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Routine antenatal ultrasound in low- and middle-income countries: first look – a cluster randomised trial

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Objective Ultrasound is widely regarded as an important adjunct to antenatal care (ANC) to guide practice and reduce perinatal mortality. We assessed the impact of ANC ultrasound use at health centres in resource-limited countries.

Design Cluster randomised trial.

Setting Clusters within five countries (Democratic Republic of Congo, Guatemala, Kenya, Pakistan, and Zambia)

Methods Clusters were randomised to standard ANC or standard care plus two ultrasounds and referral for complications. The study trained providers in intervention clusters to perform basic obstetric ultrasounds.

Main outcome measures The primary outcome was a composite of maternal mortality, maternal near-miss mortality, stillbirth, and neonatal mortality.

Results During the 24-month trial, 28 intervention and 28 control clusters had 24 263 and 23 160 births, respectively; 78% in the intervention clusters received at least one study ultrasound; 60% received two. The prevalence of conditions noted including twins, placenta previa, and abnormal lie was within expected ranges. 9% were referred for an ultrasound-diagnosed condition, and 71% attended the referral. The ANC (RR 1.0 95% CI 1.00, 1.01) and hospital delivery rates for complicated pregnancies (RR 1.03 95% CI 0.89, 1.20) did not differ between intervention and control clusters nor did the composite outcome (RR 1.09 95% CI 0.97, 1.23) or its individual components.

Conclusions Despite availability of ultrasound at ANC in the intervention clusters, neither ANC nor hospital delivery for complicated pregnancies increased. The composite outcome and the individual components were not reduced.

Keywords antenatal care, low-/middle-income countries, perinatal mortality, ultrasound.

Tweetable abstract Antenatal care ultrasound did not improve a composite outcome that included maternal, fetal, and neonatal mortality.

Linked article This article is commented on by BD Einerson, p. 1600 in this issue. To view this mini commentary visit https://doi.org/10.1111/1471-0528.15402.

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Introduction

Ultrasound (US) is used routinely at antenatal care (ANC) in high-income countries (HIC) to improve gestational age dating, reduce postdates pregnancies, and improve diagnosis of twins and abnormal presentations.[1–4] US has also been used to evaluate fetal growth and amniotic fluid abnormalities as well as congenital anomalies.[5,6] Despite these benefits, multiple systematic reviews have concluded that these potential benefits do not result in reduced maternal, fetal or neonatal mortality.[7–10]

While reduced mortality with US use during antenatal care has not generally been shown in HIC, there is speculation that US could have an impact on mortality in low-/middle-income countries (LMIC), where rates of perinatal and maternal mortality and morbidity are high and the ANC coverage and quality are poor.[11–13] The rationale for this potential impact includes US serving as an attraction for women to attend ANC earlier or more often and to identify high-risk pregnancies that may require advanced care.[14–16] Although studies have explored US use in pregnancy in LMIC, no definitive studies have evaluated the impact of US on maternal, fetal, or neonatal mortality. However, several small studies in LMIC have suggested that US may increase ANC utilisation, improve referral for obstetric conditions discovered on US, result in more hospital deliveries, and improve gestational age dating.[16–18] Several studies evaluating different types and lengths of training have suggested that lower-level obstetric providers can be trained to perform a basic obstetric US examination with intensive training conducted over a period of several weeks to months.[19,20]

Our objective was to conduct a trial to evaluate the impact of basic obstetric US at routine ANC visits on maternal, fetal, and neonatal mortality in LMICs.[21] Because trained US providers are generally not available in many regions of LMIC, especially at community clinics where ANC is provided, and many of these regions also have a shortage of physicians, training of ultrasound naïve providers was a necessary component of our study.[20,22] We evaluated whether US-naïve providers could be trained to perform basic obstetric US examinations to accurately determine gestational age and identify specific complications.[21] In previously published studies, we demonstrated the high quality of the trainees' US examinations.[23] Based on prior studies, we had two primary hypotheses. First, we tested the hypothesis that in LMIC, the availability of routine US at ANC clinics would increase the use of ANC and hospital delivery for complicated pregnancies, and second, that appropriate referrals for discovered complications would reduce the composite outcome of maternal mortality, maternal near-miss mortality, stillbirth, and neonatal mortality.

Methods

Trial design

The First Look study was a two-arm, parallel, cluster randomised trial conducted in clusters in sites in rural and semi-urban areas of Zambia, Kenya, the Democratic Republic of the Congo (DRC), Pakistan, and Guatemala under the auspices of the Global Network for Women's and Children's Health Research (Global Network). The US training intervention was overseen by the University of Washington's Department of Radiology (UW). The study design is described in detail elsewhere.[21,23]

The trial was conducted using a modification of the intent-to-treat (ITT) principle. The ITT population included all women in the study clusters who were residents of and delivered within the First Look study clusters during the site-specific analysis periods defined for this trial.

Participants

All pregnant women residing within study clusters were eligible for participation. A cluster was a defined geographic area generally served by a single health centre and its catchment area with about 500 births per year. At the time of the First Look study initiation, the government health centres in the study areas did not routinely provide US at ANC.

Each cluster, whether intervention or control, had one or more registry administrators, independent of the intervention, who were responsible for enrolling pregnant women in the Global Network Maternal Newborn Health Registry (GN MNHR) and collecting pregnancy and outcome data.[24] The GN MNHR, which began in 2008, seeks to register women as early as possible during their pregnancy, and collects relevant demographic, treatment, and outcome data at enrolment, at delivery and at 42 days postpartum. In each cluster, every pregnant woman who provided consent was included in the US study regardless of whether she received a study US examination. Prior to the study, in each intervention cluster, community meetings were held to describe the study and the potential benefits of an ultrasound examination and to ask for community input regarding the study.

Core data

The primary outcome data for the trial, including pregnancy outcomes (stillbirth >20 weeks or 500 grams), neonatal death (<28 days), and maternal near-miss or mortality were collected by the MNHR administrators. MNHR staff also collected demographic information and health care for ANC and delivery for all participants. Additional process measures, collected by the First Look study staff, included the study ultrasound examination results and referrals based on the ultrasound.

Randomisation and masking

Prior to initiation of the trial, the central data coordinating centre (RTI International, Durham, NC) generated a random assignment of the clusters at each site to intervention and control treatment groups stratified by site, with additional strata within site using the most recent year's perinatal mortality rates of the clusters collected through the MNH registry to balance on pregnancy risk. The nature of this intervention precluded masking of the study intervention. We were aware of the possibility of modifying the intervention through overattentive monitoring. To limit the risk of bias associated with unmasked reviews of study progress, the primary outcome data were collected by an independent team in each cluster associated with the MNHR.

Procedures

The intervention clusters had a pretrial training period for US-naïve healthcare practitioners who were identified to participate in the trial. During this period, a team consisting of UW-sponsored sonologists or sonographers in partnership with an in-country expert from each site provided training in basic US obstetric examinations. The training period consisted of 2 weeks of intensive hands-on training interwoven with didactic lectures followed by a 3-month pilot that took place in the trainees' antenatal clinics.[23,25] During the entire training period, every study US examination was evaluated and scored, and specific feedback was provided to the trainees, a total of 3822 examinations with 26 754 images.[23] Each trainee completed a minimum of 50 supervised examinations during the pilot. To proceed to the trial, trainees were required to pass a written examination after the 2-week course and a practical examination by the conclusion of the training period. Four practical examinations were administered during the training period to monitor the trainees' progress. Only after the trainee was certified to provide competent US examinations was he/she allowed to conduct US examinations for the trial. During the trial, a minimum of 10% of all examinations were evaluated for quality, and these results were used to guide continued training of the sonographers.

For the trial, the objective was to provide two routine US examinations at ANC, one at 16–22 weeks to determine the number of fetuses, gestational age, amniotic fluid abnormalities, and major congenital anomalies and another at 32–36 weeks to document placental location, growth abnormalities, amniotic fluid abnormalities, and fetal malposition. We chose those windows because at our network sites, most women presented for antenatal care at 20 weeks or later, and examinations around 20 weeks are reasonably accurate for determining gestational age. Examinations in the 32- to 36-week window are more accurate for predicting fetal position, growth restriction, and amniotic fluid abnormalities at delivery.[25–28] The basic examination consisted of evaluation of cardiac activity, fetal position, fetal number, placenta position, biparietal diameter, head circumference, abdominal circumference, femur length, weight percentile, and amniotic fluid measurements. Hospital referral for specific findings such as twins, breech, placenta previa, and fetal growth restriction was required. Referral algorithms for each condition were created and agreed to by the study sonographers and representatives of the referral hospital. Sex determination was prohibited for the study and was not included in the training of the sonographers.

If a study sonographer left the study, a replacement sonographer was identified and a similar training process was conducted, with local supervision and oversight by the central team at the UW through a secure website.[28] US training was also provided to sonographers at the referral hospitals to ensure consistency in addition to limited training in emergency obstetric and neonatal care. Building community awareness through community meetings, counselling patients related to the US findings, and providing an US image of the fetus to the mother were parts of the intervention.

The control clusters were equivalent to the intervention clusters in having the MNHR to enrol and track primary outcomes. Women in these clusters received standard ANC at the health centre without additional interventions provided.

Outcomes

The trial had primary outcomes that included both clinical and process outcomes. The primary composite outcome included maternal mortality, near-miss maternal mortality, stillbirth, and neonatal mortality. Maternal mortality was defined as any death during pregnancy up to 42 days postpartum. Near-miss maternal mortality was defined based on a modified definition of the World Health Organization (WHO) symptom list.[29] Stillbirth was defined as any fetal death after 20-week gestation, prior to delivery. Neonatal mortality was defined as death of a liveborn infant up to 28 days. The process outcomes were ANC and hospital delivery for complicated pregnancies. ANC use was evaluated by whether the woman received any ANC, four or more ANC visits, and the mean number of ANC visits. Complicated pregnancies were defined as those with antepartum haemorrhage, hypertensive disease/preeclampsia/eclampsia, breech/transverse or oblique lie, multiple birth, fetal growth restriction, and major congenital anomalies. These outcomes were collected at patient interviews and chart reviews conducted during enrolment, at delivery and 42 days postpartum by the GN MNHR staff. The training of US-naïve sonographers was also a secondary outcome, and the evaluation was previously reported.[23] Finally, additional process measures such as US

skills and the identification of conditions by US were collected only in the intervention clusters.

Statistical analysis

The main hypothesis was that introduction of antenatal US screening with appropriate referral would improve the composite outcome. The second hypothesis was that US would a) increase the rate of ANC utilisation and b) increase hospital deliveries for women with complicated pregnancies. The ANC outcome was evaluated by several measures of ANC utilisation. The hospital delivery outcome was evaluated using a binary measure of whether a complicated pregnancy was delivered in a hospital. The hypotheses were tested independently at a level of significance of 0.05 without controlling for multiplicity.

Both randomisation tests and model-based procedures were used to generate hypothesis tests as well as point and interval effect size estimates for the study outcomes. For the primary clinical outcome, a two-stage, cluster-level analysis proposed by Gail et al. as analogue of a randomisation test was used to test the hypothesis that the risk of the composite mortality and morbidity outcome as well as the individual components of that outcome differed by treatment arm.[30] Point and interval estimates for these outcomes were obtained from a log-binomial model that analysed data at the individual level with terms for treatment and stratification factors using generalised estimating equations (GEE) to control for correlation within clusters. The hypothesis that the number of ANC visits differed by treatment arm was tested using an extension of the proportional odds model that again used GEE to control for correlation within clusters. An extension of the log-binomial model using GEE was used to test whether the probability of the outcomes of four or more ANC visits and delivery of complicated pregnancies at appropriate facilities differed by treatment arm and to generate point and interval estimates of the relative risk of these outcomes.

All data were collected and entered at each study site; edits were reviewed at each site using both hand-held and secure computer systems. Data were transmitted using a secure system to the central data coordinating centre (RTI International) where additional data edits were performed; queries were resolved locally.

The trial sample size assumed a composite outcome baseline rate of at least 80 events per 1000 pregnancies with current care in the trial clusters, based on the most recent years' Global Network perinatal mortality rates.[21,24] Sample size estimates assumed a target reduction of 25% in the composite outcome with 80% power and alpha at 0.05, and an intracluster correlation (ICC) of 0.005, also consistent with historic Global Network data. With these assumptions, 58 clusters were required to detect a 25% reduction in the composite outcome in the intervention compared to the control clusters.

The Data Monitoring Committee appointed by National Institute of Child Health and Human Development (NICHD) reviewed the trial progress at bi-annual meetings throughout the trial. This trial is registered at clinicaltrials.gov (NCT01990625).

Ethical approvals

The ethics review committees of all implementing sites (Aga Khan University, Pakistan, Moi University, Kenya, Universidad Francisco Marroquin, Guatemala, University of Zambia, Zambia, and Kinshasa School of Public Health, DRC), the institutional review boards at the central investigators' institutions at Columbia University, University of Washington, and RTI International reviewed and approved for the study. Each participant provided informed consent prior to study participation.

Support

This trial was funded by grants from the Bill & Melinda Gates Foundation and the *Eunice Kennedy Shriver* National Institute of Child Health. The ultrasound equipment was supplied by GE Healthcare. The funders had no input into the data analyses.

Results

The trial was initiated in July 2014, and enrolment was completed in May 2016 (exact dates varied by site). Across all sites, 49 001 women were screened for study, 48 469 consented, 46 904 women delivered, and 46 768 mothers and 47 297 infants had the 42-day visit. The eligibility and lost-to-follow-up rates were similar between the intervention and control study groups. Figure S1 displays the screening and study eligibility. Guatemala had the largest number of clusters and the largest enrolment, while the DRC had the smallest number of clusters and the lowest enrolment. The larger number of women in the intervention group in Zambia is explained by one intervention cluster having a much larger number of deliveries than the others.

Table 1 provides characteristics of women in the intervention and control groups. No important differences in the characteristic between women in the intervention and control clusters were noted.

Of the 24 008 women who delivered in an intervention cluster, 18 640 (77.6%) received at least one study ultrasound examination and of these and 12 681 (68.0%) received two or more examinations. Our goal was to provide US examinations in two windows, first at 16–22 weeks and then at 32–36 weeks. Overall, first examinations were frequently performed after the 16- to 22-week window, while most second examinations were performed within

Table 1. First Look study: maternal characteristics by treatment group

	Intervention	Control
Women, *N*	24 008	22 896
Maternal age (years), *N* (%)		
<20	4306 (17.9)	4188 (18.3)
20–35	17 921 (74.7)	16 977 (74.2)
>35	1764 (7.4)	1723 (7.5)
Maternal education level, *N* (%)		
No formal schooling/illiterate	5010 (20.9)	4836 (21.1)
No formal schooling/literate	389 (1.6)	294 (1.3)
Primary	7059 (29.4)	7235 (31.6)
Secondary	10 559 (44.0)	9486 (41.4)
University	979 (4.1)	1040 (4.5)
Parity, *N* (%)		
0	5966 (25.3)	5988 (26.6)
1	5366 (22.8)	4960 (22.1)
2+	12 215 (51.9)	11 532 (51.3)

the 32- to 36-week window. Figure S2 summarises the gestational age distribution of the study examinations.

In addition to the study US examination, based on a question asked by the MNHR after delivery, 95% of the intervention group and 43% of the control group received an US during pregnancy. The use of US among women residing in the control clusters varied substantially by site, representing 95% of Pakistani, 75% of Guatemalan, and <5% of the African participants (data not shown). An informal survey performed at each site suggested that many of the nonstudy examinations occurred in hospital at the time of delivery or, if performed prior to delivery, were performed to learn when the baby was due or to determine the sex of the baby.

Findings on study US were generally within the expected ranges: multiple gestation (1.3%), fetal growth restriction (5.0%), oligohydramnios (0.9%), and polyhydramnios (1.1%). Because several findings are gestational age-dependent, we present the prevalence of placenta previa only on

Table 2. First Look study: antenatal and obstetric care by treatment group

	Intervention	Control	RR (95% CI)	*P*-value
All women, *N*	24 008	22 896		
Antenatal care utilisation, *n*/*N* (%)				
Antenatal care utilisation ≥4 visits, *n* (%)	12 021 (50.1)	10 866 (47.5)	1.03 (0.90, 1.17)	0.6376*
Delivery location, *n* (%)				
Hospital, any	8580 (35.8)	7768 (33.9)		0.4261**
Clinic, any	7936 (33.1)	7966 (34.8)		
Home/Other	7483 (31.2)	7152 (31.3)		
Delivery at facility with CS, *n*/*N* (%)	8098 (33.7)	7289 (31.8)	1.04 (0.86, 1.26)	
Delivery mode, *n* (%)				0.4280**
CS	2919 (12.2)	2808 (12.3)		
Assisted (forceps)	45 (0.2)	31 (0.1)		
Vaginal	20 998 (87.6)	20 015 (87.6)		
Complicated deliveries				
Complicated deliveries, *n*/*N* (%)	6152/24 008 (25.6)	5528/22 896 (24.1)	1.10 (1.02, 1.18)***	
ANC ≥ 4 visits	2986 (50.8)	2661 (50.7)	1.00 (0.88, 1.12)***	
Delivery location, *n* (%)				
Hospital, any	2682 (45.6)	2404 (45.8)		0.1694
Clinic, any	1433 (24.4)	1247 (23.7)		
Home/Other	1766 (30.0)	1602 (30.5)		
Delivered in a hospital with CS, *n*/*N* (%)	2569/6152 (41.8)	2252/5528 (40.7)	1.03 (0.89, 1.20)***	0.6841****
Delivery mode, *n* (%)				
CS	1199 (19.5)	1204 (21.8)		0.9747****
Assisted (forceps or vacuum)	17 (0.3)	14 (0.3)		
Vaginal	4933 (80.2)	4307 (78.0)		

CS, caesarean section capabilities.
**P*-value from a t test described by Gail
***P*-value from a generalised logit model adjusting for treatment and strata with generalised estimating equations
****Relative risks from a log-binomial model adjusting for treatment and strata with generalised estimating equations to control for cluster-level effects.
*****P*-value from a log-binomial model adjusting for treatment and strata with generalised estimating equations to control for cluster-level effects.

examinations at 28 weeks or more (0.3%) and abnormal lies at 32 weeks or more (5.6%). 9.3% of women were referred at least once for an US-diagnosed condition; 71.1% attended the referral (data not shown).

One of our hypotheses was that the ANC rates would be higher in the intervention clusters compared to the control clusters (Table 2). However, the number of visits (*P*-value 0.78), the number of women with any ANC visit (RR 1.0, 95% CI 1.00, 1.01), and four or more ANC visits (RR 1.03, 95% CI 0.90, 1.17) were not found to differ between groups. There was a small increase in the percent of women with complications noted in the intervention clusters (25.4% vs 24.0%); however, no statistically significant differences were observed between the intervention and control clusters in the percent of women with complications delivering in a hospital with caesarean section capability (RR 1.03, 95% CI 0.89, 1.20). There were also no significant differences in the type of providers or in the rate of all women delivering in a health facility.

Table 3 presents the composite outcome (RR 1.09, 95% CI 0.97, 1.23) and the individual components of the composite outcome in the intervention and control clusters. There were no statistically significant differences in any outcome between the two groups.

Table 4 shows the composite outcomes, use of ANC, and hospital delivery for complicated pregnancies by site. There was not a significant difference in the composite primary outcome, ANC utilisation, nor hospital delivery for complicated pregnancies in the intervention compared to control group at any site, although the composite outcome was greater in the treatment clusters compared to the control clusters in the Pakistan site. None of the sites had a significant difference in other measures of ANC or hospital delivery between the groups.

Discussion

Main findings

US-naïve providers were successfully trained to conduct basic obstetric US examinations.[23] However, the routine use of US during ANC did not increase women's use of ANC and the rate of hospital births for women with complications, nor did it improve the composite outcome of maternal, fetal and neonatal mortality, and near-miss maternal mortality, nor any of the individual components. These LMIC results confirm Cochrane reviews of the impact of routine use of US during ANC in HIC.[7–10]

It is important to emphasise what we did and did not study. We studied the provision of two routine basic US examinations during ANC with the earliest examinations at 16 weeks coupled with referrals to a hospital for certain obstetric conditions. We did not study the benefit of first

Table 3. First Look study: composite mortality and near-miss maternal mortality by treatment group

	Intervention	Control	RR (95% CI)*	*P*-value**	ICC
Composite outcome of maternal mortality, near-miss, stillbirth, and neonatal mortality, *n/N* (%)	2097/23 925 (8.8)	1905/22 854 (8.3)	1.09 (0.97, 1.23)	0.1803	
Secondary outcomes					
Stillbirth rate, *n/N* (rate/1000)	675/24 254 (27.8)	628/23 149 (27.1)	1.08 (0.94, 1.24)	0.2268	0.009281
Intrapartum (nonmacerated) stillbirth rate, *n/N* (rate/1000)	470/24 049 (19.5)	415/22 936 (18.1)	1.16 (0.95, 1.41)	0.1333	0.006772
Neonatal mortality <28 days, *n/N* (rate/1000)	546/23 495 (23.2)	543/22 479 (24.2)	0.99 (0.86, 1.14)	0.9462	0.007636
Maternal near-miss <42 days, *n/N* (rate/1000)	1160/23 924 (48.5)	1028/22 850 (45.0)	1.11 (0.90, 1.37)	0.3786	0.02581
Maternal mortality <42 days, *n/N* (rate/1000)	28/23 923 (117)	29/22 845 (127)	–	0.6814	0.0009625
Neonatal mortality <28 days by birthweight, *n/N* (rate/1000)					
<1500 g	119/184 (646.7)	99/153 (647.1)	1.01 (0.91, 1.13)		0.04786
1500–2499 g	196/2676 (73.2)	188/2731 (68.8)	1.02 (0.83, 1.26)		0.009464
≥ 2500 g	231/20 635 (11.2)	255/19 594 (13.0)	0.89 (0.73, 1.09)		0.003947
Outcomes of interest					
Obstructed or prolonged labour, *n* (%)	1054/23 998 (4.4)	931/22 885 (4.1)	1.10 (0.93, 1.31)		0.02544
Low birthweight (<2500 g), *n* (%)	3223/24 201 (13.3)	3223/23 111 (13.9)	1.01 (0.90, 1.13)		0.06243
Postpartum haemorrhage, *n* (%)	327/21 143 (1.5)	250/20 671 (1.2)	1.29 (0.93, 1.79)		0.01734

ICC, intracluster correlation

*Relative risks from a log-binomial model adjusting for treatment and strata with generalised estimating equations to control for cluster-level effects.

***P*-value from a t test described by Gail.

Table 4. First Look study outcomes by site

	Composite outcome			≥4 Antenatal care visits			Women with complicated pregnancy delivering in hospital		
	Intervention *n/N* (%)	Control *n/N* (%)	RR (95% CI)	Intervention *n/N* (%)	Control *n/N* (%)	RR (95% CI)	Intervention *n/N* (%)	Control *n/N* (%)	RR (95% CI)
DRC	156/2359 (6.6)	131/2449 (5.3)	1.26 (0.91, 1.74)	1003/2362 (42.5)	932/2453 (38.0)	1.11 (0.86, 1.42)	124/563 (22.0)	58/390 (14.9)	1.42 (0.54, 3.72)
Kenya	291/4497 (6.5)	291/4672 (6.2)	0.92 (0.53, 1.62)	2531/4502 (56.2)	2278/4670 (48.8)	1.12 (0.89, 1.41)	169/659 (25.6)	227/484 (46.9)	0.64 (0.39, 1.06)
Zambia	199/5421 (3.7)	140/3860 (3.6)	1.15 (0.54, 2.45)	2161/5485 (39.4)	1302/3883 (33.5)	0.92 (0.36, 2.31)	406/1033 (39.3)	160/726 (22.0)	1.55 (0.78, 3.10)
Guatemala	748/7930 (9.4)	787/8345 (9.4)	1.01 (0.93, 1.10)	4664/7993 (58.8)	4983/8353 (59.7)	0.96 (0.86, 1.08)	1500/2607 (57.5)	1590/2851 (55.8)	1.03 (0.92, 1.17)
Pakistan	703/3718 (18.9)	556/3528 (15.8)	1.20 (1.06, 1.38)	1662/3772 (44.7)	1371/3572 (38.9)	1.17 (0.79, 1.71)	370/1290 (28.7)	217/1077 (20.1)	1.55 (0.63, 3.79)

trimester examinations, either routine or for complications of miscarriages, abortions, or ectopic pregnancy. We also did not study the benefit of examinations performed at any other time in pregnancy and especially for complications at the time of labour and delivery. We also did not study the potential psychological benefit of US to women or whether US enhanced bonding with their infants. Furthermore, although some training on improving in-hospital obstetric and neonatal care was provided to hospitals involved in the study, no attempt was made to evaluate the quality of hospital care.

Strengths and limitations

The strengths of our study included its cluster randomised design, large sample size across multiple regions, consistent results across regions, and use of staff to collect outcome data who were independent of study implementation staff. We note that this is among the first if not the only trial in LMIC which has sufficient sample size to allow detection of a potential reduction in mortality or morbidity.

Because this trial was conducted in regions where perinatal research has been ongoing, it raised the issue of generalisability of results. We also found a substantial use of USA in control clusters outside of the health centres in two of our sites that may have decreased the impact of the intervention. However, because we did not find meaningful site differences in outcomes, even in regions with little US utilisation in control clusters, this is unlikely to explain the lack of impact.

Interpretation [in the light of other evidence]

It is important to place our study in context. Many HIC studies have assessed the value of routine US examinations during ANC and several Cochrane meta-analyses, one of which focused on routine ANC US examinations early in pregnancy and one on ANC US examinations later in pregnancy, all had consistent results.[7,9] In those analyses, US increased the detection of multiple pregnancy at <24 weeks, was associated with reduction in labour induction for post-term pregnancy, and provided some evidence of earlier detection of fetal abnormalities. However, routine US did not appear to reduce adverse outcomes for babies or the frequency of healthcare services use by mothers and babies. One Cochrane review concluded that introducing routine US in resource-constrained healthcare settings could place a large burden on available resources, detracting from other more beneficial services.[10]

The introduction of various interventions without proof of efficacy in achieving an important clinical outcome is not uncommon either in obstetrics or in medicine in general.[31] Adopting interventions used in high-income countries in resource-limited areas without proof of efficacy in those locations also occurs frequently.[31] Many of these interventions are diagnostic in nature and while their

ability to diagnose may be apparent, without the ability to utilise that information to improve an important outcome, introducing that test into practice will not be of benefit and may lead to harm. In an extensive study carried out in the earlier days of ultrasound, Ringa et al. concluded that the value of routine US scanning to improve gestational age dating or the diagnosis of intrauterine growth restriction was demonstrated in the randomised controlled trials. However, the results of these trials of routine US use on important health effects did not give strong evidence for its use.[31] Instead, they found that the spread of US scanning was based mainly on evaluative surveys which assessed its diagnostic value. We believe that only when US or any other technology can be shown to improve health outcomes, should it be introduced into clinical care.

Conclusions

In conclusion, this large study, one of the first in LMIC to evaluate the relationship between routine US examinations during ANC and important pregnancy outcomes, found no increase in ANC utilisation, hospital delivery for women with pregnancy complications, or reduction in maternal mortality, near-miss maternal mortality, stillbirth, or neonatal mortality. These results from LMIC confirm the prior studies of routine US use during ANC on pregnancy outcomes in HIC.[7–10] These results do not necessarily relate to the value of US to influence pregnancy management during the first trimester, labour, and delivery or to its value for gestational age dating in research projects on preterm birth or fetal growth restriction. We conclude that without improvement in the quality of care at health facilities in LMIC, there appears to be limited impact of routine ANC use of US alone. A systems-based approach focusing on the quality of facility care will likely be needed to reduce maternal mortality, stillbirth, and neonatal mortality in LMIC.

Disclosure of interests

None declared. Completed disclosure of interests form available to view online as supporting information.

Contribution to authorship

RLG and EMM wrote the first draft of the report with input from RON, JS, DS, DDW, MSH, MKT, MM, CLB, WAC, and ALG. RLG, EMM, RON, JS, and DS developed the protocol with input from DDW, ALG, HF, CLB, AT, AL, EC, WAC, NFK, KMH, EAL, FE, WM, MKT, and SS. AT, AL, EC, MM, WAC, ALG, NFK, KMH, FE, LF, EAL, DM, FN, ISP, WM, NK, FN, WLG, HF, and SS oversaw the field implementation of the study and monitoring. WM, NK, WLG, DH, VLB, RON, FN, ISP, DS, MC, MM, and JS oversaw implementation and quality monitoring of the ultrasound intervention. JM, DDW, and EMM performed the trial data analyses. All authors reviewed and approved the final manuscript.

Details of ethics approval

This trial was reviewed and approved by the institutional review committee at Columbia University (FWA00002636; New York, NY) (approved 9/30/2013); RTI International (FWA00003331 Durham, NC) (approved 7/19/2013); and the ethics review committees at Aga Khan University (FWA00001177; Karachi Pakistan) (approved 8/7/14), Kinshasa School of Public Health (FWA000003581 Kinshasa, DRC) (approved 2/13/14), Universidad Francisco Marroquin Facultad de Medicina (FWA000003581 Guatemala City, Guatemala) (approved 12/06/13), Moi University (FWA000003128; Eldoret, Kenya) (approved 6/10/14), and the University of Zambia (FWA00000338; Lusaka, Zambia) (approved 2/13/14).

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. CONSORT Diagram of trial enrolment.

Figure S2. Gestational age at study ultrasound examination. ■

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