CHARACTERISTICS OF NEONATAL AND PERINATAL DEATH IN NINE VILLAGES IN THE LORETO PROVINCE OF PERU

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ABSTRACT

Introduction: The percentage of deaths under the age of five years attributed to neonatal mortality is rising worldwide. Knowledge of sub-national neonatal and perinatal mortality rates (NMR and PMR), causes of death, and risk factors for death is imperative for developing and implementing programs to decrease rates of neonatal and perinatal death.

Objectives: Determine the NMR, PMR, causes of death, and risk factors for neonatal and perinatal death for nine villages in the Loreto Province of Peru.

Methods: Eligible women were interviewed about pregnancy outcomes for the preceding five years. Women who experienced stillbirth or neonatal death were interviewed using the World Health Organization (WHO) International Standard Verbal Autopsy Questionnaire for death of a child under four weeks of age. Verbal autopsy reviewer agreement was assessed using percent agreement. Univariate logistic regression analyses, using generalized estimating equations, provided estimates of NMR and PMR adjusted for clustering by mother and village. Fisher's exact tests were used to determine risk factors for neonatal and perinatal death.

Results: For nine villages in the Loreto Province of Peru, the NMR was 31.4 per 1000 live births (95% CI: 15.6/1000 to 62.3/1000 live births) and the PMR was 49.7 per 1000 pregnancies (95% CI: 28.5/1000 to 85.3/1000 pregnancies). Percent agreement among reviewers using verbal autopsy was 90.5% (95% CI: 69.6% to 98.8%) for cause of neonatal death, 55.6% (95% CI: 30.8% to 78.5%) for timing of stillbirth, and 38.9% (95% CI: 17.3% to 64.3%) for cause of stillbirth. The main contributor to neonatal death was infection (43%), followed by asphyxia (29%). Risk factors for neonatal and perinatal death were pregnancy with twins (p=0.001), preterm delivery (p=0.003), and delivery by cesarean section (p=0.049).

Conclusion: The NMR and PMR for nine villages in the Loreto Province were found to be among the highest of any reported in Peru. Use of the WHO International Standard Verbal Autopsy for death of a child under four weeks of age proved useful for determining cause of neonatal death with high reliability. Characteristics of pregnancy associated with neonatal or perinatal death were twin gestation, preterm delivery, and delivery by cesarean section. Knowledge of these risk factors will assist in targeting interventions to decrease neonatal and perinatal mortality in these villages.

GLOSSARY OF TERMS

Neonatal period: period from the time of birth to postnatal day of life 28

Perinatal period: period from the beginning of the 28th week of gestation to postnatal day of life 7

Neonatal mortality rate (NMR): the number of deaths in the neonatal period per 1000 live births

Perinatal mortality rate (PMR): the number of deaths in the perinatal period per 1000 pregnancies

Stillbirth: death of a fetus after the 20th week of gestation

Fresh stillbirth: death of a fetus during labor or delivery

Live birth: delivery of an infant who shows signs of life by way of movement, heartbeat, or breathing

CHAPTER 1 — BACKGROUND AND SIGNIFICANCE

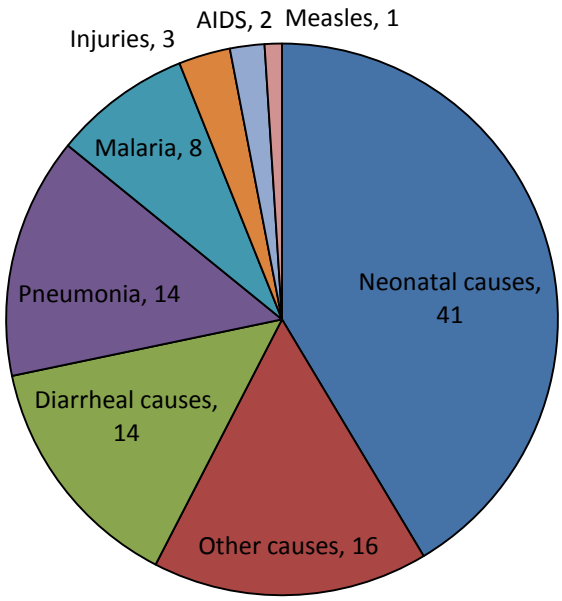
Perinatal and Neonatal Death, A Global Perspective

Faced with a new millennium, heads of State and Government from 192 countries met in September of 2000 at United Nations Headquarters in New York.[1] The United Nations Millennium Declaration was adopted at this summit and included eight Millennium Development Goals (MDG).[2] The MDGs focus on issues including poverty, education, gender equality, health, and environmental sustainability; all have the common aim "to uphold the principles of human dignity, equality, and equity at the global level.[2]" MDG4 calls specifically for the reduction of the under-age five mortality rate by two-thirds between 1990 and 2015.[3] In 1990, the global under-five mortality rate was 90 per 1000 live births; in 2008, the rate had decreased by 28% to 65 per 1000 live births.[4] In absolute numbers, this is a reduction from 12.5 million to 8.8 million under-five deaths from 1990 to 2008.[3] Although strides are being made in this critical area of child health, the rate of decline is too slow to reach the goal set forth by MDG4.[5] In fact, MDG4 will not be achieved until 2045 at the current rate of decline.[6] Many believe that MDG4 can be achieved through an expansion of interventions that target the most important causes of death.[7]

The causes of death among children under age five and the percentages of occurrence for each were reported by the United Nations in 2010 (Figure 1).[3] Four diseases of childhood—pneumonia, diarrhea, malaria, and AIDS—accounted for 38% of all deaths worldwide in children under age five in 2008.[3]

Forty-one percent of deaths among children under age five in 2008 were due to the broad category labeled “neonatal causes.” The report states that interventions should be focused on the above four key diseases, but does not address the larger category of neonatal causes.[3]

Figure 1: Causes of death among children under age five worldwide, 2008 (%) [3]



As progress is made in other causes of under-five mortality, neonatal causes of death appear to be decreasing at a slower rate. In 1970, 38.9% of deaths among children under the age of five occurred in the neonatal period; in 2008, it rose to 41%.[3,5,7] Therefore, as we see overall numbers of under-five childhood deaths decrease over time, the relative share of under-five childhood deaths that occur in the neonatal time period have increased.[5] These numbers bring neonatal mortality to the forefront: if we are going to meet MDG4, neonatal mortality must

be addressed.[7] In fact, estimations state that prevention of 70% of neonatal deaths worldwide would decrease the under-five mortality rate by 25%.[9]

Around 130 million babies are born each year, and of these, about four million will die before reaching one month of age.[10] For every neonatal death, it is estimated that one stillbirth occurs; around one million of these are thought to be intrapartum, or "fresh," stillbirths.[11,12] These deaths stem from poor maternal health, inadequate prenatal care, inappropriate management of complications during labor and delivery, poor hygiene during delivery and just after birth, and lack of the essential newborn care that is needed during the first days of life.[13] Within the neonatal period, there is great variability in the daily risk of death.[10] Mortality is highest in the initial 24 hours after birth (anywhere from 25-45%), 50% die within the first three days, and about 75% of all neonatal deaths occur in the first week of life.[10,14,15]

For reasons to be discussed, global estimates of frequency of direct causes of neonatal death exist only by means of statistical modeling.[10] In 2000, the main causes of neonatal death and their estimates of occurrence were severe infections (36%), preterm birth (28%), complications of birth asphyxia (23%), and congenital abnormalities (7%).[10] Causes of death can be correlated with timing of death. Neonatal death that occurs in the first week of life is often related to complications of birth asphyxia and prematurity, while deaths occurring after one week of life are commonly due to infectious causes.[10,13] In a study of over 1000

neonatal deaths in rural India, 31% and 26% of deaths on the first day of life were due to birth asphyxia and preterm birth, respectively.[16] For the remainder of the first week, 30% of deaths were due to preterm birth and 25% were due to sepsis and pneumonia.[16] Infection accounted for 45% of deaths during the second week of life and 36% of deaths during weeks three and four.[16]

The burden of neonatal mortality appears to be rooted in inequality. The overall neonatal mortality rate (NMR) in low-middle income countries is 33 per 1000 live births, which is over eight times the NMR seen in high-income countries (4 per 1000 live births).[14,17] In fact, 99% of neonatal deaths—a staggering 3,960,000 deaths per year—occur in developing countries.[10,14] Two-thirds of these deaths occur in the World Health Organization (WHO) African and southeast Asian regions.[10] The effect of inequality is seen within countries as well, as NMRs are highest in the poorest wealth quintile of many developing countries.[6,9,10]

Lack of access to skilled care is a major contributor to high NMRs in low-middle income countries. In about half of the deliveries in developing countries, skilled care (in the form of a birth attendant with formal education) is unavailable.[11] Nearly two-thirds of births that occur in developing countries occur in the home, and up to 90% of deliveries in the poorest wealth quintile of many developing countries occur in the home without the presence of a skilled professional.[9,11,17] Between 1995 and 2003, over 50% of neonatal deaths came after a delivery at home without the presence of a skilled birth attendant.[10] Lack of access to care

occurs before and extends beyond the time of delivery as well. Prenatal care is often unavailable, and most babies in developing countries are cared for at home without any formal medical care in the days immediately following delivery.[14]

The ability to study neonatal and perinatal mortality, as well as plan and implement programs to improve survival, is impeded by an overall lack of information.[18] Countries with the highest NMRs often lack the vital registration systems that are necessary to record information about deaths.[17] Death registration in general is reliable in only 72 of the world's over 190 countries, and vital registration coverage is available for less than 3% of the world's neonatal deaths.[1,12] Without vital registration systems, direct cause of death statistics for certain countries and regions are not available. This results in the need for global estimates based on statistical modeling.[10] In countries that do have vital registration systems, the high number of home deliveries that occur in resource-poor settings likely leads to high numbers of uncounted and uncharacterized deaths that occur in the home.[19,20] High rates of stillbirth that occur during home deliveries, and the frequent misclassification of neonatal death as stillbirth in home deliveries, further contribute to issues surrounding vital registration.[15]

Verbal autopsy (VA) is one tool that is used to determine cause of death in places lacking vital registration systems.[21] VA consists of interview with family members of the deceased using a structured questionnaire to elicit findings that can be used to determine cause of death.[20,21] Despite known limitations of VA,

including questions about validation and use for comparison between countries, this is currently the only practical tool available to monitor causes of death in developing countries without vital registration systems.[21] Because the places lacking these vital registration systems are the very places targeted by recent global health initiatives, the need for standardized verbal autopsy-derived mortality data has increased.

In 2007, the WHO published verbal autopsy standards to be used in evaluation of such initiatives, as well as to provide a source of cause of death statistics to make disease-burden estimates.[21] These verbal autopsy standards were the product of a three year effort by an expert group lead by the WHO. This expert group, consisting of researchers, data users, and other stakeholders, systematically reviewed, debated, and refined the currently available data and evidence from the most widely previously used and validated verbal autopsy questionnaires.[21] The result was the standard verbal autopsy questionnaires for three age groups: child under four weeks, child aged four weeks to 14 years, and person aged 15 years and above. They also provide standardized methods of certification, coding, and tabulation of causes of death from verbal autopsies according to the *International Statistical Classification of Diseases and Related Health Problems*, tenth revision (ICD-10). The development of these standards is the first step. Further research includes optimization of the questionnaires and the refinement of reliable methods for assigning cause of death. For now, the

knowledge of site-specific causes of neonatal death and the frequency with which they occur can help in policy planning and implementation.

Several risk factors have been identified from population-based studies for all-cause neonatal and perinatal death.[12] Pre-pregnancy risk factors include maternal age less than 18 years or greater than 35 years, maternal height less than 150 cm and weight less than 47 kg, primigravid status or parity greater than six, and poor obstetric history.[12] Antenatal risk factors include multiple pregnancy; maternal anemia, jaundice, hypertensive disorders, diabetes, syphilis, malaria, or HIV; preterm birth (<37 weeks gestation); and post-term birth (>42 weeks gestation).[12] Intrapartum risk factors include obstructed labor, prolonged second stage of labor, passage of meconium, malpresentation (including breech), vaginal bleeding, maternal fever during labor, and prolonged rupture of membranes.[12]

Perinatal and Neonatal Death in Peru

Peru is the third largest country in South America and has a population of approximately 29 million people, 30% of whom live in the Lima metropolitan area.[22] Peru is divided into regions, and the Loreto Province in northeastern Peru is the largest of these. A substantial portion of the Loreto Province consists of the upper Amazon Basin, with the jungle city of Iquitos as its main hub.[23] Government and private hospitals and clinics exist in Iquitos and other larger towns, but as one travels further into the jungle, access to medical care is limited.

Countdown to 2015 is an independent initiative that was established in 2005 with the objective of gathering and presenting data to stimulate action on the health-related MDGs.[4] The most recent report from this group came in June of 2010, and its focus is on the 68 countries that together account for at least 95% of maternal and child deaths worldwide.[4] Peru is one of these countries. According to this report, the 2008 NMR in Peru was 13 per 1000 live births and neonatal deaths accounted for 52% of all deaths in children under the age of five.[24] This information is a general estimate for all of Peru. Presumably, wide regional differences exist in terms of neonatal mortality. In fact, the Instituto Nacional de Estadistica e Informatica in Peru estimated that in 2009, the NMR of the Loreto Province was 24.5 per 1000 live births.[25]

Because of high rates of stillbirth and the frequent misclassification of neonatal death as stillbirth in developing countries, the perinatal mortality rate (PMR) has become an important measure in the assessment of programs designed to reduce neonatal mortality.[15] PMRs can give insight into the availability and skill of intrapartum care being delivered in a country or region.[13] The underreporting of stillbirth and early death, however, means that underestimation of PMRs may be occurring.[13] In 2005, the PMR in Peru was estimated to be 19.8 per 1000 pregnancies.[26] In the Loreto Province, the PMR was estimated at 20.4 per 1000 pregnancies.[26]

Countdown to 2015 also reports on some of the risk factors known to increase odds of neonatal and perinatal death. For instance, in 2006, it was estimated that 91% of all women aged 15-49 in Peru had at least one visit with a skilled health provider during pregnancy.[24] Also in 2006, 71% of deliveries were estimated to have been attended by a skilled healthcare provider.[24] The cesarean section rate in rural Peru was estimated to be 6%.[24] Finally, the percent of Peruvian newborns in 2008 estimated to be protected against neonatal tetanus (through maternal vaccination) was 67%.[24]

Thesis Objectives and Aims

Neonatal mortality is recognized worldwide for its significant contribution to under-five mortality. The fact that the overall percentage of under-five deaths attributed to neonatal death is rising means that on a global scale, there has not been enough done to combat this problem. Perinatal death is part of this problem as well, as misclassification of neonatal death as stillbirth is common in regions with high rates of home birth.

At its core, this project is a needs assessment for this area of the Loreto Province in Peru. To target interventions that have the goal of decreasing rates of neonatal and perinatal mortality, one must understand the scope of the problem and know the main site-specific causes of death and frequency of occurrence. Risk factors for neonatal or perinatal death specific to those communities must be discovered. Medical and other technological resources available to a community must be

known and seen firsthand. A better understanding of the culture and how women and infants are perceived in that culture must be sought. Perhaps most importantly, the level of acceptance by a culture of outside support must be gauged. Only then can a program be implemented with any hope of successfully helping a community.

The importance of understanding regional NMR, PMR, causes of death, and risk factors for death cannot be overemphasized. The available literature is very clear in that data on sub-national NMR, PMR, and causes of death are often times lacking, particularly in areas lacking vital registration systems. To our knowledge, this is the first time this area of Peru has been studied using direct interview techniques with the purpose of determining NMR, PMR, cause of death, and risk factors for neonatal and perinatal death. The knowledge gained will be used to plan and implement education programs tailored to the needs of this region.

Our specific aims include:

1. Through systematic survey and personal interviews, determine the NMR and PMR for nine villages in the Loreto Province and compare these rates to the currently accepted rates for Peru and the Loreto Province.
2. Use verbal autopsy to determine causes of death in those cases identified as neonatal and perinatal death and assess verbal autopsy reviewer agreement.

3. Determine characteristics of women, labor and delivery, neonates, and villages that may be associated with increased risk of neonatal and perinatal death in these nine villages in the Loreto Province of Peru.

CHAPTER 2 — METHODS

Area of Study

Amazon Promise is a United States-based nonprofit organization founded with the goal of providing medical care to the remote populations living in the Loreto Province of Peru. Since 1994, Amazon Promise has been providing routine volunteer-based medical outreach clinics in over 30 remote jungle villages in the Loreto Province. In July and August of 2010, Amazon Promise conducted clinics in nine of these villages. To conduct this study, we traveled with Amazon Promise to these villages. The general location of the villages is marked by the star in Figure 2. The locations of the nine villages visited are detailed in Figure 3.

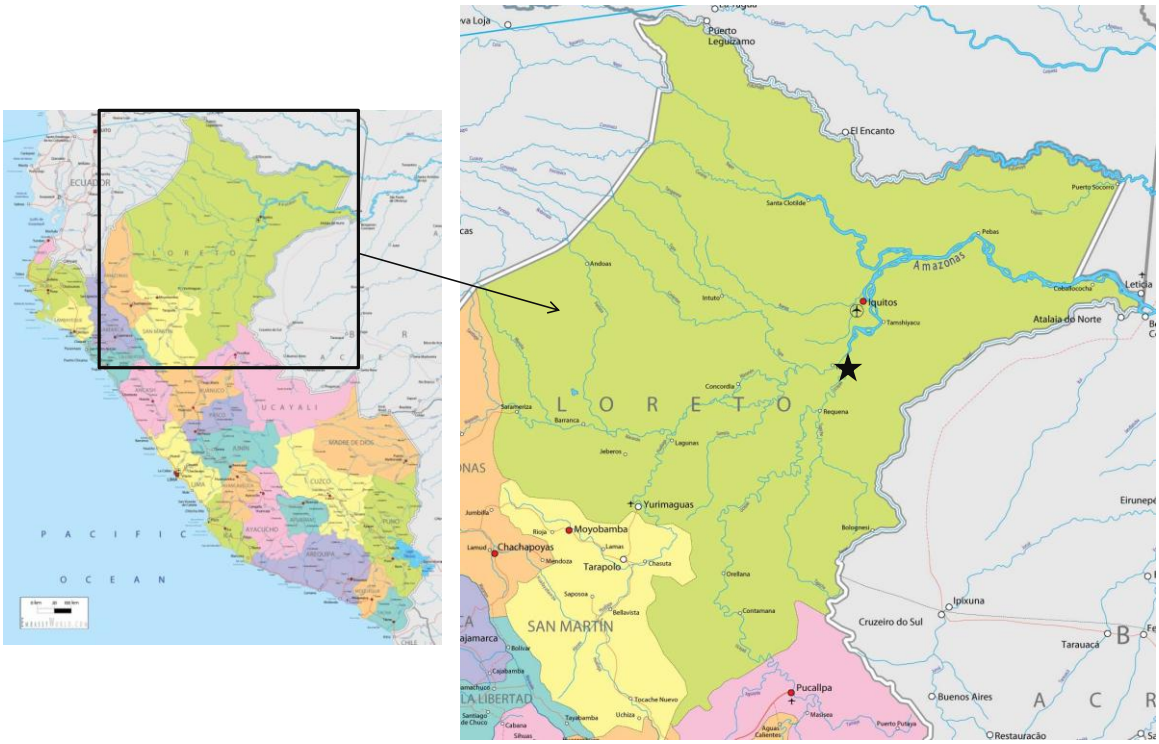
Subject Eligibility and Recruitment

Subjects who were registered to be seen in the clinics provided by Amazon Promise were eligible for recruitment. Visits to the Amazon Promise clinic are provided free of charge to any resident of the village who wishes to be seen. Patients are seen as family units, and each family member registers and receives their own paper chart with their name and birth date listed at the top. After registration, charts are placed in a central location in the clinic, and patients are called to be seen by volunteer physicians in the order in which they registered.

For this study, each paper chart was screened to determine if the patient fit eligibility criteria. Patients were considered eligible for recruitment if they were

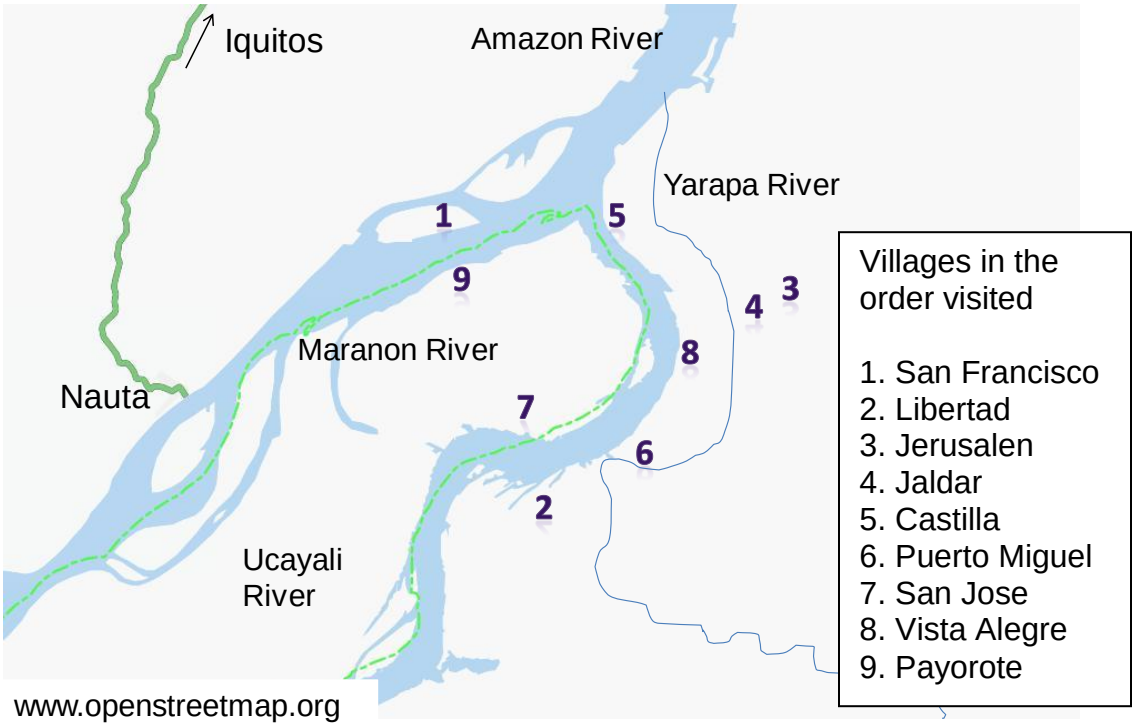
female, aged 15 years or older (local age of adulthood), and had been pregnant at least one time in the previous five years. Sex and age were determined by examining paper charts; pregnancy status was determined by verbal questioning. Once a woman was found to be eligible, she was asked to participate in the study and written informed consent was obtained using a Spanish interpreter provided by Amazon Promise. If the study participant was not able to read or write, verbal informed consent was obtained. The study was approved by the institutional review board at Oregon Health & Science University (OHSU), Portland, Oregon, USA.

Figure 2: Peru, with detail of the Loreto Province; area of interest noted with star



http://www.embassyworld.com/maps/Map_Of_Peru/

Figure 3: Location of the nine villages visited in the Loreto Province, Peru



Interview

All women who consented to participate were interviewed by Dr. Jamie B. Warren (OHSU) and a female Spanish interpreter provided by Amazon Promise. Interviews were conducted in July and August 2010. All women who were registered to be seen in the Amazon Promise clinic were screened for eligibility. Of the 132 eligible women, 130 consented to be interviewed. Any woman who had experienced a stillbirth or a neonatal death in the previous five years was interviewed using the WHO International Standard Verbal Autopsy Questionnaire

for death of a child under four weeks of age (Appendix A). Any woman who had not experienced a stillbirth or a neonatal death in the previous five years was interviewed using the questionnaire shown in Appendix B, which was developed by the author for this study and includes questions similar to those in the verbal autopsy. Women in this second category were asked to answer these questions based on their most recent pregnancy. Information from the interviews was used to determine the number of pregnancies and pregnancy outcomes in the sample, as well as demographics for use in risk factor analysis.

Outcome Variables

Each interviewed woman was asked about the number of pregnancies she had experienced in the previous five years. Outcomes for each pregnancy were obtained and included: (1) currently pregnant, (2) miscarriage, (3) stillbirth, (4) neonatal death, (5) infant death, (6) childhood death, and (7) currently living. Definitions of these outcomes are as follows:

1. Currently pregnant: current pregnancy, any gestational age
2. Miscarriage: loss of a pregnancy between conception and 20 weeks gestation
3. Stillbirth: loss of a pregnancy between 20 weeks gestation and delivery
4. Neonatal death: death of a newborn between postnatal days 0 and 28
5. Infant death: death of an infant between 1 and 12 months of age
6. Childhood death: death of a child between 1 and 5 years of age
7. Currently living: currently alive, any age

Perinatal death was also used as an outcome variable, and is defined as death occurring between the 28th week of gestation and postnatal day of life 7. Due to the lack of consistent prenatal care and accurate pregnancy dating methods in the region, determination of gestational age at the time of pregnancy loss was reliant on maternal report.

Rate Calculations

Due to the clustered nature of the data, neonatal and perinatal mortality rates were calculated using a logistic Generalized Estimating Equation (GEE) model. Data was affected by two clustering variables: the mother and the village. The rates reported here are calculated using the mother as the clustering variable, as this indirectly accounts for characteristics of the village. Use of the village as the clustering variable does not account for characteristics of the individual mothers.

Verbal Autopsy

Three independent reviewers were chosen to review the verbal autopsies (2 neonatology faculty members and 1 neonatal fellow from OHSU). Each reviewer was provided with a copy of each completed WHO International Standard Verbal Autopsy Questionnaire for death of a child under four weeks of age. For neonatal deaths, reviewers were asked to assign a most likely cause of death. For stillbirths occurring after 28 weeks gestation, reviewers were asked to assign the most likely timing of death and the most likely cause of death. Each patient had three assignments for cause or timing of death—one from each reviewer—and

agreement between each reviewer pair was assessed (i.e., reviewer pairs 1-2, 1-3, and 2-3). Overall percent agreement of the reviewers is reported.

Exposure Variables

Several risk factors have been identified from population-based studies for all-cause neonatal and perinatal death, including: maternal age less than 18 years or greater than 35 years; maternal height less than 150 cm and weight less than 47 kg; primigravid status or parity greater than six; poor obstetric history; multiple pregnancy; maternal anemia, jaundice, hypertensive disorders, diabetes, syphilis, malaria, or HIV; preterm birth (<37 weeks gestation); post-term birth (>42 weeks gestation); obstructed labor; prolonged second stage of labor; passage of meconium; malpresentation (including breech); vaginal bleeding; maternal fever during labor; and prolonged rupture of membranes.[12] Of these identified risk factors, data were collected on the following: maternal age, primigravid status, multiple pregnancy, maternal health, preterm or post-term birth, malpresentation, maternal fever, and timing of membrane rupture.

Of these identified risk factors, the following were evaluated for association with neonatal and perinatal death due to the reliability and objectivity of the data: maternal age, primigravid status, multiple pregnancy, preterm or post-term birth, and malpresentation. Other variables that were evaluated for association with neonatal and perinatal death were sex of the infant, prenatal care, home delivery, birth weight of the infant, delivery mode, maternal tetanus vaccination, distance

from Nauta (the largest town with medical care), and presence of a skilled birth attendant.

Statistical Analysis

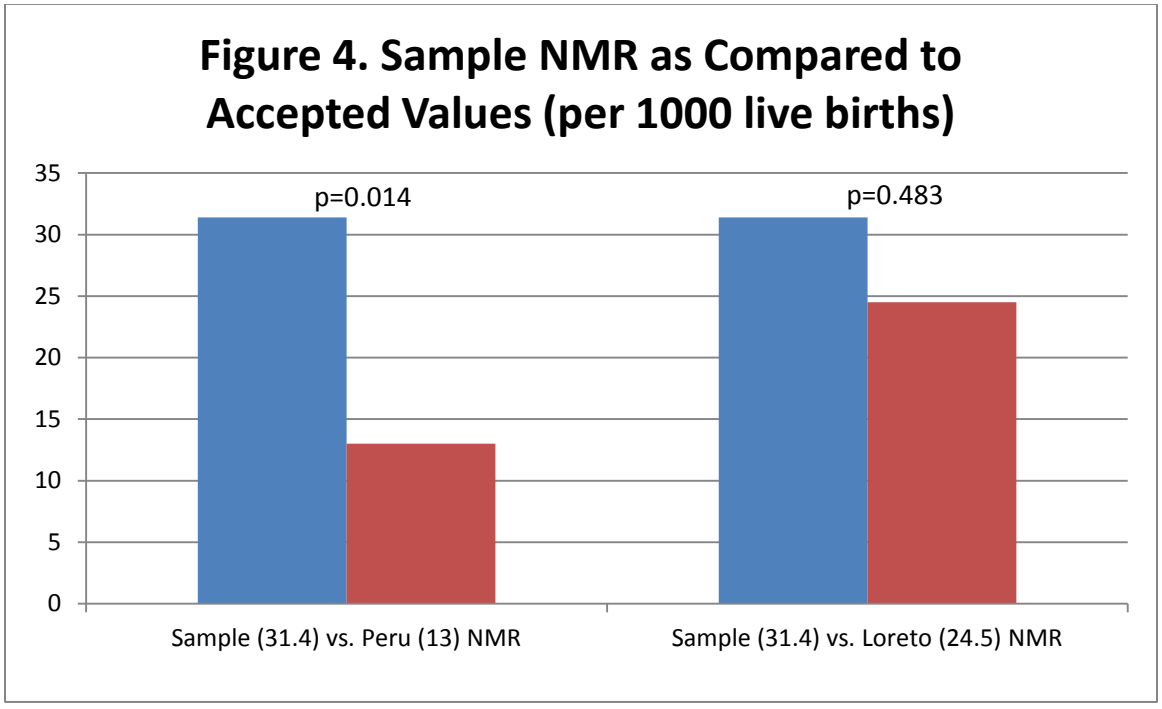
All statistical analyses were conducted in Stata 11.0 (StataCorp, College Station, TX). NMRs are expressed as the number of deaths between postnatal days 0 and 28 per 1000 live births. PMRs are expressed as the number of deaths between 28 weeks gestation and postnatal day of life 7 per 1000 pregnancies. NMRs and PMRs were calculated using a logistic GEE model; the mother was used as the clustering variable. The estimated NMR and PMR from the sample were compared to accepted values for both the Peru and Loreto Province NMRs and PMRs using linear contrast after the logistic GEE. Verbal autopsy reviewer agreement was assessed using percent agreement. With the exception of one woman who had experienced two stillbirths, each woman contributed data from one pregnancy to examine the association between exposure variables and neonatal or perinatal death using two-sided Fisher's exact tests. Exact logistic regression was performed to explore whether more than one variable could be significantly associated with neonatal or perinatal death in the regression using those variables found to be significant using Fisher's exact tests. The significance level for all tests was set at 0.05.

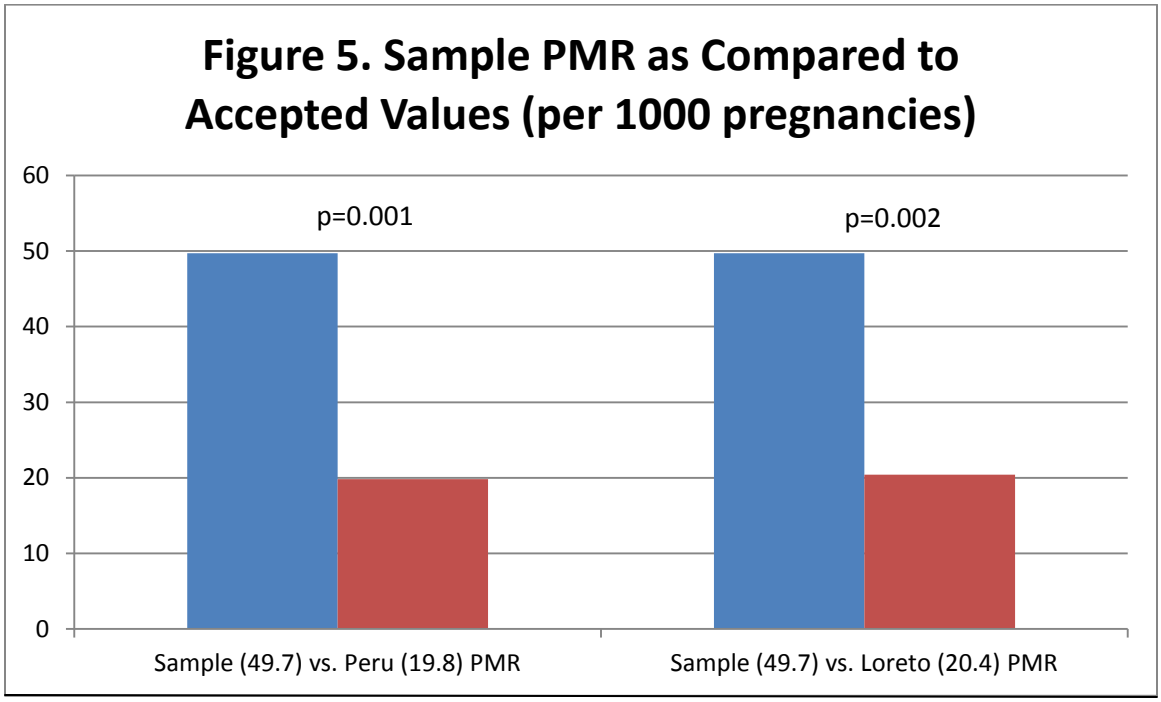
CHAPTER 3—RESULTS

One-hundred and thirty-two women met inclusion criteria; of these, 130 were consented and interviewed (two women declined interview). Data were collected on 263 pregnancies during the five years prior to interview (July 2005-July 2010). Three of the pregnancies were current at the time of interview, so outcomes were known for 260 completed pregnancies. The sample included three sets of twins. Two twin pregnancies resulted in stillbirth for both twins, while the other resulted in one live birth and one stillbirth. In order to minimize bias, as each twin pregnancy resulted in at least one stillbirth, each twin pregnancy is treated as one pregnancy and one stillbirth. Outcomes of the 260 completed pregnancies are presented in Table 1. Six stillbirths, all occurring after 28 weeks gestation per maternal report, were identified from 260 pregnancies. Seven neonatal deaths were identified from 229 live births (sum of living, neonatal death, infant death, and childhood death). Each neonatal death was an early neonatal death (occurred in the first 7 days of postnatal life); therefore, 13 perinatal deaths were identified from 260 pregnancies of known outcome.

A verbal autopsy (for stillbirth or neonatal death) or a detailed questionnaire (for live birth, Appendix B) was completed for each of the 130 interviewed women. The one exception was one woman who had experienced two stillbirths; verbal autopsies were completed for both of these stillbirths in an attempt to obtain the most amount of information on perinatal mortality for the region. General characteristics for these 131 pregnancies are detailed in Table 2.

Using the GEE model, the sample NMR estimated from the 7 neonatal deaths identified from 229 live births was found to be 31.4 per 1000 live births (95% CI: 15.6 per 1000 to 62.3 per 1000 live births). Figure 4 shows the comparison between this estimated rate and the accepted NMRs for both Peru and the Loreto Province. Using the same model, the sample PMR estimated from the 6 stillbirths and 7 early neonatal deaths identified from 260 pregnancies was found to be 49.7 per 1000 pregnancies (95% CI: 28.5 per 1000 to 85.3 per 1000 pregnancies). Figure 5 shows the comparison between this estimated rate and the accepted PMRs for both Peru and the Loreto Province.





Appendix C details other methods that could be used to calculate the NMR and PMR, including direct rate calculation and GEE rate calculation using the village as the clustering variable.

Verbal autopsy-identified cause of death assignments are shown in Table 3 (neonatal deaths), Table 4 (timing of stillbirth), and Table 5 (cause of stillbirth). Neonatal and perinatal deaths are analyzed separately as to determine efficiency of the verbal autopsy at determining cause of death between these two populations. Percent agreement among reviewers for neonatal cause of death was 90.5% (19/21), with a 95% CI of 69.6% to 98.8%. Percent agreement among reviewers for timing of stillbirth was 55.6% (10/18), with a 95% CI of 30.8% to

78.5%. Percent agreement among reviewers for cause of stillbirth was 38.9% (7/18), with a 95% CI of 17.3% to 64.3%. Additionally, kappa statistic calculations were attempted; due to the small number of observations, this was not a feasible method of assessing verbal autopsy user agreement. Kappa statistic calculations are shown in Appendix D.

The univariate association between each exposure variable and neonatal and perinatal death was assessed with Fisher exact tests. These variables included: maternal age, primigravid status, singleton vs. multiple gestation, gestational age at delivery, presentation at delivery, sex of the infant, prenatal care (at least one visit), place of delivery, birth weight of the infant, delivery mode, maternal tetanus vaccination status, distance from Nauta, and presence of a skilled birth attendant (Table 6). Pregnancy with twins (p=0.001), preterm delivery (p=0.003), and delivery by cesarean section (p=0.049) were significantly associated with neonatal or perinatal death. Presence of a doctor at delivery (p=0.061) and delivery in a medical facility (p=0.096) trended towards significance.

As previously stated, one mother in the sample had experienced two stillbirths, and, therefore, contributed two stillbirths to the six reported in the sample. A sensitivity analysis was performed to ensure that clustering from this mother did not alter risk factor analysis results. When only one stillbirth was counted for this mother (bringing the total number of perinatal deaths to 12), risk factor analysis results were not substantially different (Appendix E).

Based on the results from exact logistic regression, no single model included more than one significant variable. Of the exposure variables of pregnancy with twins, preterm delivery, and delivery by cesarean section, preterm delivery was the only variable that remained in the exact logistic regression model.

CHAPTER 4—DISCUSSION

Using direct interview techniques with women who had been pregnant in the 5 years prior to the interview, the NMR and PMR for nine villages in the Loreto Province of Peru were estimated to be 31.4 per 1000 live births (95% CI: 15.6-62.3) and 49.7 per 1000 pregnancies (95% CI: 28.5-85.3), respectively. Causes of neonatal death were attributed to infection (43%), asphyxia (29%), prematurity (14%), and congenital malformations (14%). Verbal autopsy reviewer agreement was good for cause of neonatal death and fair for timing and cause of stillbirth. Pregnancy with twins, premature delivery, and delivery by cesarean section were significantly associated with neonatal or perinatal death.

Depending on the country, information on neonatal and perinatal mortality comes from vital registration systems, survey data, or a combination of both.[13] Since only one third of the world's population has reliable vital registration data, survey data is the main source of neonatal and perinatal mortality information for most developing countries, including Peru.[13] The Instituto Nacional de Estadistica e Informatica is the Peruvian organization in charge of obtaining this survey data, and it does so through the implementation of the Demographic and Health Survey (DHS).[28] The WHO uses data from the Instituto Nacional de Estadistica e Informatica as its source of reported NMRs and PMRs.[13] All accepted NMRs and PMRs reported here come from either the WHO or directly from the Instituto Nacional de Estadistica e Informatica; therefore, all accepted NMRs and PMRs reported here come from the DHS.[24,25,26]

Our sample NMR of 31.4 per 1000 live births is substantially higher than the accepted NMR for Peru of 13 per 1000 live births (p=0.014), but not appreciably different than the accepted NMR for the Loreto Province of 24.5 per 1000 live births (p=0.483). Our sample PMR of 49.7 per 1000 pregnancies was over two-fold higher than the accepted PMR for both Peru (19.8 per 1000 pregnancies, p=0.001) and the Loreto Province (20.4 per 1000 pregnancies, p=0.002). Therefore, each rate that was estimated using the DHS was lower than the rates observed in our study.

Underestimation of NMRs and PMRs is common when survey tools are used, especially for deaths that occur close to the time of birth.[13] Underreporting, particularly of stillbirth, is the most common problem encountered in neonatal and perinatal mortality estimates.[13] The number of stillbirths at least equals (and likely exceeds) the number of neonatal deaths in developing countries; underreporting is suggested in many surveys when only one-third to one-half the number of neonatal deaths are reported as stillbirths.[13] If these surveys are not conducted in the remote areas that lack accessible health care, underreporting on a national level is likely to occur. Unfortunately, the details of how and where the DHS survey is implemented in Peru are not available. Misclassification by either the mother or the survey can also occur due to a misunderstanding of the definitions of live birth or stillbirth.[13] Oftentimes regression or other estimation methods are used in an attempt to account for these underestimations. The rates that are

provided for Peru are not altered statistically, leaving the possibility that underreporting is an issue.[13]

We found an equal number of stillbirths to early neonatal deaths, which is consistent with what is reported in the literature. Although our direct interview method and village survey appeared to capture data that may be more accurate than the reported NMRs and PMRs, this technique is not without its own potential limitations. First, we only questioned women who were registered in clinics. Women with health problems, and thus possibly adverse pregnancy outcomes, may be more likely to seek medical care. This would lead to an overestimation of NMR and PMR. We did not have the ability to compare the health between those that did and those that did not seek care. Second, recall bias may also have been an issue, as mothers were asked to remember details about pregnancy and delivery from up to five years prior to the time of interview. Inability to accurately recall the gestation at the time of fetal loss may have led to misclassification of miscarriage as stillbirth and vice versa. Also, if the timing of neonatal death was not recalled accurately, a misclassification of neonatal death as early or late may have altered the estimation of the PMR (stillbirth and early neonatal deaths only). Although the possibility of recall bias exists, in our judgment it is not likely to be an issue for misclassification because the accuracy of recall is likely to be improved by the enormity of the event of a fetal or neonatal death in the lives of the women that were interviewed.

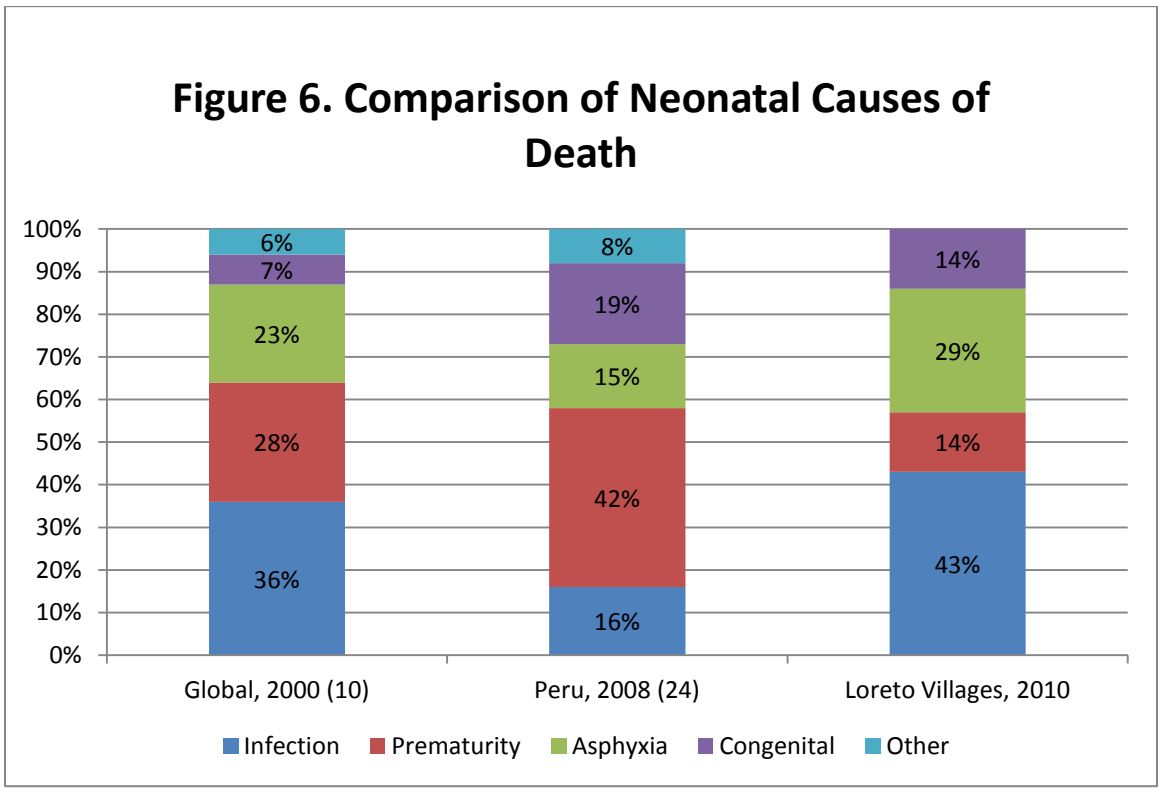
On the other hand, our methodology may also have underestimated the true NMR and PMR for these villages. Maternal mortality is strongly associated with stillbirth and neonatal death. As we did not interview family or general community members regarding maternal deaths, we may not have captured all stillbirths and neonatal deaths, biasing our results to the null. Younger maternal age is also a risk factor for perinatal and neonatal death. We excluded women under the age of 15 from this study, which may again decrease our numbers of stillbirth or neonatal death. Finally, we may have experienced underreporting simply because our study population felt uncomfortable discussing these sensitive issues with us. We feel this is not as likely, as women were informed of the nature of the questions to be asked and were given the opportunity to decline interview. Only two of the 132 women who were asked to participate declined to do so. Any bias introduced by these two women would have been minimal.

Overall, many of the shortcomings that can be seen in the direct interview technique would also be apparent in the use of the DHS. The major lack of information in this study comes from the absence of data about maternal mortality and from women under the age of 15. Since the lack of this data would likely result in a bias of the estimate towards the null, we can feel fairly certain that the differences seen between our NMR and PMR and the accepted values for Peruvian and Loreto Province NMR and PMR are at least this large, and probably underestimated.

To determine cause of death, we utilized the 2007 WHO International Standard Verbal Autopsy for death of a child under four weeks of age. Three physicians reviewed each VA and assigned cause of death and/or timing of death for each. We found good inter-reviewer agreement for the use of this tool in determining neonatal cause of death (90.5% agreement); however, this tool did not have good inter-reviewer agreement for determining timing of stillbirth (55.6%) or cause of stillbirth (38.9%).

Verbal autopsy results in this study showed that of the seven identified neonatal deaths, three were attributed to infection (43%), two to asphyxia (29%), one to prematurity (14%), and one to congenital malformation (14%). Since less than 3% of neonatal deaths worldwide have reliable cause of death data from vital registration systems, global percentages are estimates obtained through advanced statistical modeling.[29] According to the WHO, Peru had vital registration statistics with an estimated 50-74% coverage from 2007; therefore, the WHO and the Child Health Epidemiology Reference Group estimated percentages of neonatal causes of death for Peru in 2008 using a vital registration-based multi-cause model for neonatal death.[30] Figure 6 compares the results of our study to the global and Peruvian estimates. We must interpret the percentages of causes of death found in our study with caution, due to the sample size of seven. However, interestingly, the results from this study found the proportions of neonatal causes of death in these nine villages in the Loreto

Province to more closely resemble global estimates than estimates for the country of Peru.



As stated, Peru had 50-74% vital registration coverage for 2007. This coverage was likely higher in larger cities such as Lima, where the population has more consistent access to health care. Of the six stillbirths and seven neonatal deaths we recorded form the last five years in these nine villages, only one mother had received a death certificate for her child. This is well under the reported 50-74% range of vital registration coverage for Peru. While a vital registration-based multi-cause model for neonatal death may be appropriate for certain areas of countries, it may not be appropriate to generalize these results to all regions in the country. The percentages seen for Peru are closer to those percentages

seen in more developed countries, with prematurity accounting for the largest proportion of neonatal death. The percentages seen for these nine villages in the Loreto Province, where healthcare is difficult to access, are closer to the global estimates, which are heavily weighted by the large number of stillbirths and neonatal deaths that occur in rural areas with limited access to healthcare. This highlights the need for more accurate region-specific cause of death estimates.

To our knowledge, there are no published studies that have utilized the 2007 WHO International Standard VA for death of a child under four weeks of age. Over the last several years, however, studies have been published on use of VA to ascertain causes of stillbirth and/or neonatal death in specific areas. Three of these studies utilized the 2002 revised version of the WHO childhood VA that had specific modules for stillbirths and neonatal deaths. Only one of these studies, performed in Ghana in 2003-2004, attempted validation of the tool by comparing hospital records to the causes of death assigned using VA.[31] A total of 1251 VAs were coded by 3 physician reviewers; the level of agreement between physicians was at least moderate (kappa statistic ≥ 0.40) for all major causes of neonatal death or stillbirth except for congenital abnormalities causing antepartum stillbirth.[31] A total of 502 VAs for either stillbirth or neonatal death were available for comparison to the hospital record.[31] They found that 64% of the total stillbirths and 70% of the neonatal deaths were correctly classified by VA according to their major cause.[31] Sensitivity was >70% for all major causes of death except prematurity.[31] Specificity was 76% for birth asphyxia and >85% for

prematurity and infection.[31] The diagnostic accuracy for neonatal death of the VA used in this study, when compared to older studies that looked at comparisons between VA and hospital records for neonatal death, was found to be better. Specificity was generally higher and sensitivity similar or slightly lower in this Ghana study as compared to similar comparison studies done in Bangladesh, Pakistan, Nepal, and Nicaragua.[31] There are no published studies of VA diagnostic accuracy for stillbirth.[31] We did not find validation studies in the literature for the 2007 WHO International Standard VAs.

The other two studies that utilized the 2002 revised version of the WHO childhood VA were done in Nepal and Bangladesh. The Nepal study used a two physician review of VA for neonatal death or stillbirth and utilized this information to determine NMR, PMR, and causes of neonatal death.[32] The Bangladesh study used a three physician review of VA for neonatal death and utilized this information to determine NMR and causes of neonatal death.[33] Neither of these studies was able to validate VA results against the gold standard of hospital records.

In comparing our study to the Nepal and Bangladesh studies, we used the VA in a similar fashion to determine NMR, PMR, and cause of death. These studies were able to perform much larger numbers of VAs (1272 total VAs in the Nepal study and 365 in the Bangladesh study).[32,33] The results found for NMR, PMR, and causes of death are not comparable due to different populations studied.

Reviewer agreement found in the Ghana study is difficult to compare to our study, since they report reviewer agreement using kappa statistics. In general, they did seem to see higher agreement for neonatal deaths than for stillbirths, which is consistent with our findings. The sensitivity and specificity levels found in the Ghana study, although not for the particular VA used in our study, can give us some confidence in the VA's ability to estimate causes of neonatal death. The VA's ability to identifying cause of stillbirth, however, may not be as accurate, which is evident in our findings.

Despite the growing use of VA for cause of death determination in areas lacking vital registration systems, challenges for the use of the VA technique remain evident. The primary challenge is the lack of a standardized instrument and directions for its administration.[34] The WHO created the 2007 International Standard VAs in an attempt to move toward a standard method; however, the use and administration of this form has not been standardized.[34] Validation studies of this form in which causes of neonatal death or stillbirth identified by VA are compared to a gold standard of hospital record diagnoses are also lacking.[34] Other areas of research for this VA form include determining the best method for assigning causes of death that removes human bias, optimal sampling methods and size when using this tool for research purposes, and the best way to adapt this tool to different countries for specific situations.[35]

VA is also susceptible to bias. Reporting bias can occur if cultural factors associated with death prevent a mother from wanting to discuss the death of infants under one month of age.[34] This may be made worse if the interviewer is male.[34] Also, the clinical background of an interviewer may unknowingly bias results of a VA to look like a specific disease burden is higher in a certain location.[34] Recall bias is possible if there is a long period of time between the death of the infant and the timing of the interview. For adult deaths, interview within one year of death is considered acceptable for VA accuracy.[34] However, validity of mothers' responses for a period of up to 20 months has been reported to be high.[34]

In the present study, we questioned mothers about stillbirths and neonatal deaths over the last five years. This was done in order to increase our sample size, but may have introduced an element of recall bias into results. Also, 12 of our 13 stillbirths and neonatal deaths did not have medical records or death certificates; therefore, validation of the reviewer-assigned causes of death was not possible. Finally, we had physicians trained in neonatology making cause of death assignments for stillbirths. It is possible, since stillbirths are typically due to obstetric complications, that we asked the wrong group of physicians to review the stillbirth VAs. Perhaps we would have seen better reviewer agreement if we had asked obstetricians to review this data.

Strengths of the study included that the same female provider (JBW) performed all verbal autopsies with the help of female interpreters. Only two women out of the sample of 132 declined questioning. Causes of death assigned by the reviewers should not have been biased, as they were not present for the interview and had only the answers provided by the VA questionnaire to make diagnosis decisions. Finally, this is one of the only studies we are aware of to use the 2007 WHO International Standard VA for death of an infant under four weeks of age. Although this is a small study, it will add to the modest body of literature on the use of VA in developing areas.

Risk factors for stillbirth and neonatal death have been identified from several population-based studies.[12] We did not specifically assess for several of the known risk factors in this study, including maternal height <150 cm; maternal weight <47 kg; parity greater than six; poor obstetric history; maternal illness including anemia, jaundice, hypertensive disorders, diabetes, syphilis, malaria, HIV; obstructed labor; prolonged second stage of labor; passage of meconium; or vaginal bleeding. We did assess for the remaining known risk factors for neonatal and perinatal death, including maternal age <18 or >35 years, primigravid status, multiple pregnancy, gestational age < 37 weeks or >42 weeks, malpresentation, maternal fever, and prolonged rupture of the membranes >24 hours. We also assessed for some additional risk factors not identified by previous studies, including prenatal care, tetanus status of the mother, presence of a skilled birth attendant, location of the delivery, mode of

delivery, sex of the neonate, birth weight, and proximity of the village to Nauta. In this study, pregnancy with twins, premature delivery (<37 weeks' gestation), and delivery via cesarean section were found to be statistically significant risk factors for neonatal or perinatal death.

Limitations of this portion of the study include the lack of information on several of the known risk factors for neonatal and perinatal death. Due to constraints on time and inability to review medical records, information on many of these risk factors was not able to be obtained. All information gathered on risk factors was dependent on maternal memory, knowledge, and, at times, estimation. For example, information on gestational age at delivery was dependant on maternal report. Due to the lack of consistent prenatal care, many of these gestational ages were based solely on last menstrual period as reported by the mother. Due to perceived difficulties in the majority of women to report accurately on presence of fever during labor or the duration of rupture of membranes, these were not assessed for statistical significance as risk factors for neonatal or perinatal death. The discovery of only three risk factors that were significantly related to neonatal and perinatal death may have been due to the small sample size in this study. Limitations in sample size also led to the need to use exact tests to assess risk factors and the inability to use logistic regression. Use of exact logistic regression did not identify more than one significant variable in any single model.

Strengths of the risk factor analysis include the number of variables that were analyzed, including some that had not been previously reported as risk factors. The finding that pregnancy with twins or delivery of a premature infant was associated with neonatal or perinatal death was expected. The discovery that delivery by cesarean section was significantly associated with neonatal or perinatal death has not been previously reported. This finding was likely secondary to the fact that by the time women from these villages were able to get to a higher level of medical care, the problems they had to necessitate that higher level of care made it more likely for pregnancy to result in stillbirth or neonatal death. The same explanation can be made for the risk factors that trended toward significance, specifically the two variables “having a physician present at delivery” and “delivering in a medical facility.” In general, it was not typical for the deliveries of women from these villages to be attended by a doctor or occur in a medical facility. If either of these occurred, it was likely that a woman was having problems with the pregnancy that may predispose to stillbirth or neonatal death.

Overall, we feel that our estimates for the NMR and PMR for these nine villages in the Loreto Province of Peru may be more accurate than those currently published. Use of VA provided good inter-reviewer agreement for cause of neonatal death, but less agreement when looking at timing of or cause of stillbirth. Despite inherent limitations with the use of VA, we feel that the use of the 2007 WHO International Standard VA for infants under four weeks of age

provided an acceptable method of determining the difference between stillbirth and neonatal death, and classifying cause of neonatal death. Risk factor assessment found pregnancy with twins, delivery before 37 weeks' gestation, and delivery by cesarean section to be significant risk factors for neonatal and perinatal death. Even with our small sample size, we quantified neonatal and perinatal mortality rates that met expectations for rural areas such as the Loreto Province. Similarly, our clinical judgments for causes of death and risk factors for death are congruent with other available reports for developing countries and their rural populations. By conducting this needs assessment, we are now in a position to collaborate with these communities in order to plan and implement education programs focused on the needs of these villages.

Table 1. Outcomes data for each completed pregnancy over the last 5 years (130 women interviewed)

Outcome	Number
Living	211
Miscarriage	25
Stillbirth	6
Neonatal death	7
Infant death	8
Childhood death	3
Total number of pregnancies	**260**

Table 2. Characteristics of each pregnancy obtained from detailed interview

Characteristic	Number of pregnancies (n=131 unless specified)	Percent of pregnancies
Maternal age <18 or >35	34	26%
Primigravid status	43	32.8%
Singleton pregnancy	128	97.7%
Delivery at term (37-42 weeks)	116/128*	90.6%
Malpresentation	2	1.5%
Male sex of infant	66	50.4%
Prenatal care (at least one visit)	68	51.9%
Delivery at home	112	85.5%
Birth weight average for gestation	86/126^	68.3%
Delivery by Cesarean section	4	3.1%
Maternal tetanus vaccination	58/65**	89.2%
Distance from Nauta >2 hours by boat	56*^	42.7%
Birth attendant		
Traditional birth attendant	73	55.7%
Family member/alone	40	30.5%
Formally trained health professional	18	13.7%

*3 women unsure of gestation at delivery
^5 women unsure of size/birth weight of baby
**Data not collected for 66 pregnancies
*^Libertad, Jerusalen, Jaldar, Puerto Miguel, San Jose

Table 3. Verbal autopsy results: neonatal cause of death

Patient	Reviewer 1	Reviewer 2	Reviewer 3
1	Infection	Tetanus	Tetanus
2	Asphyxia	Asphyxia	Asphyxia
3	Asphyxia	Asphyxia	Asphyxia
4	Infection	Infection	Infection
5	Congenital malformation	Airway malformation	Congenital malformation
6	Bowel obstruction	Infection	Infection
7	Prematurity	Prematurity	Prematurity

Table 4. Verbal autopsy results: timing of stillbirth

Patient	Reviewer 1	Reviewer 2	Reviewer 3
1	Intrapartum	Before labor	Intrapartum
2	Intrapartum	Before labor	Intrapartum
3	Intrapartum	Intrapartum	Before labor
4	Intrapartum	Intrapartum	Intrapartum
5	Intrapartum	Intrapartum	Intrapartum
6	Intrapartum	Intrapartum	Intrapartum

Table 5. Verbal autopsy results: cause of stillbirth

Patient	Reviewer 1	Reviewer 2	Reviewer 3
1	Asphyxia	Hydrops	Asphyxia
2	Asphyxia/premature	Chorioamnionitis	Asphyxia
3	Asphyxia	Asphyxia	Asphyxia
4	Asphyxia/cord prolapsed	Unknown	Asphyxia
5	Asphyxia/premature	Chorioamnionitis	Asphyxia
6	Multiple anomalies	Chorioamnionitis	Asphyxia

Table 6. Associations of risk factors to neonatal and perinatal death

Risk factor for neonatal or perinatal death	Deaths with risk factor (%)	Deaths without risk factor (%)	P-value*
Maternal age <18 or >35 years	2/34 (5.9)	11/97 (11.3)	0.513
Primigravid status	4/44 (9.1)	9/87 (10.3)	1.000
Twin gestation pregnancy	3/3 (100.0)	10/128 (7.8)	0.001
Preterm delivery (<37 weeks' gestation)^	5/12 (41.7)	8/116 (6.9)	0.003
Non-vertex presentation	1/2 (50.0)	12/129 (9.3)	0.189
Male sex	8/66 (12.1)	5/65 (7.7)	0.561
No prenatal care	4/63 (6.3)	9/68 (13.2)	0.247
Delivery in a medical facility	4/19 (21.1)	9/112 (8.0)	0.096
Birth weight large/small for gestation**	3/40 (7.5)	8/86 (9.3)	1.000
Cesarean section delivery	2/4 (50.0)	11/127 (8.7)	0.049
Mother without tetanus vaccination*^	1/7 (14.3)	12/58 (20.7)	1.000
Distance from Nauta >2 hours by boat	6/56 (10.7)	7/75 (9.3)	1.000
Presence of a doctor at delivery	4/18 (22.2)	9/113 (8.0)	0.061

*Fisher's exact test, 2-sided
^3 unknown gestational ages
**5 unknown size (2 deaths)
*^data not collected from 66 pregnancies

Supplementary tables in Appendix F

CHAPTER 5—PUBLIC HEALTH IMPLICATIONS

Neonatal and perinatal mortality is a recognized problem in Peru and worldwide. A number of interventions have been suggested in order to decrease NMRs and PMRs globally.[11] To be successful, these interventions must target site-specific causes of neonatal and perinatal death. Unfortunately, little is known about the countries with the highest NMRs and PMRs as they do not have vital registration systems in place to obtain this information. The goal of this project was to determine the number, causes, and risks of neonatal and perinatal death for the Loreto Province of Peru. We hope to use this information to design interventions that specifically target the needs of these communities.

The main finding of our study was the estimated NMR and PMR for our targeted area that are higher than previously reported, and apparently higher than the national rates. The major causes of neonatal death as attributed by VA and expert review are, in descending order: infection, asphyxia, prematurity, and congenital abnormalities. Risk factors for perinatal death are pregnancy with twins, preterm delivery, and need for cesarean section.

Although the Demographic and Health Survey is currently implemented in Peru to capture NMR and PMR data, at the local level there are no consistent death recording systems. This lack of a local system eventually affects the accuracy and specificity of the larger recording systems. Of the 13 stillbirths and neonatal deaths identified, only one mother had a death certificate that recorded the

occurrence and probable cause of death of her child. Before the implementation of an intervention in any of these communities, it is first necessary to establish a method of recording these deaths as they occur. Without this record, it will not be possible to track the success of any intervention.

The state infrastructure is not mature enough to institute a registration system in these jungle villages. However, there are literate community members that could be trained to be responsible for the collection of these data. Each of the communities focused on had at least one traditional birth attendant. As the community members most commonly involved in the delivery of infants, traditional birth attendants would be ideal candidates to be in charge of recording stillbirths and neonatal deaths for the town, along with a perceived cause of death. If these records are kept by a single person or group, it would be possible to report these numbers to responsible government parties every 5 to 10 years. Knowledge of how a community's stillbirth or neonatal death rate changes over time will help to determine if interventions have been successful.

It is also necessary to know how causes of stillbirth or neonatal death change over time to determine if interventions have been successful. VA is a relatively easy and inexpensive method that could be routinely employed in these villages to determine causes of death. By knowing how the relative prevalence of causes of death change over time, the success of cause-specific interventions can be assessed and adjusted, if necessary. This would ideally be a government-

supported effort. VAs could be performed by a government-appointed group every 5 to 10 years, at the same time the death records are reported.

For now, VA can be used in a fashion similar to how it was used in this study. However, if VA is used in Peru on the large scale we suggest here, it is possible that its use in Peru could contribute to larger VA validation and standardization studies. Although VA has been used for many years, the International Standard VA forms developed by the WHO in 2007 are the first attempt at universal forms. Further standardization of the use and administration of these forms is needed. For example, it is unclear if these forms could be administered by individuals with non-medical backgrounds, then coded by physicians. There are also suggestions that computer algorithms might be developed to handle coding of causes of death, thus minimizing bias. If VA were used on a larger scale in Peru, we might be able to gain important knowledge about region-specific causes of neonatal death in the country while also contributing to the much-needed base of research on VA use.

In these nine villages in the Loreto Province, the main causes of neonatal death were found to be infection, asphyxia, prematurity, and congenital abnormalities. Stillbirth was found to occur as frequently as neonatal death. In looking at these main causes of death, three areas for intervention can be targeted. These include (1) recognition of the need for transport to a higher level of care, (2)

education on how to treat birth asphyxia, and (3) education on cleanliness and avoidance of infection.

Recognition of the need to transport to a higher level of care and the ability to make transport occur are necessary in certain situations. One of these situations is prematurity. Many of the stillbirths that were identified in this study occurred in preterm pregnancies and one of the neonatal deaths was attributed to prematurity. Prematurity, the leading cause of neonatal death in the developed world, will be particularly challenging to address. However, the hospitals in Iquitos have the resources and ability to care for preterm infants that might otherwise die if they remained in the jungle. Most of the women that we talked with who ended up delivering premature infants had warning signs of impending delivery or problems with the pregnancy before delivering their infant. Recognition of these issues and of the need to transport these women to a higher level of care is likely the best option to attempt to save the lives of these infants.

The recognition of the need to transport and the ability to transport are two different things. The majority of the people who live in these villages do not have the resources to easily travel to other villages or to bigger towns. All of the villages we visited are dependent on the river for transportation; there are no roads between these villages and Nauta. There is a paved road from Nauta to Iquitos. Along with the education of the local midwives about warning signs of

premature delivery and the need to transport these women to a higher level of care, an individualized emergency medical transport plan should be made for each village. This may include making rental agreements with members of the community who own boats, or simply having someone who can quickly get to a nearby village to obtain transportation. Whatever the plan may be, it should be well known throughout the village, and ideally, all community members would be willing to help with transport if needed.

Neonatal death from prematurity and congenital abnormalities will overall be difficult to overcome in settings where resources are limited. However, with a relatively small amount of education and resources, we may be able to give these communities the ability to drastically decrease rates of neonatal death caused by infection and birth asphyxia. The majority of the local midwives that we met during our time in these villages had no formal midwifery training. However, these women were extremely experienced in the delivery of babies. They were excited to gain any knowledge they could and in desperate need of supplies. Two programs that are focused on the education of traditional birth attendants such as the women we encountered are the American Academy of Pediatrics' Helping Babies Breathe (HBB), which targets those infants having trouble with transition due to birth asphyxia, and the WHO's Essential Newborn Care (ENC), an education program targeting both prenatal and postnatal care.

HBB is an evidence-based curriculum developed specifically for the education of birth attendants who are responsible for the resuscitation of infants in resource-limited areas.[36] The focus of HHB is on “The Golden Minute;” the goal is that every baby should either be breathing well or should be ventilated with a bag and mask within one minute of birth.[36] The education program is based on a pictorial action plan (Appendix G) and keys on the need for an assessment of every baby, stimulation to breathe, and assisted ventilation, if necessary.[36,37] The program is simulation-based, and training includes practice with a newborn simulator and supplies such as a suction device and bag-mask ventilator.[36] All of these supplies are able to be cleaned by boiling, and are available at cost to MDG countries.[36] The goal of HBB is to give the birth attendants in these resource-limited areas the knowledge, resources, and ability to treat those infants who do not breathe at birth as a result of birth asphyxia.

ENC is designed to improve the health of newborns through basic preventive care and the early detection of danger signs that require referral to higher levels of care.[38] The program is based on the premise that preventing newborn deaths begins with the health of the mother.[38] Prenatal care such as tetanus immunization, focus on maternal nutrition, and treatment of maternal infection can have a strong influence on newborn survival.[38] Interventions during the intrapartum time period focus on the need for clean delivery practices in order to prevent infection.[38] Postnatal care should include early and exclusive breastfeeding, attention to thermal control, and continued hygienic practices,

including the care of the umbilical cord.[38] Importantly, these interventions can be carried out in a cost-effective manner. The WHO estimates that the implementation of the full ENC program would cost US$3 a year per capita in low-income countries.[38]

Implementation of HBB and ENC in these jungle villages of Peru would potentially target the two main causes of neonatal death in the region: infection and asphyxia. Coupled with the implementation of a method of recording deaths and plan for follow-up of determining cause of death through verbal autopsy, we would have the ability to provide interventions that focus on the main neonatal causes of death for these villages and follow progress over time.

Appendix A: World Health Organization Verbal Autopsy Standard

INTERNATIONAL STANDARD VERBAL AUTOPSY QUESTIONNAIRE 1
DEATH OF A CHILD AGED UNDER 4 WEEKS

ID/CONTROL/REFERENCE NUMBER ☐☐☐☐☐☐

SECTION 1.1 INTERVIEWER VISITS

	1	2	3	FINAL VISIT
DATE				DAY ☐☐
				MONTH ☐☐
				YEAR 2 0 ☐☐
INTERVIEWER'S NAME				INT. NUMBER ☐☐
RESULT*	☐	☐	☐	RESULT ☐
NEXT VISIT: DATE				TOTAL NUMBER OF VISITS ☐
TIME				

1 COMPLETED 2 NOT AT HOME 3 POSTPONED 4 REFUSED
5 PARTLY COMPLETED 6 NO APPROPRIATE RESPONDENT FOUND 7 OTHER _____ (SPECIFY)

SUPERVISOR	FIELD EDITOR	OFFICE EDITOR	KEYED BY
NAME _____	NAME _____	☐☐	☐☐
DATE _____ ☐☐	DATE _____ ☐☐		

PLACE NAME _____

ADDRESS/DIRECTIONS TO HOUSEHOLD _____

SECTION 1.2 ADDITIONAL DEMOGRAPHIC INFORMATION
(FOR USE IN SAMPLE VITAL REGISTRATION OR DEMOGRAPHIC SURVEILLANCE SITE)

REGION/PROVINCE _____
FIELD SITE _____
HOUSEHOLD NUMBER _____
NAME OF REFERENCE PERSON _____
RESIDENTIAL STATUS OF THE DECEASED _____

REGION/PROVINCE ..... ☐☐
FIELD SITE ..... ☐☐
HOUSEHOLD NUMBER ..... ☐☐

RESIDENT IN ENUMERATION AREA 1
BODY BROUGHT HOME FOR BURIAL 2
HOME-COMING SICK 3

SAMPLE INFORMED CONSENT STATEMENT

Hello. My name is _____ and I am working with [AGENCY]. We are collecting information on the causes of death in the community. We would very much appreciate your participation in this effort. We want to ask you about the circumstances leading to the death of the deceased. Whatever information you provide will be kept strictly confidential. No information identifying you or the deceased will ever be released to anyone outside of this information-collection activity. Participation in this survey is voluntary and you can choose not to answer any individual question or all of the questions. You may also stop the interview completely at any time without any consequences at all. However, we hope that you will participate in this survey since the results will help the government improve services for people.

At this time, do you want to ask me anything about the purpose or content of this interview?

May I begin the interview now?

Signature of interviewer: _____ Date: _____

RESPONDENT AGREES TO BE INTERVIEWED ... 1 ↓ RESPONDENT DOES NOT AGREE TO BE INTERVIEWED ... 2 → END

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
SECTION 2. BASIC INFORMATION ABOUT RESPONDENT			
201	RECORD THE TIME AT START OF INTERVIEW	HOUR ..... [ ][ ] MINUTES ..... [ ][ ]	
202	NAME OF THE RESPONDENT	_____ (NAME)	
203	What is your relationship to the deceased?	FATHER ..... 1 MOTHER ..... 2 SIBLING ..... 4 OTHER RELATIVE _____ (SPECIFY) 6 NO RELATION 8	
204	Did you live with the deceased in the period leading to her/his death?	YES ..... 1 NO 2	
SECTION 3. INFORMATION ON THE DECEASED AND DATE/PLACE OF DEATH			
301	What was the name of the deceased?	_____ (NAME)	
302	Was the deceased female or male?	FEMALE ..... 1 MALE 2	
303	When was the deceased born? RECORD '9 8' IF DON'T KNOW DAY OR MONTH RECORD '9 9 9 8' IF DON'T KNOW YEAR	DAY ..... [ ][ ] MONTH ..... [ ][ ] YEAR ..... [ ][ ][ ][ ]	
304	How old was the deceased when s/he died?	AGE IN DAYS ..... [ ][ ]	
305	When did s/he die? RECORD '9 8' IF DON'T KNOW DAY OR MONTH RECORD '9 9 9 8' IF DON'T KNOW YEAR	DAY ..... [ ][ ] MONTH ..... [ ][ ] YEAR ..... [ ][ ][ ][ ]	
306	Where did s/he die?	HOSPITAL ..... 1 OTHER HEALTH FACILITY ..... 2 HOME ..... 3 OTHER _____ (SPECIFY) 6 DON'T KNOW 8	
SECTION 4. RESPONDENT'S ACCOUNT OF ILLNESS/EVENTS LEADING TO DEATH			
401	Could you tell me about the illness/events that led to her/his death? _____ _____ _____ _____ _____ _____		
402	CAUSE OF DEATH 1 ACCORDING TO RESPONDENT _____		
403	CAUSE OF DEATH 2 ACCORDING TO RESPONDENT _____		

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
SECTION 5. PREGNANCY HISTORY			
501	I would like to ask you some questions concerning the mother and symptoms that the deceased had/showed at birth and shortly after. Some of these questions may not appear to be directly related to the baby's death. Please bear with me and answer all the questions. They will help us to get a clear picture of all possible symptoms that the deceased had.		
502	How many births, including stillbirths, did the mother have before this baby?	NUMBER OF BIRTHS/ STILLBIRTHS ..... ☐☐ DON'T KNOW 98	
503	How many months was the pregnancy when the baby was born?	MONTHS ..... ☐☐ DON'T KNOW 98	
504	Did the pregnancy end earlier than expected?	YES ..... 1 NO ..... 2 → 506 DON'T KNOW ..... 8 → 506	
505	How many weeks before the expected date of delivery?	WEEKS ..... ☐☐ DON'T KNOW 98	
506	During the pregnancy did the mother suffer from any of the following known illnesses:	YES NO DK	
	1 High blood pressure?	HIGH BLOOD PRESSURE 1 2 8	
	2 Heart disease?	HEART DISEASE 1 2 8	
	3 Diabetes?	DIABETES 1 2 8	
	4 Epilepsy/convulsion?	EPILEPSY/CONVULSION 1 2 8	
	5 Did she suffer from any other medically diagnosed illness?	OTHER ..... 1 2 8 _____ (SPECIFY)	
507	During the last 3 months of pregnancy did the mother suffer from any of the following illnesses:	YES NO DK	
	1 Vaginal bleeding?	VAGINAL BLEEDING 1 2 8	
	2 Smelly vaginal discharge?	SMELLY VAGINAL DISCHARGE 1 2 8	
	3 Puffy face?	PUFFY FACE 1 2 8	
	4 Headache?	HEADACHE 1 2 8	
	5 Blurred vision?	BLURRED VISION 1 2 8	
	6 Convulsion?	CONVULSION 1 2 8	
	7 Febrile illness?	FEBRILE ILLNESS 1 2 8	
	8 Severe abdominal pain that was not labor pain?	SEVERE ABDOMINAL PAIN (NOT LABOR PAIN) 1 2 8	
	9 Pallor and shortness of breath (both present)?	PALLOR/SHORTNESS OF BREATH (BOTH) 1 2 8	
	10 Did she suffer from any other illness?	OTHER ILLNESS ..... 1 2 8 _____ (SPECIFY)	
508	Was the child a single or multiple birth?	SINGLETON ..... 1 → 601 TWIN ..... 2 TRIPLET OR MORE ..... 3 DON'T KNOW ..... 8 → 601	
509	What was the birth order of the child that died?	FIRST ..... 1 SECOND ..... 2 THIRD OR HIGHER ..... 3 DON'T KNOW 8	

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
SECTION 6. DELIVERY HISTORY			
601	Where was the child born?	HOSPITAL ..... 1 OTHER HEALTH FACILITY ..... 2 HOME ..... 3 OTHER _____ 6 (SPECIFY) DON'T KNOW 8	
602	Who assisted with the delivery?	DOCTOR ..... 1 NURSE/MIDWIFE ..... 2 TRADITIONAL BIRTH ATTENDANT ..... 3 RELATIVE ..... 4 MOTHER BY HERSELF ..... 5 OTHER _____ 6 (SPECIFY) DON'T KNOW 8	
603	When did the water break?	BEFORE LABOR STARTED ..... 1 DURING LABOR ..... 2 DON'T KNOW 8	
604	How many hours after the water broke was the baby born?	LESS THAN 24 HOURS ..... 1 24 HOURS OR MORE ..... 2 DON'T KNOW 8	
605	Was the water foul smelling?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
606	Did the baby stop moving in the womb?	YES ..... 1 NO ..... 2 DON'T KNOW 8	 →608 →608
607	When did the baby stop moving in the womb?	BEFORE LABOR STARTED ..... 1 DURING LABOR ..... 2 DON'T KNOW 8	
608	Did a birth attendant listen for fetal heart sounds during labor?	YES ..... 1 NO ..... 2 DON'T KNOW 8	 →610 →610
609	Were fetal heart sounds present?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
610	Was there excess bleeding on the day labor started?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
611	Did the mother have a fever on the day labor started?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
612	How long did the labor pains last?	LESS THAN 12 HOURS ..... 1 12-23 HOURS ..... 2 24 HOURS OR MORE ..... 3 DON'T KNOW 8	
613	Was it a normal vaginal delivery?	YES ..... 1 NO ..... 2 DON'T KNOW 8	→615 →615
614	What type of delivery was it?	FORCEPS/VACUUM ..... 1 CAESAREAN SECTION ..... 2 OTHER _____ 6 (SPECIFY) DON'T KNOW 8	
615	Which part of the baby came first?	HEAD ..... 1 BOTTOM ..... 2 FEET ..... 3 ARM/HAND ..... 4 OTHER _____ 6 (SPECIFY) DON'T KNOW 8	
616	Did the umbilical cord come out before the baby was born?	YES ..... 1 NO ..... 2 DON'T KNOW 8	

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
SECTION 7. CONDITION OF THE BABY SOON AFTER BIRTH			
701	At birth what was the size of the baby?	SMALLER THAN NORMAL ..... 1 NORMAL ..... 2 LARGER THAN NORMAL ..... 3 DON'T KNOW 8	
702	Was the baby premature?	YES ..... 1 NO ..... 2 DON'T KNOW 8	→ 704 → 704
703	How many months or weeks along was the pregnancy? INDICATE PERIOD OF PREGNANCY	MONTHS ..... 1 ☐☐ WEEKS ..... 2 ☐☐ DON'T KNOW 9 9 8	
704	What was the birth weight of the baby?	KILOGRAMS ..... ☐.☐ DON'T KNOW 9 8	
705	Was anything applied to the umbilical cord stump after birth?	YES ..... 1 NO ..... 2 DON'T KNOW 8	→ 707 → 707
706	What was it?	_____ _____ (SPECIFY)	
707	Were there any signs of injury or broken bones?	YES ..... 1 NO ..... 2 DON'T KNOW 8	→ 709 → 709
708	Where were the marks or signs of injury?	_____ _____ (SPECIFY)	
709	Was there any sign of paralysis?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
710	Did the baby have any malformation?	YES ..... 1 NO ..... 2 DON'T KNOW 8	→ 712 → 712
711	What kind of malformation did the baby have?	SWELLING/DEFECT ON THE BACK ..... 1 VERY LARGE HEAD ..... 2 VERY SMALL HEAD ..... 3 DEFECT OF LIP AND/OR PALATE ..... 4 OTHER MALFORMATION _____ 6 (SPECIFY) DON'T KNOW 8	
712	What was the color of the baby at birth?	NORMAL ..... 1 PALE ..... 2 BLUE ..... 3 DON'T KNOW 8	
713	Did the baby breathe after birth, even a little?	YES ..... 1 NO ..... 2 DON'T KNOW 8	

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
714	Was the baby given assistance to breathe?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
715	Did the baby ever cry after birth, even a little?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
716	Did the baby ever move, even a little?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
717	CHECK 713, 715, AND 716 FOR CODES 'NO': ALL THREE CODES 'NO': THE BABY DIDN'T BREATH, THE BABY DIDN'T CRY, THE BABY DIDN'T MOVE ☐	OTHER ☐	→ 801
718	If the baby did not cry, breathe or move, was it born dead?	YES ..... 1 NO ..... 2 DON'T KNOW 8	→ 801 → 801
719	Was the baby macerated, that is, showed signs of decay?	YES ..... 1 NO ..... 2 DON'T KNOW 8	→ 1001 → 1001 → 1001
SECTION 8. HISTORY OF INJURIES/ACCIDENTS			
801	Did the baby suffer from any injury or accident that led to her/his death?	YES ..... 1 NO ..... 2 DON'T KNOW 8	→ 804 → 804
802	What kind of injury or accident did the baby suffer?	ROAD TRAFFIC ACCIDENT ..... 01 FALL ..... 02 DROWNING ..... 03 POISONING ..... 04 BURNS ..... 05 VIOLENCE/ASSAULT ..... 06 OTHER _____ 96 (SPECIFY) DON'T KNOW 98	
803	Was the injury or accident intentionally inflicted by someone else?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
804	Did the baby suffer from any animal/insect bite that led to her/his death?	YES ..... 1 NO ..... 2 DON'T KNOW 8	→ 901 → 901
805	What type of animal/insect?	DOG ..... 1 SNAKE ..... 2 INSECT ..... 3 OTHER _____ 6 (SPECIFY) DON'T KNOW 8	

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
SECTION 9. NEONATAL ILLNESS HISTORY			
901	Was the baby ever able to suckle or bottle-feed?	YES ..... 1 NO ..... 2 DON'T KNOW 8	 → 905 → 905
902	How soon after birth did the baby suckle or bottle-feed?	HOURS ..... 1 DAYS ..... 2 DON'T KNOW 9 9 8	
903	Did the baby stop suckling or bottle-feeding?	YES ..... 1 NO ..... 2 DON'T KNOW 8	 → 905 → 905
904	How many days after birth did the baby stop suckling or bottle-feeding?	DAYS ..... DON'T KNOW 9 8	
905	Was the breastfeeding exclusive?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
906	Did the baby have convulsions?	YES ..... 1 NO ..... 2 DON'T KNOW 8	 → 908 → 908
907	How soon after birth did the convulsions start?	DAYS ..... DON'T KNOW 9 8	
908	Did the baby become stiff and arched backwards?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
909	Did the child have bulging of the fontanelle?	YES ..... 1 NO ..... 2 DON'T KNOW 8	 → 911 → 911
910	How many days after birth did the baby have the bulging?	DAYS ..... DON'T KNOW 9 8	
911	Did the baby become unresponsive or unconscious?	YES ..... 1 NO ..... 2 DON'T KNOW 8	 → 913 → 913
912	How many days after birth did the baby become unresponsive or unconscious?'	DAYS ..... DON'T KNOW 9 8	
913	Did the baby have a fever?	YES ..... 1 NO ..... 2 DON'T KNOW 8	 → 915 → 915
914	How many days after birth did the baby have a fever?	DAYS ..... DON'T KNOW 9 8	

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
915	Did the baby become cold to the touch?	YES . . . . . 1 NO . . . . . 2 DON'T KNOW 8	→ 917 → 917
916	How many days after birth did the baby become cold to the touch?	DAYS . . . . . ☐☐ DON'T KNOW 9 8	
917	Did the baby have a cough?	YES . . . . . 1 NO . . . . . 2 DON'T KNOW 8	→ 919 → 919
918	How many days after birth did the baby start to cough?	DAYS . . . . . ☐☐ DON'T KNOW 9 8	
919	Did the baby have fast breathing?	YES . . . . . 1 NO . . . . . 2 DON'T KNOW 8	→ 921 → 921
920	How many days after birth did the baby start breathing fast?	DAYS . . . . . ☐☐ DON'T KNOW 9 8	
921	Did the baby have difficulty breathing?	YES . . . . . 1 NO . . . . . 2 DON'T KNOW 8	→ 926 → 926
922	How many days after birth did the baby start having difficulty in breathing?	DAYS . . . . . ☐☐ DON'T KNOW 9 8	
923	Did the baby have chest indrawing?	YES . . . . . 1 NO . . . . . 2 DON'T KNOW 8	
924	Did the baby have grunting? DEMONSTRATE	YES . . . . . 1 NO . . . . . 2 DON'T KNOW 8	
925	Did the baby have flaring of the nostrils?	YES . . . . . 1 NO . . . . . 2 DON'T KNOW 8	
926	Did the baby have diarrhoea?	YES . . . . . 1 NO . . . . . 2 DON'T KNOW 8	→ 930 → 930
927	How many days after birth did the baby have diarrhoea?	DAYS . . . . . ☐☐ DON'T KNOW 9 8	
928	When the diarrhoea was most severe, how many times did the baby pass stools in a day?	NUMBER . . . . . ☐☐ DON'T KNOW 9 8	
929	Was there blood in the stools?	YES . . . . . 1 NO . . . . . 2 DON'T KNOW 8	
930	Did the baby have vomiting?	YES . . . . . 1 NO . . . . . 2 DON'T KNOW 8	→ 933 → 933
931	How many days after birth did vomiting start?	DAYS . . . . . ☐☐ DON'T KNOW 9 8	

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
932	When the vomiting was most severe, how many times did the baby vomit in a day?	NUMBER OF TIMES A DAY ..... ☐☐ DON'T KNOW 9 8	
933	Did the baby have abdominal distension?	YES ..... 1 NO ..... 2 DON'T KNOW 8	→ 935 → 935
934	How many days after birth did the baby have abdominal distension?	DAYS ..... ☐☐ DON'T KNOW 9 8	
935	Did the baby have redness or discharge from the umbilical cord stump?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
936	Did the baby have a pustular skin rash?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
937	Did the baby have yellow palms or soles?	YES ..... 1 NO ..... 2 DON'T KNOW 8	→ 1001 → 1001
938	How many days after birth did the yellow palms or soles begin?	DAYS ..... ☐☐ DON'T KNOW 9 8	
939	For how many days did the baby have yellow palms or soles?	DAYS ..... ☐☐ DON'T KNOW 9 8	
SECTION 10. MOTHER'S HEALTH AND CONTEXTUAL FACTORS			
1001	What was the age of the mother at the time the baby died?	YEARS ..... ☐☐ DON'T KNOW 9 8	
1002	Did the mother receive antenatal care?	YES ..... 1 NO ..... 2 DON'T KNOW 8	
1003	Did the mother receive tetanus toxoid (TT) vaccine?	YES ..... 1 NO ..... 2 DON'T KNOW 8	→ 1005 → 1005
1004	How many doses?	NUMBER OF DOSES ..... ☐☐ DON'T KNOW 9 8	
1005	How is the mother's health now?	HEALTHY ..... 1 ILL ..... 2 NOT ALIVE ..... 3 DON'T KNOW 8	

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
SECTION 11. TREATMENT AND HEALTH SERVICE USE FOR THE FINAL ILLNESS			
1101	Did the baby receive any treatment for the illness that led to death?	YES ..... 1 NO ..... 2 DONT KNOW 8	 → 1201 → 1201
1102	Can you please list the treatments the baby was given for the illness that led to death? COPY FROM PRESCRIPTION/DISCHARGE NOTES IF AVAILABLE	_____ _____ _____	
1103	Please tell me at which of the following places or facilities the baby received treatment during the illness that led to death:	YES NO DK	
	1 Home?	HOME 1 2 8	
	2 Traditional healer?	TRADITIONAL HEALER 1 2 8	
	3 Government clinic?	GOVERNMENT CLINIC 1 2 8	
	4 Government hospital?	GOVERNMENT HOSPITAL 1 2 8	
	5 Private clinic?	PRIVATE CLINIC 1 2 8	
	6 Private hospital?	PRIVATE HOSPITAL 1 2 8	
	7 Pharmacy, drug seller, store?	PHARMACY, DRUG SELLER, STORE 1 2 8	
	8 Any other place or facility?	OTHER ..... 1 2 8 (SPECIFY)	
1104	In the month before death, how many contacts with formal health services did the baby have?	NUMBER OF CONTACTS ..... [ ][ ] DONT KNOW 9 8	
1105	Did a health care worker tell you the cause of death?	YES ..... 1 NO ..... 2 DONT KNOW 8	 → 1201 → 1201
1106	What did the health care worker say?	_____ _____ _____	

SECTION 12. DATA ABSTRACTED FROM DEATH CERTIFICATE

1201	Do you have a death certificate for the baby?	YES ..... 1 NO ..... 2 DONT KNOW 8	 → 1301 → 1301
1202	Can I see the death certificate? COPY DAY, MONTH AND YEAR OF DEATH FROM THE DEATH CERTIFICATE.	DAY [ ][ ] MONTH [ ][ ] YEAR [ ][ ][ ][ ]	
1203	COPY DAY, MONTH AND YEAR OF ISSUE OF DEATH CERTIFICATE.	DAY [ ][ ] MONTH [ ][ ] YEAR [ ][ ][ ][ ]	
1204	RECORD THE CAUSE OF DEATH FROM THE FIRST (TOP) LINE OF THE DEATH CERTIFICATE: _____		
1205	RECORD THE CAUSE OF DEATH FROM THE SECOND LINE OF THE DEATH CERTIFICATE (IF ANY): _____		
1206	RECORD THE CAUSE OF DEATH FROM THE THIRD LINE OF THE DEATH CERTIFICATE (IF ANY): _____		
1207	RECORD THE CAUSE OF DEATH FROM THE FOURTH LINE OF THE DEATH CERTIFICATE (IF ANY): _____		

SECTION 13. DATA ABSTRACTED FROM OTHER HEALTH RECORDS			
1301	OTHER HEALTH RECORDS AVAILABLE?	YES ..... 1 NO 2	→ 1311
1302	FOR EACH TYPE OF HEALTH RECORD SUMMARIZE DETAILS FOR LAST 2 VISITS (IF MORE THAN 2) AND RECORD DATE OF ISSUE. (RECORD INFORMATION ABOUT MOTHER AND STILLBORN DECEASED CHILD)		
1303	BURIAL PERMIT (CAUSE OF DEATH) _____		
1304	POSTMORTEM RESULTS (CAUSE OF DEATH) _____		
1305	MCH/ANC CARD (RELEVANT INFORMATION) _____		
1306	HOSPITAL PRESCRIPTION (RELEVANT INFORMATION) _____		
1307	TREATMENT CARDS (RELEVANT INFORMATION) _____		
1308	HOSPITAL DISCHARGE (RELEVANT INFORMATION) _____		
1309	LABORATORY RESULTS (RELEVANT INFORMATION) _____		
1310	OTHER HOSPITAL DOCUMENTS SPECIFY: _____		
1311	RECORD THE TIME AT THE END OF INTERVIEW	HOURS ..... MINUTES	

INTERVIEWER'S OBSERVATIONS

TO BE FILLED IN AFTER COMPLETING INTERVIEW

COMMENTS ON SPECIFIC QUESTIONS:

ANY OTHER COMMENTS:

SUPERVISOR'S OBSERVATIONS

NAME OF THE SUPERVISOR: _____ DATE: _____

Appendix B: Interview script for mothers who did not experience stillbirth or neonatal death

All questions pertain to pregnancy, labor, delivery, and first month of life of the last infant delivered by the mother.

1. How old was the mother at the time of the last delivery?
2. Did the mother have prenatal care during the last pregnancy?
3. How many pregnancies has the mother had in the last five years?
4. What was the sex of the last infant delivered?
5. How old is the last infant delivered currently?
6. Was the last pregnancy with a single baby, or with multiple babies?
7. What was the mother's health like during pregnancy?
8. How is the mother's health currently?
9. At what gestation was the last pregnancy at the time of delivery?
10. Where did the last delivery take place?
11. Who assisted the mother with delivery of the last infant?
12. When in relation to labor and delivery did the water break?
13. Did the mother experience fever during labor or delivery?
14. How was the last baby delivered?
15. What part of baby was delivered first?
16. What was the birth weight of the infant?
17. Describe the umbilical cord care:
    a. What was used to cut the cord?
    b. What was used to tie the cord?
    c. Was anything used in order to prevent infection?
18. Did the baby need assistance to begin breathing right after delivery?
19. In the first month of life, did the baby have any of the following signs of infection:
    a. Fever?
    b. Cough?
    c. Vomiting?
    d. Diarrhea?
    e. Umbilical stump redness?
20. If the baby had any of these signs of infection, did the baby receive medical treatment?
21. Did the baby receive any medical care during the first month of life?
22. Did the mother receive any vaccinations against tetanus before delivery of this infant?
23. If yes, when was the last tetanus vaccine received?

Appendix C: Other methods of Neonatal Mortality Rate (NMR) and Perinatal Mortality Rate (PMR) calculation

Aside from the GEE method, a direct rate calculation can be used to compute the NMR and PMR. Exact tests to obtain the NMR and PMR with 95% confidence intervals were used (*cii* command). P-values to compare these rates to the currently accepted rates in Peru and the Loreto Province were obtained using linear contrast. These results are provided below.

In the main results section of this report, we use the GEE method using the variable of the mother as the clustering variable. It is also possible to use the village as the clustering variable. The results of using the village as the clustering variable, obtained using the same methods as reported in the main body of the text, are reported below.

NMR (7 neonatal deaths from 229 live births):

Direct: NMR = 30.6/1000 live births (95% CI: 12.4/1000 to 62/1000 live births)
The NMR of our sample is significantly different than the currently accepted NMR of Peru of 13/1000 live births (p=0.011) but is not significantly different than the currently accepted NMR of the Loreto Province of 24.5/1000 live births (p=0.202).

$GEE_{village}$: NMR = 30.4/1000 live births (95% CI: 17.5/1000 to 52.6/1000 live births)

The NMR of our sample is significantly different than the currently accepted NMR of Peru of 13/1000 live births (p=0.003) but is not significantly different than the currently accepted NMR of the Loreto Province of 24.5/1000 live births (p=0.442).

PMR (13 perinatal deaths from 260 pregnancies):

Direct: PMR = 50/1000 pregnancies (95% CI: 26.9/1000 to 84/1000 pregnancies)

The PMR of our sample is significantly different from the currently accepted PMRs of Peru (19.8/1000 pregnancies) and the Loreto Province (20.4/1000 pregnancies), both with p-values of 0.001.

$GEE_{village}$: PMR = 49.9/1000 pregnancies (95% CI: 29.9/1000 to 82.1/1000 pregnancies)

The PMR of our sample is significantly different than the currently accepted PMR of Peru of 19.8/1000 pregnancies (p<0.001), as well as the currently accepted PMR of the Loreto Province 20.4/1000 pregnancies (p=0.001).

Appendix D: The Kappa statistic

The kappa statistic is a commonly used measure to determine inter-observer agreement. Calculation of a kappa statistic was attempted using the data from the verbal autopsy assignments for neonatal deaths, but due to the small number of verbal autopsies, we found that the kappa statistic was not a valid measure of correlation between reviewers.

Use of the kappa statistic for more than two raters with two ratings was initially attempted. Results of this test varied with differing methods of data entry. A kappa statistic of 0.45 with a p-value of 0.02 and a kappa statistic of -0.05 with a p-value of 0.59 were both obtained using the same data set.

Use of the kappa statistic for more than two raters with more that two ratings was also attempted. For cause of neonatal death, a kappa statistic of 0.85 with a p-value of <0.001 was obtained. For timing of stillbirth, a kappa statistic of -0.29 with a p-value of 0.89 was obtained. For cause of stillbirth, a kappa statistic of -0.18 with a p-value of 0.88 was obtained.

Appedix E: Sensitivity Analysis for Risk Factors (eliminating one stillbirth)

Risk factor for neonatal or perinatal death	Number of deaths with risk factor (%)	Number of deaths without risk factor (%)	P-value*
Maternal age < 18 or > 35 years	2/34 (5.9)	10/96 (10.4)	0.731
Primigravid status	4/44 (9.1)	8/86 (9.3)	1.000
Twin gestation pregnancy	2/2 (100.0)	10/128 (7.8)	0.001
Preterm delivery (<37 weeks gestation)^	4/11 (36.4)	8/116 (6.9)	0.011
Non-vertex presentation	1/2 (50.0)	11/128 (8.6)	0.177
Male sex	7/65 (10.8)	5/65 (7.7)	0.763
No prenatal care	4/63 (6.3)	8/67 (11.9)	0.367
Delivery in a medical facility	4/19 (21.1)	8/111 (7.2)	0.075
Birth weight large/small for gestation**	3/40 (7.5)	7/85 (8.2)	1.000
Cesarean-section delivery	2/4 (50.0)	10/126 (7.9)	0.042
Mother without tetanus vaccination*^	1/7 (14.3)	11/57 (19.3)	1.000
Distance from Nauta > 2 hours by boat	6/56 (10.7)	6/74 (8.1)	0.761
Presence of a doctor at delivery	4/18 (22.2)	8/112 (7.1)	0.075

*Fisher's exact test, 2-sided
^3 unknown gestational ages
**5 unknown size (2 deaths)
*^data not collected from 66 pregnancies

APPENDIX F: Supplementary Tables

Table S1. Number of women interviewed per village

Village name	Number interviewed per village
San Francisco	20
Libertad	17
Jerusalen	9
Jaldar	1
Castilla	22
Puerto Miguel	20
San Jose	9
Vista Alegre	17
Payorote	15
Total	**130**

Table S2. Detail of maternal characteristics

Maternal characteristic	Number of respondents	Percent of mothers (131 total)
Age		
15-19	26	19.8%
20-24	33	25.2%
25-29	30	22.9%
30-34	21	16%
35-39	12	9.2%
40-44	7	5.3%
>44	2	1.5%
Number of prior pregnancies*		
0	43	32.8%
1	51	38.9%
2	22	16.8%
3	15	11.5%
Health during last pregnancy^		
Healthy	83	63.4%
Unhealthy	48	36.6%

*in previous 5 years
^self-reported

Table S3. Additional delivery characteristics

Delivery characteristics	Number of respondents	Percentage of deliveries (total 131)
Timing of membrane rupture*		
Just prior	79	60.3%
2-12 hours	7	5.3%
12-24 hours	7	5.3%
>24 hours	5	3.8%
Unknown	33	25.2%
Fever during labor/delivery		
No	110	84%
Yes	21	16%
Neonatal assistance with breathing		
None	92	70.2%
Stimulation	20	15.2%
Suction	17	13%
Positive pressure ventilation	1	0.8%
Unknown	1	0.8%
Umbilical cord care		
Yes^	95	72.5%
No	27	20.6%
Unknown	9	6.9%

*In relation to delivery
^Any form of cord care

Table S4. Health characteristics of the first month of life

Characteristic	Yes (%)	No (%)	Unknown (%)	N/A (%)
Fever	52 (39.7)	71 (54.2)	1 (0.8)	7 (5.3)
Cough	42 (32.1)	81 (61.8)	1 (0.8)	7 (5.3)
Vomiting	12 (9.2)	112 (85.5)	0 (0.0)	7 (5.3)
Diarrhea	35 (26.7)	88 (67.2)	1 (0.8)	7 (5.3)
Umbilical redness/ discharge	21 (16.0)	103 (78.6)	0 (0.0)	7 (5.3)
Healthcare (any, 1st month of life)	67 (51.1)	58 (44.3)	0 (0.0)	6 (4.6)

Table S5. Maternal age and outcome

	Neonatal/perinatal death	No neonatal/perinatal death
<18 or >35 yrs (n=34)	2	32
18-35 yrs (n=97)	11	86

Fisher's exact = 0.513

Table S6. Primigravid status and outcome

	Neonatal/perinatal death	No neonatal/perinatal death
Primigravid (n=43)	4	39
Multiparous (n=88)	9	79

Fisher's exact=1.000

Table S7. Multiple gestation pregnancy and outcome

	Neonatal/perinatal deaths	No neonatal/perinatal death
Twins (n=3)	3	0
Singletons (n=128)	10	118

Fisher's exact=0.001

Table S8. Gestation* at delivery and outcome

	Neonatal/perinatal deaths	No neonatal/perinatal death
Preterm (n=12/128^)	5	7
Term (n=116/128^)	8	108

*No post-term infants in this sample
^3 unknown gestational ages
Fisher's exact=0.003

Table S9. Presentation at delivery and outcome

	Neonatal/perinatal deaths	No neonatal/perinatal death
Malpresentation (n=2)	1	1
Vertex (n=129)	12	117

Fisher's exact=0.189

Table S10. Sex of infant and outcome

	Neonatal/perinatal deaths	No neonatal/perinatal death
Male (n=66)	8	58
Female (n=65)	5	60

Fisher's exact=0.561

Table S11. Prenatal care and outcome

	Neonatal/perinatal deaths	No neonatal/perinatal death
No prenatal care (n=63)	4	59
At least 1 visit (n=68)	9	59

Fisher's exact=0.247

Table S12. Place of delivery and outcome

	Neonatal/perinatal deaths	No neonatal/perinatal death
Home (n=112)	9	103
Medical facility (n=19)	4	15

Fisher's exact=0.096

Table S13. Birth weight* and outcome

	Neonatal/perinatal deaths^	No neonatal/perinatal death
Average for gestation (n=86/126^)	8	78
Small or large for gestation (n=40/126^)	3	37

*Determined using growth charts, birth weight, and given gestation, or by maternal estimation
^Overall, 5 pregnancies were unknown size; 2 of these were neonatal or perinatal deaths
Fisher's exact=1.000

Table S14. Mode of delivery and outcome

	Neonatal/perinatal deaths	No neonatal/perinatal death
Cesarean-section (n=4)	2	2
Vaginal (n=127)	11	116

Fisher's exact=0.049

Table S15. Maternal tetanus vaccination status and outcome

	Neonatal/perinatal deaths	No neonatal/perinatal death
Vaccinated (n=58/65*)	12	46
Not vaccinated (n=7/65*)	1	6

*Data not collected from 66 pregnancies
Fisher's exact=1.000

Table S16. Distance from Nauta and outcome

	Neonatal/perinatal deaths	No neonatal/perinatal death
>2 hours (n=56*)	6	50
</=2 hours (n=75)	7	68

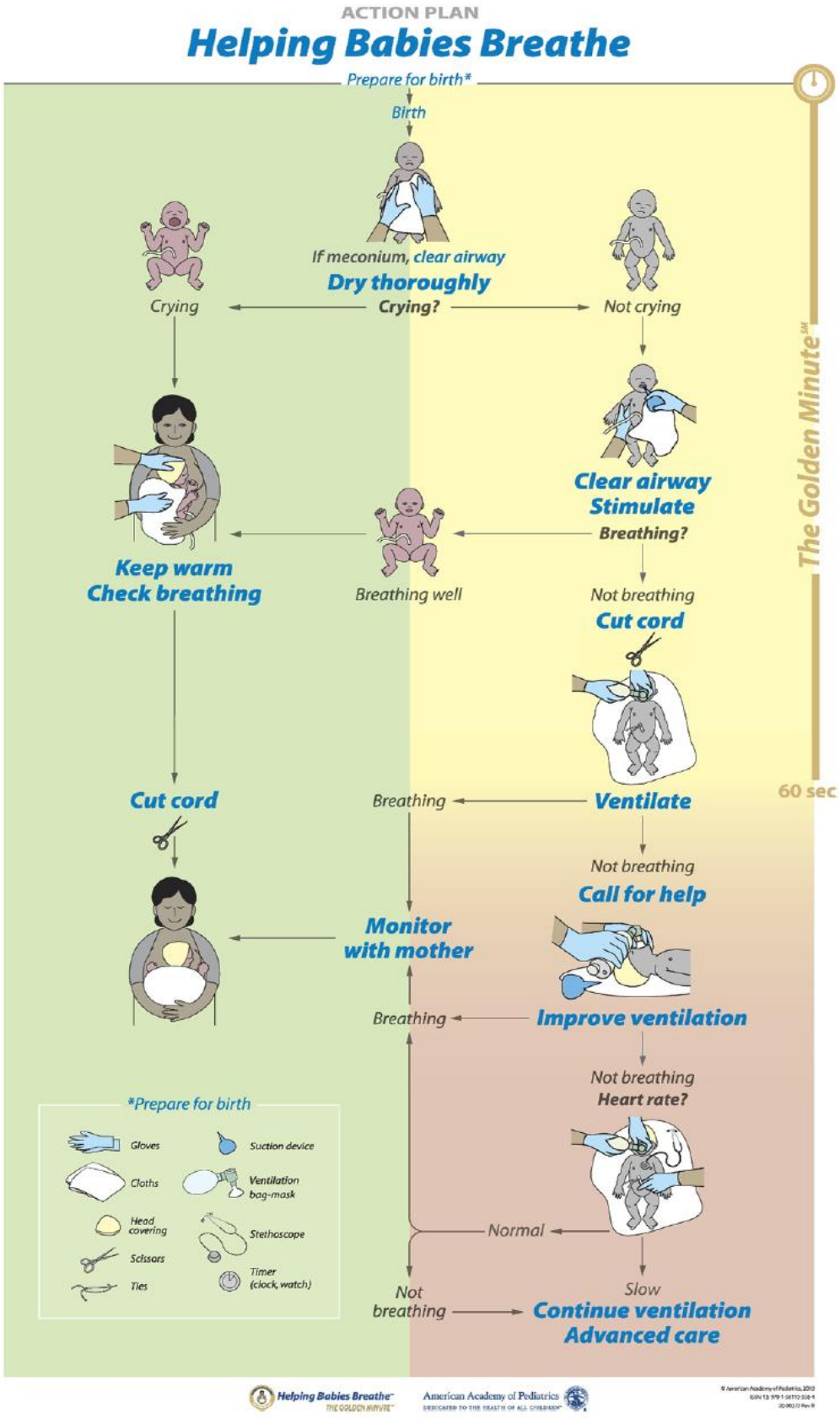
*Villages > 2 hrs from Nauta: Libertad, Jerusalen, Jaldar, Puerto Miguel, and San Jose
Fisher's exact=1.000

Table S17. Type of birth attendant and outcome

	Neonatal/perinatal deaths	No neonatal/perinatal death
Doctor (n=18)	4	14
Traditional (n=73)	4	69
Other (n=40)	5	35

Fisher's exact=0.061

APPENDIX G:


ACTION PLAN
Helping Babies Breathe
Prepare for birth*
Birth
If meconium, clear airway
Dry thoroughly
Crying?
Crying
Not crying
Clear airway
Stimulate
Breathing?
Keep warm
Check breathing
Breathing well
Not breathing
Cut cord
Ventilate
Cut cord
Breathing
Not breathing
Call for help
Monitor
with mother
Improve ventilation
Breathing
Not breathing
Heart rate?
Normal
Slow
Not
breathing
Continue ventilation
Advanced care
The Golden Minute℠
60 sec
*Prepare for birth
Gloves
Suction device
Cloths
Ventilation
bag-mask
Head
covering
Stethoscope
Scissors
Timer
(clock, watch)
Ties
Helping Babies Breathe
THE GOLDEN MINUTE
American Academy of Pediatrics

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