intervention was rolled out, who were contacted by the social marketing campaign and the professional midwifery liaison; 3) clinic providers who attend births working in the selected health centers were invited to participate in emergency obstetric and newborn care simulation training.

Study design

The 33 health centers were grouped into six sub-districts of 4 to 6 adjacent centers each to receive the intervention in a step-wise fashion (Figure 1), aiming to facilitate intervention implementation. Randomization consisted of random allocation of the six

sub-districts to one of the six study sequences, with the following restrictions: (i) the sub-district allocated to the first sequence was pre-specified and not randomly allocated; (ii) the sub-districts selected for subsequent sequences alternated between the two districts to create a balance of the roll-out across districts. This increased the acceptability of the trial design and mitigated against any large imbalances between the two districts. These limitations reduced the available randomizations to 12 possible allocations. Each health center was informed of the date they would be exposed to the intervention 4 months before the start of the intervention to allow time to embed the intervention into practice. Baseline data were collected at all facilities from January-September 2014, during which time no health center was exposed to the intervention. Following this, the intervention package was rolled out sequentially, every 4 months, until all centers in all sub-districts received 4 months of intervention exposure. Data collection continued in all facilities until 4 months after the final group of health centers completed the 4-month intervention (January, 2017). Trained field monitors visited each center once a month beginning at baseline and continuing until 4 months after the intervention ended in the last sub-district (January, 2017).

Outcomes and measurements

The outcomes measures of the study were: 1) counts of health center births (≥ 28- week gestation); 2) incidence of severe acute maternal morbidity defined as conditions related directly to maternal mortality (severe post-partum hemorrhage, eclampsia, pre-eclampsia, and sepsis) prior to discharge; 3) incidence of perinatal morbidity, defined as a newborn of ≥ 28 weeks of gestational age with an Apgar score ≤ 7 at the fifth minute or respiratory difficulties that required use of positive pressure ventilation or cardiac

massage reported on the outcome form prior to discharge; 4) incidence of perinatal mortality, defined as stillbirths and newborn deaths of ≥ 28 weeks of gestational age which occurred at health facilities or before the mother and/or baby were discharged or referred; and 5) incidence of perinatal mortality before discharge defined as health center newborn deaths excluding stillbirths. This outcome was added post-hoc to evaluate the improvement of quality of care for births delivered in health centers. Data were extracted from health center records using an adapted 30-question tool previously used in a pilot phase of the study [15]. Field workers were trained in data collection procedures including data protection and privacy. All data were initially collected on a paper form and once they were entered electronically they were assigned codes to maintain individual anonymity and confidentiality. Once data was extracted from the paper form, all individual identifiers were removed; leaving only unique codes designating health center and patient. By the nature of the intervention, neither patients nor health care practitioners could be blinded to the intervention. Data analysts were not masked to intervention exposure due to the sequential roll-out of the intervention. Data collection included total number of health center births, and individual maternal and perinatal morbidity and mortality outcomes.

Intervention

The intervention package included 1) PRONTO provider training, a low-cost simulation and team training program using a low-technology birth simulator PartoPants [18] to teach birth attendants maternal and perinatal emergency management as well as teamwork and communication skills, and provision of culturally sensitive care [19]. 2) a social marketing campaign, *Qué Vivan Las Madres!* (Long Live the Mothers) lasting

during the entire 4 month period, distributed promotional material in intervention communities in seven native languages including radio and TV spots, posters at health facilities and other public places, calendars, flyers, bracelets, stickers and baby beanies. The campaign aimed to encourage pregnant women to choose to give birth in the nearest health center rather than at home. 3) Four professional midwives conducted outreach activities in the communities and with TBAs to also promote health center births; promotion of professional midwifery and inclusion of traditional midwifery practices into the formal health care system. Professional midwives were tasked with raising awareness among clinic providers on the importance and benefits of integrating midwifery-based care and traditional midwifery practices into the formal sector (Table 1). The project emphasized the cultural factors at play and included activities to bridge the cultural divide.

Sample Size Justification

The sample size in this study was fixed by the number of women giving birth in the participating health centers over the study period. All second-level healthcare facilities that fulfilled the eligibility criteria from the two selected districts received the intervention.

Data Analysis

All analyses were conducted in STATA versions 13 and 15. We used mixed effects Poisson regression with a log link, clustering by health center, using robust variances to allow for inflated variances and analysis of binary outcomes. Treatment effects are

therefore reported on a relative risk scale (with 95% confidence intervals). Time trends were incorporated by including months as a fixed effect categorical variable in all analyses. Heterogeneity across clusters in time trends was incorporated by including a random cluster by month interaction. Treatment effect heterogeneity across clusters was incorporated by including a random interaction between cluster and intervention. Initially, all analyses allowed for unstructured covariance so random intercepts and random intervention effects could be correlated; however perinatal mortality, neonatal mortality and perinatal morbidity analyses did not converge under this assumption and used an independent covariance structure instead. Due to the expected differences between the two districts, district was initially included as a covariate in all analyses. Analysis of neonatal mortality did not converge when including the district covariate. For the outcome health center deliveries, numbers were standardized by including an offset of the log of estimated number of live births for that district based on the number of births registered. This denominator data was available for years 2014 to 2016, but not for the last month of the study, January 2017, for which the values from January 2016 were imputed. We did not exclude any transition periods as it was expected that the effect of the intervention would appear beginning after the first month of intervention. Plots of estimated rates for each outcome are produced by first generating marginal estimates for each observation with the intervention arm covariate turned on (intervention) or off (control). These estimates are then summed over all observations at each time point for each arm and smoothed lines are plotted by arm.

Ethical Considerations

Pregnant women, unborn babies and indigenous communities are considered vulnerable populations. This study strictly adhered to ethical principles and guidelines and is registered in University of California, San Francisco's Committee on Human Research, Institutional Review #14-13057 as well as the Institutional Review Board of the Guatemalan Ministry of Health under 47-2014. All of the activities of this study were voluntarily and participants did not receive compensation. Providers who participated in training consented to participate at the beginning of each training.

Results

Study flow chart describes in detail each step of the study from baseline to post-roll-out period. Shows how all zones start in the control condition and move to the intervention condition sequentially (Figure 2)

There were a total of 24,412 health center births between the beginning of intervention roll-out and the end of the study (September 2014 to January 2017). This equated to an average of 690 (SD 78) combined births per month in participating health centers and an average of 21 (SD 20) births per month per health center. There were 982 cases of severe and acute maternal morbidity, 912 cases of perinatal morbidity and 309 cases of perinatal mortality (Table 2).

Overall, during the trial period, the number of health center deliveries increased by 26% from about 230 per 1,000 live births at baseline to 290 per 1,000 live births at end (Figure 3). After adjusting for temporal trends and clustering, the estimated effect of the intervention on institutional births was increasing but was not statistically significant (aRR 1.04 (95% CI 0.97 - 1.17) (Table 3).

Maternal morbidity decreased over the study period (Figure 3). After adjusting for temporal trends and clustering, we determined that the effect of the intervention was a reduction of 22% in risk and marginally statistically significant for the effect of the intervention [aRR 0.78 (95% CI: 0.60 - 1.02)] (Table 3).

Perinatal morbidity showed a decreasing trend over the study period (Figure 3). After adjusting for temporal trends and clustering, the estimated effect of the intervention on perinatal morbidity was a 16% reduction in risk (aRR 0.84 (95% CI 0.68 - 1.05) (Table 3).

Perinatal mortality decreased over the study period (Figure 3). After adjusting for temporal trends and clustering, the estimated effect of the intervention on perinatal mortality was a 13% reduction in risk [aRR 0.87 (95% CI 0.65 - 1.17)] (Table 3).

Finally, for the outcome perinatal mortality before discharge (Figure 3), the estimated effect of intervention on neonatal mortality was a 15% reduction in risk [aRR 0.85 (95% CI 0.45 – 1.62)] (Table 3).

Discussion

We found that the intervention package was marginally associated with a reduction of maternal morbidity. We did not find a significant association between the intervention package and our other outcomes, number of health center births, perinatal morbidity and mortality and perinatal mortality before discharge. To our knowledge, this is the first cluster randomized stepped wedge design study to measure the impact of this type of intervention package including a social marketing campaign, liaison with TBAs, and

obstetric and perinatal emergency simulation and team training, on maternal and perinatal health indicators in a rural setting.

Our findings are consistent with other studies that have found that simulation-based training programs can be effective in the reduction of maternal and perinatal and perinatal morbidity in developing settings. For example, a hospital-based cluster randomized trial in Mexico found that simulation and team-training increased the number of evidence-based practices at birth contributing to quality of care [20]. Another cluster randomized trial in Ghana found that a training program using simulation and skill stations resulted in sustained decrease in facility-based newborn mortality and intrapartum stillbirths and retained knowledge among birth attendants after two years [21].

Even though the number of health center births showed a notable increase over the study period, the difference between control and intervention groups was negligible. One possible explanation for this was contamination between the adjacent sub-districts as a result of the social marketing campaign spilling over to adjacent districts. Furthermore, previous studies suggest that the decision to give birth at home is partially driven by social and cultural traditions where TBAs provide not only obstetric but also social and spiritual care [22]. These traditions have prevailed for millennia. An intervention package to further impact the decision to deliver at a health center may require interventions more focused on addressing cultural birthing norms, and other structural and economic barriers (i.e. mother’s educational attainment, decision-making power in the household and fear of cesarean sections) as drivers of women giving birth

at health centers. These underlying issues were not within the scope of the intervention and will require further consideration.

Although not statistically significant, the magnitude of the intervention effect is similar across perinatal morbidity and mortality and perinatal mortality outcomes. These positive trends are consistent with other quality improvement programs that employ resuscitation training in low-resource settings [23] to address these problems. The non-significance in the result might either represent an intervention that does not work, or lack of statistical certainty. Our budget constraints prevented us from enrolling additional health facilities. Larger studies are needed to properly assess the effect of the intervention on these indicators. Importantly, any other larger studies must also be of rigorous design and not simply be before and after studies.

This study has several limitations. First, geographic proximity of the health facilities and the communities they serve create the potential for contamination between control and intervention groups with women crossing between sub-districts. Second, due to the heterogeneity of the study population (indigenous population, diverse languages, traditions and beliefs) and low literacy level in Huehuetenango and Alta Verapaz the generalizability of these results is unclear. Third, few cases of perinatal mortality were seen in the health centers resulting in wide confidence intervals and large p-values for the effect estimates. In addition, data collection on perinatal morbidity and mortality was limited to pre-discharge events. No follow-up or referrals were captured and thus these two outcome measures only included cases that occur in the health center, usually during a 24-hour stay. The morbidity outcome indicators were limited to diagnoses we felt were accurately captured by providers. Furthermore, as has occurred in similar

stepped-wedge design studies, no sample size or power analysis calculation were performed as all second-level health facilities as well as all women giving birth in the health facilities who met met the eligibility were enrolled in the study [24].

Despite these limitations, our data suggest that in a predominantly indigenous region in Guatemala, an integrated approach to encouraging women to deliver at health facilities and simultaneously training providers in obstetric and neonatal emergency management may have an impact on maternal and perinatal health outcomes. Although the results were not statistically significant, from a public health stand point, a 20% decrease in maternal and perinatal morbidity and mortality, if repeated in future studies, would be meaningful. This type of intervention package deserves further investigation with lessons learned from this trial to modify the intervention (particularly the demand side) and improve data collection on morbidities. Qualitative research would also be a valuable addition to better understand the various drivers that motivate women to deliver in the health facility and inform future innovations and designs.

Contributors

EK: Principal investigator, conceived the intervention package trial, writing the first manuscript, review and editing

GA: data analysis and first manuscript writing, interpretation and review

KH: data analysis and interpretation and manuscript writing and editing

JPH: study design, data analysis and interpretation and manuscript writing and editing

JM: review and data interpretation

MM: review and data interpretation

SM: literature review, manuscript design and writing, data interpretation

DW: Co-principal investigator, conceived the project, manuscript writing and editing

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Table 1: Summary of intervention dosage and exposure

Intervention component	Realized exposure
PRONTO Training	1. 3-day training on obstetric and neonatal emergency training using simulation and team training 2. 544 providers trained on obstetric and neonatal emergency and teamwork and communication 3. 162 simulations performed at health centers
Professional midwife liaison	1. 1089 TBAs contacted 2. 450 workshops with pregnant women 3. 260 obstetric and neonatal emergency simulations with TBAs
Social marketing campaign	1. 1,611 posters distributed 2. 11,124 posters distributed 3. 25,000 silicon bracelets distributed 4. 122,119 stickers distributed 5. 301,269 flyers distributed 6. 4,236 baby beanies distributed 7. 2,119 CDs and DVDs distributed 8. 20,115 calendars distributed

Table 2. Baseline characteristics of health centers in each sub-district of the trial

	Sub-district 1	Sub-district 2	Sub-district 3	Sub-district 4	Sub-district 5	Sub-district 6
Average number of deliveries per month (SD)	48 (9)	88 (9)	45 (9)	135 (20)	71 (7)	182 (15)
Severe maternal morbidity rate [1] (SD)	76 (55)	85 (35)	86 (89)	61 (18)	122 (105)	58 (44)
Perinatal mortality rate [1] (SD)	0 (0)	14 (8)	27 (27)	21 (11)	69 (110)	5.0 (2.4)
Perinatal morbidity rate [1] (SD)	64 (42)	69 (21)	46 (33)	88 (30)	93 (76)	58 (40)
Neonatal mortality before discharge [1] (SD)	0 (0)	2.0 (2.7)	5.0 (7.7)	1.7 (3.8)	19 (37)	1.0 (1.4)

[1] *Rates per 1,000 live births per month; * Before discharge*

Table 3. Estimated impact of intervention on outcomes

Outcome	Total number of cases at health center	Rate per 1,000 live births	Intervention effect [1] aRR (95% confidence interval)	P-value
Health center based vaginal deliveries [2]	24,412	214	1.04 (0.97 - 1.17)	0.24
Maternal morbidity*	1,322	54	0.78 (0.60 - 1.02)	0.07
Perinatal morbidity*	1,214	50	0.84 (0.68 - 1.05)	0.13
Perinatal mortality*	345	14	0.87 (0.65 - 1.17)	0.35
Neonatal mortality*	52	2	0.85 (0.45 - 1.62)	0.62

[1] Intervention effects are adjusted for temporal trends and clusters (for full details see statistical analysis section).
[2] Excluding deliveries of pregnancies with less than 28 weeks (52 cases) and excluding cases from outlier health center (43 cases)
* Before discharge