"Too" Much Maternal Mortality: The Effects of Reproductive Patterns in Matlab, Bangladesh

Mizanur Rahman
International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B)
Mizanur20wood@gmail.com

Julie DaVanzo
RAND Corporation

Abdur Razzaque
International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B)

Abstract

We investigate the association between maternal mortality and reproductive patterns using longitudinal data on nearly 215,000 pregnancy outcomes that occurred during 1978-2008 from the Matlab Demographic Surveillance System. Among the four "too's" that are commonly believed to increase maternal mortality risk – too young, too short (an interval), too many (children), and too old -- only too old is found to be a significant risk factor. Women in their 20s have the lowest risk of maternal mortality, which then increases with age after 35. First pregnancies have 2.00 times the risk of second or higher order pregnancies. We find evidence of an additional "too" -- too long; interpregnancy intervals of 75 months or longer have 1.52 times higher maternal mortality risk than those with intervals of 27-50 months. Additional risk factors include a history of pregnancy loss(es) and of child death(s), and index outcomes of induced abortion, miscarriage, and stillbirth.

Introduction

Maternal mortality is unacceptably high in developing countries -- 290 deaths per 100,000 thousand live births compared to only 14 per 100,000 in developed countries -- and more than 99% of the annual worldwide maternal deaths occur in developing countries (WHO 2010). A better understanding of the factors associated with maternal mortality will help health and family planning programs develop strategies to make pregnancy and childbirth safer for women. Because of unavailability of adequate data, little is known about the demographic, socioeconomic, and programmatic factors that may affect maternal mortality in developing countries. In this paper, we use high-quality, longitudinal data from the Matlab Demographic Surveillance System (DSS) on nearly 215,000 pregnancy outcomes to examine correlates of maternal mortality during the period 1978-2008. We assess how maternal mortality is associated with reproductive patterns -- maternal age, gravidity (pregnancy order), and the duration of the preceding interpregnancy interval.

Reproductive Patterns and Maternal Mortality

The presumed relationship between demographic factors and maternal mortality can best be captured by a commonly cited assertion found in the demographic and reproductive health literature that four "too's" are associated with higher risks of maternal mortality (and infant and child mortality) in developing countries. It is believed that *too young* motherhood, *too short* an interval between pregnancies, having *too many* pregnancies, and having a pregnancy at *too old* an age are each pernicious for mothers' health in general and are associated with a greater likelihood of maternal mortality in particular. We now review the reasons for these expectations.

Too Young

A female continues to grow physiologically and mentally until age 20 and beyond. It is widely believed that her physiology is not yet fully ready to bear a child before this age; or putting it differently, when a teenager gets pregnant there is competition between her own growth and that of her fetus. Therefore, a pregnancy before age 20 or especially before age 18 may lead to relatively greater physiological stresses and, because of this, to higher maternal morbidity and mortality. There is a hypothesis of biologic immaturity -- that the pelvic bones and the birth canal of young adolescents may still be in the process of growth, leading to increased risks of prolonged and obstructed labor, episiotomy, use of forceps and ventouse, and

puerperal endometritis (Zabin and Kiragu 1998). If there is a high incidence of these complications among adolescents, one would expect higher incidence of cesarean delivery; however, studies show that adolescent women are at lower risk of such deliveries (Conde-Agudelo et al. 2005; Jolly et al. 2000; Smith and Pell 2001).

In developing countries where childbearing often takes place at early age, it is often found, in the bivariate relationship, that both maternal mortality and infant and child mortality are higher among mothers under age 20 than others. However, research in the United States that controls for the effects of socioeconomic, behavioral, familial, and environmental factors shows that teenagers do not experience greater risks of maternal mortality than older women (Geronimus 1987). It is argued that it is not the young mother's biology but the other (e.g., socioeconomic) factors that lead to higher risks of poor outcomes associated with childbearing (Geronimus 1987). In a companion study in Matlab, we found that teenagers actually have significantly *lower* risks of having pre-eclampsia and proteinuria (Razzaque et al. 2005), and other studies found lower rates of gestational diabetes, breech presentation, induction of labor, and postpartum hemorrhage (Jolly et al. 2000).

A large-scale study from Latin American countries did find higher maternal mortality risk among women ages 15 years or younger compared to women ages 16-24 (Conde-Agudelo et al. 2005). The study also observed higher risk of puerperal endometritis, postpartum hemorrhage, episiotomy, and anemia, but lower risk of gestational diabetes, third-trimester bleeding, and cesarean delivery for these very young women compared to those ages 20-24. However, the incidence of episiotomy, postpartum hemorrhage, and puerperal endometritis was higher among the 16-19–year-old women than those aged 20-24. The high mortality risk for very young women, below age 16, may be explained by the biological immaturity hypothesis mentioned above. It is also possible, as mentioned by the authors, that the young women may have been a selected high-risk group that sought care from hospitals.

Too Old

Women in developing countries not only begin their childbearing at an early age but also sometimes continue it till their late 40s, mainly because of their lack of use of contraception. It is believed that maternal mortality can be improved if women cease childbearing before they are "too old." Compared to the young women's risk of mortality, there is less controversy in the literature that advanced maternal age carries a greater risk of maternal adverse outcomes in most

societies, especially in societies with limited access to advanced medical technologies, most likely because of the physiology of aging. Older women are more likely to experience common chronic diseases that may affect the healthiness of a pregnancy -- hypertension, diabetes, and arthritis. Older women are more likely than younger ones to have placenta previa, which can cause severe bleeding during delivery.

Adverse pregnancy outcomes and complications have been observed for older women in many studies in industrialized countries. Women aged 35 or over had increased risk of miscarriage, perinatal mortality, and low birth weight in the U.S. (Cleary-Goldman et al. 2005). In Belgium, Sweden, and the U.S., preterm birth, very preterm birth, small for gestational age, large for gestational age, and intrauterine fetal death were all more prevalent among women age 40 and older compared to women aged 20-29 (Jacobson et al 2004; Paulson et al. 2002; Delbere et al. 2006). After adjusting for multiple fetuses, the risks of low birthweight, very low birthweight, preterm delivery, small for gestational age, and fetal mortality were all significantly greater for women aged 50 or over in the U.S. (Salihu et al. 2003). Women aged 40 or over had a higher incidence of pregnancy complications, including severe preeclampsia, in Sweden (Jacobson et al. 2004); diabetes and hypertensive disorder in Israel and the U.S. (Simchen et al. 2006*;* Paulson et al. 2002); chromosomal abnormality, caesarian delivery, gestational diabetes, placenta previa, and placental abruption in U.S. (Cleary-Goldman et al. 2005); and large placental infarcts and growth retardation in the U.S. (Naeye 1983). Mortality was higher among women aged 40 or over in Belgium (Temmerman et al. 2004).

In Bangladesh, women aged 30 or over are at higher risk of anemia, high blood pressure, edema (Razzaque et al. 2005), and induced abortion and stillbirth (DaVanzo et al. 2011).

Too Short (an Interpregnancy Interval [IPI])

It has been asserted that births that are too closely spaced carry a risk both for the child's and mother's health. For both the mothers' and the children's health the main postulated mechanism is maternal depletion; it is believed that it takes time for a woman to recover from the physiological stresses associated with the previous pregnancy (e.g., Khan et al. 1998; Miller 1991; Winikoff 1983; Winkvist et al. 1992). (For children's health, sibling competition may also play a role.) Repeated pregnancies in a short period can lead to certain morbidities and nutritional deficiencies that are risk factors for women's own survival and for their children's health (Winkvist et al. 1992).

Closely spaced births have been found to be associated with poorer child health and survival in many countries (e.g., Cleland et al. 1984; Rutstein 2005; DaVanzo et al. 2008). There have been relatively few studies of whether there is such an effect on *maternal* health. Some studies have documented in bivariate analyses that short intervals are risk factors for maternal mortality in developing countries (e.g., Anandalakshmy et al. 1993; Miller et al. 1992; and Winikoff 1983). In a multivariate analysis of a large number of pregnancies in Latin America that controlled for the effects of a number of relevant variables, Conde-Agudelo and Belizán (2000) found that maternal mortality was 2.5 times higher among women who had an IPI of less than six months compared to those with an IPI of 18-23 months. However, in a case-control study in Matlab, Bangladesh, Ronsmans and Campbell (1998) found no evidence of a relationship between maternal mortality and the duration of the preceding IPI after controlling the effects of some confounding demographic and socioeconomic variables.

The effects of short IPIs on maternal and child health outcomes vary by the type of outcome that began the interval (e.g., DaVanzo et al. 2008). Short intervals elevate the risk of abortion, miscarriage, or stillbirth (DaVanzo et al. 2007), and women with such outcomes have a higher risk of maternal death compared to women with a live birth (Rahman et al. 2010).

Too Long (an Interpregnancy Interval)

Our studies of maternal morbidity and of pregnancy outcomes in Matlab found a new "too": too long. Interpregnancy intervals of more than six years were found to be associated with an elevated risk of the pregnancy ending in abortion, miscarriage, or stillbirth (DaVanzo et al. 2007) and of pre-eclampsia, high blood pressure, and edema (Razzaque et al. 2005). It has been hypothesized that pregnancies after very long intervals may be similar physiologically to first pregnancies, which have a high risk of maternal morbidity and mortality (Conde-Agudelo and Belizán 2000). Razzaque et al. (2005) found that in Matlab, Bangladesh, the incidences of pre-eclampsia, high blood pressure, and edema were significantly greater among women with long intervals (75+ months). Similarly, Conde-Agudelo and Belizán (2000) found significantly higher incidences of pre-eclampsia, eclampsia, and third-trimester bleeding among women with long intervals (60+ months) in their study of Latin America. First pregnancies have been found to be associated with pre-eclampsia, proteinuria, high blood pressure, premature rupture of membranes, or edema (Conde-Agudelo and Belizán 2000; Razzaque et al. 2005), which are risk factors of maternal mortality. It seems women with one or more pregnancies enjoy a protective

effect against morbidities such as pre-eclampsia or high blood pressure, and those with very long intervals lose this protective effect and therefore are at higher risk of morbidity and mortality after long intervals. It is also possible that higher maternal morbidity after a long IPI is a reflection of poor maternal health that prevented the woman from becoming pregnant for a long time (Razzaque et al. 2005).

Too Many (Pregnancies)

It has been hypothesized that maternal mortality increases with the number of pregnancies (also known as gravidity or pregnancy order). This relationship may be confounded by IPI duration and maternal age, since, for a given age at first pregnancy, the number of pregnancies by some subsequent age will be greater if those pregnancies are more closely spaced and also because when number of pregnancies increases, maternal age also increases.

Too many pregnancies, short IPI, or both can adversely affect pregnancy outcomes, pregnancy complications, and maternal, infant, and child health. The mechanism as mentioned above is maternal depletion associated with repeated pregnancies and/or short pregnancy intervals that do not allow mothers to recuperate from nutritional deficiency and/or physiological stress during the preceding pregnancy (Winkvist et al.1992).

Maternal depletion is more likely to be at work in populations with nutritional deficiency, inadequate prenatal care, or women's continuation of breastfeeding until the next conception or even during gestation. The detrimental effect of short intervals on infant mortality in Malaysia was significant only among women more likely to have inadequate nutrition (DaVanzo et al. 1986). A study in Guatemala found that the overlap of breastfeeding and gestation increased nutritional stress (Merchant et al. 1990a and 1990b). Bangladesh has high prevalence of under-nutrition of women, a relatively low level of antenatal care (ANC) coverage, and high fertility until recently (NIPORT 2009), and thus it is likely that maternal mortality may be associated with the number of pregnancies through the mechanism of maternal depletion.

Setting, Data, and Methods

This study uses data from Matlab, typical rural subdistrict of Bangladesh. Our data on pregnancies and their outcomes have been collected through the Demographic Surveillance System (DSS) of the International Center for Diarrhoeal Disease Research, Bangladesh (ICDDR,B). The DSS data on the timing of pregnancy outcomes should be of very high quality

because they have been collected during regular household visits (every two weeks until 1997, every month since 1999, and every two months since 2007) by trusted female community health workers (CHWs) (D'Souza 1981; Van Ginneken et al. 1998).

Since October 1977, half of the DSS area has been exposed to the Maternal Child Health-Family Planning (MCH-FP) intervention of the ICDDR,B, which provides better family planning and health services than the standard government services available to people in the other half of the area, known as the Comparison Area (Van Ginneken et al. 1998). In the MCH-FP Area, basic ANC screening began in 1982, and safe motherhood interventions, including home-based deliveries, began in 1987. Maternal mortality began to decline in 1991 (Chowdhury et al. 2007). In 1996 home-based deliveries were discontinued in an effort to promote institutional deliveries. In the MCH-FP Area, well-trained CHWs visited married women of reproductive age every two weeks to provide counseling about family planning services and to deliver injectables, pills, and condoms at the doorstep. Since 2001, CHWs visit the doorstop only to collect data; they no longer deliver services, and women in the MCH-FP Area must now go to a health center to receive the services. Married women in the Comparison Area were supposed to (but did not always) receive the standard visits every two months from female welfare assistants working for the government family planning program, who provide counseling and supply oral contraceptive pills and condoms. Hence, at least until 2001, the MCH-FP Area was characterized by greater contact among clients, workers, and supervisors as well as greater availability and a broader mix of contraceptive methods than is available in the Comparison Area. In addition to the standard government Health and Family Welfare Centers available in both areas, the MCH-FP Area also has ICDDR,B sub-centers in the communities that provide maternal and child health and family planning services that are better than those available in the Comparison Area.

Data on Maternal Mortality

The Matlab DSS records causes of death. In general, the completeness of death enumeration is very high, especially for adults, but maternal death may be underreported due to misclassification of cause of death. According to the Tenth Revision of the International Classification of Diseases (ICD-10), a maternal death is "the death of a woman during pregnancy or within 42 days of pregnancy outcome from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes" (WHO 1992).

Investigators studying maternal mortality in Matlab have collected further information to improve the identification of maternal deaths that occurred between 1976 and 2005 (Fauveau et al. 1991; Koenig et al. 1988; Ronsmans et al. 1997; Dieltiens 2005; and Chowdhury et al. 2007) and have updated the DSS death files accordingly[1]. These investigators followed an extended definition of maternal death -- a death within 90 days of a pregnancy outcome (AMA 1964) -- and this is the definition we use in this study. We repeated the analysis for maternal deaths within 42 days, and the main findings were the same as those shown here.

We analyze maternal mortality for a sample of 214,937 singleton pregnancy outcomes that occurred in Matlab during the period 1978-2008. We matched death records with the pregnancy outcomes through the unique DSS identification numbers. We exclude 2,165 pregnancies (just over 1% of all pregnancies) that had multiple outcomes (twins and triplets) because these outcomes carry a special risk of maternal deaths that should be separately studied.[2] We consider a total of 715 maternal deaths that occurred between 1978 and 2008. Accidental deaths during pregnancy or within 90 of the outcome are not treated maternal mortality.

Methods of Analysis

We first examine the bivariate relationships between the likelihood of maternal mortality, defined as maternal deaths per 100,000 pregnancies, and maternal age, gravidity or pregnancy order, and IPI. We then estimate multivariate models of maternal mortality risks using logistic regression to examine the net effect of the factors considered while also controlling for the influences of socioeconomic, programmatic, and other factors; we present the multivariate results as odds ratios. We have more than one observation of pregnancies for some women, and since the outcome (i.e., the death) can occur only once, we do not have to adjust our analysis for multiple observations.

Independent Variables

We consider the following reproductive-pattern factors in our bivariate and multivariate analyses: maternal age at the time of pregnancy outcome (or at death for women who died during pregnancy), gravidity (number of pregnancies, including the one under consideration),

[1] Maternal mortality data collected during 2006-2008 are based on the routine verbal autopsy investigation, which is less rigorous than the special investigations.

[2] We consider 221 women who died during pregnancy. We don't know whether any of them were carrying multiple fetuses.

and the length of the interpregnancy interval (IPI) preceding the index pregnancy. These variables can all be computed from information in the DSS database.

The duration of IPI is defined as the amount of time between the preceding pregnancy outcome and the estimated date of conception of the index pregnancy; the latter is calculated as the date of last menstrual period (DLMP) plus 14 days. The DSS has recorded women's DLMP as part of women's reproductive history for pregnancies since 1978 in the MCH-FP Area and for those since 2000 for the Comparison Area. In order to include the IPI variable all pregnancies in both areas, for observations for which we don't know DLMP, we estimated the date of conception assuming that the duration of the index pregnancy will be the same as the average for that outcome for cases for which we know the DLMP.[3] The analysis also includes a variable that identifies cases where the duration of the IPI is unknown (e.g., because the previous pregnancy occurred before the woman moved to the Matlab area). All continuous variables are included as categorical variables in the analyses in order to allow for non-linear relationships.

We include several kinds of variables as control variables in the analysis. First, as health indicators, we consider four variables that are likely to capture the household health environment and the health of the woman herself. They are (a) the cumulative numbers of child death(s), (b) number of pregnancy losses (induced abortions, miscarriages, or stillbirths) the woman experienced prior to the pregnancy in question, (c) type of outcome of the previous pregnancy, and (d) type of outcome of the index pregnancy. Second, as socioeconomic indicators, we consider the woman's education (0, 1-5 years, 6-16 years), household economic condition, and, religion (Muslim and Non-Muslim). Household economic condition is measured by household space, which has been found in Matlab to be associated with mortality and other health indicators (D'Souza et al. 1981); we have categorized it into roughly four quartiles as <170 square feet, 170-249 sq. ft., 250-349 sq. ft., and 350+ sq. ft. We control for woman's residence in the MCH-FP Area as an indicator of programmatic factors. As noted above, since 1977 the MCH-FP Area has received a number of health care and family planning interventions. We also control for the year of the pregnancy outcome, using the categories 1978-1981, 1982-1986, 1987-1990, 1991-1995, 1996-2000, and 2001-2008**; t**hese calendar-year categories roughly correspond to the introduction of safe motherhood interventions or changes in the service delivery strategies.

[3] The average durations of pregnancies for cases with reported DLMP are 36 weeks for live births, 34 weeks for stillbirths, 10 weeks for miscarriages, and 7 weeks for induced abortions.

In the descriptive analysis, we examine the association between maternal mortality and cross-tabulated categories of maternal age and pregnancy order, because these two variables are highly correlated. We also examine the association between IPI and mortality, controlling for the type of outcome at the previous as well as index pregnancy. The type of outcome can confound the association between mortality and IPI for two reasons: Pregnancies that end in abortion, miscarriage, or stillbirth have markedly higher risk of maternal mortality than those than end with live births, and they lead to similar outcomes in the next pregnancies and with short IPI. If the previous pregnancy ended with a live birth, the pregnancy is usually of full term and the child is likely to be breastfed, and for both reasons the woman is more likely to be depleted compared to a pregnancy with an outcome other than a live birth. If the index pregnancy also results in a live birth, that should be more depleting than those with other outcomes, which are of shorter gestation. Thus, IPIs for a pair of two live births are likely to have the highest level of depletion, those for pairs of two non-live-birth pregnancies should have the least, with those of a live birth and a non-live-birth pregnancy in between. However, miscarriages, induced abortions, and stillbirths are associated with higher risks of maternal mortality (Rahman et al., 2010), so this will offset the depletion effects. We examine these relationships in cross-tabulations as well as in the logistic regression.

In order to investigate the independent effect of each of the reproductive pattern variables -- maternal age, pregnancy order, and IPI -- and to understand the mechanisms through which they may affect maternal mortality, we estimate eight logistic models in a stepwise approach. In Model 1, we examine the effects of maternal age. In Model 2, we add gravidity (pregnancy order). In Model 3, we add IPI. Model 4 tests for an interaction between first pregnancy and maternal age. A significant interaction term associated with particular age group will indicate that having the first pregnancy in those ages is riskier (or less risky) than having first pregnancy at other ages. Our particular interest here is to examine whether women who have their first pregnancy at older are at higher risk of mortality. Model 5 includes all the socioeconomic and other control variables and the main effects of the above three reproductive pattern variables as in Model 3, to see if the effects of reproductive-pattern variables change when variables that may be correlated with them are controlled. In Model 6, we add two proxy health indicators -- (a) the number of previous child deaths and (b) the number of previous pregnancy losses, to see the extent to which controlling the household health environment affects (and explains) the effects of

reproductive-pattern variables estimated in the earlier models. Model 7 includes two variables that measure whether both the preceding and index pregnancies are live births. We expect greatest adverse effect of short IPI when both the pregnancies are live birth, and, therefore, the depletion effect if there is one should be observed in this model. Model 8 again tests for interactions between the first pregnancy and age after adjusting for the effects of all the variables considered in our analysis.

Descriptive Analyses

Maternal Age and Gravidity

During the 1978-2008 period, the average likelihood that a pregnancy resulted in a maternal death in Matlab was 333 per 100,000 pregnancies. In Table 1 we examine maternal mortality rates cross-tabulated by mother's age *and* gravidity (the total number of pregnancies or pregnancy order). The mortality risks and their odds ratios (OR) in the "total" column show the effect of age without considering the effect of gravidity. They show that mortality was significantly higher among women aged 16-17 and 18-19 and 30 or older than among those aged 20-24. Mortality risk was 30% higher for women aged 15 or younger than for those aged 20-24, but the difference is not statistically significant.

The "total" row indicates how the risk of mortality varies with gravidity. We see that first pregnancies are associated with significantly higher risks of maternal mortality than second or third pregnancies, and that mortality risk is lowest for third pregnancies and increases thereafter, with significantly elevated risks (compared to second pregnancies) for fifth and higher-order pregnancies

The bivariate effects of age and pregnancy order just discussed are confounded by the effect of correlation between these two variables. Pregnancies to young women are more likely to be first pregnancies, while women with a large number of pregnancies are likely to be old. In our data, 77% of pregnancies to teenagers were first pregnancies, compared to 33% among 20-24 year olds and 7% among 25-29 year olds.

Figures 1a and 1b graph the data in the body of Table 1 to illustrate how the variations in the risk of maternal mortality by age differ by gravidity. For first pregnancies, the risk is lowest at age 20-24 and then increases with age; it is about three times higher at age 30-34 and about four times higher at age 35-39, compared to age 20-24. Therefore, we find that women who get their first pregnancy at older ages are at very high risk of mortality. The mortality risks for

second and third pregnancies do not vary by age; but for women of fourth or higher-order pregnancies there is a consistent pattern of increasing risk with age, except for one or two cells.

For first pregnancies, those to women below age 20 have higher risk of maternal mortality than those to women aged 20-24, but the difference is not statistically significant. There is no evidence that the mortality risk is higher among women below 20 with second or higher-order pregnancies. However, it should be noted that the cell frequencies for women under age 20 with second or higher-order pregnancies are sometimes small and therefore may not allow a valid comparison of risk.

The mortality risks observed in various cells in Table 1 can also give a sense of whether repeated pregnancies (resulting in short intervals) can have an adverse effect on mortality. Holding constant the age of first pregnancy, the more pregnancies a woman has by a certain age, the shorter the average interval between them. We do not observe any consistent patterns of positive association between mortality risk and pregnancy order within an age group, and hence see no evidence in Table 1 that repeated pregnancies in short intervals are a risk factor for maternal mortality. We next look directly at the effects of durations of interpregnancy intervals.

Interpregnancy Interval (IPI)

Maternal mortality risks by duration of the preceding IPI are shown in Table 2 for all second and higher-order pregnancies. We show the risks for three subsamples: (A) all intervals regardless of the type of pregnancy outcome in the index and previous pregnancy, (B) intervals which began with a live birth, but the index pregnancy ended with any type of outcome, and (C) intervals that both began and ended with live births. The last two subsamples should be more affected by maternal depletion, because the IPIs began with full-term pregnancies and, for subsample C, because in Bangladesh live-born children who do not die immediately after birth are typically breastfed, which may further deplete the mother nutritionally. However, we do not observe an elevated risk of mortality among women with short IPI for any of the three subsamples in Table 2. In fact, the shortest IPIs (<6 months) are associated with the *lowest* risks of maternal mortality for all three subsamples, and the next shortest category (6-14 months) is associated with the next lowest risks for IPIs that began with live births (subsamples B and C).

We do, however, see adverse effects of very long intervals. In all three subsamples women who had an IPI of 75 months or longer had a significantly higher risk of mortality than women with an IPI of 27-50 months. The mortality risk associated with an IPI of 75 months or

longer was 361 per 100,000 pregnancies when we consider all IPIs (regardless of the outcomes with which they began or ended). This risk is quite close to the risk associated with the first pregnancy of 406 per 100,000 (Table 1). However, the mortality risk for such long intervals that began with a live birth is considerably lower -- 219 per 100,000 where the index pregnancy is of any type (Panel B); it is even lower -- 133 per 100,000 -- when we consider cases where the pregnancies at the beginning and end of the interval both ended in live births (Panel C). This lower mortality is due to the exclusion of pregnancies that ended in abortion, miscarriage, and stillbirth from the samples in Panels B and C. As we have noted, our companion study showed that women whose pregnancies ended in these outcomes had significantly higher risk of mortality than those women who end their pregnancies with a live birth (Rahman et al. 2010).

Multivariate Analyses

We present the logistic regression models in Table 3. In Model 1, which evaluates the age pattern of maternal mortality without controlling for any other variables (and hence the odds ratios (ORs) are equivalent to those in the total column in Table 1), mortality risk is significantly higher among women aged 16-19 than women aged 20-24. Women under age 16 also had higher risk but the difference is not statistically significant. Mortality risk monotonically increases with age after 30 and is significantly higher than for ages 20-24.

When pregnancy order is controlled, in Model 2, the age effects attenuate slightly; risks for women 35 and older are still significantly higher than those for women 20-24, but the risk for women under age 20 is no longer significantly higher. Risks are 1.77 times higher for first pregnancies ($p<0.001$) than for second-order pregnancies. Risks are similarly high for high-order pregnancies (gravidity ≥ 6).

In Model 3, in which IPI is added, we see further attenuation of the age effect. The mortality risk is significantly higher at age 40 and higher compared to ages 20-24. Most effects of gravidity remain the same when IPI is controlled, though the effects of the highest gravidity group (8+) increase somewhat (to OR = 1.86; $p<0.01$)). We see an elevated risk of maternal mortality following long IPIs of 75+ months compared to those of 27-50 months (OR=1.46; $p<0.05$).

In Model 4 we include interaction terms between age and first pregnancy to test whether the higher risks of maternal mortality for first pregnancies at older ages that we saw in Table 1 and Figure 1a are statistically significant. The ORs for age in the top panel for Model 4 are the

effects of age for second and higher-order pregnancies; none of these is statistically significant at $p<0.05$. The ORs for the interaction terms between maternal ages and first pregnancy indicate that having the first pregnancy at age 35 or higher is significantly much riskier (OR of 6.00 or higher at age 35 or over) than at younger ages.

Models 2-4 indicate that women of sixth or higher pregnancy order had significantly higher risk of mortality after controlling for the effects of age and IPI.

In Models 5-8, we add controls for socioeconomic and programmatic factors and for the year when the pregnancy occurred.[4] When we control for these variables in Model 5, the effects of older maternal age become larger and more significant than in Model 3; the effects of first pregnancy and very long IPI (75+ months) become more perverse, while those of high gravidity disappear.

Consistent with the bivariate analysis, Model 3 shows that women did not experience significantly higher risk of mortality following short IPIs while those with IPIs of 75 months or more had significantly higher risk of mortality, 1.46-1.56 times higher ($p< 0.05$) in the multivariate analysis, compared to those with IPI of 27-50 months.

Model 6 adds to Model 5 the two proxies for the woman's and her family's health environment -- previous child deaths and previous pregnancy losses (induced abortion, miscarriage, or stillbirth) -- so that we can see whether the effects of the reproductive variables change when we control for the family health environment. Women who had prior child deaths or pregnancy losses have higher risk of maternal mortality. The likelihood of mortality is 1.39 times higher for women with two or more child deaths prior to the index pregnancy ($p<0.05$). Similarly, mortality risk is 1.42 ($p<0.01$) and 1.96 ($p<0.001$) times higher among women with one and two or more previous pregnancy losses. When previous child deaths and pregnancy losses are controlled, the effect of high pregnancy order becomes much smaller and in fact some are significantly lower than those for pregnancy order 2. Women with higher pregnancy order had more opportunities to experience pregnancy losses and child deaths. When the effects of these are netted out, high gravidity itself no longer has a deleterious effect, but instead the lower

[4] In Model 5, women with 1-5 years of schooling and six or more years of schooling had 15 percent ($p<0.05$) and 35 percent ($p<0.01$) lower risk of dying than women with no schooling. Maternal mortality was 17 percent ($p<0.05$) lower in the MCH-FP Area than the Comparison Area during the period 1978-2008. Mortality declined over the study period but the decline appeared to be significant beginning in 1991. Compared to the period 1978-1981, mortality was 26 percent lower ($p<0.05$) during 1991-1995, 37 percent lower ($p<0.001$) during 1996-2000, and 61 percent lower ($p<0.001$) during 2001-2008. We find no significant differences by religion or household space (proxy measure of household wealth) when all other variables are controlled.

risk for high gravidity seems to indicate that the women who made it to these high gravidities without experiencing child deaths and pregnancy losses were able to do so because they were very healthy and able to become pregnant easily. It is noteworthy that after controlling for the effect of household health environment and women's own health through the child death and pregnancy loss variables, women with an IPI of less than six months have significantly *lower* mortality risk than women with an IPI of 27-50 months. This probably indicates a selectivity effect in that healthier women are more likely to conceive at an early postpartum duration than average healthy while relatively less healthy women take longer to conceive.

Model 7 adds variables that control for the effect of the type of outcome of the previous and index pregnancies. The ORs of the IPI categories will represent the intervals between two live births when the effect of non-live birth in each of the previous and index pregnancies is included as it is done in Model 7. As mentioned above, interval between two live births are likely to be most depleting. Consistent with Rahman et al. (2010), the results of Model 7 indicate that women with a non-live-birth outcome (miscarriage, induced abortion, or stillbirth) in the index pregnancy are at a significantly and markedly higher risk of mortality than women with a live birth.[5] Once the effect of women's experience of non-live birth pregnancies is controlled, we no longer see significant effects of any of the IPI variables. The effects of some other factors are modified as well. The higher mortality at older ages remains significant but is smaller in magnitude than in Models 5 and 6. This probably reflects the fact that some deaths at older ages are associated with higher likelihoods of abortion, miscarriage, or stillbirth, which are more likely at old ages in Bangladesh. Once these are controlled in Model 7, the age effect is reduced and is likely to be the direct effect of relatively old maternal age.

The final model (Model 8) again includes interactions between maternal age and first pregnancy to see if the effects of these that we saw in Model 4 remain the same after adjusting for the variables added in Models 5-7. The results are roughly similar to those seen in Model 4 in terms of the direction of association between mortality and the reproductive and other factors but the strength of these associations attenuates. For example, the interactions between first pregnancy and ages 45-49 is still large and significant, though not as much so as in Model 4, but

[5] The type of pregnancy outcome is highly correlated between two successive pregnancies. This may be a reason why the effect of previous pregnancy outcome is not significant in Model 7. The OR associated with "Non-live birth" for the variable "Previous pregnancy outcome" is 1.60 ($p<0.01$) when the variable "Index pregnancy outcome" is excluded from Model 7.

the interactions with age 35-39 and age 40-44 are smaller and no longer statistically significant at $p < 0.05$. The effects of first pregnancy, the number of previous child deaths, and the type of index pregnancy outcomes remain statistically significant and almost unchanged in magnitude.

Discussion

We analyze high-quality longitudinal data from the Matlab DSS on nearly 215,000 pregnancies over a period of three decades, 1978-2008, to investigate the relationship between three reproductive-pattern variables -- age, gravidity (pregnancy order), and interpregnancy interval (IPI) -- and maternal mortality. By controlling for the effects of some socioeconomic and programmatic factors and of some proxy indicators of health at the community, time-period, household, and woman's personal level, we try to understand the pathways through which these reproductive patterns affect maternal mortality. These data are highly unlikely to suffer from the underreporting usually encountered in on maternal mortality data in developing countries. Also our data on maternal mortality, coming from frequent prospective data collection in an entire population, rather than, say, only deaths occurring in a hospital or relatives' reports of women's deaths, are likely to cover a much more representative sample than those used in many previous studies.

We have assessed the effect on maternal mortality of four "too's" that are commonly believed to be associated with maternal mortality -- *too young* motherhood, *too short* intervals *(i.e., too closely spaced* births), having *too many* births, and *too old* motherhood. We find that only one of these -- too old -- is associated, with an increased risk of maternal mortality. Pregnancies among teenage women, after short intervals, or to women already having many children do not have excessive risk of maternal mortality.

Our maternal mortality findings on the four "too's" have both similarities and dissimilarities with that of others in the field of maternal, newborn, and child health. For example, Menken et al. (2004) found in Matlab that women's survival was not significantly associated with early childbearing, pace of childbearing or short intervals, and repeated childbearing or too many pregnancies. Ronsmans et al. (1998) found no significant association between maternal mortality and the length of interpregnancy intervals in Matlab. However, in their studies of in Latin America, Conde-Agudelo and Belizán (2000) found a significant association between short intervals and maternal mortality, and Conde-Agudelo et al. (2005) found higher maternal mortality among very young women (age ≤15 years). DaVanzo et al.

(2008) observed adverse effects in Matlab of short intervals on early and late neonatal mortality, post-neonatal mortality, and child mortality and adverse effects of young motherhood (<20 years or <18 years) on early and late neonatal and post-neonatal mortality. Thus, we find that in Matlab young motherhood and short intervals adversely affect newborn health but not maternal health, as measured by maternal mortality or morbidity. The incidences of pre-eclampsia and proteinuria were significantly lower among the women under 20 than their counterparts in the 20s (Razzaque et al. 2005).

These dissimilarities or similarities should be evaluated at least at two levels. First, the level of statistical analysis; the relevant confounding variables should be considered to find the net effect of a particular factor. We find that the risk of maternal mortality is similar among teenagers (separately for ≤15 years, 16-17 years, and 18-19 years) and women aged 20-24 years, once the effects of gravidity are controlled. The relationship observed in bivariate analysis is confounded by the fact that pregnancies at a young age are likely to be first pregnancies, and first pregnancies have higher risks for maternal mortality.

Similarly, when investigating the depletion effects of IPIs on maternal and newborn health outcomes, the type of pregnancy outcome should be considered in the analysis; the depleting effect is likely to be stronger when both pregnancies are live births than for pregnancies one or both of which are non-live birth because they have shorter gestation (and the breastfeeding of a live birth at the beginning of an IPI will further deplete the women). Studies that have investigated the association between these demographic variables and health outcomes have either selected a particular type of pregnancy outcome or did not distinguish between outcomes. For example, in their study of the effects of interpregnancy intervals on maternal health outcomes Conde-Agudelo and Belizán (2000) considered pregnancies with live births for the index pregnancy and a live birth or stillbirth for the previous pregnancy. Similarly, in their study of maternal health outcomes and adolescent pregnancy Conde-Agudelo et al. (2005) considered only those pregnancies that ended with a birth. DaVanzo et al. (2008) found that the effect of IPI on infant and child mortality in Matlab varied by the type of pregnancy outcome that began the interval. Similarly, DaVanzo et al. 2007 found that the pregnancy outcome at the end of the interval was affected by the type of the preceding outcome as well as the interval between the two. And, maternal mortality risk greatly varies by the type of pregnancy outcome

(Rahman et al. 2010). Most studies of maternal mortality do not distinguish the type of pregnancy outcome.

Second, the findings may be evaluated in the context of maternal depletion through which the four "too's" can adversely affect maternal, newborn, and child health outcomes. The adverse effects on the mother and the fetus (or newborn) are hypothesized to occur mainly through maternal nutrient depletion. The consequences of the depletion on the fetus are well known but that on maternal under-nutrition and other health outcomes are less well documented (King 2003). One hypothesis is that in the state of maternal depletion, nutrients are partitioned differently by a delicate metabolic mechanism between the mother and the offspring, and the former gets preference at the expense of the growth of the latter. Scholl and colleagues (1994) showed in a U.S. study that nutrition effects on the mother and the fetus are different. For example teens gained weight during pregnancy but gave birth to smaller infants. Data from the Dutch famine during 1944-1945 show that in the circumstance of nutritional deterioration fetal growth was more reduced than maternal body weight (King 2003). The implication of this finding is that the adverse effect of depletion may be greater on the newborn than on the mother. Therefore, our findings that maternal mortality is not affected by early childbearing, short intervals, or large number of pregnancies but infant mortality is, is consistent with the partition theory of nutritional stores during gestation.

That very young (≤15 years) and young (16-17 years and 18-19 years) women do not experience higher risk of mortality than their counterparts at ages 20-24 is consistent with the findings that teenage women in Matlab had significantly lower incidences of pre-eclampsia and proteinuria during pregnancy than older women (Razzaque et al. 2005). As mentioned above, research in the United States that controls for the effects of socioeconomic, behavioral, familial, and environmental factors shows that teenagers do not experience greater risks of maternal and child health outcomes than older women. Some have argued that teenage pregnancy is neither a public health nor a clinical problem but instead a manifestation of the social and economic exclusion of teenage mothers in the context of the USA or UK (Lawlor and Shaw 2002; Rich-Edwards 2002; and Scally 2002).

In Matlab, like in many developing countries, young women under age 20 are at significantly higher risk of abortion (DaVanzo et al. 2011), yet those in Matlab do not have excess risk of maternal mortality when we control for pregnancy order and other variables. This

has may occur for two reasons. First, our data on cause of death show that proportional mortality for abortion was not higher for younger women than other women. Second and more importantly, the incidence of stillbirth, a strong risk factor of maternal mortality, was significantly *lower* among younger women than older women. This counteracting mechanism leads to younger women's lower risk of maternal mortality.

Although we do not find a direct adverse effect of short intervals on maternal mortality, our research shows indirect evidence that short intervals can lead to higher morbidity and mortality[6].

We find that first pregnancies carry an elevated risk of mortality for women. Typically, reproductive health counseling emphasizes delayed childbearing beyond teenage on health grounds. Our analysis shows that mortality is found to be high among teenagers because most of them have the first pregnancy in this age range. First pregnancy is the real risk factor. However, our results also indicate that the occurrence of first pregnancy at age 35 or later ages is especially high risk. First pregnancies at such older ages are rare in Bangladesh -- they account for only 168 of the 50,515 first pregnancies in our sample – and the deferment of the first pregnancy till women's 30s in Matlab is probably not by choice. We do not know at this time whether first pregnancy at higher ages is causally associated with the high risk of mortality, or whether it reflects adverse health, familial, and social factors that led to the pregnancy delay. Further research should try to understand the causes of women's delaying first pregnancy in Bangladesh.

We find that mortality risk declines with pregnancy order until the third pregnancy, which has the lowest risk maternal mortality, and then, both in bivariate analysis and in multivariate analyses where maternal age and pregnancy spacing are controlled, the risk of maternal mortality increases monotonically as gravidity increases thereafter. However, when we control for socioeconomic status and programmatic factors, we no longer see a higher risk associated with high gravidity; and when we control for previous child deaths and pregnancy losses, we find that higher-order pregnancies are associated with a *lower* risk of maternal mortality. These finding suggest that there are three types of women who have a large number of

[6] Short intervals are associated with a greater likelihood that the pregnancy outcome at the interval will be an induced abortion, miscarriage, and stillbirth rather than a live birth (DaVanzo et al. 2007), and these non-live-birth outcomes are associated with higher risk of maternal mortality (Rahman et al. 2010). Moreover, the non-live births tend to repeat among women (DaVanzo et al. 2007) and thus a certain proportion of women become a special high-risk group for maternal mortality as a result of the short pregnancy spacing. Short intervals also are risk factor for morbidities like pre-eclampsia and high blood pressure (Razzaque et al. 2005).

pregnancies: (1) women of lower SES who have many pregnancies and also have higher rates of maternal mortality; (2) women who experience child deaths and involuntary pregnancy losses, which reflect a poor family health situation that increases the woman's risk of maternal death and which lead to many pregnancies as she tries to "replace" those that did not result in a surviving child; and (3) very healthy women who are able to conceive easily and have many healthy pregnancies and children. The last is consistent with the observation that there are some women who do not experience depletion during their reproductive cycles and produce healthy infants and keep healthy themselves (Winkvist et al. 1991).

We find that maternal mortality risk increases with age after women's 20s. Some of the excess mortality at older ages is due to the fact that the incidence of abortion, miscarriage, and stillbirth increases with age, and such pregnancy outcomes are strong risk factors of maternal mortality. Second, significant age-first pregnancy interaction indicates that the excess mortality associated with older ages is mostly due to the first pregnancies that occur in those ages. As we hypothesize above, women with first pregnancies at older ages may acquire the high mortality risk from their underlying health or other vulnerabilities. We reiterate that further studies should be undertaken to better understand the reasons behind women's delaying the first pregnancy beyond age 35 years.

Our finding that a part of the excess mortality at older ages is due to the high incidence of abortion has strong policy implications for developing countries where unsafe abortion is common and maternal mortality is high. Most abortions in these countries are due to lack of access to appropriate and quality contraceptive supplies. Bangladesh is an interesting case study where the health and family planning programs have been successful in reducing fertility. Because of early marriage and childbearing, most women achieve their desired family size, which currently averages 2.5 children (NIPORT 2009), before age 30. During the ages 30-49, women on average give birth to about one excess child (NIPORT 2009), and many of the women of these ages terminate their unintended pregnancies (DaVanzo et al. 2011). This is mainly because of couples' reliance on spacing methods like pills, injectables, and condoms and traditional methods. Women who have already achieved their desired family size continue to use these spacing methods, which have high rates of use-failure and discontinuation. Permanent contraceptive methods or long-acting methods that are appropriate for limiting fertility are not popular in Bangladesh, and many women thus encounter unintended pregnancies. Some abort

their pregnancies, and others end up with a live birth leading to excess births. Strong family planning behavior change activities coupled with quality services should be designed to have a balanced contraceptive method mix in which more and more couples will adopt long-acting and permanent methods for limiting purposes or they use the short-acting methods more effectively to avoid use-failure. This can help reduce the incidence of childbearing beyond age 35 and thus reduce maternal mortality.

We find that *too long* pregnancy intervals (75+ months) have pernicious effect on maternal mortality, but the effect reduces when the type of pregnancy outcome of both the previous and current pregnancies is controlled for. The apparent excess risk of long intervals stems from those intervals in which either or both of the pregnancies end in abortion, miscarriage, or stillbirth. We know these non-live birth outcomes are risk factors for maternal mortality and that they are more likely following long intervals (DaVanzo et al. 2007; Rahman et al. 2010). For induced abortion this is primarily because women with long intervals are probably mostly limiters, but conceptions occur due to use-failure or interrupted use of short-acting contraceptive methods, which, as mentioned just above, is common in Bangladesh. Women with an abortion have significantly higher risk of mortality than those with a live birth (Rahman et al. 2010). The likelihood of miscarriage and stillbirth, both of which are risk factors for mortality, is significantly higher following long (75+ months) intervals than those with 27-74 months (DaVanzo et al. 2007). This is probably a selectivity effect of women's poor health. A woman in poor health may have difficulty becoming pregnant, this may lead to a very long interpregnancy interval, and that pregnancy is more likely to end in a miscarriage or stillbirth. The incidence of intrauterine mortality was found to be high in Matlab as was that of maternal malnutrition, and malnutrition was a risk factor of intrauterine mortality (Ford et al. 1989). The incidences of malnutrition, anemia, reproductive tract infections, and other maternal morbidities, alone or in combination with other illnesses, are high in Bangladesh (NIPORT 2003), as they are in many developing countries. It is possible that women with these conditions are sub-fecund, take a long time to conceive, and that their pregnancies often end in miscarriage or stillbirth. In our data, about five percent of pregnancies occurred after interpregnancy intervals of 75 or more months. Further research is needed to investigate the causes of long interpregnancy intervals and associated women's health risks.

Regardless of the explanations of the cause-and-effect mechanisms, our findings provide a number of indicators that can be used for screening for and monitoring of high-risk groups: first pregnancies, older maternal age, long interpregnancy intervals (75+ months), a history of pregnancy loss(es) and of child death(s), and non-live-birth index outcomes (induced abortion, miscarriage, and stillbirth). In Table 4, we present the percentage of all pregnancies in our sample that are in high-risk categories. Substantial proportions of pregnancies are from high-risk groups. Women aged 35 or over and who are pregnant for the first time have a particularly high risk of maternal mortality (however, their proportion is small) and should be carefully monitored.

Although we don't find that young motherhood or short pregnancy intervals increase the risk of maternal mortality, it is important to note that these groups are associated with higher risk of infant and child mortality and therefore "too young" to be mother and "too short" of an interval should be avoided in order to improve family health. Furthermore, early marriage and childbearing limit women's opportunities for human capital and life skills development, with negative familial, social, economic, and health impact (Raj et al. 2009). In addition, early childbearing exacerbates the problems of population momentum, a factor affecting population growth in many developing countries.

As fertility declines in Bangladesh and other developing countries, a greater proportion of all pregnancies will be first pregnancies, which have a significantly higher risk of maternal mortality. This will put upward pressure on maternal mortality rates, ratios, and risks.[7]

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[7] Bongaarts (1987) made the same observation for infant mortality, since first births have a higher risk than higher-order births.

of the authors and do not reflect the opinions of WHO, USAID, ESD, RAND, or ICDDR,B.

References

American Medical Association (AMA) Committee on Maternal and Child Care, *A Guide for Maternal Death Studies, Council of Medical Services,* Chicago, IL, USA: AMA, 1964.

Anandalakshmy, P. N., P. B. Talwar, K. Buckshee, and V. Hingorani. 1993. Demographic, socio-economic and medical factors affecting maternal mortality-an Indian experience. *Journal of Family Welfare* 39:1-4.

Bongaarts, John. Does family planning reduce infant mortality rates? 1987. *Population and Development Review* 13(2):323-334.

Chowdhury M.E., R. Botlero, M. Koblinsky, et al. 2007. Determinants of reduction in maternal mortality in Matlab, Bangladesh: a 30-year cohort study. *Lancet* 370:1320-28.

Cleary-Goldman Jane, Fergal Malone, John Vidaver et al. 2005. Impact of maternal age on obstetric outcome. *Obstetrics and Gynecology* 105 (5) I: 983-990.

Cleland, John G. and Z. A. Sathar. 1984. The effect of birth spacing on childhood mortality in Pakistan. *Population Studies* 38: 401-418.

Conde-Agudelo, Agustin, and José Belizán. 2000. Maternal morbidity and mortality associated with interpregnancy interval. *British Medical Journal* 321:1255-9.

Conde-Agudelo, Agustin, José Belizán, and Cristina Lammers. 2005. Maternal-perinatal morbidity and mortality associated with adolescent pregnancy in Latin America: cross-sectional study. *American Journal of Obstetrics and Gynecology* 192:342-49.

Conde-Agudelo, Agustin, José Belizán, R Breman, SC Brokman, and A Rosas-Bermudez. 2005. Effect of the interpregnancy interval after an abortion on maternal and perinatal health In Latin America. *International Journal of Gynecology and Obstetrics* 89 (Suppl 1):S34-40.

DaVanzo, Julie, Lauren Hale, Mizanur Rahman, and Abdur Razzaque. 2011. The effects of pregnancy spacing after a miscarriage on subsequent pregnancy outcomes: evidence from Matlab, Bangladesh, draft.

DaVanzo, Julie, Lauren Hale, Abdur Razzaque, and Mizanur Rahman. 2008. The effects of pregnancy spacing on infant and child mortality in Matlab, Bangladesh: How they vary by the type of pregnancy outcome that began the interval. *Population Studies* 62(2):131-154.

DaVanzo, Julie, Lauren Hale, Abdur Razzaque, and Mizanur Rahman. 2007. Effects of interpregnancy interval and outcome of the preceding pregnancy on pregnancy outcomes in

Matlab, Bangladesh. *BJOG (British Journal of Obstetrics and Gynecology): An International Journal of Obstetrics and Gynaecology* 114(9):1079-1087.

DaVanzo Julie and Jean-Pierre Habicht. 1986. Infant mortality decline in Malaysia, 1946-1975: the roles of changes in variables and changes in the structure of relationship. *Demography* 23:143-160.

DaVanzo, Julie, Mizanur Rahman, Shahabuddin Ahmed, and Abdur Razzaque. 2011. Influences on pregnancy-termination decisions in Matlab, Bangladesh, draft.

D'Souza S. 1981. A population laboratory for studying disease processes and mortality -- the demographic surveillance system, Matlab Bangladesh, *Special Publication* #13.

Dieltiens G, Dewan H, Botlero R, et al. 2005. Met need for life-saving obstetric surgery in Bangladesh: the Matlab-ICDDR,B cohort-study of maternal mortality 1990-2001 and the results for a new indicator to assess met need for life-saving obstetric surgery. Dhaka: International Centre for Diarrhoeal Disease Research, Bangladesh.

Delbaere Ilse, Hans Verstraelen, Sylvie Goetgeluk, Guy Martens, Guy De Backer, and Marleen Temmerman. 2006. Pregnancy outcome in primiparae of advanced maternal age. *European Journal of Obstetrics & and Gynecology and Reproductive Biology* 135(1):41-46.

Fauveau V., Stewart K., Khan S. A., and Chakraborty J. Effect on mortality of community-based maternity-care programme in rural Bangladesh. *Lancet* 1991; 338: 1183-86.

Ford, Kathleen, Sandra L. Huffman, AKMA Chowdhury, Stan Becker, Hubert Allen, and Jane Menken. 1989. Birth-interval dynamics in rural Bangladesh and maternal weight. *Demography* 26 (3):425-437.

Geronimus, A.T. 1987. On teenage childbearing and neonatal mortality in the United States. *Population and Development Review* 13(2):245-279.

Jacobsson, Bo, Lars Ladfors, and Ian Milsom. 2004. Advanced maternal age and adverse perinatal outcome. *Obstetrics and Gynecology* 104 (4):727-733.

Jolly MC, Sebire N, Robinson HS, et al. 2000. Obstetric risks of pregnancy in women less than 18 years old. *Obstetrics and Gynecology* 96(6):962-966.

Khan, K.S., P.F. Chien, N.B. Khan. Nutritional stress of reproduction. 1998. *Acta Obstetrics Scandinavia* 77: 395-401.

King, Janet C. 2003. The risk of maternal nutritional depletion and poor outcomes increases in early or closely spaced pregnancies. *Journal of Nutrition* (Suppl.): 1732-1736.

Koening M. A., Fauveau V., Chowdhury A. I. et al. 1988. Maternal mortality in Matlab, Bangladesh. *Studies in Family Planning* 19(2): 69-80.

Lawlor, Debbie A and Shaw Mary. 2002. Too much too young? Teenage pregnancy is not a public health problem. *International Journal of Epidemiology* 31:552-554.

Menken Jane, Linda Duffy, and Randall Kuhn. 2003. Childbearing and women's survival: new evidence from rural Bangladesh. *Population and Development Review* 29(3):405-429.

Merchant K, Martorell R, and Haas J. 1990. Maternal and fetal responses to the stress of lactation concurrent with pregnancy and of short recuperative intervals. *American journal of Clinical Nutrition* 52: 280-288.

Merchant K, Martorell R, and Haas J. 1990. Consequences for maternal nutrition of reproductive stress across consecutive pregnancies. *American journal of Clinical Nutrition* 52: 616-620.

Miller, Jane E. Birth intervals and perinatal health: an investigation of three hypotheses. 1991. *Family Planning Perspectives* 23:62-70.

Naeye, Rachard L. 1983. Maternal age, obstetric complications, and the outcome of pregnancy, *Obstetrics and Gynecology* 61(2):210-216.

National Institute of Population Research and Training (INPORT), ORC Macro, Johns Hopkins University (JHU) and International Centre for Diarrhoeal Disease Research (ICDDR,B). 2006. *Bangladesh Maternal Health Services and Maternal Mortality.* Dhaka, Bangladesh.

Paulson RJ, Boostanfar R, Saadat P, Mor E, Tourgeman DE, Slater CC, et al. 2002. Pregnancy in the sixth decade of life: obstetric outcomes in women of advanced reproductive age. *JAMA* 288:2320–3.

Rahman M, DaVanzo J, Razzaque A. 2010. The role of pregnancy outcomes in the maternal mortality rates of two areas in Matlab, Bangladesh. *International Perspectives on Sexual and Reproductive Health* 26(4):170-177.

Raj A, Saggurty N, Bilash D, and Silverman JG. 2009. Prevalence of child marriage and its effect on fertility and fertility-control outcomes of young women in India: a cross-sectional, observational study. *Lancet* 373:1883-89.

Razzaque A., DaVanzo J., Rahman M., et al. 2005. Pregnancy spacing and maternal morbidity in Matlab, Bangladesh. *International Journal of Gynecology & Obstetrics* 89 (Suppl. 1):S41-49.

Rich-Edwards, Janet. 2002. Teen pregnancy is not a public health crisis in the United States. It is time we made it one. *International Journal of Epidemiology* 31:555-556.

Ronsmans C., Vanneste A. M., Chakraborty J., and van Ginneken J. 1997. Decline in maternal mortality in Matlab, Bangladesh: a cautionary tale. *Lancet* 350: 1810-14.

Ronsmans C. and Campbell O. 1998. Short birth intervals don't kill women: evidence from Matlab, Bangladesh. *Studies in Family Planning* 29: 282-90.

Rutstein, Shea. 2005. Effects of preceding birth intervals on neonatal, infant, and under-five years mortality and nutritional status in developing countries: evidence from the Demographic and Health Surveys. *International Journal of Gynecology & Obstetrics* 89 (Suppl. 1):S7-24.

Salihu, Hamisu M. M. Nicole Shumpert, Martha Slay, Russell S. Kirby, and Greg R. Alexander. 2003. Childbearing beyond maternal age 50 and fetal outcomes in the United States. *Obstetrics and Gynecology* 102 (5I):1006-14.

Scally, Gabriel. 2002. Too much too young? Teenage pregnancy is a public health, not a clinical, problem. *International Journal of Epidemiology* 31:554-555.

Scholl, Theresa O, Mary L Hediger, Joan I Schall, Chor-San Khoo, and Richard L Fischer. 1994. Maternal growth during pregnancy and the competition for nutrients. *American Journal of Clinical Nutrition* 60: 183-188.

Simchen, Michal J., Yoav Yinon, Orit Moran, Eyal Schiff, and Eyal Sivan. 2006. Pregnancy outcome after age 50. *Obstetrics and Gynecology* 108:1084-88.

Smith GCS and Pell JP. 2001. Teenage pregnancy and risk of adverse perinatal outcomes associated with first and second births: population based retrospective cohort study 323:476-79.

Temmerman M, H. Verstraelen, G. Martens, and A. Bekaert. 2004. Delayed childbearing and maternal mortality. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 114 (1):19-22.

Van Ginneken J., Bairagi A., De Francisco A., Sarder A. M., and Vaughan P. 1998. *Health and demographic surveillance in Matlab: past, present, and future*, Scientific Publication No. 72.

Winikoff, Beverly. 1983. The effects of birth spacing on child and maternal health, *Studies in Family Planning* 14 (10): 231-245.

Winkvist, A., K. M. Rasmussen, and J. P. Habicht. 1992. A new definition of maternal depletion syndrome. *American Journal of Public Health* 82: 691-694.

World Health Organization. 1992. *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision.* Geneva: WHO.

World Health Organization (WHO), United Nations Children's Fund (UNICEF), and United Nations Population Fund (UNFPA), and World Bank. 2010. *Trends in Maternal Mortality: 1990 to 2008,* Geneva: WHO.

Zabin L.S. and Kiragu K. 1998.The health consequences of adolescent sexual and fertility behavior in sub-Saharan Africa. *Studies in Family Planning* 29: 210-232.

Table 1. Probability of maternal deaths per 100,000 pregnancies by age and gravidity, Matlab, 1978-2008

(Number of pregnancies in parentheses)

Maternal age	Gravidity (Pregnancy order)									
	1	2(RC)	3	4	5-6	7-8	9+	Unknown	Total	Odds ratio
≤15	402 (1,244)	0 (179)	-- (41)	-- (9)	-- (3)	-- (1)			339 (1,477)	1.30
16-17	431 (7,193)	204 (1,470)	0 (238)	1,299 (77)	-- (18)	-- (1)		-- (10)	411 (9,007)	1.58**
18-19	469 (14,939)	220 (5,002)	95 (1,056)	0 (313)	685 (146)	-- (14)	-- (3)	-- (31)	386 (21,504)	1.48***
20-24 (RC)	329 (22,491)	244 (24,159)	194 (12,864)	192 (5,733)	208 (2,891)	1,294 (309)	-- (22)	0 (274)	260 (68,743)	1.00
25-29	392 (3,827)	181 (9,960)	184 (13,564)	247 (11,736)	401 (12,218)	390 (2,562)	267 (375)	289 (346)	271 (54,588)	1.04
30-34	613 (653)	160 (1,871)	198 (4,541)	358 (6,144)	317 (11,981)	498 (7,024)	394 (2,537)	383 (261)	348 (35,012)	1.34**
35-39	2308 (130)	0 (332)	109 (914)	361 (1,663)	377 (4,774)	498 (5,222)	683 (4,980)	1,042 (192)	494 (18,207)	1.90***
40-44	-- (22)	-- (47)	0 (113)	0 (244)	682 (880)	943 (1,378)	700 (2,714)	1,235 (81)	748 (5,479)	2.89***
45+	-- (16)	- (8)	-- (17)	-- (23)	3,125 (96)	1,015 (197)	362 (553)	-- (10)	1,087 (920)	4.21***
Total	406 (50,515)	221 (43,028)	186 (33,348)	266 (25,942)	367 (33,007)	539 (16,708)	590 (11,184)	581 (1,205)	333 (214,937)	
Odds ratio	1.84***	1.00	0.84	1.21	1.66***	2.45***	2.68***	2.64**		

-- Mortality risk is not shown for 50 or fewer cases
**p<0.01; ***p<0.001
RC = Reference category for marginals.

Table 2. Maternal mortality risk by duration of preceding interpregnancy interval (IPI) for second or higher order pregnancies, by types of pregnancy outcome at the beginning and end of the IPI

	Outcome of previous and index pregnancy								
	(A)			(B)			(C)		
	Both any type			Previous only live births; index outcomes any type			Both previous and index only live births		
IPI (months)	Deaths per 100,000	Odds ratio	No. pregnancies	Deaths per 100,000	Odds ratio	No. pregnancies	Deaths per 100,000	Odds ratio	No. pregnancies
< 6	189	0.86	12,167	197	0.93	4,568	101	0.80	3,941
6-14	241	1.09	21,170	206	0.97	15,059	122	0.90	13,110
15-26	214	0.97	46,663	210	0.99	43,806	125	0.98	39,233
27-50 (RC)	220	1.00	49,003	212	1.00	47,095	127	1.00	41,668
51-74	217	0.99	15,189	212	1.00	14,613	135	1.06	12,623
75+	361	1.64*	8,036	339	1.60*	7,660	217	1.71*	5,993
Unknown	416	1.89	12,194	369	1.74	1,083	414		966
Total	227		164,422	219		133,884	133		117,534

Any type = induced abortion, miscarriage, stillbirth, or live birth
*p<0.05
RC = reference category

Table 3. Odds ratios of reproductive-pattern factors associated with maternal mortality, from logistic regression (n=214,937)

					Background variables also controlled[a]			
							(b)	
Model:	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Maternal age								
<=15	1.30	1.00	1.00	1.09	0.76	0.74	0.71	0.78
16-17	1.58*	1.23	1.24	1.07	1.00	0.98	0.72	0.70
18-19	1.48**	1.22	1.22	0.92	1.07	1.06	0.84	0.45+
20-24 (RC)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
25-29	1.04	1.10	1.07	0.96	1.28+	1.32*	1.40*	1.29
30-34	1.34*	1.20	1.13	0.96	1.51*	1.61**	1.55*	1.34
35-39	1.90***	1.52*	1.37+	1.11	1.94**	2.13***	2.01**	1.65*
40-44	2.89***	2.19***	1.91**	1.52+	2.75***	3.03***	1.99*	1.60
45-49	4.21***	3.16***	2.70**	1.75	3.78***	4.18***	2.40*	1.51
Gravidity/Pregnancy order								
First pregnancy		1.77***	1.74***	1.47*	2.00***	2.09***	2.25***	1.87**
2 (RC)		1.00	1.00	1.00	1.00	1.00	1.00	1.00
3		0.82	0.81	0.83	0.72+	0.66*	0.61**	0.59*
4-5		1.22	1.21	1.28	0.92	0.74+	0.71+	0.72+
6-7		1.77***	1.83***	2.00**	1.10	0.75	0.78	0.84
8+		1.71*	1.86**	2.21***	1.00	0.55*	0.57*	0.64
Maternal age x First pregnancy								
16-17 x First pregnancy								
18-19 x First pregnancy				1.30				1.13
20-24 x First pregnancy (RC)				1.54				2.29+
25-29 x First pregnancy				1.00				1.00
30-34 x First pregnancy				1.28				0.95
35-39 x First pregnancy				1.88				1.42
40-44 x First pregnancy				6.20**				3.27+
45-49 x First pregnancy				9.42*				4.41
				22.91***				15.67**
Interpregnancy interval (IPI)								
0-5 months								
6-14 months			0.74	0.73	0.76	0.60*	0.72	0.71
15-26 months			1.18	1.17	1.18	1.05	0.94	0.94
27-50 months (RC)			0.96	0.95	0.89	0.88	0.92	0.91
51-74 months			1.00	1.00	1.00	1.00	1.00	1.00
75+ months			1.07	1.10	1.26	1.27	1.04	1.06
Unknown			1.46*	1.56*	1.93**	1.94***	1.41	1.49+
			0.83	0.89	0.82	0.79	1.07	1.12
No. previous child deaths								
None (RC)						1.00	1.00	1.00
1						1.24+	1.24	1.24
2+						1.39*	1.65**	1.65**
No. previous preg. losses								
None (RC)								
1						1.00		
2+						1.42**		
						1.96***		
Previous pregnancy outcome								
Live birth (RC)							1.00	1.00
Non-live birth							1.25	1.27
Index pregnancy outcome								
Live birth (RC)							1.00	1.00
Non-live birth							7.40***	7.37***
-2 Log likelihood	4,760.83	4,737.04	4,731.86	4,724.40	4,669.42	4,657.69	3,380.00	3,373.89

[a] Control variables include maternal education, household space as a proxy for household wealth, religion, area, and calendar years. [b]221 women who died during pregnancy are excluded.

+p<0.10; *p<0.05; **p<0.01; and ***p<0.001

Table 4. Maternal mortality high-risk groups and their percentages of all pregnancies in the sample

High-risk group	Percent of the sample
Age 35 years or higher	11.5
First pregnancies	23.5
First pregnancy and age 35 years or higher	0.3
Preceding interpregnancy interval = 75 months or longer	4.9
History of two or more child deaths	10.1
History of one or more pregnancy loss	21.6
Index pregnancy outcome = induced abortion, miscarriage, or stillbirth	12.1

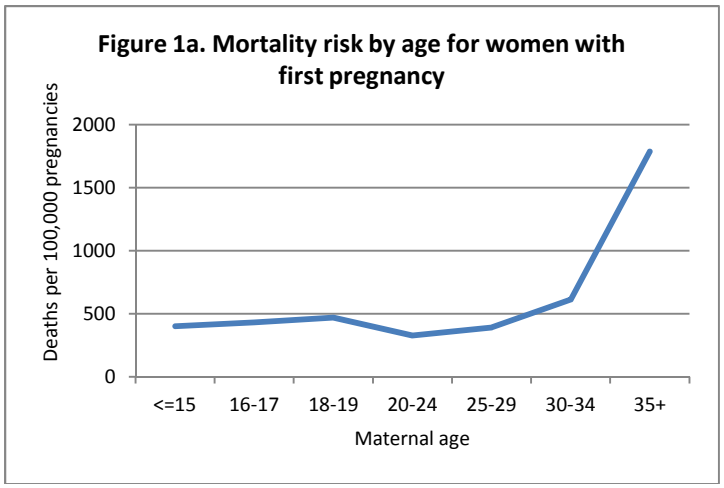
Figure 1a. Mortality risk by age for women with first pregnancy
Deaths per 100,000 pregnancies
2000
1500
1000
500
0
<=15
16-17
18-19
20-24
25-29
30-34
35+
Maternal age

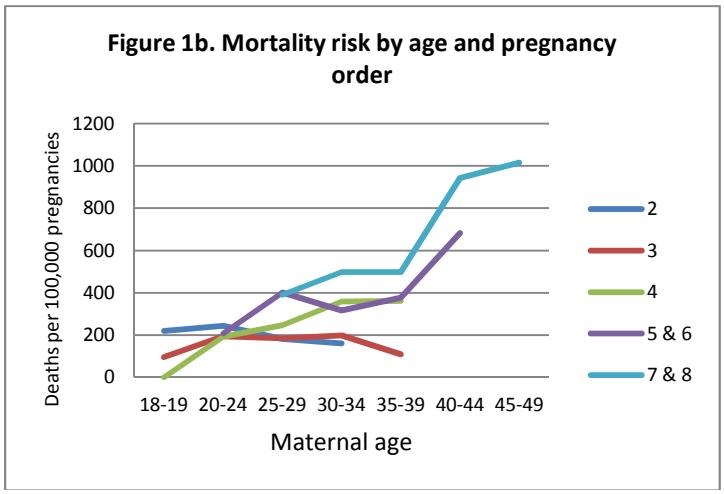
Figure 1b. Mortality risk by age and pregnancy order
Deaths per 100,000 pregnancies
1200
1000
800
600
400
200
0
18-19
20-24
25-29
30-34
35-39
40-44
45-49
Maternal age
2
3
4
5 & 6
7 & 8