Increased Antenatal Visits and Deliveries Attended by Skilled Health Care Providers Following the Introduction of Antenatal Ultrasound in Rural Uganda

By

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CERTIFICATE OF APPROVAL

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Introduction

Background

In the year 2000, 189 member states came together to sign the United Nations Millennium Declaration, a road map of ambitious goals to address the many faces of poverty widely prevalent in the world's developing nations. Improving maternal health became Millennium Development Goal 5 (MDG 5) with a focus on decreasing maternal mortality and increasing access to family planning[1]. The World Health Organization defines maternal mortality as the death of a woman while pregnant or within 42 days of termination of pregnancy. This is tracked by the indicator of maternal mortality ratio (MMR) which is the number of maternal deaths per 100,000 live births. Two targets were selected to monitor progress towards MDG 5: the maternal mortality ratio with a goal of reducing MMR by 75% between 1990 and 2015 and increasing the proportion of births attended by skilled health care personnel with a goal of a 90% increase by 2015.

Maternal mortality has been a priority of the global health community for many years, certainly pre-dating the Millennium conference, with such committed initiatives as the Safe Motherhood Initiative of 1987. More recently the launch of the UN's Global Strategy for Women's and Children's Health in 2010 and the Obama administration's Global Health Initiative have continued the effort to make progress towards MDG 5.

Despite this global effort, concern has been expressed over the feasibility of achieving the Millennium Development Goals, including MDG 5, by the 2015 target[2-4]. The challenges identified are numerous and varied, and include inadequate health care systems, low numbers of skilled birth attendants, high fertility rates, and low levels of education. These problems are most acute in the rural areas of the developing world leading to staggering inequities in the burden of maternal death. For example, in 2005 MMR in sub-Saharan Africa was estimated at 905 (453-1480, 95% CI), an astonishing 100 times the estimate of MMR for developed countries in the same year[5]. The wide confidence interval reflects the difficulty in obtaining accurate data but do not dilute the magnitude of the disparity. The need for continued investigation into effective interventions is acute.

Skilled health care during pregnancy and delivery, a key strategy to reduce MMR

A strategy which has shown consistent promise in reducing MMR is attendance at birth by skilled health care personnel[6,7]. This number has been easier to track than MMR and is used as a proxy indicator in marking progress toward MDG 5. Skilled care during the antenatal, peri-partum, and post-partum period is an explicit priority of the global health community, with all countries asked to ensure access to such care in a joint statement from the WHO, UNFPA, UNICEF, and World Bank[8]. The majority of maternal deaths occur in the intrapartum period and many of these cannot be anticipated[3]. The presence of a skilled birth attendant working within a health care system that provides an avenue for referral and management of obstetric emergencies allows for early detection and treatment of unanticipated complications. A skilled birth attendant working within an appropriate health care system with access to basic drugs, equipment, and supplies can often successfully manage the most common causes of peripartum maternal death, listed in descending order by the World Health Organization as hemorrhage, sepsis, unsafe abortion, eclampsia, and obstructed labor[9]. Current evidence suggests that as countries increase the availability of skilled birth attendance, maternal mortality will decline, and this has been shown to be a more successful strategy than relying on the training of traditional birth attendants[10,11]. Policies to increase the number of deliveries attended by skill birth attendants remain an important focus of international efforts to decrease the MMR[12].

The efficacy of prenatal care in reducing maternal mortality has been and continues to be controversial[13] but remains an important component of efforts to decrease both maternal mortality and perinatal death, particularly in the developing world. Prenatal visits allow opportunities for maternal education regarding safe birthing and home care practices including umbilical stump hygiene, lactation practices, and the types of circumstances when mothers should seek skilled medical care outside the home or village environment. In sub-Saharan Africa, HIV, parasites, and anemia are common co-morbidities in pregnancy. Prenatal visits also allow opportunities for screening and appropriate treatment of a variety of co-morbid conditions, decreasing maternal mortality, and in the case of HIV, actions to reduce vertical transmission of the virus to the newborn. Developing relationships with pregnant women during prenatal visits may also increase the likelihood of having a skilled birth attendant present at delivery. Practical strategies to encourage prenatal visits and skilled care at delivery remain an important area of investigation to inform international health policy efforts.

Uganda health overview

Uganda is a country of approximately 31.7 million people with a high birth rate, exceeding the average for sub-Saharan Africa with an annual population growth of 3.4%[14]. Like most of sub-Saharan Africa, Uganda has a high burden of maternal mortality. (See table 1). Although overall there has been increasing availability to health care over the last decade–in 2010 72% of the population lived within 5 km of a health care facility compared with 49% in 2000[14]–access to skilled maternal care remains split with the poor and those living in rural areas significantly less likely to have access to health care resources[14]. Maternal mortality ratio has decreased over the last 20 years from 600 per 100,000 live births in 1990 to 310 in 2010. Nonetheless this remains unacceptably high with woman facing a 1 in 49 lifetime risk of dying during childbirth. In the United States the lifetime risk is 1 in 2,400.

Public health efforts in Uganda have focused on increasing attendance at delivery by a skilled health care provider, frequently a nurse midwife. Many of these providers are trained in the Active Management of the Third Stage of Labor program, a set of recommendations to prevent postpartum hemorrhage which remains the leading cause of maternal mortality resulting in 36% of deaths. Particularly in the rural areas of Uganda simply encouraging women to give birth with a trained and skilled birth attendant remains a challenge, with the overall percentage of attended births having only increased slightly from 38% in 1989 to 42% in 2006, and with women in the top quintile of household income more than twice as likely to have a skilled provider present at delivery than women in the bottom quintile.

Nawanyago is a small village in Eastern Uganda, approximately 125 kilometers away from the capital, with a population of approximately 21,000. Health care resources in this rural area are limited. Women typically give birth at home attended by a traditional birth attendant, as is common in much of the developing world. A small community health care center is located in Nawanyago with a district hospital capable of providing emergency obstetric care in Kamuli, 35 kilometers to the south. Efforts to provide avenues for rural women to access skilled maternity care, both at the local health care center and at the district hospital, have encountered challenges. Local women may have few resources for transportation or payment, may be intimidated by the prospect of coming to an urban center, and may be influenced by traditional views of pregnancy and delivery[15].

Ultrasound and the "Imaging the World" program

In June of 2010 a program was put in place to provide access to basic antenatal ultrasound at the Nawanyago community health care center. This program was co-founded by Dr. DeStigter, residency program director and vice-chair of radiology at University of Vermont and Dr. Garra, associate professor in radiology formerly of University of Vermont, now in the Department of Radiology at the Veterans Affairs Hospital in Washington, D.C. Initially implemented at the Nawanyago clinic, the program has been expanded to several other rural clinic sites in Uganda with eventual plans for deployment in other countries and is now named "Imaging the World."

Historically, implementing ultrasound in a rural environment faces numerous obstacles. The hardware and personnel requirements are considerable. A standard, full-sized ultrasound machine may cost over $100,000, requires a stable power supply, protection from dust and moisture, and cannot be easily transported from clinic to clinic or even up a flight of stairs. Training a sonographer to capture diagnostic quality images is typically a two-year full-time endeavor. A trained radiologist or obstetrician who can interpret the images represents an even greater training commitment. Implementing this type of prenatal ultrasound program in a resource constrained environment has previously not been considered cost effective. However, as ultrasound technology has improved with more affordable and portable systems available, implementation in developing countries has become more feasible[16]. Portable ultrasound units are now available that are the size of a laptop computer. A rechargeable battery system enables use in an area where the power supply is unreliable and can also be charged from solar power. These portable units are becoming increasingly affordable and are easily transported, simplifying delivery to the clinic, transport between clinics, and if needed, removal for repair.

The Imaging the World ultrasound program relies on several additional technologies and training innovations. To address the difficulty with finding trained sonographers in low resource settings, scanning protocols have been developed which use surface anatomy landmarks and volumetric scanning. The ultrasound probe is passed across the patient's abdomen in several prescribed sweeps and a series of static images are collected which can be scrolled through by the reviewer like a short video. An initial feasibility study has confirmed that the obtained images are of diagnostic quality[17]. The advantage of such a system is that a person can learn to successfully master the protocols in a few days of training. The acquired images are then stored locally on a laptop computer before being compressed and transmitted digitally via cell phone modem to a remote internet server where they can then be accessed by a credentialed reviewer for interpretation. An abbreviated report of the findings is sent via SMS to the nurse midwife's cell phone, and the full report is sent by email. Cell phones are ubiquitous in Uganda and coverage is widely available, allowing for the transmission of images and receipt of reports even in remote rural areas. The full program methodology has been previously reported[18].

Previous research on ultrasound during pregnancy

The vast majority of previous investigation into the use of routine antenatal ultrasound has taken place in populations in the developed world where full size ultrasound machines are used by trained sonographers to acquire detailed fetal surveys to identify congenital anomalies along with other detectable complications of pregnancy. The images are interpreted by radiologists and obstetricians and access to the necessary follow-up is typically available. This type of high cost program has been found to be unfeasible in the low resource setting. Work by Geerts et al. drawing on a mix of high risk urban and rural patients at a hospital in South Africa demonstrated only a small benefit; specifically fewer women were induced for post-dates delayed labor with the more accurate pregnancy dating afforded by ultrasound[19]. This small benefit was not felt to be worth the large cost of the program. Van Dyk et al. reached similar conclusions in a more recent study also based in South Africa[20]. The findings are limited by a high percentage of study participants lost to follow up but found no benefit on rates of miscarriage, perinatal death, prenatal hospitalization, or low birth weight. The number of study participants did not provide adequate statistical power to examine maternal mortality. Other maternal outcomes such as the development of rectovaginal fistula–a prevalent and debilitating problem in the developing world–were not reported.

Numerous studies based in more affluent areas of the developing world have also shown mixed benefit for the routine use of antenatal ultrasound. The RADIUS study group reported no benefit on perinatal outcome for the use of routine screening ultrasound, although the control group in this instance received an average of 0.6 scans per pregnancy, instigated at the judgement of the clinician rather than as a routine screen[21]. A more recent Cochrane review aggregated results from 11 trials with over 37,000 women and found a similar pattern of increased detection of multiple gestations prior to 24 weeks, decreased number of inductions for post-dates, but no significant benefit on perinatal outcome[22]. Maternal deaths are so rare in the developed world that even an aggregated meta-analysis does not accrue enough data to accurately assess this outcome.

The acceptability of ultrasound to mothers in low resource settings has been evaluated in a few studies. Rijken et al. found that women on the Thai-Burmese border were likely to view ultrasound favorably as a technology which could increase safety during pregnancy and delivery[23]. Offsetting the potential benefits is concern for overuse of ultrasound scanning during pregnancy with multiple follow up scans recommended, potentially as a way for private clinics to increase revenue[24,25]. Clearly the introduction of antenatal ultrasound scanning into a low resource and ultrasound naive setting must be done cautiously.

In summary, although previous research on antenatal ultrasound has shown only a small benefit with questionable cost-effectiveness, these studies have mostly taken place in developed countries and–even when done in a low resource setting–have looked at high-cost, comprehensive ultrasound screening programs. There is a need for research into the use of low-cost ultrasound programs focused on identifying high risk conditions of pregnancy as an early warning system to allow for appropriate triage and referral of patients at greatest risk for a poor outcome.

Area of investigation

Important differences exist between the bulk of the previous research on antenatal ultrasound and the environment in Nawanyago. Studies in developed countries assess a population of women that is already receiving highly skilled care at pregnancy and delivery with easy access to emergency obstetric services including surgical delivery. Even the limited studies done in more resource constrained environments–although they draw on a mixed rural and urban population–are based at referral hospitals where women can access these types of emergency obstetric services. The cost-benefit analyses have also been based on the expense of full-sized equipment operated by trained sonographers. At Nawanyago and thousands of similar rural health care clinics, skilled midwives are available but higher level emergency obstetric services require referral to a regional hospital which may be hours away. Early detection of high risk pregnancies in this environment is critical. Additionally the cost-benefit equation may shift in the context of low-cost equipment and decreased training requirements for personnel.

Ultrasound can diagnose many of the most common causes of maternal and neonatal mortality including multiple gestations, sequelae of abortion, causes of obstructed labour, and specific causes of maternal hemorrhage such as placenta previa[9], and this is the focus of the Imaging the World program. The implemented scanning protocols allow for reliable identification of fetal presentation and number and placental position. Early identification of high risk pregnancies allows for timely referral to the district hospital in Kamuli for a higher level of obstetric care. Previous authors have stated the importance of well designed longitudinal studies to directly assess the effect of ultrasound on maternal mortality in low resource settings[16]. Whether access to antenatal ultrasound in this rural environment will lead to improved maternal health outcomes is the subject of ongoing, prospective investigative effort at the Nawanyago site and at other sites as the Imaging the World Program is more widely implemented. There is also a need to examine the broader context of introducing a prenatal ultrasound program into a resource constrained environment.

A consensus framework for evaluating the use of technology in developing countries has previously been proposed with these parameters: impact on improving health, appropriateness and cultural acceptability, feasibility, decreasing the knowledge gap, and the provision of other indirect benefits to the community[26]. To succeed, a technology must not only be effective but also acceptable to the traditions and attitudes of the local communities. Whether the addition of ultrasound scanning to prenatal visits at the health center would encourage or discourage potential patients was an unknown question of critical interest. Data is routinely collected at health care clinics regarding the number of antenatal clinic visits (ANCs) and deliveries. This allows analysis of trends in ANCs and deliveries at the clinic to confirm or refute the anecdotal impression that overall visits increased after the introduction of the ultrasound program. An additional, secondary analysis is performed to analyze the number of women tested and treated for common co-morbidities of pregnancy, including deworming for parasites, intermittent preventive treatment (IPT) for malaria, HIV testing, and prophylactic folate and iron administration for pregnancy related anemia.

Treatment of co-morbidities in pregnancy

An important component of prenatal visits in any context is testing for and treating pregnancy co-morbidities that can impact maternal and fetal health. Some of these conditions such as parasitic infection and malaria, are unique to tropical areas of the world. Others such as anemia and HIV, are more prevalent in sub-Saharan Africa than in the developed world. This heightens the importance of high quality prenatal visits in rural sub-Saharan Africa and, indeed, treatment of these co-morbidities has been shown to be of benefit[27-30].

Malaria is a leading overall cause of mortality and morbidity in Uganda with a disproportionate impact on pregnant women and children less than five years old[31]. Because of changes in the immune system during pregnancy, women living in malaria endemic areas lose some of their immunity to local malarial strains. Malarial infection during pregnancy contributes to maternal anemia and results in a higher proportion of low birth weight babies. Strategies to combat maternal malarial infection include the use of insecticide treated bed nets and presumptive treatment with anti-malarial drugs during pregnancy–Intermittent Preventative Treatment (IPT)–regardless of whether the woman shows clinical symptoms or tests positive for the *plasmodium* parasite. ANCs provide a venue for administration of IPT and distribution of bed nets. IPT during pregnancy has been demonstrated to be a cost-effective way to reduce maternal and neonatal mortality and morbidity[32].

The prevalence of HIV in Uganda has fallen since its peak in the early 1990s when it was estimated that nearly ten percent of the population was infected with the virus. Nonetheless, prevalence remains high, particularly compared to Western countries and prevention of vertical transmission is a high priority[33]. Routine counseling and testing for HIV at ANCs is recommended. Treatment of HIV positive mothers dramatically reduces the chances of vertical transmission to the child[34].

Presumptive treatment for parasites with albendazole has not been as comprehensively studied as malaria and HIV treatment, but there are many indications that this may provide benefit for both mother and child. Helminth infection during pregnancy contributes to maternal anemia and may reduce available micronutrients with anorexia, vomiting, and diarrhea common during infection[35]. Maternal anemia is strongly linked with low birth weight, impaired cognitive development, and other long term health outcomes for the child[36]. Deworming treatment is recommended empirically in endemic areas, as is supplementation with iron and folate to replete maternal iron stores[37,38].

Antenatal interventions at Nawanyago

At the Nawanyago clinic, guidelines dictate that at each antenatal visit women will be provided with folate and iron for prevention of anemia and–in the case of folate–decreased neural tube defects. Additionally serum hemoglobin is measured and if less than ll mg/dL more aggressive iron supplementation is recommended. Albendazole is distributed empirically for deworming. HIV tests are performed. If positive, women are offered antiretroviral therapy and counseled to receive treatment to prevent vertical transmission of the virus to the child. Over the course of a pregnancy, women are treated twice with doses of IPT for malaria using sulfadoxine/pyrimethamine concordant with international guidelines. Blood pressure is monitored and the tetanus vaccine offered, although these data points are not measured in this study.

These services are received inconsistently at antenatal visits both at Nawanyago and elsewhere in Uganda. A community based survey in Entebbe, Uganda showed women reported high rates of blood pressure monitoring and tetanus vaccination at 95% and 91% respectively, but IPT (66%), deworming (58%), and HIV testing (47%) were the least reported interventions[39]. The current study evaluates trends in the proportion of women at ANCs who are tested and treated for anemia, HIV, malaria and parasites. Improving the quality of antenatal visits is an important avenue for improving health outcomes in this environment.

Methods

The study design was a historically-controlled retrospective analysis with the primary endpoints being the number of antenatal visits and the number of deliveries at Nawanyago HC III before and after the introduction of the antenatal ultrasound screening program. Secondary endpoints included the proportion of women who presented for an ANC who received IPT dose 1 and 2; received iron and folate supplementation; were tested for HIV; and who received empiric deworming treatment. Data for all variables was available in the form of counts aggregated by month. Records at the clinic were reviewed for the period of January 2007 through March 2012 to obtain the relevant data including the number of births and antenatal visits at the clinic per month for the 41 months preceding the introduction of the ultrasound program and for the 22 months following. Data for the secondary endpoints was available only for 22 months prior to the intervention and 21 months following. Data for IPT1 and IPT2 were only available for 11 and 8 months prior to the intervention, respectively. All clinic records were subsequently audited by an independent research associate from the Makerere University School of Public Health in Kampala and found to be concordant with the numbers provided to the research team by clinic staff. Antenatal visits were analyzed both in total and by each visit category (first time visit through fourth return visit).

Ethics statement

IRB approval was obtained from the Mengo Hospital research review committee, (IRB title Evaluation of Simple Ultrasound Protocols for Improving Access to Ultrasound in Low Resource Settings, study number 013/05-10). Written informed consent was obtained from all study participants with appropriate translation resources provided as necessary. The consent form and process were approved by the IRB. Data were coded anonymously for analysis. For ethical reasons, fetal gender determination is not performed and the program is periodically audited to ensure compliance with this requirement.

Statistical analysis

Statistical analysis was carried out using Stata v11 (Statacorp 2009). Primary and secondary outcome variables were characterized with descriptive statistics which is summarized in table and graphical format. The number of ANCs was examined separately by number of visit (first time visit through fourth return visit) and as the total number of ANC visits. As these data represent counts collected over time (monthly), the outcome variables were initially modeled as a Poisson distribution. The Poisson model for each outcome variable was then assessed for evidence of over-dispersion, with observed variation of at least 20% greater than expected from a Poisson model being evidence of this extra variation. All of the primary and secondary outcome variables greatly exceeded this threshold with the variance significantly exceeding the mean (summarized in table 6). Thus a negative binomial distribution was selected as the most appropriate distribution for analysis[40,41]. The negative binomial distribution model was assessed for evidence of autocorrelation for each of the outcome variables to the lag-1 level using a Box-Jenkins test applied to the Pearson residuals. No evidence of autocorrelation was found to the lag-1 level for any of the variables to an alpha of 0.15 (summarized in table 7). The secondary outcome variables are all treatments offered at ANC visits. Thus if they were being consistently provided at every ANC visit, they should track perfectly with the ANC numbers and a separate analysis would be unnecessary. However these are inconsistently provided at ANCs and the average number of women receiving these recommended treatments per ANC visit was also an area of investigative interest. These outcomes were also analyzed as over-dispersed count data using a negative binomial distribution but with total number of ANC visits included as an offset variable. Specifically, the number of total ANC visits was used as an exposure variable to capture the varying opportunities for these treatments to be provided as ANC numbers changed month to month. All Stata code used in the analysis can be found in the Appendix

Results

Summary statistics for the primary and secondary outcome variables over the course of the study period are summarized in table 2 and figures 1-2. It can be seen that the variation for all of the primary and secondary outcome variables is considerable month to month. Another trend worth noting is that the number of women returning for each subsequent ANC visit declined rapidly with an estimated 95.19 (88.96-101.42, 95% CI) women coming on average each month for a first time ANC visits and only a monthly mean of 9.41 (7.37-11.45, 95% CI) women coming for their fourth return visit. This trend was observed both pre and post ultrasound program.

Statistically significant increases were seen in the monthly mean number of deliveries and ANC visits of all categories following the introduction of the antenatal ultrasound program at Nawanyago. This is summarized in figures and tables 3-4. The mean number of monthly deliveries at the clinic prior to ultrasound was 28.39 (26.59 - 30.31, 95% CI) which increased by 59.73% (44.70% - 76.32%, 95% CI) to a post-ultrasound program mean of 45.35 (42.12 - 48.83). All categories of ANC visits showed statistically significant increases in monthly mean following the introduction of ultrasound as summarized in table 3 with the greatest relative increase shown for fourth return ANC visits which increased from 4.14 (3.53 - 4.88, 95% CI) to 19.23 (16.95 - 21.81, 95% CI), a relative increase of 363.72% (77.67 - 469.37, 95% CI).

Prior to the introduction of ultrasound, the most frequently received prenatal treatment was prophylactic treatment for anemia with the receipt of folate and iron, a treatment which was received by an average 80.1 women per 100 ANC visits (74.71 -85.82, 95% CI) of ANC visits. This was followed closely by HIV testing, received by an average of 79.9 women per 100 ANC visits (71.5 - 89.2, 95% CI) of clinic visits and then by first dose of IPT for malaria [50.4 (43.3 - 58.7, 95% CI)], presumptive administration of deworming therapy [48.5 (45.0 - 52.2, 95% CI)], and finally second dose of IPT for malaria received by an average of 20.6 (15.1 - 28.0, 95% CI) of ANC visits. Two of these treatments showed a statistically significant ($p<0.001$) increase in the proportion of women receiving them at ANC visits. Specifically the proportion of women receiving deworming treatment increased by 21.72% (10.23% - 34.41%, 95% CI) to 59.00% (55.18% - 63.08%, 95% CI) and the proportion of women receiving supplementation for anemia increased by 22.60% (11.38% - 34.95%, 95% CI) to 98.17% (91.87% - 100.50%, 95% CI). The proportion of women receiving HIV testing remained virtually unchanged ($p=0.73$), whereas the proportion of women receiving IPT 1 actually declined significantly ($p<0.001$), down 23.15% (7.52 - 38.78%, 95% CI). The proportion of women receiving IPT 2 also declined by 23.50% (from a 46.76% reduction to a 9.93% increase, 95% CI) although this did not reach statistical significance ($p=0.148$).

Discussion

These results indicate a clear increase in the number of deliveries and antenatal clinic visits performed at Nawanyago after the introduction of ultrasound. The increase is robust, well timed with the advent of ultrasound, and durable throughout the follow-up period. However careful analysis must be made of any study before sound conclusions can be drawn, and that is particularly important in a retrospective, historically controlled study where the presence of confounding must be carefully assessed. Causality can be difficult to determine in a retrospective analysis. However, randomized trials are frequently unfeasible or unethical in the realm of maternal health and cautious analysis of epidemiologic data must be undertaken instead.

Some interesting pattens were apparent during the data analysis. Not unexpectedly the number of women returning for each subsequent return ANC visit declined with only a small minority of women coming back for all four ANC visits. This trend continued after the introduction of ultrasound. The greatest relative increase was observed in the number of women coming back for a fourth return visit, an impressive 363.72% (77.67 - 469.37, 95% CI), but this still only resulted in an post-ultrasound monthly mean of 19.23 visits (16.95 - 21.81, 95% CI). ANC visits later in pregnancy may be the best time for ultrasound to identify high risk pregnancies and triage the patient to deliver in the most appropriate environment. It could be stressed that the patient should avoid delivering at home and return to the clinic, or–in more acute cases–transfer to the regional hospital in Kamuli could be arranged. It is a failing of our study that it is not recorded at what gestational date women presented for their ANC visit. A first time visit for a woman who comes only once, but late in pregnancy, would be counted as an ANC 1. This makes it harder to understand the pattern of prenatal care utilization.

Qualitative questionnaires may be the best research tool to try to explain why ultrasound attracted women to the clinic and this should be considered as part of any future study on the matter. Lacking that tool, we do have anecdotal observations made by clinic staff. One observation was that husbands were more likely to accompany their wives to prenatal visits because they enjoyed watching the ultrasound scan. This could be included as a measurable data point in a future study. Husbands are frequently the health care decision makers in Uganda[15] and it is possible that their apparent increased involvement in pregnancy care may in part explain the observed effect. Previous studies have found that women in low resource countries perceive ultrasound positively, as a chance to view the baby and receive reassurance that the pregnancy is progressing normally. They also reacted well to education on pregnancy as a part of these visits[24]. This may play an important role in attracting women to the clinic.

Prenatal care throughout pregnancy is important to maximize the chances of positive health outcomes for mother and baby, particularly in the developing world where pregnancy co-morbidities such as anemia, HIV, malaria, and parasites can be tested for and treated. The effect of ultrasound on these secondary outcome measures is harder to interpret. The data show that similar to other studies treatments are received inconsistently. Also concordant with the literature, treatment for deworming and distribution of supplemental folate and iron were the most consistently received whereas IPT, particularly the recommended second dose, were much less likely to be received by patients[39]. The changes in utilization following the introduction of ultrasound are hard to interpret. Some interventions significantly increased in prevalence: deworming treatment and anemia supplementation; the prevalence of IPT 1 significantly decreased in prevalence; and the proportion of women tested for HIV and receiving the second dose of IPT did not significantly change. The absolute numbers of all treatments increased, as would be expected given the significant increase in the number of ANCs, providing more opportunities to offer the treatments to women in the clinic. It is not clear that ultrasound directly impacted the likelihood of women presenting for ANCs to receive all recommended interventions. Improving the quality of care received at ANC visits remains an important goal.

Study limitations

It is prudent to begin with a discussion of the limitations of this study. One central assumption that must be acknowledged is that the increased numbers of women coming to the clinic for ANCs and deliveries represent women who would otherwise seek care from traditional birth attendants in the environment of their home village. If these women were being diverted from a competing, but equally adequate, clinic the importance attached to the results would decrease substantially. However in the experience of the clinic staff, the catchment area for the Nawanyago clinic is quite rural with few other competing modern health care resources. As best as can be assessed, this increase therefore represents a true increase in the number of women receiving any prenatal care or skilled assistance at delivery. An improvement in the study design—which would need to be in place prospectively—would be the addition of a questionnaire both to collect quantitative demographic information about the patients, but also to qualitatively assess their experience in seeking care during pregnancy. This could better answer the question of where they would have gone if they had not come to Nawanyago and perhaps assess whether it was the presence of the ultrasound which had attracted them.

The presence of unmeasured confounding must also be considered. A number of confounders could at least partially account for the observed increase in the outcome variables. One possibility is that the increase could represent an underlying trend influenced by external factors which could include population growth, changing political stability, improved transportation infrastructure within the region. This is felt to be less likely as the regional conditions—although difficult to measure quantitatively—were felt to be stable by clinical staff and other local experts, including the Ugandan members of the research team. More difficult to easily dismiss is whether factors associated with the introduction of ultrasound played a role in increasing the number of clinic visits.

The introduction of the ultrasound program was accompanied by a number of other changes at the clinic. This included an increase in the number of visits from outsiders, including both investigators from Kampala as well as members of the ITW program from abroad. It is possible that this contributed to the observed increase in deliveries and ANC visits. However the increase has been both durable and consistent over the follow up period and thus the occasional spike in outside visitors is felt unlikely to play a dominant role. Additionally an education program was undertaken to inform the local population about the ultrasound program. This utilized an existing health education outreach group associated with the Nawanyago clinic and already active in the region. It is not clear that the educational outreach should be considered a confounder. Certainly if ultrasound is attracting patients to the clinic, they must hear about the program from somewhere. It should also be stated that a modest fee is collected from patients in exchange for ultrasound services. Thus they are not attracted to the clinic to receive a new, free service.

It should be noted that the clinical workflow itself is not designed to gratuitously increase the number of visits. For example, if the women were asked to return on a separate day to receive the results of their scan and these return visits were counted as ANCs the increase would be easily explained and less meaningful. Also if numerous follow up scans were recommended, the increased ANCs would be less meaningful. However, the clinic adhered to the WHO recommendations of four ANCs during pregnancy, and this is the basis on which women were advised. The methodology for counting and recording ANC visits and deliveries at the clinic did not change.

Despite these assurances, the possibility of uncontrolled confounding cannot be summarily dismissed and tempers the strength of our conclusions. A prospective trial with an appropriate control site would be a better study design and may be the best, next step. A control site was sought for the current study, but other similar clinics either had their own NGO activities over this time period or did not have the relevant records available for outside review. Nonetheless the observed effect of ultrasound on the primary outcomes in this study of ANCs and deliveries at Nawanyago is plausible, strong, well timed with the advent of ultrasound, and durable throughout the follow up period. I feel that it cannot be completely explained by unmeasured confounding and is not accounted for by bias. Thus I conclude a causal link between ultrasound and the increase in ANCs and deliveries.

It is important to consider the generalizability of these findings to avoid applying conclusions too broadly. Cultural norms and attitudes regarding antenatal ultrasound may well vary considerably between countries. Generalizing the conclusions of this study to a low resource environment in the Middle-East or Asia would be potentially problematic. However, it seems fair to conclude that the study results would apply to most places and cultures with sub-Saharan Africa, a region of the world which bears a considerable burden of maternal and neonatal mortality and morbidity. It should also be noted that this study involves a unique type of ultrasound program, using low cost equipment and training local personnel to target identification of specific high risk pregnancy conditions. As mentioned in the introduction, most prior research on antenatal ultrasound in the developing world has been with a more conventional type of program. This may influence external validity of the study when looking at different types of antenatal ultrasound programs, even if they are within a culturally similar region.

Avenues for future research

An appropriate next step would be a larger, prospective, controlled longitudinal study comparing similar health care clinics with and without the introduction of an antenatal ultrasound program. This would more strongly establish a causal link between the introduction of an ultrasound program and an increase in the numbers of women coming to the clinic for ANCs and delivery. The addition of a qualitative research questionnaire could help determine if women identify ultrasound as a motivating factor in coming to the clinic and could identify where they would otherwise have sought care, bolstering the assumption made in this study that these are women who otherwise would have delivered at home under the care of a TBA. Such a study could also be designed to follow important clinical outcomes including maternal and neonatal mortality and specific morbidities. Although the magnet effect of ultrasound may have substantial benefit in increasing utilization of existing health care resources, few would likely find the expense worthwhile unless it could also be shown to more directly impact clinical care by identifying and triaging high risk pregnancies, its intended function. It would also be important to look for evidence of over-utilization or other harms associated with the introduction of ultrasound. Research in rural and low-resource environments remains a challenge with poor infrastructure and often inadequate or incomplete record keeping. Yet appropriately implemented research protocols have the potential to inform policy decisions that could benefit the lives of millions.

Conclusion

Our study demonstrates promising initial data that the introduction of a low cost, antenatal ultrasound program at a low resource, rural health care clinic in sub-Saharan Africa can attract more women to come to the clinic to receive skilled prenatal care and skilled care at delivery. These well-recognized quality measures are thought likely to directly impact maternal and neonatal mortality and morbidity. Increasing the number of women in the developing world who give birth with the assistance of a skilled attendant remains an important global public health priority. The increased access to prenatal care provides an increased opportunity for the administration of specific tests and treatments such as supplementation to prevent anemia, testing and treatment for maternal HIV, presumptive deworming therapy, and the administration of the recommended doses of Intermittent Preventative Therapy for malaria (IPT). Our study demonstrated that these treatments are provided inconsistently, as shown in other studies, and this remained true after the introduction of the ultrasound program. Prenatal visits also present an opportunity for education on a variety of topics including the use of insecticide treated mosquito nets, hygiene, and lactation among others.

A skilled birth attendant cannot work in isolation; at least a rudimentary health care system allowing for referral and management of emergency obstetric complications is required. Similarly the addition of antenatal ultrasound to a low resource health care system is no guarantee of improved maternal and neonatal outcomes. Our analysis indicates a strategy for increasing utilization of existing health care resources, but it cannot be implemented in isolation or within a system incapable of providing emergency obstetric services. Successful strategies to reduce maternal mortality must be integrated into existing health care infrastructure and be part of a unified, multi-faceted, systems-based approach. To meet the ambitious maternal health goals of MDG 5 will require the full resolve and ingenuity of the global health community.

Tables

Table 1. Uganda health profile base on 2009 data from WHO[42].

Uganda Health Profile	
Population	32,710,000
Population in rural areas (%)	87
Life expectancy at birth	52
Maternal mortality ratio (per 100,000 live births)*	430
Births attended by skilled health personnel (%)	
Rural	38
Urban	80
Poorest quintile	28
Wealthiest quintile	77
Physicians per 10,000 population	1·2
Nurse or midwife per 10,000 population	13·1

**Indicates data from 2008 estimates.*

Table 2. Primary and secondary outcome means.

Variable	N = Months	Mean (95% CI.)	Min	Max
Deliveries	64	34.48 (31.99-37.17)	15	58
1st ANC	63	95.19 (88.96-101.42)	57	163
2nd ANC	63	44.19 (40.13-48.24)	4	76
3rd ANC	63	18.76 (15.62-21.90)	0	49
4th ANC	63	9.41 (7.51-11.79)	0	32
All ANCs	63	167.56 (154.01-181.10)	69	271
Deworming Tx	46	99.47 (87.45-111.51)	31	184
Anemia Tx	46	166.26 (146.02-165.10)	62	271
HIV Testing	45	147.29 (129.49-165.09)	38	260
IPT 1	32	83.16 (74.94-91.37)	45	146
IPT 2	29	35.21 (29.08-41.34)	9	74

Table 2. Descriptive statistics of the primary and secondary outcome variables.

Table 3. Mean number of monthly deliveries and ANCs pre and post ultrasound program.

Variable	Mean (95% CI)	Percent Change (95% CI)	P value
Deliveries			
Pre-Ultrasound (n=41)	28.39 (26.59-30.31)	+59.73% (44.70-76.32)	p<0.001
Post-Ultrasound (n=23)	45.35 (42.12-48.83)		
1st ANC			
Pre-Ultrasound (n=41)	82.21 (77.80-86.89)	+45.18% (32.71-58.82)	p<0.001
Post-Ultrasound (n=22)	119.36 (111.20-128.12)		
2nd ANC			
Pre-Ultrasound (n=41)	35.56 (32.66-38.73)	+69.49% (47.78-94.40)	p<0.001
Post-Ultrasound (n=22)	60.27 (54.14-67.10)		
3rd ANC			
Pre-Ultrasound (n=41)	11.61 (10.3-13.44)	+176.41% (120.11-247.12)	p<0.001
Post-Ultrasound (n=22)	32.09 (26.96-38.20)		
4th ANC			
Pre-Ultrasound (n=41)	4.14 (3.53-4.88)	+363.72% (77.67-469.37)	p<0.001
Post-Ultrasound (n=22)	19.23 (16.95-21.81)		
All ANCs			
Pre-Ultrasound (n=41)	133.54 (126.62-140.83)	+72.95% (58.56-88.65)	p<0.001
Post-Ultrasound (n=22)	230.95 (215.62-247.38)		

Table 3. The monthly mean number of ANC visits and deliveries performed at Nawanyago clinic are compared before and after the introduction of the ultrasound program base on NB model.

Table 4. Mean number of monthly ANC treatments pre and post ultrasound program.

Variable	Mean (95% CI)	Percent Change (95% CI)	P value
Deworming Tx			
Pre-Ultrasound (n=24)	66.29 (60.95-72.10)	+104.67% (82.31-129.78)	p<0.001
Post-Ultrasound (n=22)	135.68 (125.29-146.93)		
Anemia Tx			
Pre-Ultrasound (n=24)	110.79 (99.74-123.07)	+104.68% (76.29-137.65)	p<0.001
Post-Ultrasound (n=22)	226.77 (203.95-252.15)		
HIV Testing			
Pre-Ultrasound (n=24)	109.04 (95.90-123.99)	+75.16% (45.41-111.00)	p<0.001
Post-Ultrasound (n=21)	191.00 (166.93-218.54)		
IPT 1			
Pre-Ultrasound (n=11)	71.91 (62.01-83.38)	+23.83% (3.29-48.47)	p=0.021
Post-Ultrasound (n=21)	89.05 (80.18-98.89)		
IPT 2			
Pre-Ultrasound (n=8)	32.13 (23.21-44.47)	+13.25% (-23.35-65.81)	p=0.522
Post-Ultrasound (n=21)	36.38 (29.81-44.39)		

Table 4. The mean monthly numbers of specific tests and treatments provided at ANC visits at Nawanyago are compared before and after the introduction of the antenatal ultrasound program based on the NB model.

Table 5. Mean number of prenatal treatments per 100 ANC visits before and after the introduction of the ultrasound program.

Variable	Mean (95% CI)	Percent Change (95% CI)	P value
Deworming Tx			
Pre-Ultrasound (n=24)	48.47 (45.04-52.16)	+21.72 (10.23-34.41)	p<0.001
Post-Ultrasound (n=22)	59.00 (55.18-63.08)		
Anemia Tx			
Pre-Ultrasound (n=24)	80.07 (74.71-85.82)	+22.60 (11.38-34.95)	p<0.001
Post-Ultrasound (n=22)	98.17 (91.87-1.05)		
HIV Testing			
Pre-Ultrasound (n=24)	79.84 (71.46-89.20)	+0.03 (-12.46 - +20.69)	p=0.73
Post-Ultrasound (n=21)	82.12 (73.18-92.14)		
IPT 1			
Pre-Ultrasound (n=11)	50.42 (43.34-58.65)	-23.15 (-23.15 - -7.52)	p<0.001
Post-Ultrasound (n=21)	38.75 (34.82-43.11)		
IPT 2			
Pre-Ultrasound (n=8)	20.56 (15.09-28.01)	+13.25% (-23.35-65.81)	p=0.148
Post-Ultrasound (n=21)	15.72 (13.02-19.00)		

Table 5. The mean number of prenatal treatments per 100 ANC visits are compared before and after the introduction of the ultrasound program at Nawanyago based on the NB model.

Table 6. Model analytics, testing for over-dispersion with mean and variance of primary and secondary outcome variables.

Variable	Mean	Variance	Poisson (Pearson/df)
Deliveries	34.48	115.17	1.36
1st ANC	95.19	611.25	3.10
2nd ANC	44.19	259.61	2.75
3rd ANC	18.76	155.22	3.36
4th ANC	9.41	65.73	1.60
All ANCs	167.56	2892.06	4.47
Deworming Tx	99.48	1640.79	4.02
Anemia Tx	166.26	4647.13	9.13
HIV Testing	147.29	3511.35	13.58
IPT 1	83.16	518.91	5.92
IPT 2	35.21	259.74	7.97

Table 6. The mean and variance of the outcome variables is shown. For all variables the variance greatly exceeds the mean, violating the assumption of a true Poisson distribution that the variance is equal to the mean. The variables are initially modeled with a Poisson distribution and the model Pearson chi square statistic divided by the residual degrees of freedom to estimate the degree of over-dispersion. A threshold of 1.2 (20% greater than expected dispersion if the data came from a true Poisson distribution) was selected and all of the variables exceeded this threshold requiring refitting of the model within a negative binomial distribution to account for over-dispersion.

Table 7. Model analytics, testing for auto-correlation with Box-Jenkins distribution and Pearson residuals.

Variable	Poisson	Negative Binomial
Deliveries	p=0.78	p=0.73
1st ANC	p=0.89	p=0.88
2nd ANC	p=0.90	p=0.90
3rd ANC	p=0.80	p=0.79
4th ANC	p=0.74	p=0.74
All ANCs	p=0.95	p=0.95
Deworming Tx	p=0.97	p=0.43
Anemia Tx	p=0.43	p=0.42
HIV Testing	p=0.99	p=0.81
IPT 1	p=0.78	p=0.75
IPT 2	p=0.96	p=0.96

Table 7. Tests were performed for auto-correlation to the lag-1 level within both the Poisson and negative binomial models. Using a Box-Jenkins distribution with the Pearson residuals no evidence of carry over from the previous month was found at an alpha of 0.15.

Figures

Figure 1. Box plot of deliveries and ANC visits.

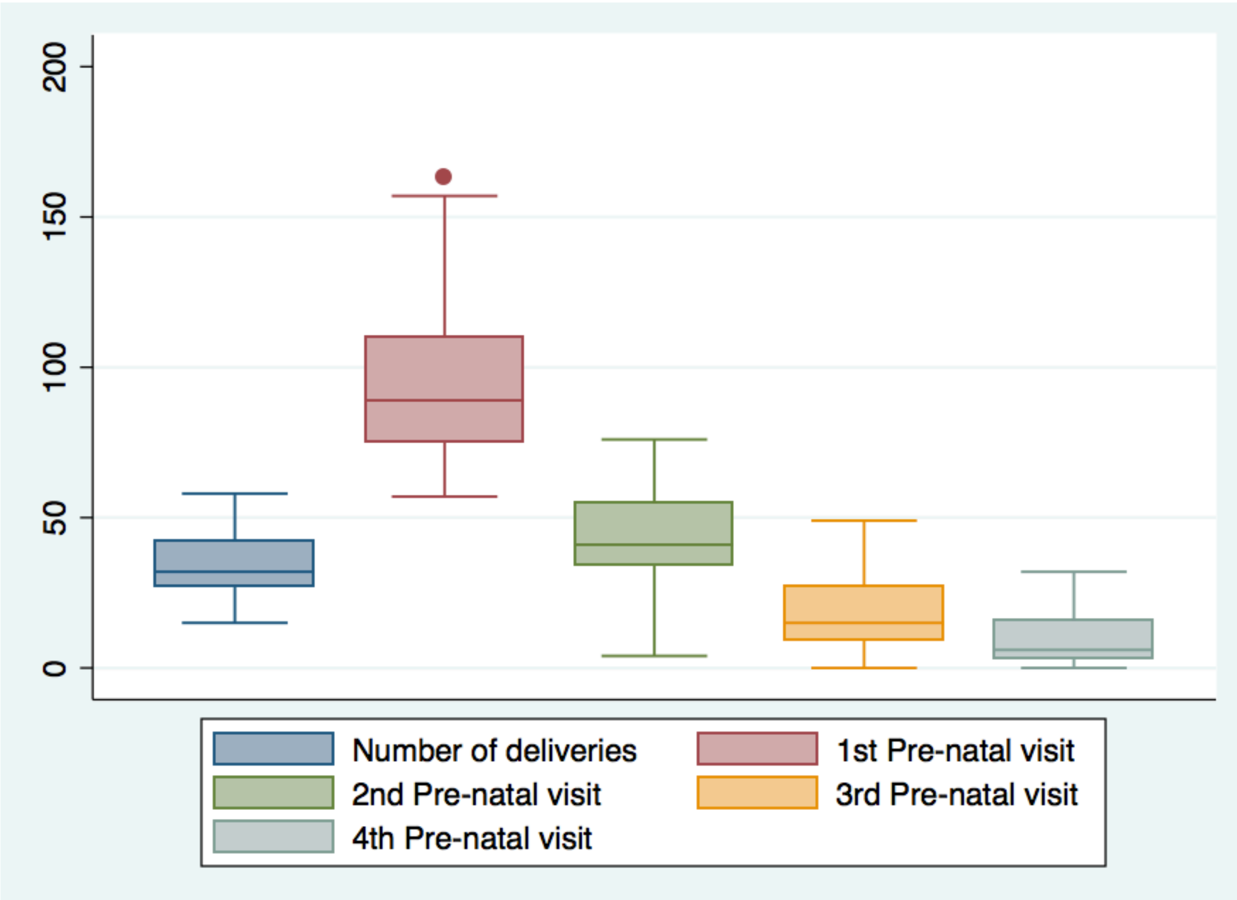

Figure 1. Box plot of numbers of monthly deliveries and ANC visits at Nawanyago during the study period.

Figure 2. Box plot of secondary outcome variables.

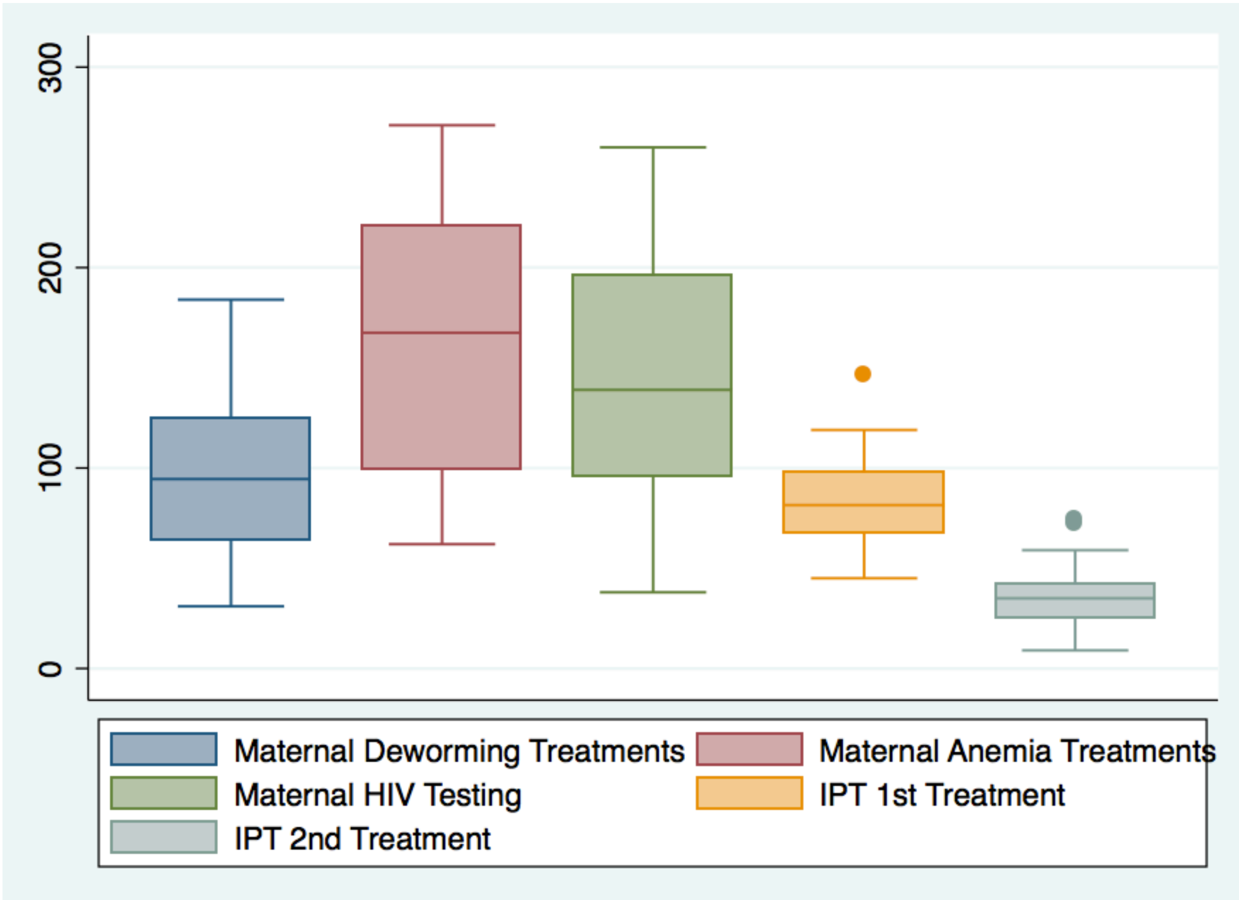

Figure 2. Box plot of numbers of prenatal tests and treatments performed at Nawanyago at ANC visits during the study period.

Figure 3. Number of ANCs by month at Nawanyago.

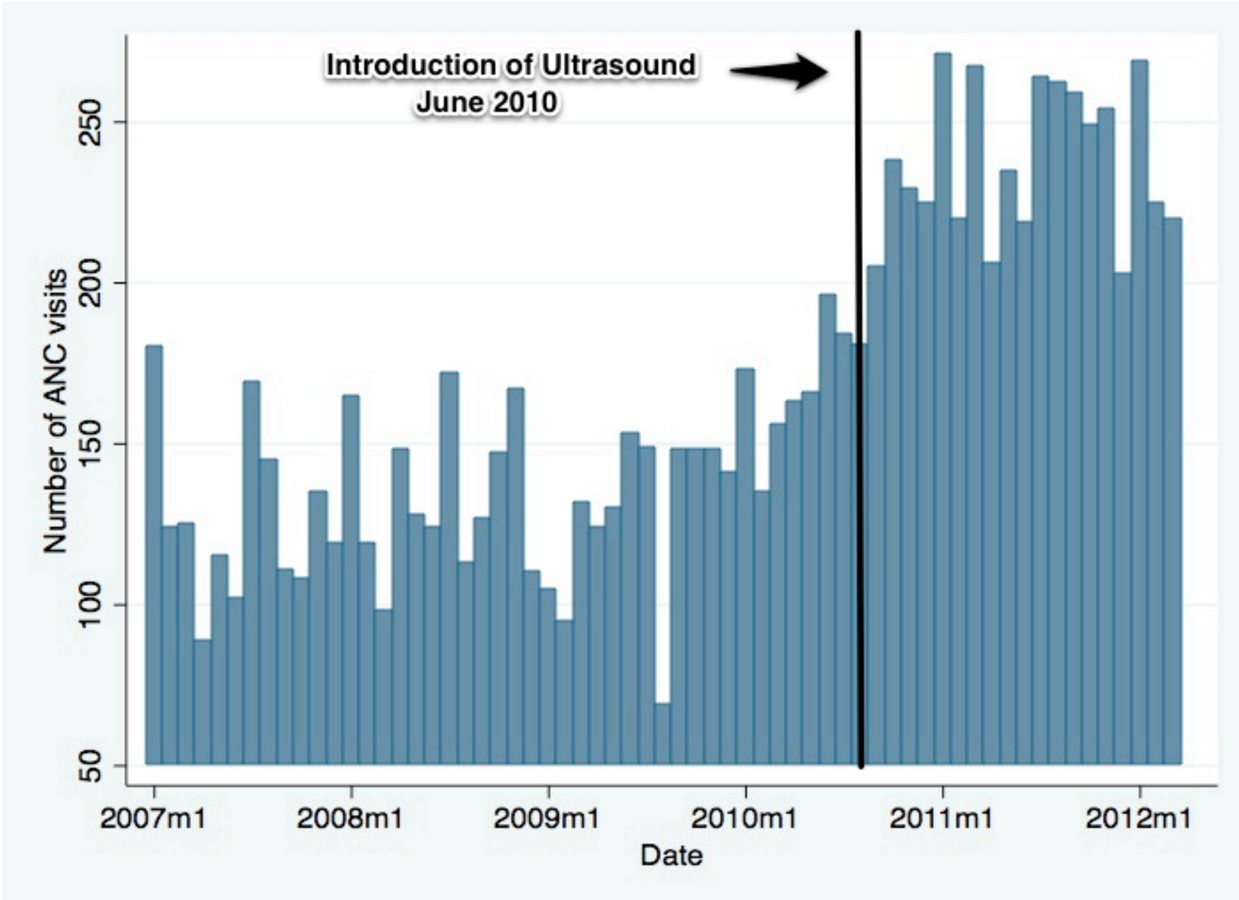

Figure 3. The monthly number of ANC visits (all categories) at Nawanyago is show over time. The ultrasound program was introduced in June of 2010.

Figure 4. Number of deliveries by month at Nawanyago.

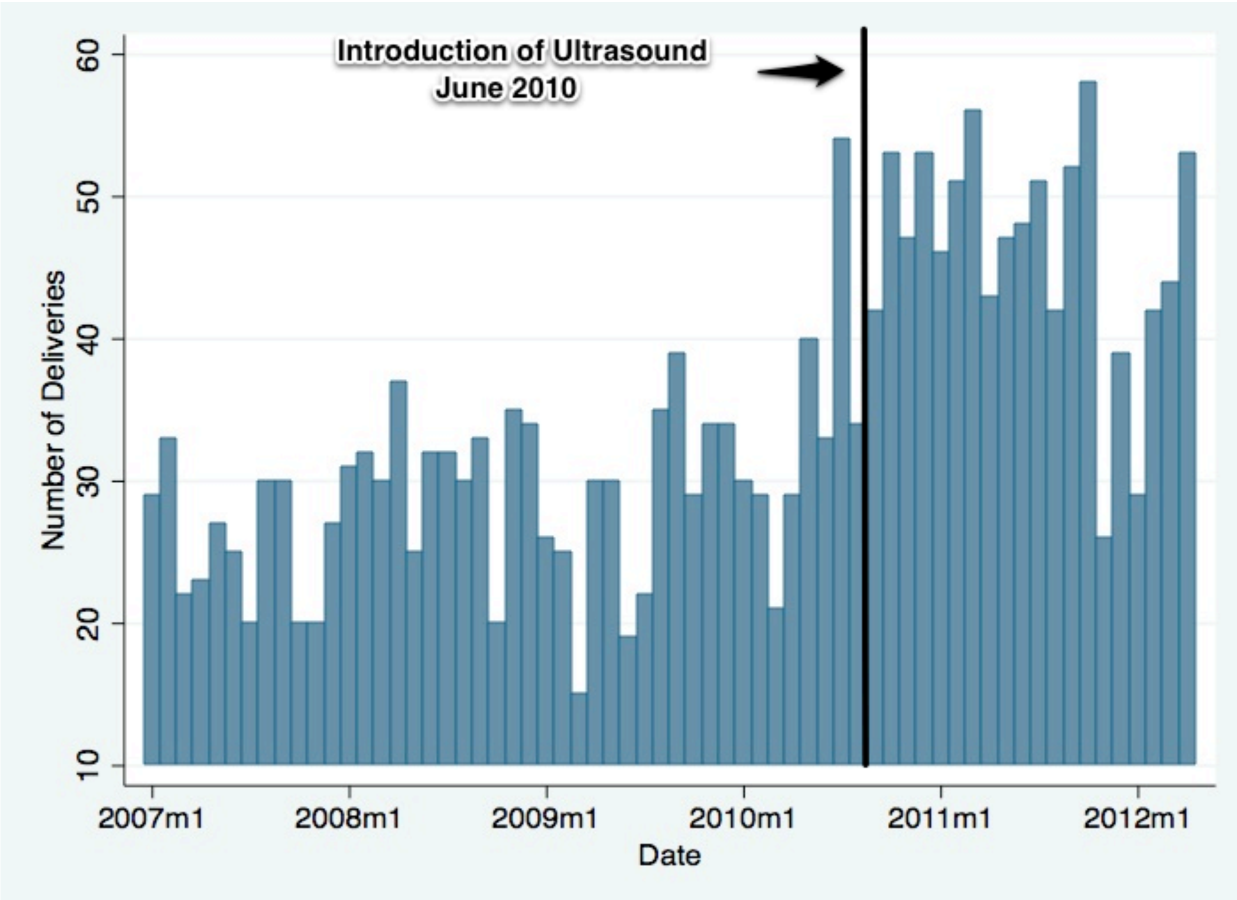

Figure 4. The monthly number of deliveries performed at Nawanyago is shown over time. The ultrasound program was introduced in June of 2010.

Figure 5. Box plot of primary outcome variables sorted by ultrasound status.

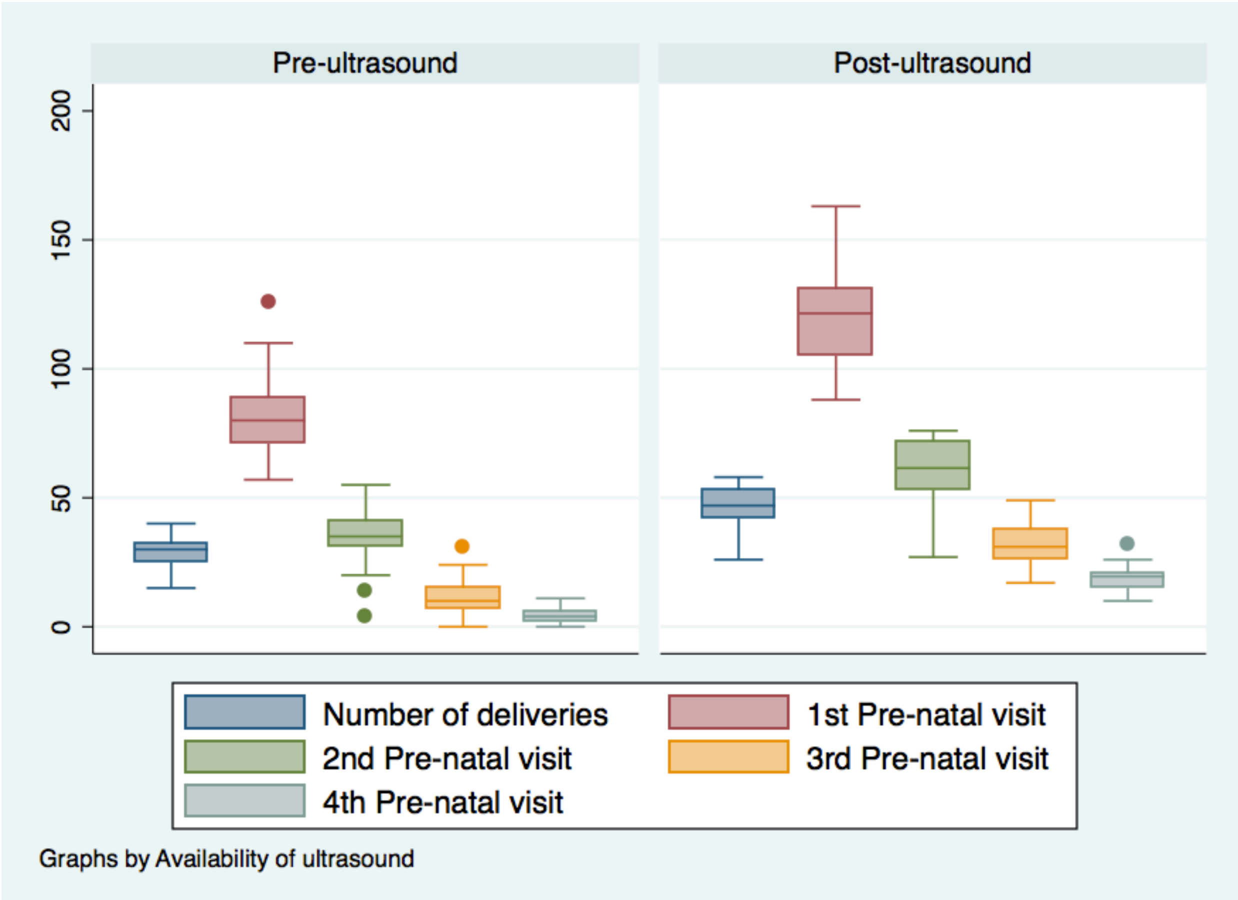

Figure 5. The number of deliveries and ANC visits at Nawanyago displayed in box plot form stratified by pre and post ultrasound status.

Figure 6. Box plot of secondary outcome variables sorted by ultrasound status.

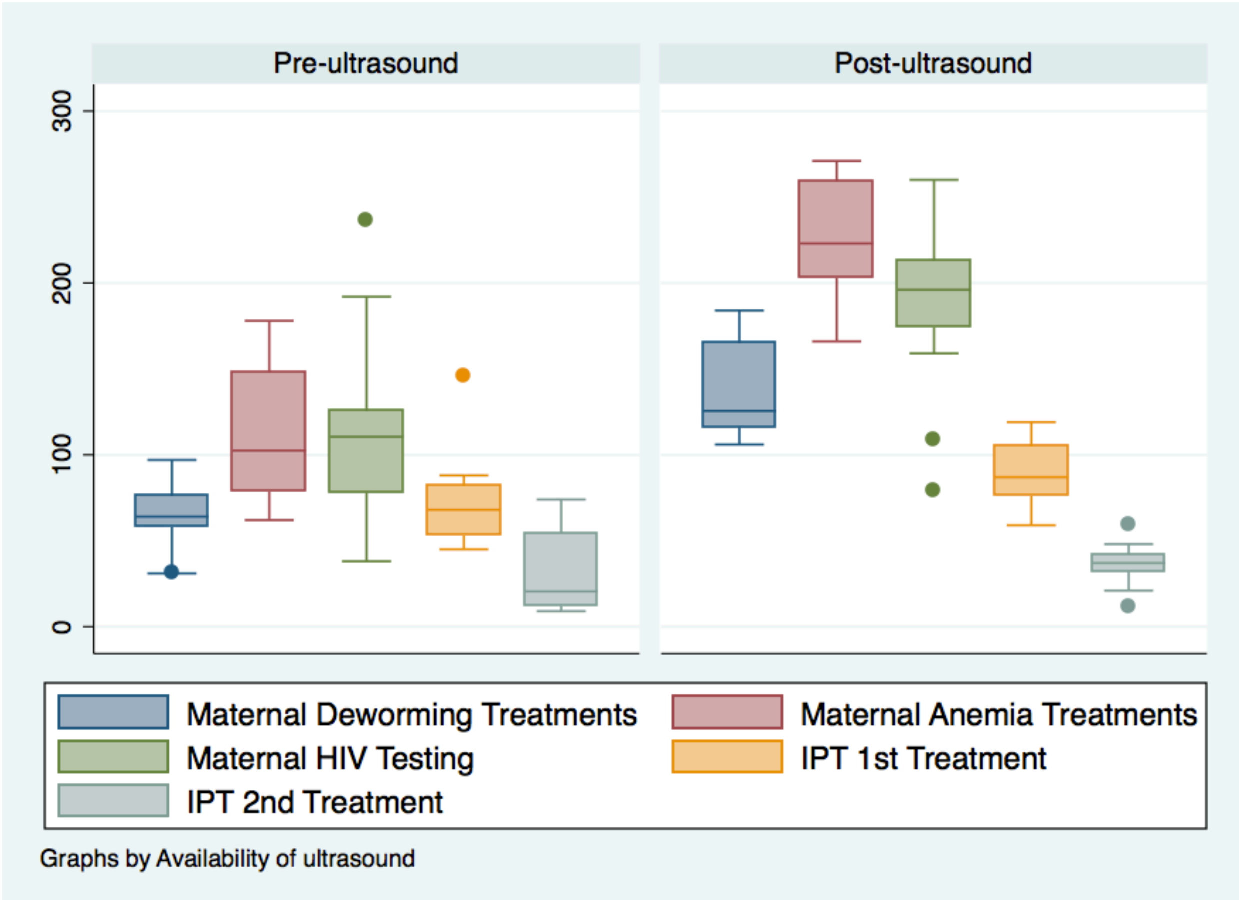

Figure 6.The numbers of prenatal tests and treatments performed at ANC visits at Nawanyago is shown in box plot form before and after the introduction of ultrasound.

Appendix

Stata code:

***Non-sorted summary statistics**
```
tabstat deliveries anc1 anc2 anc3 anc4 anc_all deworming anemia_tx hiv_test
IPT_1 IPT_2 , statistics(min, max, n, mean, sd) by(us)
```

***Summary statistics for outcome variables sorted by ultrasound status**
```
tabstat deliveries anc1 anc2 anc3 anc4 anc_all deworming anemia_tx hiv_test
IPT_1 IPT_2 , statistics(min, max, n, mean, sd) by(us)
```

***create histograms for all outcome variables and store in memory**
```
histogram deliveries, discrete frequency name(graph1)
histogram anc1, discrete frequency name(graph2)
histogram anc2, discrete frequency name(graph3)
histogram anc3, discrete frequency name(graph4)
histogram anc4, discrete frequency name(graph5)
histogram anc_all, discrete frequency name(graph6)
histogram deworming, discrete frequency name(graph7)
histogram anemia_tx, discrete frequency name(graph8)
histogram hiv_test, discrete frequency name(graph9)
histogram IPT_1, discrete frequency name(graph10)
histogram IPT_2, discrete frequency name(graph11)
```

***combine histograms for primary outcomes and export**
```
graph combine graph1 graph2 graph3 graph4 graph5 graph6
graph export Primary_Outcomes_Histogram.png , replace
```

***combine histograms for secondary outcomes and export**
```
graph combine graph7 graph8 graph9 graph10 graph11
graph export Secondary_Outcomes_Histogram.png , replace
```

***Create box plots for primary and secondary variables**
```
graph box deliveries anc1 anc2 anc3 anc4
graph export Primary_Outcomes_Boxplot.png , replace

graph box deworming anemia_tx hiv_test IPT_1 IPT_2
graph export Secondary_Outcomes_Boxplot.png
```

***Boxplots for primary and secondary variables sorted by ultrasound status**
```
graph box deliveries anc1 anc2 anc3 anc4, by(us)
graph export Primary_Outcomes_Stratified_Boxplot.png, replace

graph box deworming anemia_tx hiv_test IPT_1 IPT_2, by(us)
graph export Secondary_Outcomes_Stratified_Boxplot.png, replace
```

```
tabulate us , summarize( deliveries )
sort eventdate
```

***Model fitted as Poisson and assessed for over-dispersion. Variable deliveries is used in this example but the same code is used for all of the primary outcome variables.**

```
glm deliveries i.us , family(poisson) link(log)
```

***Check for autocorrelation of Poisson model with Pearson residuals**

```
predict muhat , mu
predict rp , pearson
regress rp , noconstant //SSResidual is Pearson Chi_square statistic
generate rr = (deliveries - muhat)
generate lag_del = deliveries[ _n-1 ]
generate lag_rp  = rp[ _n-1 ]
generate lag_rr  = rr[ _n-1 ]

*Box-Jenkins
generate top = rp*lag_rp
```

***Test statistic top/ssr**

```
drop top muhat rp lag_del lag_rp lag_rr
```

***fitting negative binomial model**

```
glm deliveries i.us , family(nbinomial ml) link(log)
```

***Determining point estimates, IRR, and CIs.**

```
lincom _cons , eform
lincom _cons + 1.us , eform
lincom 1.us , eform


glm deliveries i.us , family(nbinomial ml) link(log)
```

***Check for autocorrelation of NBR model with Pearson residuals**

```
predict muhat, mu
predict rp , pearson

generate lag_del = deliveries[ _n-1 ]
generate lag_rp  = rp[ _n-1 ]
generate lag_rr  = rr[ _n-1 ]

regress rp, noconstant
generate top = rp*lag_rp
total top
```

***Test statistic top/ssr**

***A similar approach is used for the analysis of the outcome variables with the addition of an offset variable to account for the varying opportunities to provide the prenatal tests and treatments as the number of ANCs varied month to month. The exp() option was utilized.**

***Poisson model fitted and examined for evidence of over-dispersion. Variable anemia_tx used in this example but the same code is used for all of the secondary outcome variables.**
```
glm anemia_tx i.us , family(poisson) link(log) exposure(anc_all)
```

***Check for autocorrelation of Poisson model with Pearson residuals**
```
predict muhat , mu
predict rp , pearson
regress rp , noconstant //SSResidual is Pearson Chi_square statistic
generate lag_del = anemia_tx[ _n-1 ]
generate lag_rp  = rp[ _n-1 ]

generate top = rp*lag_rp
total top
```

***Test statistic top/ssr**

```
drop top muhat rp lag_del lag_rp
```

***Fit NBR model**
```
glm anemia_tx i.us , family(nbinomial ml) link(log) exposure (anc_all)
```

***Determining proportion of visits at which treatment or test was provided, IRR, and CIs.**
```
lincom _cons , eform
lincom _cons + 1.us , eform
lincom 1.us , eform
```

****Check for autocorrelation of NBR model with Pearson residuals**
```
predict muhat , mu
predict rp , pearson
regress rp , noconstant //SSResidual is Pearson Chi_square statistic
generate lag_del = anemia_tx[ _n-1 ]
generate lag_rp  = rp[ _n-1 ]

generate top = rp*lag_rp
total top
```

***Test statistic top/ssr**

```
drop top muhat rp lag_del lag_rp
```

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