The Long-Term Effects Of Childbearing On The Mortality Of Adults In Matlab, Bangladesh

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It is argued that reproduction impairs female survival in the long term, as pregnancy is thought to drain maternal physical resources. However, a review of the literature revealed that there was little evidence to suggest that mortality of highly parous women exceeded that of less parous women. In fact, mortality appeared to be highest in nulliparous women or women with only one birth. In addition, women whose first births were later were found to have consistently lower mortality. There was no evidence that female reproductive histories affected the risk of mortality in males.

The aim of this thesis was to examine whether reproductive history was associated with all-cause mortality after age 45 in women and men who had completed their reproduction in Matlab, Bangladesh. A cohort study was conducted using demographic data collected by the International Centre for Diarrhoeal Disease Research, Bangladesh. Essential data were found to be missing in the sample and multiple imputation was used in an attempt to adjust for the potential bias that this missing data may have introduced.

Trends in crude mortality rates with the reproductive exposures were examined. Poisson regression was then used to examine the association between reproductive history and all-cause mortality, adjusting for potential confounders. Crude mortality rates for the reproductive variables, stratified by age, education, religion and marital status, were also examined for effect modification and likelihood ratio tests for interaction performed.

There were no differences in the mortality of women with parity, either when comparing the parous with the nulliparous or when looking at trends with the number of children born. However, mortality did decrease with the number of surviving children. These differences were statistically significant and persisted when the rate ratios were adjusted for potential confounders. The patterns in the husbands were strikingly similar to those seen in the women. The results suggest that there are few negative long-term biological consequences of bearing children in these women. Even if they exist, they may be outweighed by the social advantages of having a family and a healthy pregnant woman effect. These conclusions are strengthened by the fact that the reduction in mortality with the number of surviving children persisted after adjusting for potential confounders and by the remarkable consistency in the associations in the females and their husbands.

NB. The appendices are numbered according to the Chapter to which they refer.

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Abbreviations

Adj	Adjusted
ANOVA	Analysis Of Variance
BFS	Bangladesh Fertility Survey
BDHS	Bangladesh Demographic and Health Survey
CHW	Community Health Worker
CI	Confidence Intervals
DSS	Demographic Surveillance System. (One of the data collection systems of the ICDDR, B)
FL (on a figure)	Fetal Losses
HDL	High Density Lipoprotein
HR	Hazard Ratio
ICDDR, B	International Centre for Diarrhoeal Disease Research, Bangladesh
LR	Likelihood Ratio
MAR	Missing At Random
MCAR	Missing Completely At Random
MCH-FP	Maternal Child Health and Family Planning (The "intervention" area in the Matlab surveillance system)
MI	Multiple Imputation
NIS	National Impact Survey, Bangladesh
OPCS study	Office of Population Censuses and Surveys Longitudinal Study
OR	Odds Ratio
P (on a figure)	Parity
RR	Rate Ratio, when referring to my results; Relative Risk, when referring to the studies reviewed
RSFM	Retrospective Survey of Fertility and Mortality, Bangladesh
SC (on a figure)	Surviving Children
SD (on a figure)	Surviving Daughters
SD	Standard Deviation
SS (on a figure)	Surviving Sons
SMR	Standardised Mortality Ratio

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This work would never have been completed without the endless support and friendship of the following people: my supervisor Dr Carine Ronsmans, from whom I learnt so much and whose patience seems limitless; Dr Oona Campbell, who was always helpful and full of good ideas; Professor Mike Kenward, for introducing me to a world in which missing data became an interesting challenge rather than a fatal flaw and for answering my many questions; Maria Quigley, who was always on hand to help with all the other confusing statistical things; all of the ICDDR, B staff who were wonderful during my stay in Dhaka, Sajal Saha in particular; and my other lovely friends in Bangladesh and London, who have all been very tolerant of late! I would also like to acknowledge the financial support given to me by the Medical Research Council.

This thesis is dedicated to my family: dad, mam, Iwan and Chris – *y teulu gorau yn y byd*!

1.1 Introduction

The concept of a "cost of reproduction" is age-old, with Aristotle noting that "*most trees, if they have borne an excessive amount of fruit, wither away when the crop is over, when no nourishment is left over for themselves*" (Jonsson, Tuomi 1994). It is therefore argued that repeated reproduction depletes physical resources and impairs long-term survival. For example, Hill and Hurtado (1996) stated that "*energy harvested during the life cycle can be used for maintenance and repair of the soma, growth, storage, or reproduction. Since the energy used for one purpose cannot be used for another purpose, living organisms face a series of trade-offs...individuals who engage in high reproductive expenditure at some point in time should have lower reproductive output or lower survival in subsequent time periods*". These reproductive costs have been discussed in terms of effects on future fertility, the well-being of offspring and the welfare of the adults who reproduce (Bell, Koufopanou 1986). They have also attracted the attention of the popular press (Figure 1.1, next page). In this work, I will concentrate on the costs to those who reproduce and specifically on the association with long-term mortality risks.

Zoologists have found diverse effects of reproduction on survival. In a review of available evidence, Partridge and Harvey (1985) found that female sparrows rearing large broods tend to live longer, whereas red deer giving birth during one calving season may be less likely to survive to the next. They concluded that increased reproduction was associated with reduced survival in laboratory experiments, but that it was uncertain whether these effects were sustained under real life conditions.

In humans the risk of mortality changes during pregnancy, both as a result of the direct effects of pregnancy and because underlying disease conditions may be exacerbated or alleviated (AbouZahr, Royston 1991). Mortality rates in pregnant women may be twice or three times higher than those in non-pregnant women of the same age (Khlat, Ronsmans 2000). In addition, previous reproductive history alters the risk of death. Maternal mortality tends to be higher in the first pregnancy and at high birth orders. Short birth spaces have also been hypothesised to increase the risk of maternal mortality, although the evidence to date is inconsistent (Ronsmans, Campbell 1998; Conde-Agudelo, Belizan 2000).

Figure 1.1: The effects of reproduction are not just of concern to the scientific community

Daily Mail, February 19th, 2001

How having a baby can damage your health decades on

Motherhood has long-term risks

HAVING a baby appears to increase greatly a woman's chances of developing some devastating illnesses, according to research.

Cells from the foetus left in the mother's bloodstream act as 'enemies within' and trigger health problems decades later.

They could be responsible for multiple sclerosis, rheumatoid arthritis, diabetes, lupus and up to 100 other so-called autoimmune diseases.

The findings offer an explanation for why these diseases strike women up to ten times more often than men.

They could also open the way for new treatments for many autoimmune disorders.

Dr Lee Nelson, of the University of Washington in Seattle, said the persistence of foetal cells may affect the mother's immune system, causing it to malfunction.

The presence of foreign cells can

By **James Chapman**
Science Correspondent

send the immune system into overdrive. In all the auto-immune diseases, the mechanism that nature created to protect us becomes the enemy, deciding that parts of the body are alien and attacking them.

'Traditionally, the auto-immune diseases are described as your cells attacking your own, healthy tissue,' explained Dr Nelson.

'Our findings raise the question as to whether some auto-immune diseases are not entirely auto-immune, whether they actually have a component that is non-self.

'It seems pregnancy is a minigene transfer. It is exposure to a being that's half foreign. You are getting genes that aren't your own by being exposed to the cells of the child.

'With women who have had a son, we are looking 20 to 30 years later at their blood and finding male cells in it.'

The scientists have identified significantly higher levels of foetal cells circulating in the blood of women with scleroderma – an auto-immune disease in which skin and internal tissues thicken and harden, often fatally.

There are about 3,000 people in Britain with the condition – far more women than men.

Those diagnosed with the worst form survive only five years on average.

The scientists, who unveiled their findings at the American Association for the Advancement of Science conference in San Francisco, said cells could move in both directions during pregnancy.

This means each of us is probably walking around with some of our mother's cells in our bloodstream.

And this would account for the development of scleroderma in women without children and men.

The discovery of the harmful role of foreign cells could pave the way for new treatments for autoimmune diseases.

These would include rheumatoid arthritis, which affects 750,000 Britons and is the biggest cause of pain and disability, systemic lupus, which can affect any part of the body, thyroid disorders and rarer conditions such as Goodpasture's syndrome, which destroys the kidneys.

Type-1 diabetes, the more serious version, is also an autoimmune condition.

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National news

American Association What babies leave behind ● Immortality still a pipe dream ● The first domestica

Alien cells may cause arthritis in women

Tim Radford
Science editor

Women could be 10 times more likely than men to suffer from rheumatoid arthritis, lupus, multiple sclerosis and other autoimmune diseases because they carry alien tissues in their bloodstreams – cells from their children and mothers.

Lee Nelson of the University of Washington told the American Association for the Advancement of Science in San Francisco that even 30 years after the birth of a son, male foetal cells could be detected in a woman's blood stream at levels of one in a million.

The presence of these alien cells could indirectly affect the mother's immune system. Immune systems work by detecting and attacking invading cells – bacteria, viruses and so on. Sometimes, immune systems attack their own host, to cause scleroderma, multiple sclerosis and up to 100 other diseases. Autoimmune diseases are

that is non-self. It's really an entirely new paradigm."

Her research began with rheumatoid arthritis, which goes into remission when women are pregnant but returns after delivery. Immunologists have been interested for decades in why babies aren't rejected after conception, in the way that transplanted organs are rejected by the immune system. But the invasion by a "stranger" turned out to last far longer than nine months.

"In women who have had, for example, a son, you can look 10, 20 or 30 years later at a drop of blood, and find a male cell in there. Similarly you would find cells from a daughter. It's just a little easier to track a male cell in a woman," Dr Nelson said. "The basic theme is that pregnancy is an immunologic event. It is not just a change in hormones, it's actually exposure to a being who is half yours, because half the genes come from the father."

Some of the mother's cells went into the child as well. There were other ways of

there are of the genes that help you determine what is self, what is other," said Dr Nelson. It could explain why women had more autoimmune disease than men, because there were more chances of carrying alien immune system cells.

These were a set of genes on the sixth chromosome, essential to distinguishing self and non-self, called the human leukocyte antigens, or HLA genes. Knowledge of how these genes work could help scientists think of widely different illnesses as stemming from one source. It could also explain why some diseases retreated during pregnancy, and then became better or worse afterwards. It might also explain why one twin might have the disease, but another did not. One child would develop multiple sclerosis, but his or her identical twin had only one chance in 20 of developing the same disease.

"It's a fascinating area and it will give us, hopefully, a whole new way of treating these diseases because we can target

The Guardian, February 19th, 2001

There is also substantial evidence that reproductive history is associated with changes in both incidence and mortality from specific diseases. For example, mortality from cardiovascular disease and cervical cancer increases with parity (Pike 1987; Ness *et al* 1994) whereas deaths from breast, endometrial and ovarian cancer reduce (Pike 1987; Kelsey *et al* 1993). Studies relating reproductive history to other conditions, such as diabetes and non-reproductive cancers, have produced inconclusive results (Beral 1983; La Vecchia *et al* 1993; Ness *et al* 1994). For example, early cross-sectional studies suggested that there may be a relationship between parity and the incidence of diabetes in later life but recent cohort studies that have adjusted for age, socio-economic status and body weight have shown little or no association (Ness *et al* 1994). Data relating reproductive history to other cancers is also inconsistent. For example, Plesko *et al* (1985) found a significant trend in increasing mortality from stomach cancer with parity in Slovakian women whereas Miller *et al* (1980) showed that the trend in Canadian women was only of borderline significance. However, in an Italian case-control study, no relationship between parity and the incidence of stomach cancer was seen (La Vecchia *et al* 1993).

The long-term effects of childbearing on all-cause mortality have received less attention. Life history theory suggests that there is a trade-off between reproduction and survival. It has been proposed that genes promoting early and intensive reproduction may carry mutations that affect later survival ("*antagonistic pleiotropy*", where pleiotropy refers to a gene that has multiple effects, Medawar 1952; Williams 1957) or that somatic maintenance is reduced with reproduction, as physical resources used during reproduction cannot be used for repair ("*disposable soma theory*", Kirkwood 1977; Kirkwood, Rose 1991). In addition, Powys (1905) concluded that women with six or more children had higher mortality for reasons that were "*sufficiently obvious.....the incessant strain upon the physique of women who bear large families during the periods of gestation, parturition and lactation must be very prejudicial to longevity, whilst the mental strain involved in the rearing of such families cannot be regarded as other than detrimental.*" Data to corroborate these assertions are limited.

1.2 Aims and Objectives of the Thesis

The empirical evidence to support the existence of long-term effects of reproduction on mortality in humans has never been comprehensively reviewed, despite the assumptions stated above and despite a clear need to quantify how the effects of reproduction on specific diseases affect the overall risk of mortality. Thus, the first aim of this thesis is to discuss how reproduction may affect long-term survival and to review the literature relating reproductive history with all-cause mortality.

The second aim is to examine the association between reproductive history and all-cause mortality after age 45 in a developing country setting, using secondary analysis of routine surveillance data collected in Matlab, Bangladesh. The relationships will be examined in two cohorts: women, aged between 45 and 55 years on entry, who have completed their reproduction and the husbands of these women.

The specific objectives of the study are:

- **In ever-married women aged 45 years and older living in Matlab, Bangladesh between June 30th 1982 and December 31st 1998:**

1. To examine the association between reproductive and all-cause mortality.
2. To examine the effects of age, time period, religion, socio-economic status, area of residence, and changes in marital status on the strength of these associations.

- **In the husbands of these women who lived in Matlab, Bangladesh between June 30th 1982 and December 31st 1998:**

1. To examine the association between reproductive history in the wives and the husbands' all-cause mortality.
2. To examine the effects of age, time period, religion, socio-economic status, area of residence and changes in marital status on the strength of these associations.

1.3 Thesis Structure

The thesis has the following structure. Chapter Two contains a discussion of how pregnancy may affect long-term mortality risk, an examination of how reproductive exposures are defined and a detailed critique of the literature relating reproductive history to all-cause mortality. In Chapter Three, the design of the current study and a description of the data sources used are presented. Missing reproductive histories may have

introduced an important bias in this study. A description of this missing data and the methods used in an attempt to correct for this potential bias are presented in Chapter Four. The next three chapters contain the results of the study. Chapter Five includes a description of the socio-demographic status of both cohorts, and the results of a Poisson regression analysis relating these characteristics with mortality. Chapter Six contains a description of the reproductive histories of the female cohort and the results of the Poisson regression analysis relating reproductive history to female mortality. Chapter Seven contains the equivalent analyses in the men. A discussion of the strengths and weaknesses of the study along with the conclusions that can be drawn and the questions that remain unanswered are given in the final chapter. The bibliography of cited references is presented at the end of the thesis.

2.1 Introduction

A woman's body undergoes many changes during pregnancy, which serve to protect the mother and fetus during the gestation and to prepare the mother for delivery and the postpartum period. It is known that women who suffer medical complications during pregnancy are at a higher risk of morbidity and mortality in the long term. For example, women who develop gestational diabetes are at an increased risk of becoming diabetic later in life (Damm 1998) and women who suffer from pre-eclampsia are more likely to develop hypertension (Sibai *et al* 1992; Marin *et al* 2000). But what are the long-term risks associated with an uncomplicated pregnancy? The first section of this chapter examines whether it is plausible that changes occurring during pregnancy affect the risk of mortality in the long-term.

The lack of information on the long-term effects of reproduction on survival is due in part to the lack of data and necessary research, but may also be attributable to the complexity of the exposure. Thus, in the second section of the chapter, I briefly examine how reproduction may be defined as an exposure.

The main aim of the chapter is to review the literature that has examined the association between reproductive history and all-cause mortality. This review is presented in the final section of the chapter. Maternal mortality and the effects of childbearing on mortality from specific diseases will only be mentioned where relevant, as they have been extensively explored elsewhere.

2.2 How might pregnancy affect mortality in the long-term?

It has been suggested that the biological changes that take place during pregnancy in some way alter the risk of mortality after pregnancy. In Table 2.1 (next page), examples of these anatomical and physiological changes are given, along with evidence indicating whether the changes persist or have long-term effects. Evidence linking parity (number of live births) with the changes or effects is also given. In most instances, the changes are thought to affect the risk of specific diseases and, for many, current evidence linking the change to the disease or to mortality is speculative.

Table 2.1: Examples of anatomical and physiological changes during pregnancy	
Change	**Does the change persist in the long term and is there evidence of a long-term link with mortality?**
Endocrine system ↑ oestrogen, progesterone and other steroid hormones	Patterns of disease-specific mortality with parity similar to those with oral contraceptives (Oldfield *et al* 1998; Beral *et al* 1999). Parity not related to post-menopausal blood hormone concentrations in healthy women (Ness *et al* 2000).
Cardiovascular system ↑ plasma volume, ↑ cardiac output, ↑ heart rate, ↑ blood pressure	Cardiovascular system changes do not persist (Abraham 1999). Cardiovascular disease mortality increases with parity (Ness *et al* 1994). No association or a possible negative association demonstrated between parity and hypertension in long-term (Ness *et al* 1994)
Metabolic system ↓ insulin secretion and ↑ insulin resistance	No consistent relationship between parity and impaired glucose tolerance or diabetes (Henry, Beischer 1991; Dornhorst, Rossi 1998; Damm 1998).
Metabolic system Changes in lipid metabolism: Total cholesterol levels increase during pregnancy.	Multigravid/parous women have ↓ HDL cholesterol (and ↑ mortality from cardiovascular disease) than nulligravid/parous women (Ness *et al* 1994)
Immunology Exposure to fetal antigens and serum levels of IgG, IgA and IgM decrease.	Rheumatoid arthritis improves during pregnancy but worsens after. Effects on other autoimmune diseases less consistent (Nelson 1998, Reichlin 1998) Fetal antigens persist in maternal blood postpartum (Nelson 1998). This may immunise against various cancers (Janerich 1994)
Alimentary system Relaxation of intestinal musculature → greater absorption of nutrients	The more weight gained during pregnancy, the higher the risk of postpartum obesity (Scholl *et al* 1995). High parity is associated with higher postpartum body mass index in well-nourished populations (Ness *et al* 1994, Scholl *et al* 1995). Evidence for maternal depletion in malnourished subjects inconsistent (Winikoff 1978; Winkvist *et al* 1992; Ronsmans, Campbell 1998)
Reproductive system Endometrium is quiescent during pregnancy and endometrial lining is shed during delivery	Mortality from endometrial cancer ↓ with parity (Pike 1987)
No ovulation during pregnancy	Mortality from ovarian cancer ↓ with parity; similar to the effects seen with oral contraceptive (Pike 1987, Beral *et al* 1999)

Many of the changes that occur during pregnancy are mediated by hormones that are secreted by the placenta (Abraham 1999). Blood levels of oestrogen, progesterone, cortisol, and other steroid hormones in pregnant women are markedly higher than in non-pregnant women (Ness *et al* 1994). It has been suggested that these hormones are associated with changes in long-term mortality risks, as the disease-specific effects of parity are similar to those seen with oral contraceptive use (Oldfield *et al* 1998; Beral *et*

al 1999). However, Ness *et al* (2000) found no relationship between reproductive history and post-menopausal levels of steroid hormones in the blood.

There is an increase in blood volume and plasma volume during pregnancy. Cardiac output increases by between 30 and 50 percent and the woman's heart rate increases by approximately 15 percent. After the thirtieth week, there is also a tendency for blood pressure to rise. Following birth, the cardiovascular system returns to the pre-pregnancy state (Abraham 1999). However, high parity has been shown to be associated with increased cardiovascular disease mortality later in life. The mechanisms behind this association are not well understood.

In late pregnancy, tissues become resistant to insulin and its secretion diminishes. It is not known how these changes are mediated (Damm 1998). There is some evidence that glucose tolerance is impaired following an uncomplicated pregnancy, but the duration of this change remains unknown (Henry, Beischer 1991; Dornhorst, Rossi 1998; Damm 1998). However, there is no consistent evidence linking parity with the long-term incidence of non-insulin dependent diabetes mellitus (Ness *et al* 1994).

Lipid metabolism also changes during pregnancy. Levels of low-density lipoproteins, high-density lipoproteins and triglycerides all increase and, at their peak, equal those in patients with coronary heart disease. After pregnancy, levels of HDL cholesterol (so-called "good cholesterol") decrease and it has been shown that multigravid and multiparous women have lower HDL cholesterol levels than nulligravid and nulliparous women (Ness *et al* 1994). It is therefore possible that parity increases the risk of heart disease through a long-term effect on HDL cholesterol (Bush *et al* 1988, Ness *et al* 1994)

During pregnancy, a mother is exposed to HLA molecules inherited by the fetus from the father. It is not fully understood why the maternal immune system does not reject the growing foetus (Buyon *et al* 1996). There is a reduction in the immune response to antigens from the 'father' in pregnant mice, whereas exposure to the same paternal antigens after pregnancy triggers a normal immune response (Perks, Coulton 2001). In humans levels of circulating immunoglobulins reduce during pregnancy, possibly

mediated by placental hormones such as progesterone and human chorionic gonadotropin (HCG) (Abraham 1999; Perks, Coulton 2001). The long-term effects of these changes in immunity are not well understood. It has been suggested that pregnancy may "immunise" against certain cancers, prompting research into the development of tumour vaccines (Beral 1983, Janerich 1994). However, patterns in autoimmune diseases with pregnancy and parity are confusing. For example, rheumatoid arthritis often remits during pregnancy and recurs post-pregnancy (Nelson 1998; Wilder 1998), whereas systemic lupus erythematosus may improve, exacerbate or remain unchanged with pregnancy (Reichlin 1998). Evidence for long-term changes in autoimmune diseases with parity is limited.

Nutrients are absorbed more efficiently from the intestine and maternal metabolism slows during gestation to ensure that the foetus receives adequate nourishment (Abraham 1999). The more weight gained during pregnancy, the higher the risk of postpartum obesity (Scholl *et al* 1995). There is also a moderate association between high parity and an increase in body mass index (Ness *et al* 1994). Excessive weight gain is, in turn, associated with increased mortality (Poston *et al* 1998). However, it has also been suggested that frequent reproductive cycling may lead to "maternal depletion" in poorly nourished populations (Jelliffe, Jelliffe 1978) such that increasing parity and short birth spaces are thought to be detrimental when combined with maternal malnutrition. The evidence to support the existence of a "maternal depletion syndrome" is, however, weak (Winikoff 1987; Winkvist *et al* 1992; Ronsmans, Campbell 1998).

Finally, there are changes within the reproductive organs themselves that may be related to later mortality from specific diseases. It has been suggested, for example, that endometrial cancer reduces with parity as the endometrium is quiescent during pregnancy thereby discouraging malignant transformation (Pike 1987), and that the mechanical exfoliation of the endometrium at delivery results in the shedding of any malignant cells that may be present (Kvale *et al* 1991). In addition, it is thought that parity protects against ovarian cancer as ovulation ceases during gestation reducing the damage to the epithelial surface of the ovary (Pike 1987).

Therefore, many of the changes occurring during pregnancy are well described. However, surprisingly little comprehensive data exists as to the long-term effects of these

changes and whether they are more likely to persist with a particular reproductive history. An assessment of the long-term mortality risks in women with different reproductive histories is therefore not possible from this data alone.

2.3 Is exposure to pregnancy the same as exposure to reproduction?

Thus far, I have focused on the effects of pregnancy itself. But is there more to a reproductive history than exposure to pregnancy, as shown in Figure 2.1. Does counting the number of pregnancies adequately reflect a woman's exposure to reproduction or could other reproductive factors also influence long-term mortality risks? For example, although gravidity (number of pregnancies) and parity (number of live births) are highly correlated they may not be interchangeable. If exposure to a pregnancy of any length is related to changes in mortality risk, then excluding fetal losses may result in an underestimation of the effects of reproduction. If, on the other hand, the effects of the biological exposures accumulate with time then including all pregnancies may underestimate the risks associated with full term pregnancies. In addition, fetal losses may affect mortality in their own right, both directly and through an effect on other reproductive factors such as breast-feeding, contraception use and birth spacing. Other reproductive factors may also influence mortality risks. For example, if reproduction affects survival through an effect on somatic maintenance, we would expect women with shorter spaces between births and women who had all of their children within a short time span to have higher mortality. The effects of pregnancy may also be mediated through other reproductive factors. For example, highly parous women may be at an increased risk of becoming depleted owing to repeated breastfeeding, thus altering their risk of long-term mortality. Women who reproduce are also exposed to less tangible factors such as a "family", which may influence mortality through the close physical contact it entails with others or through an effect on the psychological or social well-being of the parent. Finally, reproductive factors may not influence survival in isolation. For example, it has been suggested that parity and birth spaces may interact in "maternal depletion". It therefore seems conclusive that exposure to reproduction constitutes more than just exposure to a series of pregnancies.

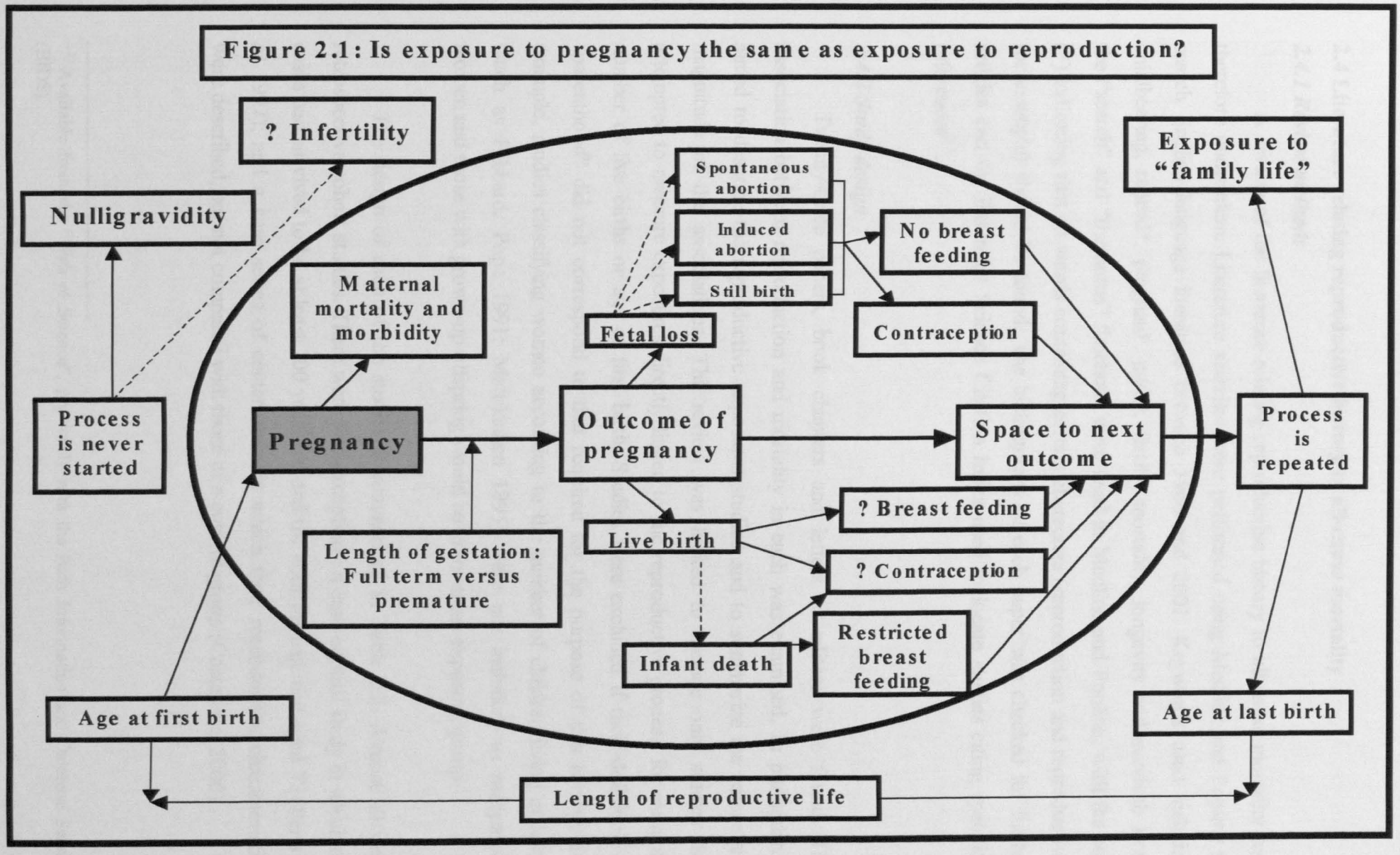


Figure 2.1: Is exposure to pregnancy the same as exposure to reproduction?
? Infertility
Nulligravidity
Process is never started
Maternal mortality and morbidity
Pregnancy
Length of gestation: Full term versus premature
Spontaneous abortion
Induced abortion
Still birth
Fetal loss
Outcome of pregnancy
Live birth
Infant death
No breast feeding
Contraception
? Breast feeding
? Contraception
Restricted breast feeding
Space to next outcome
Exposure to "family life"
Process is repeated
Age at last birth
Age at first birth
Length of reproductive life

2.4 Literature relating reproductive history to all-cause mortality

2.4.1 Review methods

A review of the literature relating reproductive history to all-cause mortality was therefore undertaken. Literature searches were performed using Medline and Popline to search English language literature between 1966 and 2001. Keywords used included childbearing, reprod*, pregnan*, parity, fertil*, mortality, longevity and survival. Both the "search" and "thesaurus" functions were used in Medline and Popline, with the star (*) indicating that all words containing certain characters (reproduction and reproductive, for example) should be found. The bibliography of each paper was checked for further articles and the Extended Science Citation Index used to locate studies citing specified references[2.1].

2.4.2 Study design

Twenty-three papers, book chapters and letters to editors were found. The association between reproduction and mortality in each was examined. In particular, I aimed to describe the reproductive exposures studied and to summarize the nature and magnitude of the associations. The review was limited to include only studies that attempted to measure exposures directly linked to the reproductive process, for example, number of live births or age at first birth. Studies were excluded if their definition of "parenthood" did not correspond to that required for the purpose of this review. For example, studies classifying women according to the number of children living at home (such as Hibbard, Pope 1991; Martikainen 1995) were not included, as nulliparous women and those with grown-up offspring would be in the same exposure group.

The design of each of the studies is summarised in Table 2.2. Almost all were retrospective cohort studies. There were two exceptions: a case-control study in which the cases had survived to be at least 100 years old and the controls had died aged 73 (Perls *et al* 1997); and a case series of centenarians in which their reproductive characteristics were described, but not compared with those of a control group (Costa *et al* 2000).

[2.1] Available from the "Web of Science", previously with the Bath Information and Database Service (BIDS).

In Table 2.2, the studies are grouped according to the source of the reproductive exposure data. Nine studies used census data to obtain the women's reproductive histories (Kitagawa, Hauser 1973; Fox, Goldblatt 1982; Green *et al* 1988; Lund *et* al 1990; Moser *et al* 1990; Weatherall *et al* 1994; Costa *et al* 2000; Doblhammer 2000; Manor *et al* 2000). Five of these used data from the Office of Population Censuses and Surveys Longitudinal Study (OPCS), which is a follow-up study of a random sample of the 1971 England and Wales census population (Fox, Goldblatt 1982; Green *et al* 1988; Moser *et al* 1990; Weatherall *et al* 1994; Doblhammer 2000). Three studies used other sources of routinely collected data, such as registrations of births (Powys 1905; Arvay, Takacs 1966) and death certificates (Beral 1985[2.2]). Exposure data was acquired in another three studies from on-going studies (Kotler, Wingard 1989; Kvale *et al* 1994; Friedlander 1996), and two further studies used the next of kin to provide some or all reproductive information (Perls *et al* 1997; Cooper *et al* 2000). The remainder used "*historical demographic records*". These were poorly described in most studies, but included family trees collected by genealogists (Westendorp, Kirkwood 1998) and parish records of births (Phillipe, Yelle 1976; Voland, Engel 1989; Le Bourg *et al* 1993; Korpelainen 2000; Lycett *et al* 2000). All used data from mortality registrations to obtain information on the outcome.

The studies were conducted using data from relatively affluent societies, including England and Wales, Norway, Hungary and Israel. The ages of the women selected varied substantially between studies. Some included women of all ages. For example, Lund *et al* (1990) included women who were 25 years and older at the census and three of the studies using OPCS data included women who were between the ages of 15 and 59 at the start of follow-up. Others attempted to restrict their samples to women who had completed their reproduction. However, these also varied, in that some included women who were over the age of 45 (Kitagawa, Hauser 1973; Manor *et al* 2000) whilst others included women over the age of 50 (Arvay, Takacs 1966; Cooper *et al* 2000). There were also differences in the birth cohorts included. Sixteen studies included women who had been born in the late nineteenth and early twentieth century. In the studies using historical sources of data, the birth cohorts included were usually considerably earlier, although many of these study populations were poorly described.

[2.2] Death certificates in England and Wales used to contain a question relating to a woman's parity.

The number of subjects varied from less than 150 (Phillipe, Yelle 1976; Perls *et al* 1997; Costa *et al* 2000) to over a million (Arvay, Takacs 1966; Doblhammer 2000). Some studies described the numbers of women included whilst others mentioned only the numbers of deaths. None showed the results of power calculations estimating the required population.

In the studies that used census data, we can assume that non-response was not a problem. However, in the studies that had recruited subjects anew, there were varying degrees of non-response. For example, 14% of Kotler and Wingard's (1989) sample did not respond to the initial request for subjects compared with 37% of the sample of Cooper *et al* (2000). Subjects were also excluded if exposure or covariate data was missing. In one extreme example, 87% of the original sample was excluded due to missing data (Phillipe and Yelle 1976)! Only one study (Kitagawa, Hauser 1973) attempted to adjust their results for the bias that the missing data may have introduced. Loss to follow-up is not described in most studies and, in the studies that relied on routine or historical data, the completeness of recording is usually not discussed.

The reproductive exposure most frequently studied was parity and its definition varied between studies. Green *et al* (1988), for example, had data on "*all children born in marriage*", whilst Lund *et al* (1990) had information on live births from a current marriage only. Kvale *et al* (1994) included information on "*all full-term deliveries*" (that may include stillbirths) whereas Friedlander (1996) had data pertaining to the "*number of biological children*". No further definition was given in most of the remaining papers. Five studies also examined the effect of age at first birth (Lund *et al* 1990; Le Bourg *et al* 1993; Westendorp, Kirkwood 1998; Doblhammer 2000; Korpelainen 2000). A further three looked at age at last birth (Le Bourg *et al* 1993; Cooper *et al* 2000; Korpelainen 2000) and two examined mortality in women who had given birth after age 40 (Perls *et al* 1997; Doblhammer 2000). Finally, two studies examined the effects of the length of a woman's reproductive life, measured as the time between her first and last births. In studies using census or other ongoing cohorts, exposure was ascertained at entry and no further information was collected during follow-up even though some women may have continued to reproduce during follow-up. In studies including subjects who were all already dead, reproductive history at death was obtained. No papers were found that

examined the relationship of other reproductive factors, such as fetal losses or breast-feeding, with all-cause mortality in women.

The association between reproduction and mortality was assessed in two different ways. In the first, women were classified according to their reproductive history and the relative risk of mortality was calculated, either by comparing women in different exposure groups using methods such as logistic regression (Kvale *et al* 1994; Weatherall *et al* 1994; Doblhammer 2000) and Cox's proportional hazards (Friedlander 1996), or by comparison with a standard population using standardised mortality ratios (Kitagawa, Hauser 1973; Beral 1985; Green et al 1988). Alternatively women were classified according to their age at death, and the reproductive characteristics of women at each age at death were compared using a variety of statistical methods such as multiple regression (Westendorp, Kirkwood 1998; Lycett *et al* 2000) and analysis of variance (Lycett *et al* 2000). Some statistical methods used were not ones that are frequently used to describe associations in current epidemiological practice such as Duncan's test (Phillipe, Yelle 1976), principal components analysis (Le Bourg *et* al 1993) and Gompertz function (Doblhammer 2000). Only one study included no hypothesis testing (Costa *et al* 2000).

All studies adjusted for the potential confounding effects of age. Most also restricted their samples to women who were currently or ever married. Adjustment for other factors such as socio-economic status was variable.

The results of the studies will be summarised in the next section. This summary includes a description of the results and summary figures where appropriate. No meta-analysis of the results could be performed, as the studies were too different in terms of the populations they included and the methodologies employed. Instead, possible sources of heterogeneity between the results will be identified.

The results of one study will not be included due to its methodological weaknesses. Phillipe and Yelle (1976) excluded 87% of their original sample due to missing or inconsistent data. They may therefore have studied a sample that was systematically different from the population of interest. Findings of other studies should be interpreted with caution. In particular, the studies using historical populations (Powys

1905; Arvay, Tacaks 1966; Voland, Engel 1989; Le Bourg et al 1993; Westendorp, Kirkwood 1998; Korpelainen 2000; Lycett et al 2000) contained only brief descriptions of the populations selected, the completeness of the data and the methods used. Assessing the methodological quality of these studies is thus difficult. Their results are included however, as they approach their hypotheses from an evolutionary standpoint and, as such, may provide a different and important perspective.

Table 2.2: Study design

Studies using CENSUS for exposure data

Study	Setting	Age (years) and Period	Year of Birth	Sample Size	Percentage of Population Excluded	Reproductive Exposure	Statistical Analyses	Control for Confounding
Kitagawa, Hauser 1973	United States	≥45 years at census in 1960	Not stated -1915	**36,183** deaths	Observed deaths weighted for the non-matched records.	Number of children ever borne	Standardised mortality ratios in parity groups	Restricted to ever-married white women. Standardised on age and education.
Fox, Goldblatt 1982	England, Wales (OPCS)	15-59 at census in 1971, follow-up 1971-1975	1912-1956	**958** deaths	Not stated	Number of children born in marriage, age at first birth, length of reproductive life	Standardised mortality ratios in parity groups	Restricted to ever-married women at entry. Standardised on age & social class.
Green, Beral, Moser 1988	England, Wales (OPCS)	16-59 at census in 1971, follow up 1971-1981	1912-1955	**3298** deaths	4% excluded due to missing parity; unknown % excluded due to missing data on social class	Number of live born children in marriage	Standardised mortality ratios in parity groups	Restricted to women currently married at entry. Standardised on age & social class or standardised on age & stratified by social class
Lund, Arnesen, Borgan 1990	Norway	≥ 25 years at census in 1970, follow-up 1970-1985	1886-1945	**822,593** women **112,023** deaths	245 (0.03%) women excluded due to missing data on parity or age of child	Number of live born children in present marriage, age at first birth	Mortality rates; Mantel-Haenszel relative risks of mortality by parity	Restricted to women currently married at entry. Adjusted for and stratified by age, husband's occupation and woman's education.
Moser, Pugh, Goldblatt 1990	England, Wales (OPCS)	15-59 at death, follow-up 1976-1981	Unclear, may be 1912-1961	**1085** deaths	Excluded women "*about whom there is no information*" - % unknown	Nulliparity[1a], Youngest child aged 0 to 16 years, youngest child aged 17+	Standardised mortality ratios in parity groups	Restricted to ever-married women. Standardised on age. Stratified by female and husband's occupation
Weatherall, Joshi, Macran 1994	England, Wales (OPCS)	15-59 at census in 1971, follow-up 1976-1985	1912-1956	**4667** deaths	Not stated	Nulliparity or age of youngest child	Logistic regression → relative risk of mortality by parity	Restricted to women currently married at entry. Adjusted for age, year, occupation, car ownership, social class.
Costa, Luzza, Mattace 2000	Italy	100-108	Unclear, 20th century	**88** centenarians	Not stated	Number of children [1b]	Descriptive analysis	Restricted to ever-married women
Doblhammer 2000	Austria	50-94 at census in 1981, follow-up 1981-1982	1887-1931	**1,245,153** women **35,234** deaths	Not stated	Number of children[1b], age at first and last birth	Logistic regression → relative risk of mortality by parity	Restricted to ever-married women. Adjusted for other reproductive variables, age, education, and marital status.
Doblhammer 2000 (same paper as above)	England, Wales (OPCS)	40-59 at census in 1971, follow-up 1971-1996	1912-1931	**56,164** women **16,941** deaths	Not stated	Number of children[1b], age at first and last birth	Force of mortality, using Gompertz function	Restricted to women currently married at entry. Adjusted for age and occupation.

1a: Those with "parity not stated" included in this group **1b:** No further definition of "number of children" given **1c:** Not clear whether this includes stillbirths or not

Table 2.2 (continued): Study design								
Studies using CENSUS for exposure data (continued)								
Study	**Setting**	**Age (years) and Period**	**Year of Birth**	**Sample Size**	**Percentage of Eligible Population Excluded**	**Reproductive Exposure**	**Statistical Analyses**	**Control for Confounding**
Manor, Eisenbach, Friedlander, Israeli 2000	Israel	45-89 at census in 1983, follow-up 1983-1992	1894-1938	**79,623** women **14,332** deaths	Excluded subjects with missing data – % not stated	Number of children[1b]	Logistic regression → relative risk of mortality by parity	Restricted to married and widowed. Stratified by age at entry. Adjusted for age, country of origin, education.
Studies using OTHER SOURCES OF ROUTINELY COLLECTED DATA for exposure data								
Powys 1905 'Published records', New South Wales	Australia	All ages, deaths in 1898-1902	Unclear, from 1800's to 1880's	**15,548** deaths	Not stated	Mean size of family	Comparison of mean family size by age at death	Restricted to married women.
Arvay, Takacs 1966 'Demographic Yearbook' Hungary	Hungary	≥50 in 1959-1960	Not stated -1910	**1,330,362** women	Not stated	Number of children[1b]	Life expectancy from current age compared by parity	Restricted to ever-married women. Stratified by age.
Beral 1985 Death certificates	England, Wales	45-74 at death in 1959-1960	1885-1915	**101,262** deaths	Excluded women for whom parity was not recorded - % unknown	Any children by current or former husband? (at death)	Standardised mortality ratios in parity groups	Restricted to ever-married women. Standardised on age.
Studies using DATA FROM ONGOING STUDIES for exposure data								
Kotler, Wingard 1989 "Alameda County Study"	United States	35-64 at entry, follow-up 1965-1982	1901-1930	**1457** women	14% excluded due to non-response; further 26% excluded due to inadequate data on occupation	Number of children[1b], presence of child aged 3-19 years in the home	Logistic regression → relative risk of mortality by parity	Stratified by female occupation. Adjusted for age, marital status, presence of children in home, physical health, smoking, alcohol, life satisfaction, and friends
Kvale, Heuch, Nilssen 1994 Study of breast cancer screening	Norway	32-74 at entry, follow-up 1961-1980	1887-1929	**61,774** women, **13,622** deaths	26% excluded due to non-response; 2% excluded due to missing data on parity	Number of full term deliveries[1c]	Stratified logistic regression → relative risk of mortality by parity	Adjusted for age, county, urban or rural residence, and husband's job
Friedlander 1996 "Rancho Bernado Heart and Chronic Diseases Study"	United States	43-92 at entry, follow-up 1972-1990	1880-1929	**1533** women	18% excluded due to non-response; 34% excluded due to missing data on parity	Number of biological children	Cox's proportional hazards → relative risk of mortality by parity	Stratified by birth cohort. Adjusted for age, body mass index, oestrogen use, employment.

1b: No further definition of "number of children" given **1c:** Not clear whether this includes stillbirths or not

Table 2.2 (continued): Study design								
Studies using DATA FROM NEXT-OF KIN for exposure data								
Study	**Setting**	**Age (years) and Period**	**Year of Birth**	**Sample Size**	**Percentage of Eligible Population Excluded**	**Reproductive Exposure**	**Statistical Analyses**	**Control for Confounding**
Perls, Alpert, Fretts 1997	United States	Cases ≥100 yrs; Controls 73 years	1896	**73** cases, **54** controls	Not stated	Having given birth at or beyond age 35 or 40	Logistic regression → relative risk of mortality by parity	Restricted to married women and single year birth cohort.
Cooper, Baird, Ephross, Sandler Weinberg, 2000 "Menstruation and Reproductive History Study"	United States	Follow-up from age 50 to death or 1991	Unclear, <25 in 1934-1939	**826** women, **106** deaths	37% excluded from original study; 5% of original sample not located for this study; 12% excluded due to incomplete data	Number of children[1b], age at last birth (at follow-up)	Discrete-time survival model based on logistic regression → relative risk of mortality by parity	Adjusted for age, age at menopause, smoking, and oestrogen replacement therapy.
Studies using HISTORICAL DEMOGRAPHIC RECORDS for exposure data								
Phillipe, Yelle 1976	Canada	≥47 yrs at death	1800-1880	**119** deaths	87% of original sample excluded due to incomplete data!	Number of live children born in first marriage	Mean age at death compared in parity groups	Restricted to married women.
Voland, Engel 1989 [1d]	Germany	≥47 yrs at death	1700-1750	**811** deaths	Excluded all women who had any missing data - % unknown	Number of pregnancies, all births, live births and children surviving to age 15	Life expectancy from age 47, by reproductive history	Restricted to married women.
Le Bourg, Thon, Legare, Charbonneau Desjardins, 1993	Canada	16-100 years	1603-1699	2 cohorts of **694 & 3495** deaths	34% of immigrants and 37% of Canadians excluded due to incomplete data	Number of children[1b]; age first and last birth; duration of childbearing period	Principal components analysis	Restricted to married women and those with at least one child.
Westendorp, Kirkwood 1998	Britain	All ages	40? (unclear) - 1876	Numbers presented differ	Not stated	Proportion childless, mean number of children[1b], mean age at first childbirth	Mean reproductive exposure compared by age at death	Restricted to married aristocracy. Adjusted for calendar time. Age at first birth adjusted for parity.
Korpelainen 2000	Europe	Unclear	1700-1899	**527** deaths	Not stated	Number of children[1b], number surviving to age 18, age at first and last birth, duration of reproduction	Mean reproductive exposure compared by age at death	Restricted to married only. Adjusted for socio-economic status.
Lycett, Dunbar, Voland 2000	Germany	≥50 at death	Unclear, between 1720-1870	**1073** deaths; less when data was missing	Those with missing socio-economic data excluded from some analyses	Number of children[1b], age at first and last birth	Mean reproductive exposure compared by age at death	Restricted to women in their first marriages. Some analyses stratified by age and social class.

1b: No further definition of "number of children" given **1d:** Methods described in an earlier German language paper, little description given in this book chapter.

2.4.3 Results[2.3]

All-cause mortality of nulliparous women compared with the parous

Figure 2.2 shows the results of studies that examined the relative risk of mortality in nulliparous women compared with the parous. All of the studies examining such relative risks are included, as none were considered too scientifically weak. However, it is important to remember that the studies often include women of different ages and from different time periods and have adjusted for different potential confounders, as documented in Table 2.2.

Six studies (a total of nine cohorts) showed that the nulliparous had higher mortality than the parous, and two found that they had lower mortality than the parous. Two of the studies finding higher mortality in the nulliparous found statistically significant differences (Green *et al* 1989, adjusted RR 1.16, $p<0.01$; Lund *et al* 1990, adjusted RR 1.66 95%CI 1.63-1.68), whilst one was not statistically significant (Cooper *et al* 2000, adjusted RR 1.22, 95%CI 0.79-1.89) and three performed no statistical comparisons (Fox, Goldblatt 1982, Kvale *et al* 1994, Moser *et al* 1994). Both studies finding that nulliparous women had lower mortality found statistically significant differences (Beral 1985: age-standardised mortality ratio 83, $p<0.05$; Friedlander 1996: adjusted HR 0.70 95%CI 0.55-0.89).

There was one further study that supported the finding that nulliparous women had higher mortality, one that refuted the finding and two that found no discernable pattern. Three of these studies had examined the proportion of women childless at each age at death (Figure 2.3, Westendorp, Kirkwood 1998; Costa *et al* 2000; Lycett *et al* 2000), the assumption being that when the proportion childless decreases with an increasing age at death, nulliparous women have higher mortality and vice versa. Costa *et al* (2000) found that only 4 of the 88 centenarians (4.5%) had never given birth, suggesting that the nulliparous had higher mortality. However, Westendorp and Kirkwood (1998) showed that almost a half of women (47%) who died after the age of 80 had never given birth, compared with lower percentages of women who had died at earlier ages. Lycett *et al* (2000) found no pattern in the percentage childless with age at

[2.3] Supplementary tables and figures can be found in Appendix 2.1

death, suggesting no difference in the mortality of nulliparous and parous women. No confidence intervals or statistical comparisons of the percentages were presented.

Therefore, ten of fifteen cohorts found higher mortality in the nulliparous than the parous. However, only two of these found statistically significant results, whereas two of the studies that found lower mortality also showed statistically significant differences.

All-cause mortality by the number of live births

Figures 2.4 (non-OPCS studies) and 2.5 (OPCS studies) show the results of studies that examined the risk of mortality, relative to the nulliparous, by the number of children borne. All of the studies examining such relative risks are included, except for the results of Friedlander (1996). They found a significant linear increase in mortality "per child born" (HR "per child born" 1.09, 95%CI 1.01-1.18), but did not show individual rates or rate ratios for the reader to assess whether these trends were truly linear.

A relatively consistent trend in mortality with parity emerged, with a reverse-j or u-shaped pattern in the risk of death in eleven of the fourteen cohorts. Mortality was high in the nulliparous, lower in women with one birth and generally lower still in women with two or three births. The pattern at higher parities was not so clear. In five cohorts there was a reverse j-shape pattern in mortality with parity, with mortality at higher parities similar to that of women with two or three live births (Lund *et al* 1990; Kvale *et al* 1994, <50 years; Manor *et al* 2000, 45-69 years and >70 years; Cooper *et al* 2000). In six cohorts there was a u-shaped pattern in mortality with parity, with mortality at higher parities rising markedly above that of women with three live births (Kitagawa, Hauser 1973, 45-64 years; Fox, Goldblatt 1982, <35 years and 35-49 years; Green *et al* 1988; Doblhammer 2000, Austrian and British cohorts). In the remaining three cohorts, there was no clear pattern in mortality with parity (Kitagawa, Hauser 1973, 65+ years; Fox, Goldblatt 1982, 50-59 years; Kvale *et al* 1994, >50 years). Not all studies performed statistical comparisons of the above relationships. Where comparisons were performed, they showed statistically significant differences in the mortality of nulliparous and parous women, but did not compare the mortality of women with two or three live births with the mortality of women of higher parities.

The studies using data from the OPCS study are shown on a separate figure as these results were obtained from the same population. There was a prominent u-shaped pattern in mortality with parity in women who were under 35 years of age on entry in Fox and Goldblatt's study (1982), a less pronounced u-shape in women between 35 and 49 years old at entry, and no trend in mortality in women who were between 50 and 59 at entry. Green *et al* 1988 found a less obvious u-shaped trend in mortality with parity in women who were aged between 15 and 59 at entry. There is also a suggestion of a u-shaped trend in mortality with parity in the final study (Doblhammer 2000), which included women between the ages 40 and 59 years. The results of these studies are generally consistent, although trends may become less apparent with the age of women at entry.

The remaining studies used different methods to examine the relationship between reproduction and parity. The papers did not always contain sufficient methodological detail for the quality of the study to be adequately assessed. Three of these studies found some evidence of increasing mortality with an increasing number of live children born, one found no pattern and one found that mortality reduced with an increasing number of live births. Korpelainen (2000) showed that women who had given birth to more children died at younger ages, suggesting that they had higher mortality (mean number of children in women who died aged 50-79 years 5.40 (SD 3.17), significantly different from the value of 4.34 (SD 3.18) in women who died over the age of 80 years). Powys (1905) and Westendorp and Kirkwood (1998) also found that women who had given birth to more children had higher mortality, but the differences were small and not significant. Lycett *et al* (2000) found no corresponding pattern in equivalent analyses (*see Figure 2.6 for a comparison of the results of the three aforementioned studies*). Arvay and Takacs (1966) described small increases in life expectancy from current age with an increased number of live births, suggesting a reduction in mortality with an increasing number of live births, but no significance tests of these associations were presented.

The majority of these studies therefore suggested that mortality is highest in nulliparous women and lowest in women with two or three live births. The patterns at higher parities are less clear.

All-cause mortality by other reproductive factors

All five studies looking at the effects of age at first birth found that women with an increasing age at first birth tended to have lower mortality (Fox, Goldblatt 1982; Lund *et al* 1990; Westendorp, Kirkwood 1998; Doblhammer 2000; Korpelainen 2000). For example, Westendorp and Kirkwood (1998) found that women who died over the age of 90 years had a mean age at first birth of 27.0 years (95% CI 24.8-29.2) whereas women who died between the ages of 61 and 70 years had a mean age at first birth of 23.8 (95% CI 23.0-24.6). Doblhammer (2000) found higher mortality in women who had first given birth before the age of 20 years compared with women who had their first birth after the age of 20 (OPCS cohort, adjusted RR 1.26, $p < 0.01$; Austrian cohort, adjusted RR 1.09, $p < 0.01$).

In addition, three studies found that births at later ages were associated with reduced mortality. For example, giving birth after age 40 was associated with reduce mortality (Doblhammer 2000: England and Wales, RR 0.95, $p < 0.10$; Austria, RR 0.95, $p < 0.05$) and was more likely in women who lived to be a hundred years old (Perls *et al* 1997, OR 4.00, 95% CI 1.02-18.70). Voland and Engel (1989) found a weak but significant positive correlation between age at last birth and age at death. However, Cooper *et al* (2000) found that, in women who had lived to be at least 50 years of age, those whose last birth was between the ages of 40 and 48 had twice the mortality risk of those whose final birth had been between 30 and 34 years (adjusted risk ratio 2.14, 95% CI 1.05-4.38).

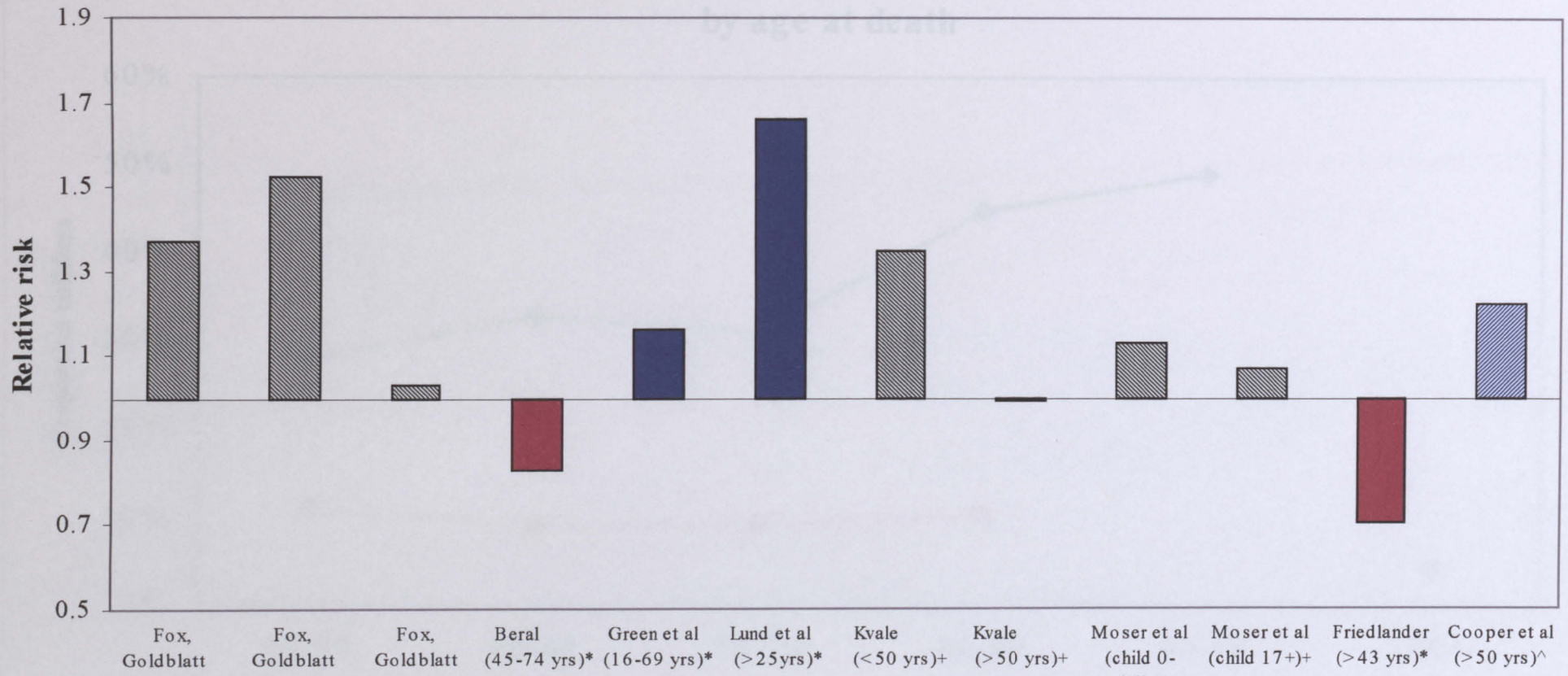
There was no clear pattern in mortality with length of reproductive life in Fox and Goldblatt's data (1982), but Korpelainen (2000) found that women with shorter mean reproductive life spans lived longer. Women who died between 50 and 79 years of age had a mean reproductive life span of 12.4 years (SD 7.1), which was significantly longer than the reproductive life span in women who died over the age of 80 years (mean 10.5 years, SD 6.7).

None of the studies reviewed examined the effects of other reproductive variables, such as birth spacing or breastfeeding, on all-cause mortality. Short birth spaces have been hypothesised to increase the risk of maternal mortality, although the evidence to date

is inconsistent. In a nested case-control study in Bangladesh, the length of the preceding birth-to-conception interval was not found to affect the risk of maternal mortality (Ronsmans, Campbell 1998), whereas a cross-sectional study in Uruguay showed that women with a birth-to-conception interval of less than 6 months had significantly higher maternal mortality than those conceiving 18 to 23 months after the preceding birth (Conde-Agudelo, Belizan 2000). No studies were found that examined the association of previous birth spacing with all-cause mortality, and the overall effects of birth spacing on survival remain unknown.

It has also been suggested that breastfeeding may influence female mortality. Breastfeeding mothers are protected from haemorrhage in the immediate postpartum period, due to the oxytocin released with each feed (Dermer 1998). They are also at a lower risk of iron deficiency, due to an increased absorption of iron from the gut during breastfeeding and lactational amenorrhoea (Labbok 1999). Furthermore, measurable bone loss occurs during lactation. However, this bone density is regained during and after weaning, to the extent that breastfeeding may protect against osteoporosis in the long term (Kennedy 1994, Dermer 1998). In addition, full breastfeeding is associated with maternal weight loss, and has been implicated in the development of "maternal depletion" (Gigante et al 2001). However, women who partially breastfeed (during weaning for example) have been shown to maintain their weight, even when they are malnourished (Kennedy 1994). A small but significant reduction in breast cancer risk, which was more pronounced in pre-menopausal women, was shown in a meta-analysis of published case-control studies (Bernier et al 2000), an effect confirmed in two recent studies (Zheng et al 2001; Tryggvadottir et al 2001). It has also been suggested, in a randomised controlled trial in Kenya, that HIV-infected women who breastfeed have higher mortality than HIV-infected women who feed their babies with formula (Nduati et al 2001). This controversial finding was not supported in a randomised controlled trial of the effects of vitamin A in South Africa (Coutsoudis et al 2001), and further investigation of this association is required (Newell 2001). No studies were found that related previous breastfeeding history with all-cause mortality in the long-term. Therefore, although breastfeeding seems to impact on the development or progression of specific diseases, an assessment of its overall effect on survival cannot be made on the basis of current evidence.

Figure 2.2: Relative risk of mortality in the nulliparous compared with all parous women (and the ages of women included)



*	Relative difference between mortality of nulliparous and parous statistically significant
^	Relative difference not statistically significant
+	Relative risk not presented, but could be calculated from numbers given in the papers – no statistical comparisons therefore performed
OPCS studies	Fox and Goldblatt 1982, Green *et al* 1988, Moser *et al* 1990

Figure 2.3: Proportion of women who remained "childless" by age at death

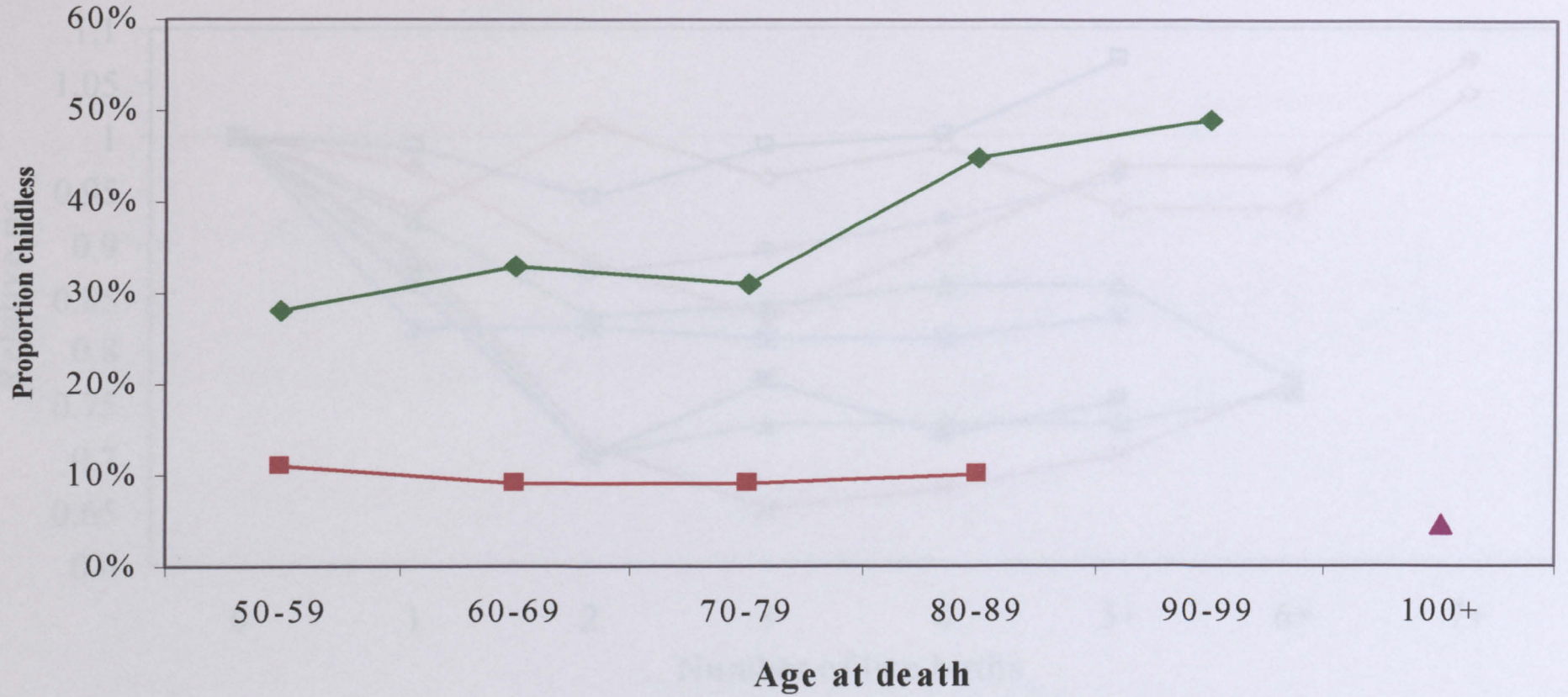


Figure 2.4: Risk of mortality, relative to the nulliparous, by the number of live births (non-OPCS studies)

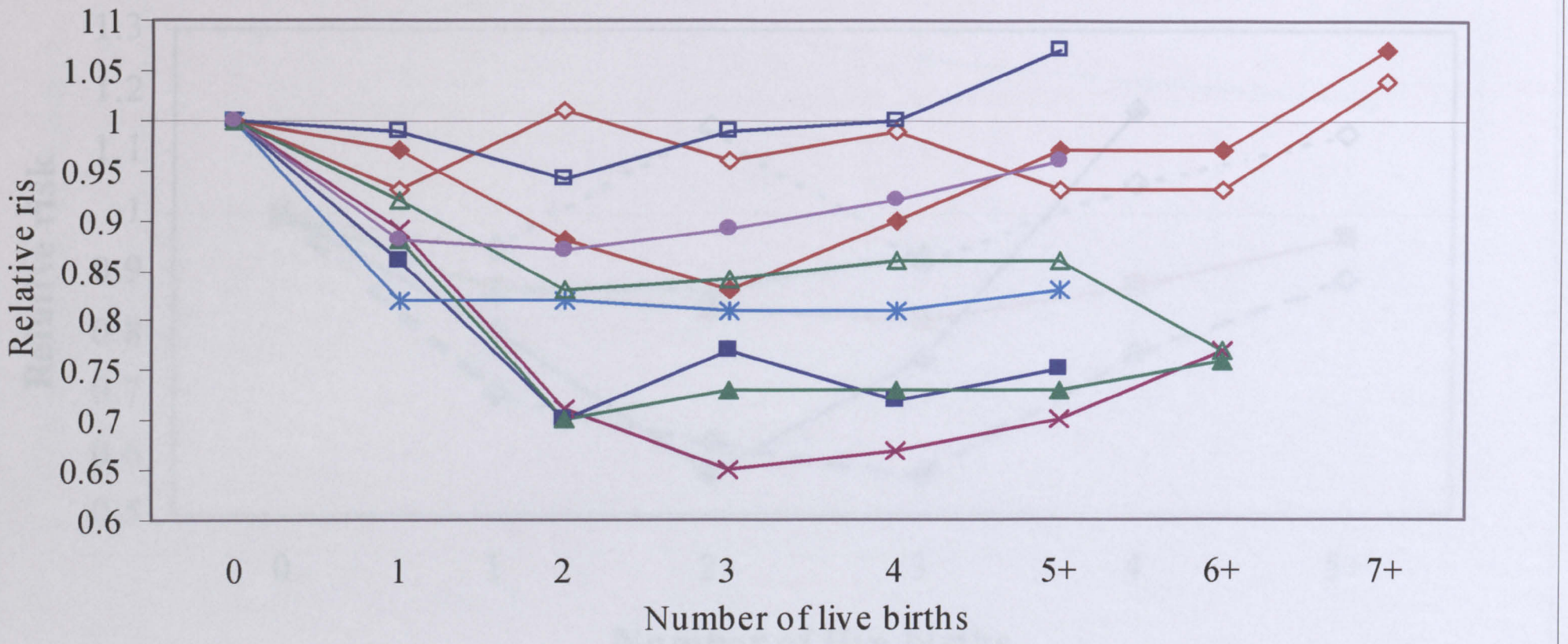


Figure 2.5: Risk of mortality by number of live births, relative to the nulliparous (OPCS studies)

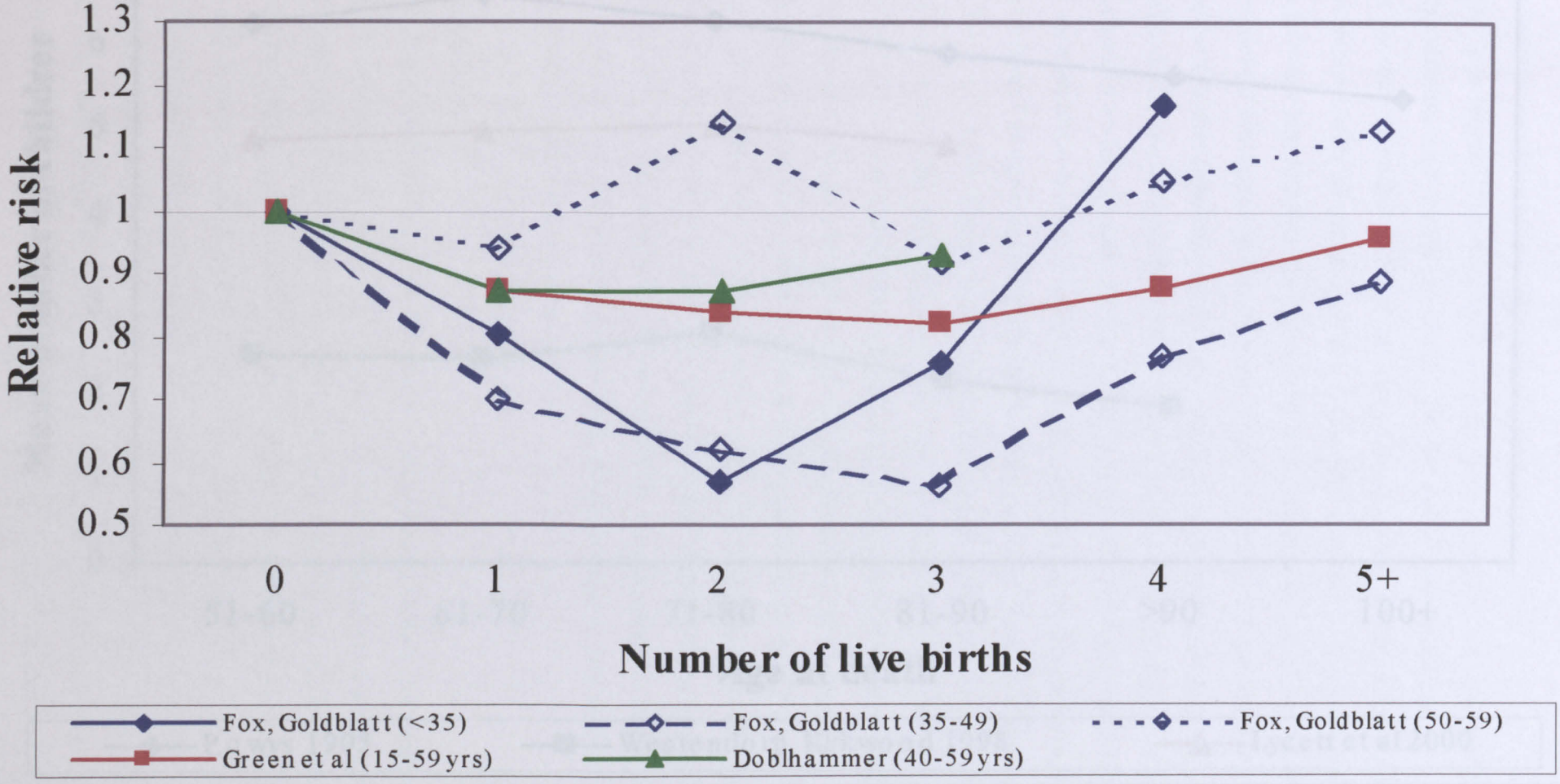
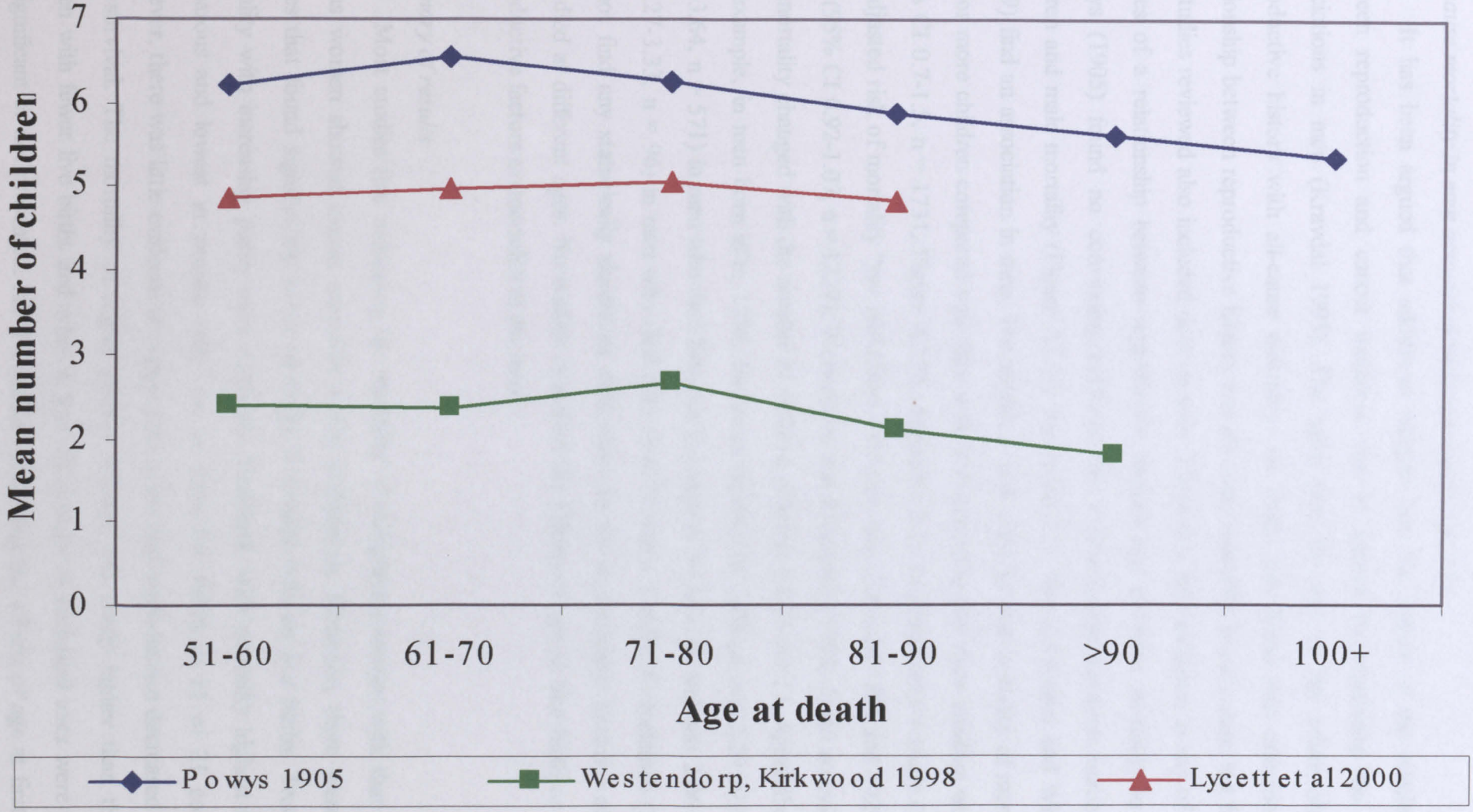


Figure 2.6: Mean number of children by age at death



All-cause mortality in men associated with reproductive factors

It has been argued that additional insights into the nature of the relationship between reproduction and cancer incidence can be gained by examining the same associations in men (Kravdal 1995). The same may be true of the relationship of reproductive history with all-cause mortality. No study was found that examined the relationship between reproductive history and all-cause mortality in men alone but five of the studies reviewed also included data on men. There was little evidence in any of these studies of a relationship between reproductive factors and all-cause mortality in men. Powys (1905) found no convincing evidence for a relationship between number of children and male mortality (Figure A2.10, Appendix 2.1). Nor did Kotler and Wingard (1989) find an association in men. The adjusted odds ratio for the mortality of men with four or more children compared with men with between none and three children was 1.0 (95% CI 0.7-1.5, n = 1731, Figure A2.11, Appendix 2.1). In Friedlander's study (1996) the adjusted risk of mortality "*per child born*" for men born between 1880 and 1929 was 1.00 (95% CI 0.92-1.07, n = 1229). Westendorp and Kirkwood (1998) found no evidence that mortality changed with the number of children (Figures A2.16-A2.17, Appendix 2.1). For example, in men born after 1700, the mean number of children was 2.29 (95% CI 1.44-3.64, n = 571) in men who died between the ages of 81 and 90, and was 2.06 (95% CI 1.27-3.33, n = 96) in men who died later than 90 years. Finally, Korpelainen (2000) did not find any statistically significant differences in the reproductive histories of men who died at different ages. No studies examined the effects of age at first birth or other reproductive factors on mortality in the men.

Summary of results

Most studies that compared the mortality of nulliparous women with that of all parous women showed excess mortality in the nulliparous. However, there were two studies that found significantly lower mortality in women with no live births. Trends in mortality with increasing parity were relatively consistent, with mortality highest in the nulliparous and lowest in women with two or three live births in 11 of 21 cohorts. However, there was little evidence to support the claim that reproduction decreased long-term survival. The mortality of highly parous women was rarely higher than that of women with fewer live births and when it was, the results of statistical tests were either not significant or not presented. All five studies examining the effects of age at first birth

showed that mortality reduced with an increasing age at first birth. Mortality also reduced with older births in three studies, although one additional study found significantly higher mortality in women who had experienced a pregnancy between 40 and 48 years of age. There was no consistent relationship between length of reproductive life and mortality. Nor was there evidence of a relationship between the number of children and all-cause mortality in men.

2.4.4 Introduction to interpretation

The studies reviewed therefore showed some relationships between reproductive factors and mortality, although these were not necessarily consistent or straightforward. Some of the inconsistencies in the results may have arisen because different populations of women were studied. Alternative explanations may also be found in the study methods, and include the roles played by chance, information bias, selection bias and confounding.

2.4.5 Differences in the study populations

Women's age

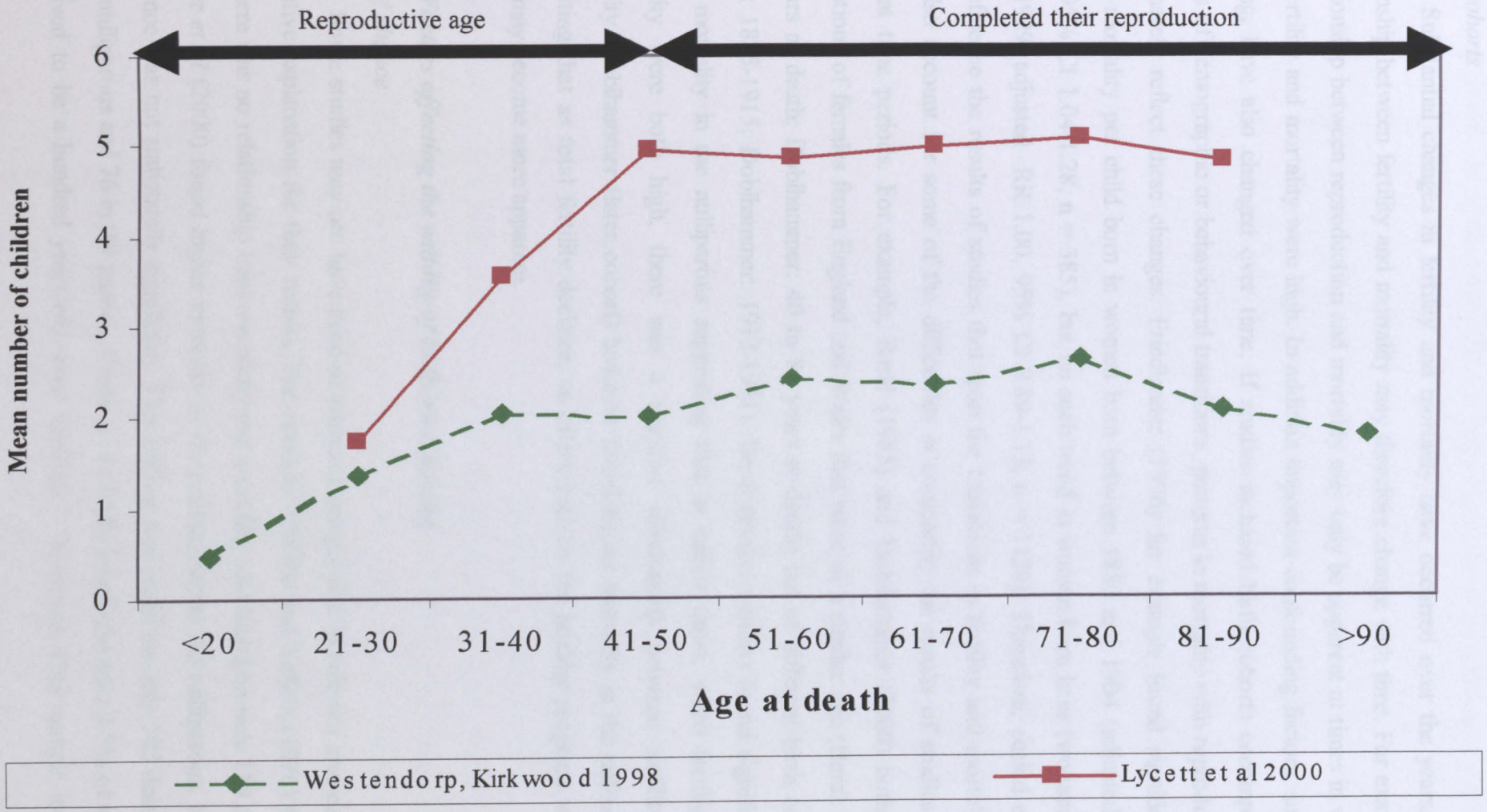
Studies that included women of all ages assumed that all of these women experienced the same exposure to childbearing, regardless of age. This is clearly not the case. For example, women who experienced pregnancies during follow-up may have been at risk of maternal mortality, whereas women who had already completed their reproduction were not. We may therefore expect to see parity-specific trends in mortality in studies including women of reproductive age, as the risk of maternal mortality changes with previous reproductive history (AbouZahr, Royston 1991). In fact the results are similar to these well-documented patterns, particularly in younger cohorts (Fox and Goldblatt for example). However, it is extremely unlikely that the patterns seen were due to pregnancy related deaths, as five of the cohorts showing a reverse-j or u-shaped pattern in mortality with parity included only women who had completed their reproduction (Kitagawa, Hauser 1973, 45-64 years; Cooper *et al* 2000; Doblhammer 2000; Manor *et al* 2000, 45-69 years and 70+ years). In addition, the studies showing these trends were all conducted in affluent societies and all included follow-up periods from the 1960's onwards. Maternal mortality would therefore not be an important cause of death in these cohorts. For example in England and Wales in 1961, maternal deaths accounted for only

2% of all deaths in females who died between the ages of 15 and 50 (Registrar General's Statistical Reviews 1963).

More important may be the fact that women who die young may not have had the opportunity to have many children, so that women with none or one live birth may appear to have higher mortality. This phenomenon is well illustrated in two of the historical studies (Figure 2.7, Westendorp, Kirkwood 1998; Lycett *et al* 2000). The mean number of children borne increases with age at death until the age of 50, after which there is no discernable trend. It is clearly less likely that a woman who dies at the age of 20 has had a large family than a woman who dies at age 50 but the trends could erroneously be interpreted as showing that women with fewer children have higher mortality.

In addition, women who are ill (or are in some way inherently weaker) may have fewer live births than healthy (or stronger) women. Women who experience fewer live births may therefore appear to have higher mortality than women with many live births. This "healthy pregnant woman" effect has been demonstrated in Bangladesh (Khlat, Ronsmans 1999) where, once direct obstetric deaths and injuries were excluded, pregnant women experienced substantially lower death rates than non-pregnant women. This effect could occur in all studies but may be exaggerated in studies that included women of reproductive age, as an illness that lowers fertility may have a greater effect on the mortality of women who are still in the reproductive years.

Figure 2.7: Mean number of children by age at death



Birth cohorts

Substantial changes in fertility and mortality have occurred over the years. The relationship between fertility and mortality may therefore change with time. For example, a relationship between reproduction and mortality may only be apparent at times in which both fertility and mortality were high. In addition important confounding factors, such as smoking, have also changed over time. If studies included birth cohorts encompassed periods of demographic or behavioural transitions, patterns in mortality with reproduction may merely reflect these changes. Friedlander (1996) for example found significantly higher mortality per child born in women born between 1880 and 1904 (adjusted RR 1.15, 95% CI 1.04-1.28, n = 385), but no such trend in women born later (women born 1905-1929, adjusted RR 1.00, 95% CI 0.89-1.13, n = 1138). Therefore, period effects may influence the results of studies that span the transitions in fertility and mortality. It may also account for some of the difficulties in comparing the results of studies from different time periods. For example, Beral (1985) and Doblhammer (2000) both used populations of females from England and Wales that were of a similar age (Beral: 45 to 74 years at death; Doblhammer: 40 to 84 years at death) but of different birth cohorts (Beral: 1885-1915; Doblhammer: 1912-1931). Beral (earlier cohort) found significantly lower mortality in the nulliparous suggesting that in earlier times, when fertility and mortality were both high, there was a negative relationship between fertility and mortality. Doblhammer (later cohort) however found higher mortality in the nulliparous, suggesting that as total fertility declines, an effect such as the healthy pregnant woman effect may become more apparent.

2.4.6 Factors affecting the validity of individual studies

Role of chance

Some studies may not have been of adequate sample size to rule out chance as an alternative explanation for their results. For example, Phillipe and Yelle's (1976) finding that there was no relationship between parity and mortality was based on only 119 deaths. Cooper *et al* (2000) found higher mortality in the parous than in the nulliparous, but the difference was not statistically significant. This finding was based on only 106 deaths, 30 in the nulliparous and 76 in the parous. Costa *et al* (2000) found that only 4.5% of women who lived to be a hundred years old were "childless". However, their sample included

only 88 centenarians. In addition they did not include a comparison group and performed no statistical hypothesis testing.

Misclassification of exposure

Reproductive histories are difficult to determine precisely. Women tend to recall the number of live births relatively accurately (Harlow, Linet 1989) but underreporting increases with time since pregnancy, particularly when children have died or left home (Chidambaram *et al* 1992). It is therefore possible that the reporting of parity was erroneous. In addition, women may not have given a complete or accurate account of their reproductive histories due to the way in which questions were phrased. For example, the Norwegian census asked for information on the number of live children born in a present marriage (Lund *et al* 1990) whereas the UK census (used in the OPCS studies) asked for information on all live births in any marriage. Furthermore parity may have been misclassified if women of reproductive age experienced additional pregnancies during follow-up, as no attempt was made in the studies using census data for instance to update reproductive histories. It is unlikely that any of these sources of misclassification were related to female mortality. Such random misclassification may therefore have resulted in an underestimation of the associations under investigation.

Moreover, the woman herself was not always the source of the exposure data. Beral (1985) used data from death certificates to calculate observed deaths in parous and nulliparous women and census data to estimate expected deaths. Therefore, when calculating SMRs, the denominator data may have been more accurate than the numerator data. The effect of this error on the results would depend on whether parity or nulliparity was most accurately recorded on death certificates. Both Perls *et al* (1997) and Cooper *et al* (2000) collected exposure information from the next of kin if the subjects of interest had died. Data for women who were still alive may thus be more accurate than data for women who were dead. The effect of this misclassification depends on how the next of kin reported the deceased's reproductive exposure. Males, for example, have been found to underestimate past reproductive events when compared with their partners (Fikree *et al* 1993). Mortality in low parity groups could thus have been overestimated in Cooper *et al*'s data for example.

Misclassification of exposure may be exaggerated in historical records. Prior to the compulsory registration of births and deaths, parish records in the United Kingdom documented baptisms and not births[2.4] (Macfarlane, Mugford 1984). It is difficult to assess the effects of this misclassification on the historical studies, as the data sources are poorly described.

Selection bias

Loss to follow-up is not discussed in the majority of the papers. In studies that included birth cohorts from the twentieth century, it may be fair to assume that mortality registration was relatively complete, and that loss to follow-up was thus not an important source of bias. However, this may not be the case in the cohorts that were based on historical demographic records. These study populations were defined on the basis of mortality records, which may have been incomplete. Just as parish records of birth were based on baptisms, parish mortality records were based on burials not deaths. Individuals whose burials were recorded may thus be different from those whose burials were not noted and it is possible that subjects who were included were systematically different from those who were excluded. The effects on the results are difficult to assess, as it is not possible to estimate the fertility and mortality of those who may have been left out.

Women with missing exposure data were also usually excluded. This may also introduce a selection bias, as those who were included may be systematically different from those who are excluded. For example, Green *et al* (1988) showed that women with missing reproductive histories had significantly higher mortality than those in the comparison population (SMR 129, 95%CI 111-149). If these women were all parous for instance, mortality in parous women would have been underestimated in this study. Nevertheless, it is again impossible to discern the effect of these exclusions on the results, as it is not possible to guess the reproductive histories of the women with missing data.

Selection of the comparison group

In many of the studies reviewed, nulliparous women were used as the "unexposed" comparison group. They should therefore have been similar to the parous in

[2.4] The UK bill for compulsory registration of births, marriages and deaths was passed in 1837

all but reproductive history, such that any associations found could be attributed to differences in reproduction.

This may not be the case, however, as the nulliparous are not a homogenous group. Some are involuntarily childless whereas others may have voluntarily controlled their fertility (Kiernan 1989). In fact, it is possible that the factors influencing mortality risk in nulliparous women have little to do with the fact that they have not been exposed to pregnancy, but are instead related to the reason why they are nulliparous. Examples may include women who were infertile due to an illness such as tuberculosis or an iatrogenic cause such as radiation or chemotherapy. Roman *et al* (1985) on the other hand noted that "*parity is a determinant of patterns of disease in working women, and the relative excess of cancers of breast, ovary and uterine body in professional and clerical workers probably reflected the high proportion of nulliparous women in these groups*".

Attempts have been made to examine a homogenous group of childless women in a study of nuns' mortality (Butler, Snowdon 1996). The mortality of the Catholic sisters was significantly lower than the mortality of women in the general population (SMR 73, 95% CI 69-77 for nuns 50-84 years in 1965-1989, comparison population white American females). The nuns were, however, too different from women in the general population to draw conclusions about nulliparous women as a whole from this data. In addition, mortality from cancers of the breast and reproductive organs (except cervical cancer) were higher, possibly related to their nulliparity.

Therefore, although it is important to study the risk of mortality in the nulliparous, the comparison between parous and nulliparous women may not always be informative. The studies finding both significantly higher and significantly lower mortality in the nulliparous may have found true effects, and their results may say more about the characteristics of the nulliparous in their samples than the fact that they had not been exposed to pregnancy.

Few studies statistically compared the mortality of women of medium parity (for example, two or three live births) with that of women of high parity (for example, four or more live births). Although these women may also differ on characteristics other than

reproduction, the comparison may reveal more about the different mortality risks associated with reproductive history. The results of the study that found higher mortality "per child born" (Friedlander 1996) must also be viewed with caution as crude mortality rates are not presented and it is unclear whether the trends seen were truly linear. There was no relationship between the number of children and all-cause mortality in men. We would expect most of the biological exposures associated with reproduction to be confined to females (except for exposures such as the increased infection burden in large families) but these results suggest that there are few negative social consequences of having a family either, certainly for males.

Confounders

The association between reproductive history and mortality may be confounded by many factors including age, marital status and social class. All studies controlled for age and most restricted their sample to include only women who were currently or had ever been married. Adjustment for other factors was variable and it is not clear that one confounder could explain the differences in the results (final column, Table 2.2). However it is possible, for example, that the results of Beral (1985) were confounded by socio-economic status. If there were more women of low socio-economic status (who may be of high fertility and high mortality) in this sample, then the protective effects of nulliparity seen may have been overestimated.

It is also necessary to note that the results of most of the studies reviewed can only be generalised to ever-married women as their samples were restricted. This is important, as the unmarried are likely to have different fertility and mortality patterns to the married.

Effect modification

Three studies showed that the effect of nulliparity reduced with age (Fox, Goldblatt 1982; Lund *et al* 1990; Kvale *et al* 1994), whilst in another the effect reduced with time since last pregnancy (Moser *et al* 1994). In addition three studies found no discernable trend in with parity in women who were older than 50 years of age in populations where there had been a reverse-j or u shaped pattern in mortality in younger cohorts (Kitagawa, Hauser 1973; Fox, Goldblatt 1982; Kvale *et al* 1994; see Figure 2.8). These findings are important because they suggest that, even if reproduction does affect

mortality, the effects may diminish with age or with time since reproduction. This cannot be concluded with certainty, as this interaction was not examined in all studies.

In addition, Green *et al* (1988) showed that the pattern in mortality with number of live births modified with social class. When their results were stratified by socio-economic status, the u-shaped association of mortality with number of live births persisted in women with a husband in a manual occupation, but was no longer apparent in women of higher socio-economic status (Figure 2.9). Kotler and Wingard (1989) also found that there might be an interaction with socio-economic status. They showed no effect of number of children in working women, but lower mortality in housewives with none to three children compared with housewives with four or more offspring (RR 0.53, 95%CI 0.30-0.91). These findings are noteworthy as they may suggest that the effects of reproduction are exacerbated in situations where women are under other forms of stress. Once again, this conclusion is limited by the fact that other studies did not examine these differences.

Figure 2.8: Risk of mortality, relative to the nulliparous, stratified by age (older women in darker colours)

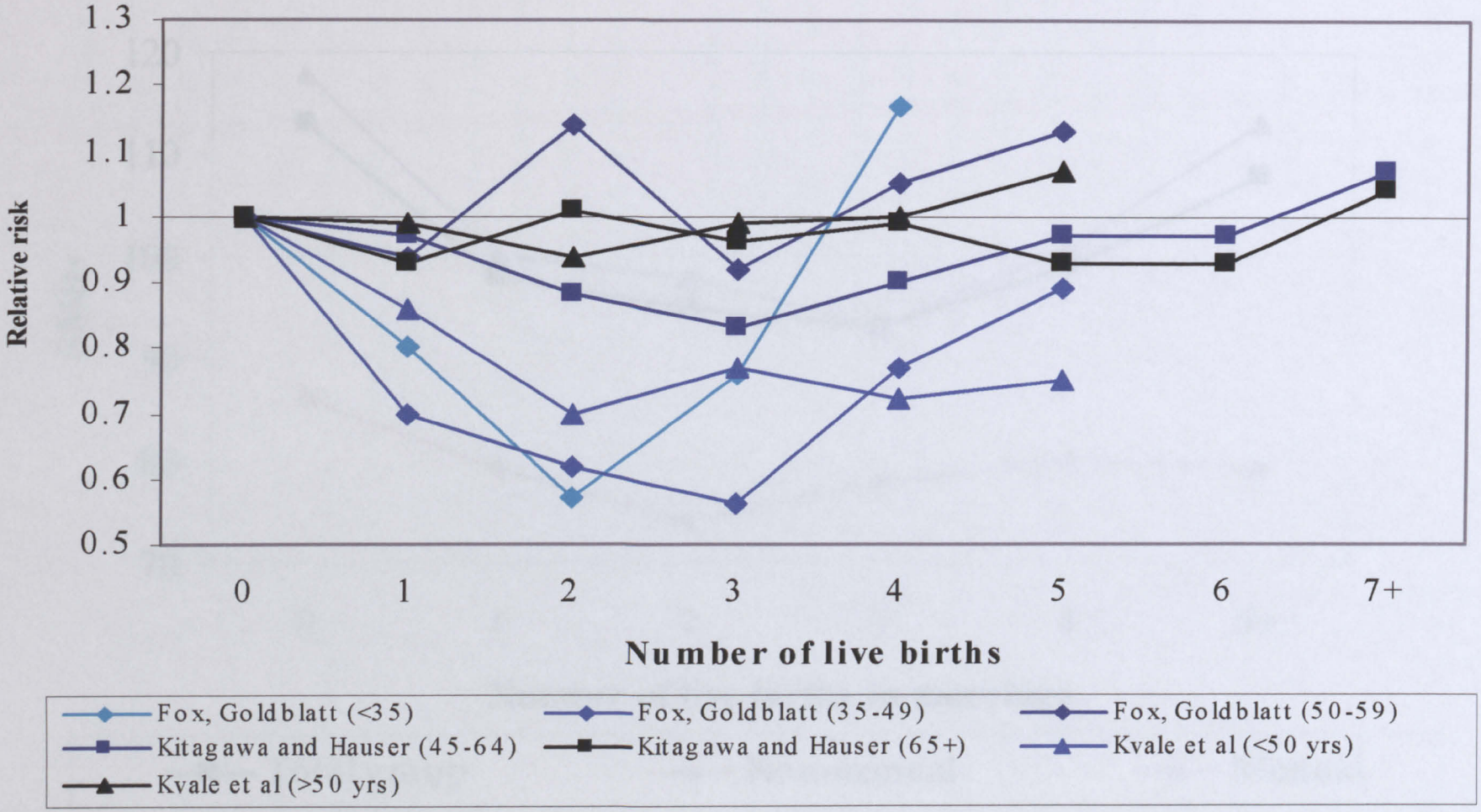
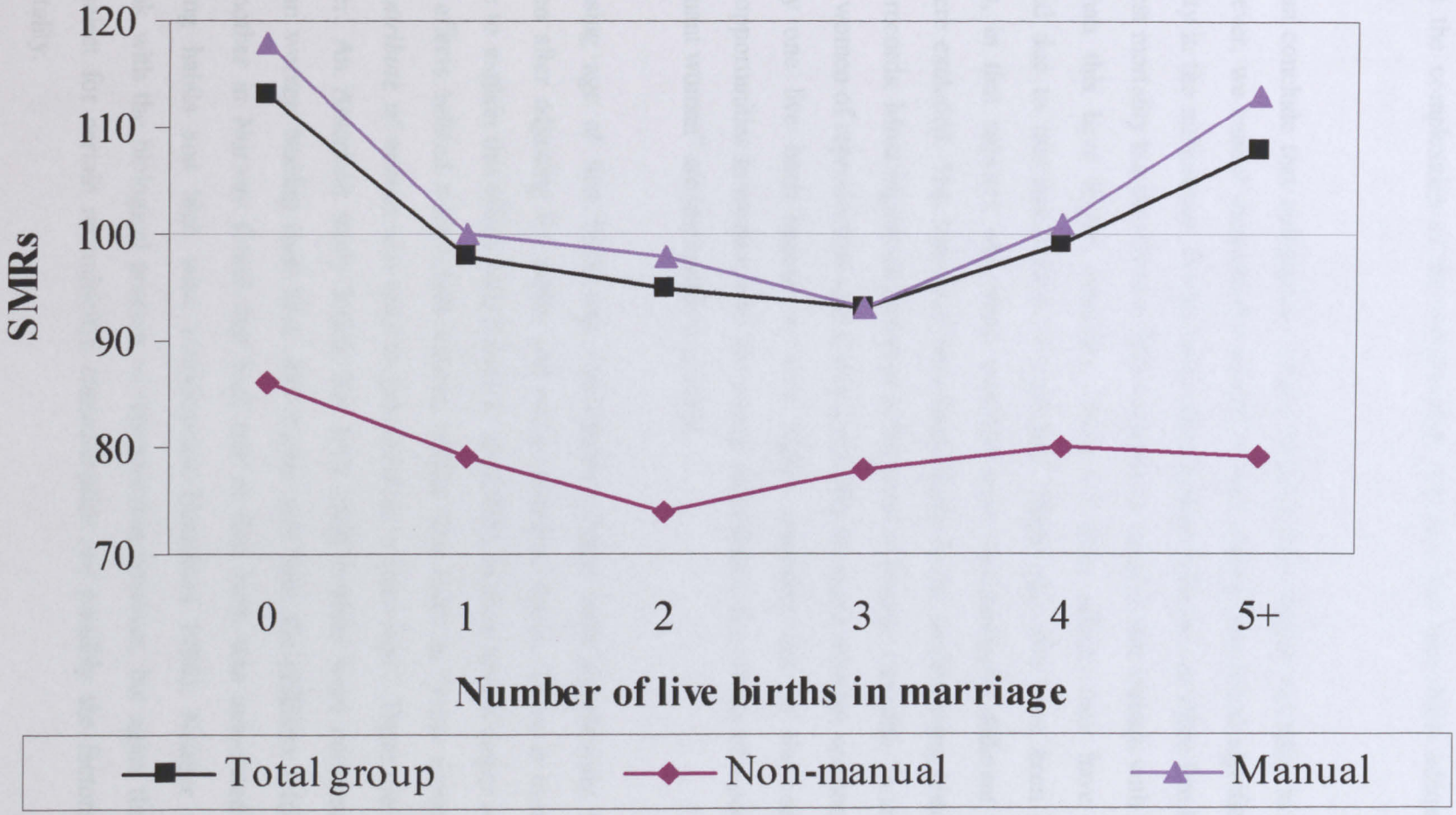


Figure 2.9: Standardised mortality ratios by live births in marriage in the different social classes (Green et al 1988)



2.5 The need for further study

An association between reproduction and mortality in the long term is therefore plausible, but the complexities of the relationships may not yet have been adequately described.

We can conclude that nulliparous women seem to have higher mortality in most studies. However, we cannot discount the results of two studies that found significantly lower mortality in the nulliparous. It also seems that women with two or three live births have the lowest mortality but that there is little evidence to suggest that women with more live births than this have higher mortality. Some of these effects may have been underestimated due to misclassification of exposure. There may also have been some selection bias, in that subjects who were included were systematically different from those who were excluded. This may have been most likely in the studies using historical demographic records. Most important however is the issue of reverse causality. In studies that included women of reproductive age, it is not possible to assess whether women with none or only one live birth appear to have higher mortality due to the reduced reproductive opportunities in women who die young. In addition, the effects of a possible "healthy pregnant woman" are impossible to discern.

Increasing age at first birth was consistently related with significantly lower mortality, even after adjusting for parity and socio-economic status. There is currently little evidence to explain this effect with Kelsey *et al* (1993), in their review paper on the reproductive effects related with breast cancer, noting that there is "*some heretofore unidentified attribute of women who tend to give birth at a later age*". There are some clues however. An American study found that later child bearers were economically better off than women bearing their first child earlier and than the childless (Hofferth 1984) and another in Norway found that high age at first birth was associated with healthier eating habits and high wine consumption (Jacobsen 1996). Neither result suggests a link with the biological process of reproduction however, but again that the factors that select for certain reproductive characteristics are possibly the factors that influence mortality.

Perls et al (1997) claim to have found evidence in support of the disposable soma theory in that "*the ability to have children in the fifth decade may be a marker for slower ageing and subsequent ability to achieve extreme longevity*". This may be the case but, in truth, we still understand very little about the way in which these other reproductive effects are mediated and it is possible that the picture of the effects of childbearing is incomplete. Many of the reproductive factors seen in Figure 1.2, such as gravidity and birth spacing, have received no research attention and it is impossible to tell how reproductive factors, such as parity and birth spacing, may interact to influence mortality risk.

In addition, the studies reviewed were all conducted in relatively affluent societies. The associations between parity and mortality seen may not be indicative of the relationships that exist in other populations, specifically in developing countries. Reproductive patterns may differ, with less affluent women tending to have more children, for example (dos Santos Silva, Beral 1997). There were very few 'grand multiparous' women in the studies reviewed. The evolutionary pressure for a reduction in survival with repeated reproduction may not therefore be obvious at these low levels of fertility. It has also been estimated that most women in the developing world who have not given birth are involuntarily childless (Poston, Kramer 1983). The nulligravid or nulliparous women may therefore be a more homogenous group in such populations.

The next chapter describes a cohort study, conducted to examine the relationship between reproduction and all-cause mortality after age 45 in adults who have completed their reproduction in Bangladesh. The aim of this study is to examine the associations described in a malnourished, natural fertility population where the nulliparous are believed to be a relatively homogenous group. In addition, the data available will allow for adjustment by more potential confounders than in previous studies and will provide accurate reproductive data for both females and their husbands.

3.1 Hypotheses

In adults who have completed their reproduction in Matlab, it is hypothesised that:

1. Nulligravid, nulliparous women or women with few live births have higher mortality

In this population "*offspring are critical to familial economic and social security, since wealth traditionally flows from children to parents and the labor value of children is manifest at an early age. Moreover, children represent insurance against risk in the face of social and environmental uncertainty that characterises rural Bangladesh*" (Phillips *et al* 1988). This is a society in which almost all women marry and, once they are married, try to have children. It is therefore hypothesised that women who do not succeed in having children are the women who are ill, and who may also have increased mortality. Women with none or few children may also have higher mortality for similar reasons.

2. Women of high gravidity and high parity have higher mortality

The women of Matlab are "*chronically malnourished and do not gain more than 5kg on average during pregnancy*" (Fauveau 1994). In addition their diets are restricted during pregnancy and lactation, when they avoid meat, eggs, fish and occasionally milk (Yunus *et al* 1994). They also breastfeed for an average of 29 months (Jain, Bongaarts 1981). Therefore, if reproduction has detrimental evolutionary or depleting effects, it is possible that they would be more apparent in this undernourished population. It is therefore hypothesised that multigravid or multiparous women have higher mortality.

3. Women who have given birth to more boys than girls have lower mortality

Male children are also highly valued in many developing societies (Miller 1990). Phillips *et al* (1988) also observed in Bangladesh that "*sons are a resource, not only for their direct contribution to household income, but also for their importance in establishing and maintaining vital family ties to village patronage groups. They are thus a source of prestige to mothers, and a source of security to parents*". Women who give birth to many sons may therefore have lower mortality, particularly if most of these sons survive.

4. Women who suffered many fetal losses have higher mortality

Experiencing a fetal loss is associated with a higher risk of losing future pregnancies (Leridon 1976, Roman 1983). However, little is known about the effects of a fetal loss on the mortality of the mother (except, of course, for the tragic effects of unsafe abortions). It is hypothesised that women in Matlab who experience many fetal losses will have higher mortality. They may have an illness that affects both their ability to maintain a viable pregnancy to term and their survival. They may also suffer negative psychological and social consequences of losing numerous pregnancies and hence have increased mortality.

5. The effect of reproductive variables on mortality may be confounded by age, marital status and socio-economic status and may modify with age and socio-economic status

Age, marital status and socio-economic status may all be independently related to fertility and mortality, and hence are potential confounders for the relationship between reproduction and all-cause mortality. In the studies reviewed, the relationship between reproduction and mortality was seen to modify with age and socio-economic status. Similar trends may be seen in Bangladesh.

6. A separate analysis for women and their husbands may help to determine the aetiology of any associations seen

An association between reproduction and mortality in the women of Matlab, Bangladesh may be mediated through both biological and social pathways. Comparing the relationships in women and men may allow for the different mechanisms involved to be identified (Kravdal 1995). Similar results in the men and their wives may suggest a social origin for the effects, whereas an increase in mortality with childbearing in the women but not in the men may point to a biological origin for the relationship. A reduction in the risk of mortality in the women but no effect or an increased risk in the men may indicate a more complicated relationship, such as the "healthy pregnant woman" effect.

3.2 Study setting

3.2.1 Bangladesh

Bangladesh was partitioned from India along with Pakistan in 1947, as an independent Muslim home state. It gained independence in its own right in 1971, following a chaotic and violent period that left it one of the world's poorest and least developed nations. It is small and densely populated, with over 120 million people living within its 58000 square miles[3.1]. In 1996, only 37% of adults were literate and a similar percentage (36%) was living below the poverty line (www.virtualbangladesh.com). A significant demographic transition has occurred in recent times, with a rapid decline in both fertility and mortality. The current total fertility rate is 2.27 births per woman and average life expectancy from birth is 59 years for men and 58 years for women (Bangladesh Demographic and Health Survey [BHDS] 1997).

3.2.2 Matlab

This study was conducted in Matlab, a rural area 35 miles southeast of the capital Dhaka. It is typical of the delta areas of rural Bangladesh, and is subject to annual flooding between June and September during the monsoon season. Travel around the area is on foot, by rickshaw or in a country boat (Aziz 1994). Travel to the capital and other urban centres is by motorised boat, although road access has improved of late. Almost 70% of the population of Matlab were under the age of 30 in 1990 (ICDDR,B 1994). The populace is predominantly Muslim (around 88%), with the remainder being Hindus. Marriage is almost universal. 99% of females older than 30 years and 98% of men older than 35 years had ever been married in a recent census (Razzaque *et al* 1998). In 1996 around 40% of individuals were illiterate. Notably, over 80% of women over the age of 50 had received no formal education at all (Razzaque *et al* 1998). The major sources of local income are fishing and agricultural labour. Only a small proportion of workers own the land or the boats on which they work (Aziz 1994). The total fertility rate in the area has declined, from 6.6 in 1976 to 2.7 in 1996 (van Ginneken *et al* 1998). The crude death rate has also fallen, from 12.2 deaths per 1000 population in 1978 to 8.5 deaths per 1000 population in 1990 (ICDDR,B 1994).

[3.1] In comparison, 59.5 million people live within 95000 square miles in the United Kingdom (including Northern Ireland)

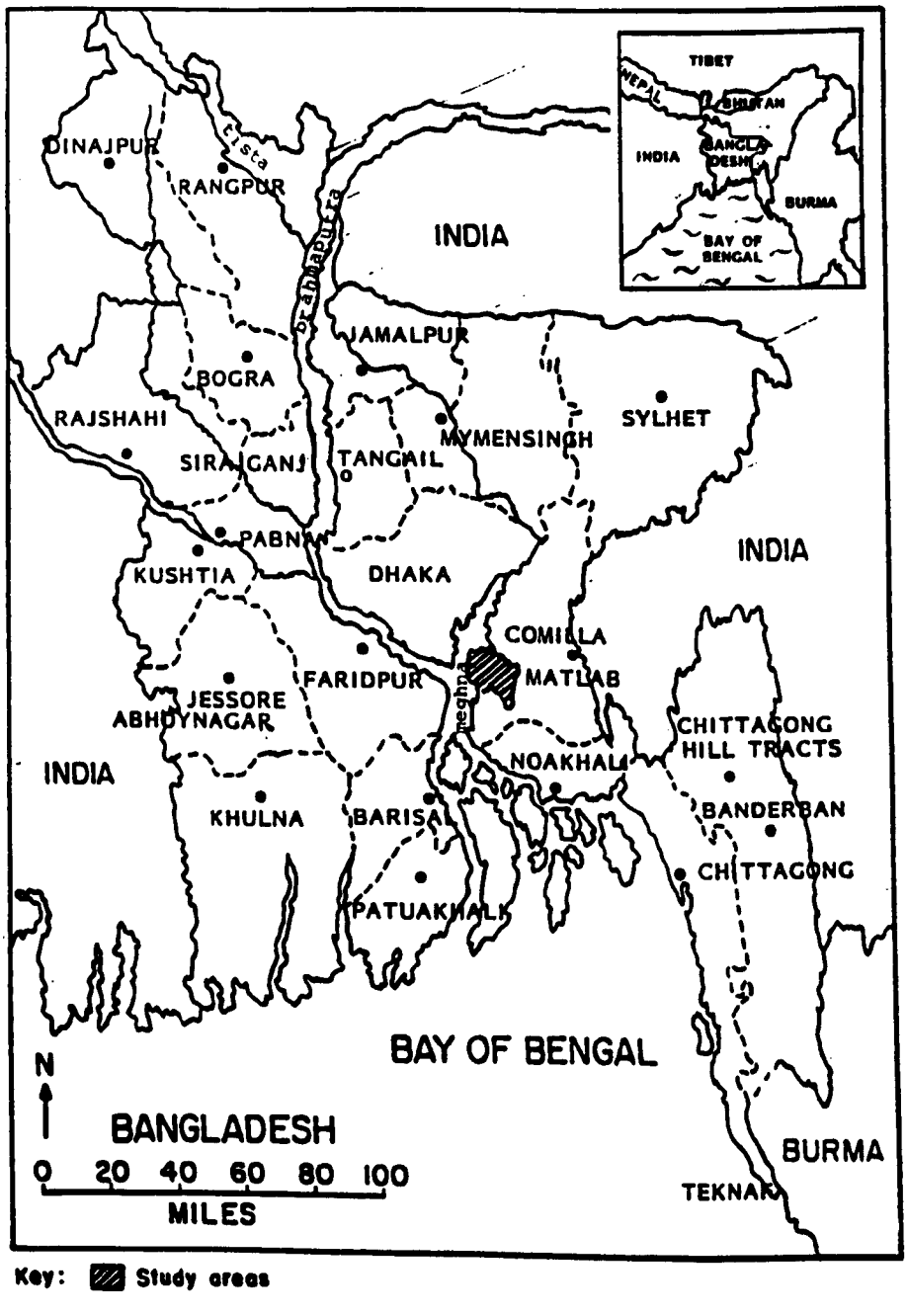


Figure 3.1: Map of Bangladesh, showing the location of the Matlab study area

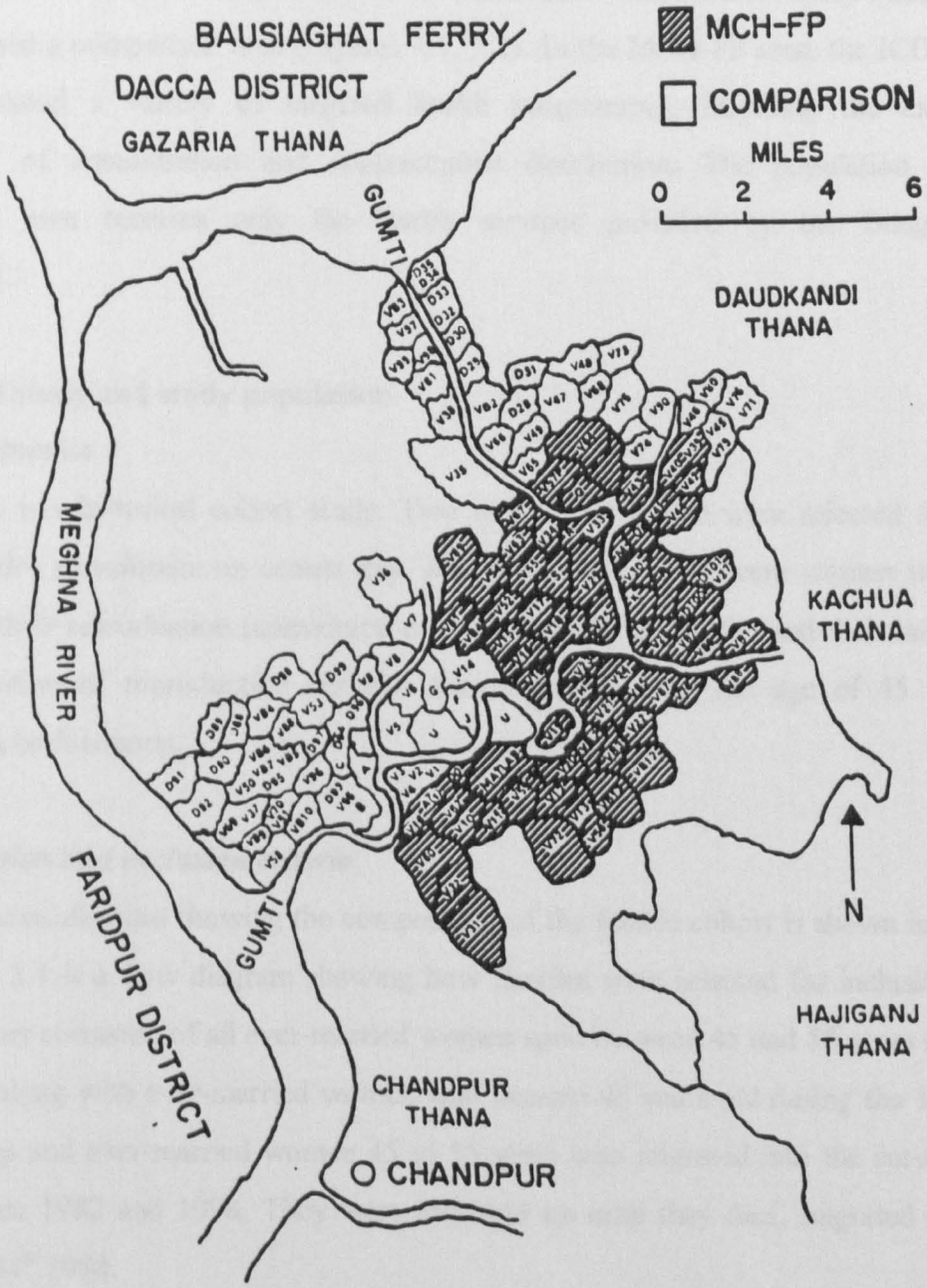


Figure 3.2: Map of the Matlab study area, showing the distribution of the intervention (MCH-FP) and comparison areas

The International Centre for Diarrhoeal Disease Research Bangladesh (ICDDR,B) has maintained a demographic surveillance programme in Matlab since the late 1960's (van Ginneken *et al* 1998). The area under surveillance consists of 142 villages and is divided equally into two sections - an intervention (Maternal and Child Health-Family Planning or MCH-FP) and a comparison area (Figures 3.1, 3.2). In the MCH-FP area, the ICDDR, B has coordinated a variety of targeted health programmes, including the extended programme of immunisation and contraceptive distribution. The population of the comparison area receives only the health services provided by the Bangladeshi government.

3.3 Type of study and study population

3.3.1 Introduction

This is a historical cohort study. Two cohorts in Matlab were selected from all subjects under surveillance on census day, June 30th 1982. They were women who had completed their reproduction (considered as those aged 45 and over) and their husbands. The association of reproductive histories with mortality after the age of 45 will be examined in both cohorts.

3.3.2 Inclusion and exclusion criteria

A Lexis diagram showing the composition of the female cohort is shown in Figure 3.3. Figure 3.4 is a flow diagram showing how females were selected for inclusion. The female cohort consisted of all ever-married women aged between 45 and 55 years on June 30th 1982, along with ever-married women who became 45 years old during the 16 years of follow-up and ever-married women 45 to 55 years who migrated into the surveillance area between 1982 and 1998. They were followed up until they died, migrated or until December 31st 1998.

There were 20402 ever-married women who fitted the inclusion criteria. To ensure that no deaths were due to the direct effects of childbearing, recent pregnancy histories were examined. 313 women experienced a pregnancy outcome in the year before entry or during the follow-up period. 19 of these were excluded as they died in the year following this last pregnancy. The remaining 294 entered the cohort one year after this last

pregnancy outcome, with their childbearing histories altered to include this latest outcome. The female cohort therefore included 20383 women.

Men who were alive on the day their wives entered the cohort were identified (see Figure 3.5). They entered if they were married to a woman who was between 45 and 55 years on June 30th 1982, married to a woman who became 45 years old during the 16 years of follow-up, or married to a woman aged 45 years and above who migrated into the surveillance area between 1982 and 1998. They entered on the same date as their wives and were followed until they died, migrated or until December 31st, 1998.

4117 women were widowed or divorced on entry into the cohort and 1880 were married to men who were absent from the area and not currently under surveillance[3.2]. This left 14886 men for whom data was accessible. 17 of these were excluded as their wives had died in the year following a recent pregnancy. 125 men had what seemed to be unreasonable dates of birth (for example, born in 1990). These inconsistencies were investigated with the data managers and the dates of birth were corrected for 59 men. For the remaining 66, the discrepancy could not be rectified. These were excluded from the analyses as it was not certain that they were the husbands of the women rather than their sons. The final cohort consisted of 14803 men.

[3.2] Migration from the area to Dhaka, India and the Middle East is common.

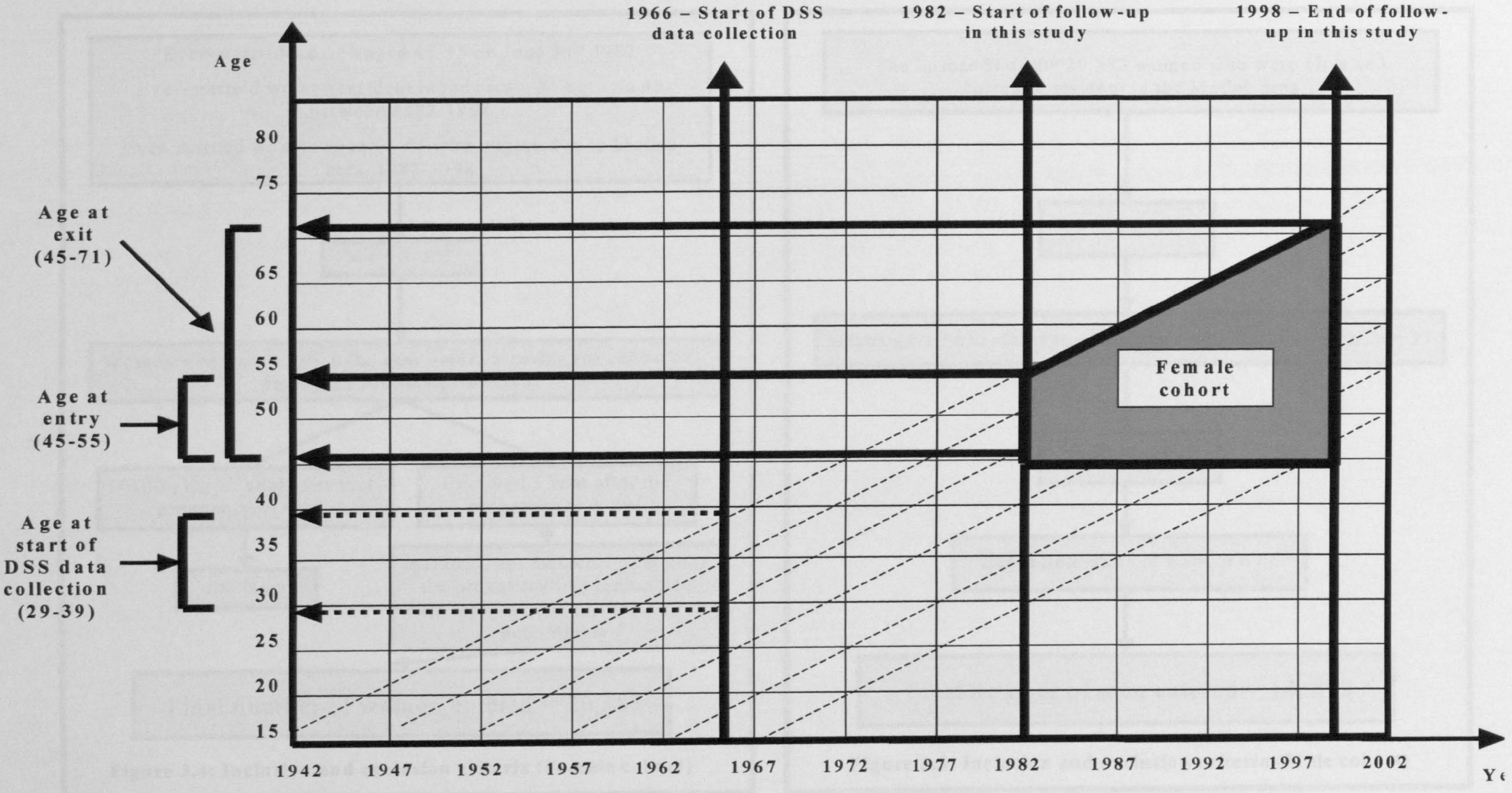


Figure 3.3: Lexis diagram of the female cohort

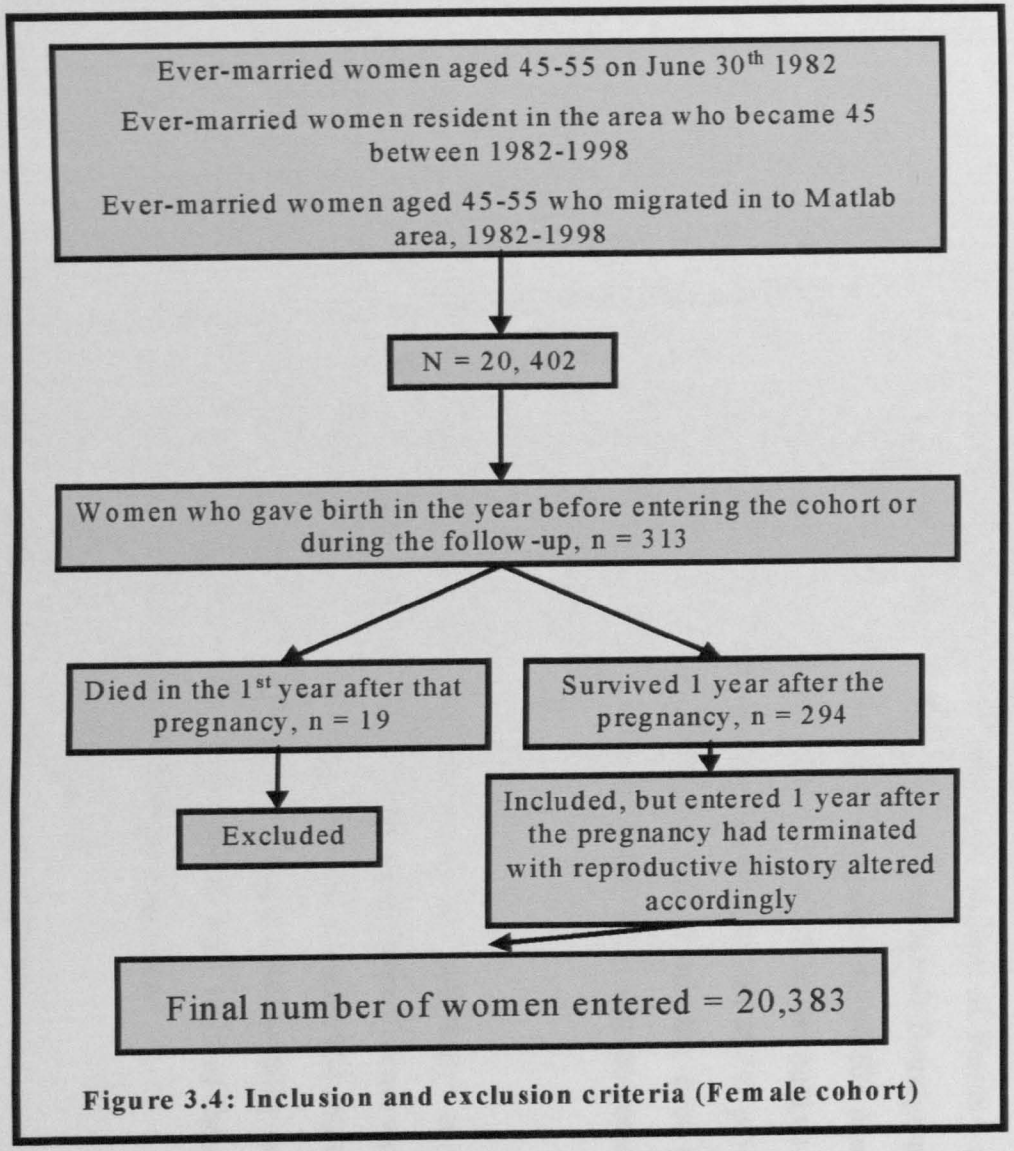


Figure 3.4: Inclusion and exclusion criteria (Female cohort)

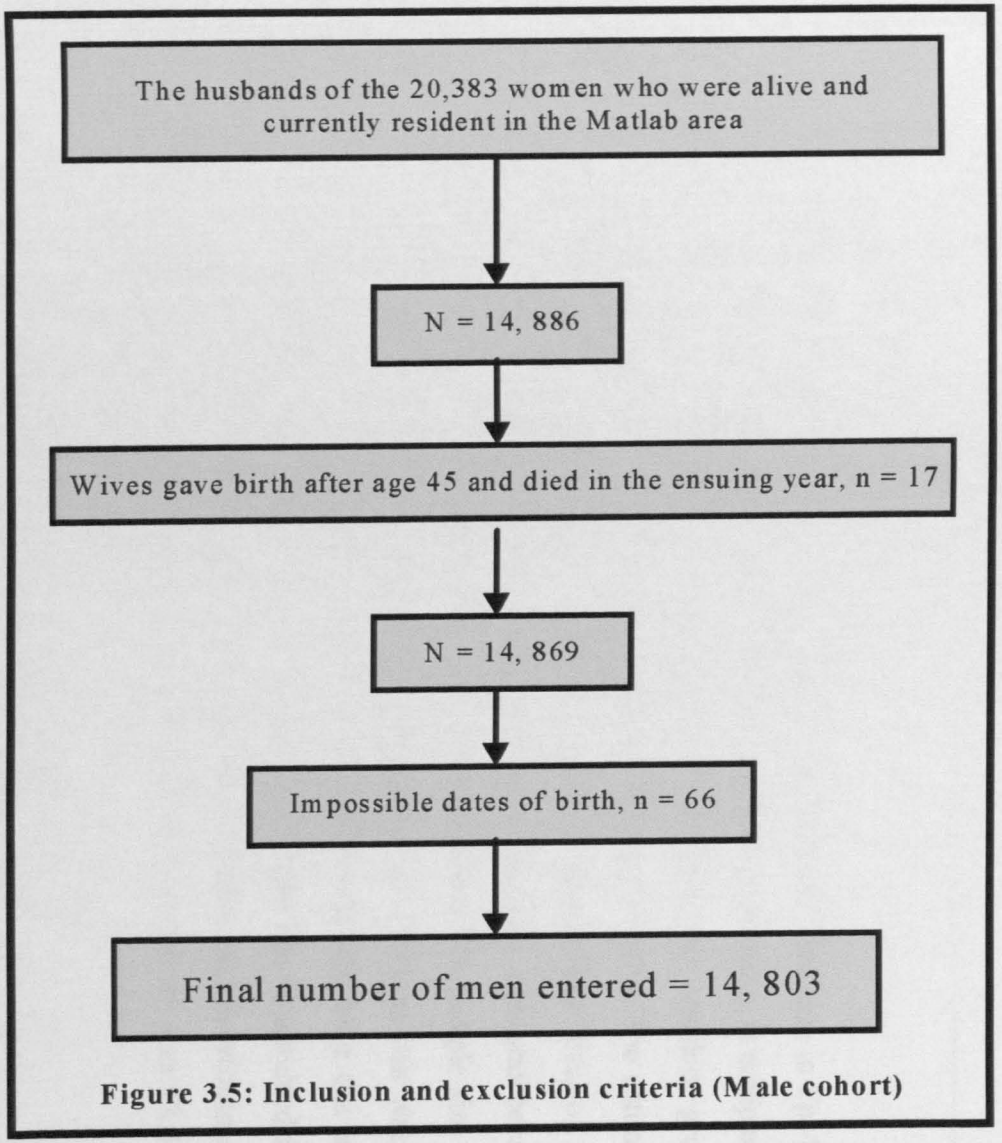


Figure 3.5: Inclusion and exclusion criteria (Male cohort)

3.3.3 Sample size

Sample size calculations were performed using the "Statcalc" function in Epi-Info 6. The estimates for both cohorts were based on the comparison of mortality in nulliparous and parous adults, as the nulliparous were expected to form the smallest group. Calculations were performed separately for the female and male cohorts. The estimates were based on a power of 80% to detect differences with a significance level of 5%. Estimates were obtained for both an increase and decrease in mortality. This was because the direction of the effect remained unknown from previous studies. The sample size was calculated based on the mortality experience of the population in 1990, as this was the approximate mid-point of the study and mortality had declined steadily over the study period. All-cause mortality rates for adults over the age of 45 years can be obtained from the Demographic Surveillance System annual reports. The mortality rate in women over age 45 in 1990 was 19.3 per 1000 women-years and in men over age 45 was 28.3 per 1000 men-years (ICDDR,B 1994).

It was estimated that 3% of ever-married women 45 years and over were nulliparous, based on data from the Bangladesh Retrospective Survey of Fertility and Mortality 1974, the Bangladesh Fertility Survey 1975 and the Bangladesh Demographic and Health Survey 1996. A sample of 1994 nulliparous women-years and 65802 parous women-years was necessary to detect a relative mortality rate of 1.5 in the nulliparous women compared with the parous, with 1477 nulliparous women-years and 48741 parous women-years required to detect a halving of the mortality rate. When the data was obtained there were 202323 female-years of follow-up in total, 2702 women-years in nulliparous women and 199621 for parous children.

The men were assumed to experience the same levels of "nulliparity" as the women. A sample of 1339 childless men-years and 44187 "men with children" years would be necessary to detect a relative mortality rate of 1.5 in the childless men and 994 childless men-years and 32802 "men with children" years to detect a halving of the mortality rates. The total number of person-years in the male cohort was 124498, with 1329 of these in childless men and 123169 in men whose wives had given birth at least once.

3.4 Data

3.4.1 Data sources

Two of the routine sources of data collected by the ICDDR,B were used to provide information for this study – the Demographic Surveillance System (DSS) and the 1982 census.

The DSS provides longitudinal data on demographic events since 1966. In 1996, approximately 200,000 individuals were under surveillance. In the MCH-FP area, 80 female community health workers (CHW) visit each house in every village twice a month. During the first visit they collect demographic data, and during the other they provide basic healthcare such as family planning, nutritional education and the treatment of diarrhoeal diseases. In the comparison area, 30 CHWs visit each household every month to record demographic events but provide no healthcare. Every CHW covers a population of around 1000 individuals and almost all are resident in the area or village in which they work. Each CHW also visits the villages accompanied by senior health assistants every two months, to verify the data collected. All pregnancy outcomes (live births, still births and spontaneous abortions), deaths, marriages and migrations are recorded. Changes in family composition are noted in a Family Register during the CHWs visit and additional information about vital events is obtained during the joint visit with the health assistant. During these visits, family members are interviewed using structured forms that are specific to each event. Prior to 1989, these forms were taken to the main ICDDR,B headquarters in Dhaka to be checked manually and entered into the appropriate data files. Since 1989 the data has been entered at the DSS field office in Matlab, using a data entry programme that automatically detects inconsistencies.

The DSS is updated using periodic censuses that serve to record changes or errors in the demographic information and to supplement the data with other information such as socio-economic indicators (religion, education, occupation).

3.4.2 Data available for this study (see Figure 3.6)

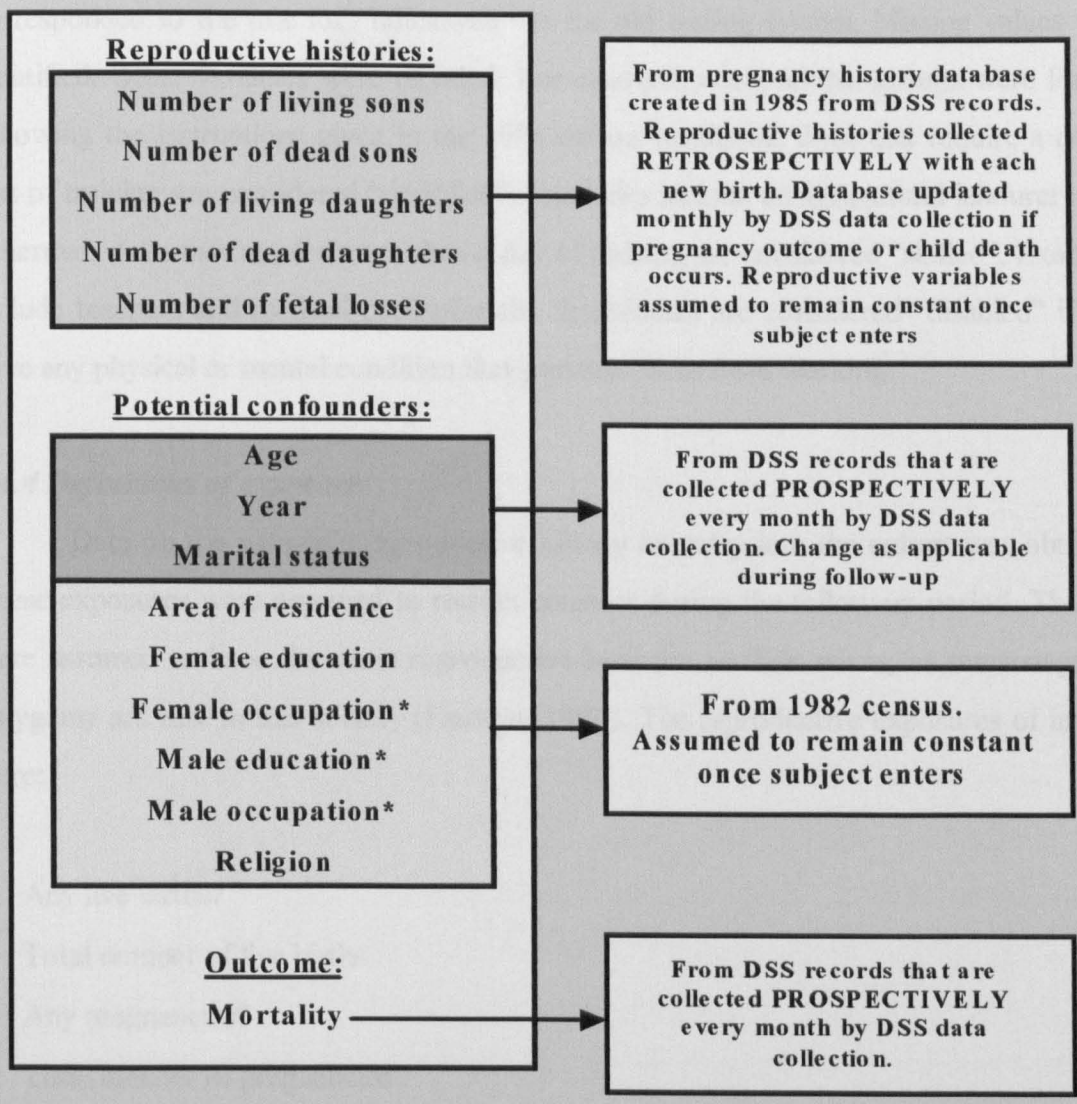
Since 1966 reproductive histories have been collected from all ever-married women experiencing a pregnancy outcome in the study area. In addition, ever-married

women under 55 years of age who migrated into the Matlab area after 1982 were asked to provide details of their pregnancy histories. These retrospective reproductive histories consist of information on the number of living sons, number of dead sons, number of living daughters, number of dead daughters and the number of fetal losses. The fetal loss data consists of a record of both spontaneous abortions and stillbirths. There is neither separate data on the two events nor is there information on induced abortions, which are illegal in Bangladesh. Reproductive information is only available for the ever married. Collecting pregnancy histories from the unmarried was, and still is, considered inappropriate in this cultural setting. The data was originally stored in a birth file that contained an individual record for each pregnancy outcome and the pregnancy history at the time of that outcome. A woman who had experienced two live births and one fetal loss would therefore have three records in this file. In 1988, a separate database was set-up for completed reproductive histories, which contains one record per woman and is updated as further pregnancy outcomes or child deaths are recorded.

Information on date of birth, area of residence, migrations, changes in marital status, and mortality were obtained from the DSS data collected prospectively each month. Additional socio-economic variables (female education, female occupation, male education, male occupation, male education, religion) were available from the data collected during the 1982 census.

Each person living in the study area has a unique identification number consisting of a code for their village, their family and for the individual within a family. This number is common to each data file and allows for linkage of information between each DSS file and between each data collection system, for example the DSS and the census. Data could also be linked between wife and husband.

Figure 3.6: Variables and data sources



3.4.3 Data management

The data was extracted in collaboration with a programmer at the ICDDR,B in Dhaka. Visits to the field site at Matlab allowed me to see the data collection at first hand. The data was obtained as ASCII text files, with separate files containing basic demography (female and male), pregnancy history, marriage history, and socio-economic data (female and male). The files were converted into Stata 6 data files, and all subsequent data cleaning and analysis was conducted using this package. Consistency checks were performed before file merges were undertaken. Discrepancies were corrected in consultation with the DSS

employees. For example, 90% of females were found to be employed as "catering managers". It transpired that employment codes had recently changed and the new code corresponded to the one for "housewife" in the old coding system. Missing values were identified. Other variables were recoded. For example, occupational groups were formed following the instructions given in the 1996 census handbook. Jobs that require a day or less of training are considered "unskilled". Examples include an agricultural labourer and a fisherman. Jobs that require more than a day of training are considered "skilled". Examples include teachers and medical professionals. Individuals are considered "disabled" if they have any physical or mental condition that prevents them from working.

3.4.4 Definitions of exposure

Data on the women's reproductive history on entry into the cohort was obtained. These exposures were assumed to remain constant during the follow-up period. The men were assumed to have the same reproductive histories as their wives, as remarriage and polygamy are rare in this society (Fauveau 1994). The reproductive exposures of interest were:

- Any live births?
- Total number of live births
- Any pregnancies?
- Total number of pregnancies
- Any surviving children?
- Number of surviving children
- Number of surviving sons
- Number of surviving daughters
- Percentage of children surviving
- Percentage of children borne who were male
- Any fetal losses?
- Number of fetal losses

Variables to represent exposures such as "parity" and "gravidity" were created from the individual components in the pregnancy history. Breast-feeding and contraception data was not available for this cohort, nor was it possible to calculate age at first birth or spaces between pregnancies. Potential confounders were age, time period, female education, female occupation, male education, male occupation, religion, area of residence, marital status at entry and changes in marital status during follow-up.

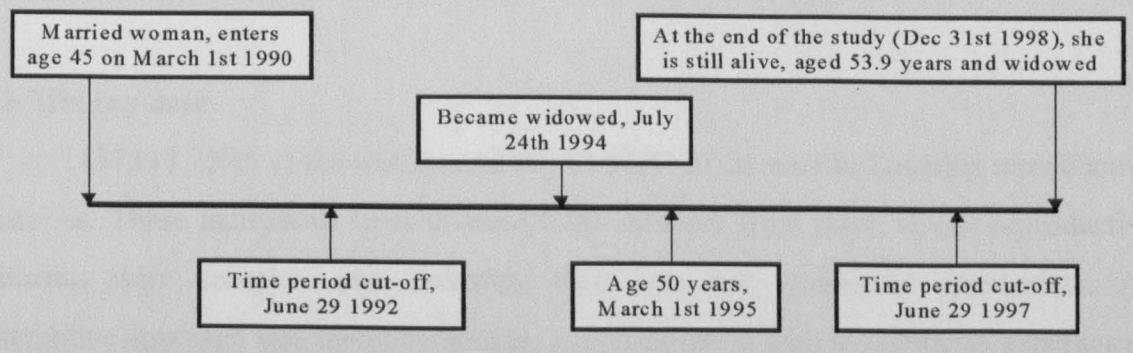
3.4.5 Definition of outcome

The outcome of interest will be all-cause mortality after the age of 45 years. A small proportion of the males were younger than their wives, and the outcome in the male cohort therefore became all-cause mortality after the age of 40 years.

3.5 Data analysis

Analyses were conducted separately for each sex. Person-years of follow-up for each exposure category of interest were calculated from the date each subject entered until they died, migrated or until December 31st 1998. The person-years for subjects who migrated out of the area were censored on the exact date that they moved away. Each subject's follow-up was split according to age (five year groups for the females, ten year groups for the males), time (five year intervals) and marital status (if a subject's status changed during follow-up). An example of one woman's follow-up is given in Figure 3.7.

Figure 3.7: An example of one woman's follow-up



This women contributes **8.8 years** of follow-up in total:

- **2.3 years** as a married woman in the 45-50 age group between 30 June1987 and 29 June 1992
- **2.1 years** as a married woman in the 45-50 age group between 30 June1992 and 29 June 1997
- **0.6 years** as a widowed woman in the 45-50 age group between 30 June1992 and 29 June 1997
- **2.3 years** as a widowed woman in the 50-55 age group between 30 June1992 and 29 June 1997
- **1.5 years** as a widowed woman in the 50-55 age group between 29 June 1997 and the end of the study

Crude mortality rates and their 95% confidence intervals were calculated for each of the exposures of interest. Poisson regression was used to compare the mortality rates between the members of the cohort at different exposure levels. It was assumed that the probability of death was proportional to the size of the age-time-exposure interval in question, that each age-time-exposure interval was sufficiently small for the rate of death to be constant within that interval, and that each death in the cohort was independent of all others (Breslow, Day 1987).

The multivariate survival analysis was conducted using the following strategy. The association between the potential confounders and all-cause mortality was assessed. Likelihood ratio tests were used to assess the statistical significance of each variable on the Poisson regression models. The association of reproductive variables with all-cause mortality was then estimated, adjusting for the potential confounders. Changes in crude estimates with each of the confounders were noted. Likelihood ratio tests were used to assess which reproductive variables significantly affected mortality, both with and without the potential confounders in the models. The Wald test for linear trends in mortality and likelihood ratio test for departures from the linear trend in mortality were performed for the discrete or ordered categorical variables. Mortality rates for the reproductive variables stratified by age, education, religion and marital status were examined for effect modification. Likelihood ratio tests for an interaction between each potential effect modifier and the reproductive variables, with and without the other variables included in the models, were performed.

3.6 Missing data

1573 (7.72%) of the women and 861 (5.82%) of the men had missing reproductive histories. These individuals were systematically different from those whose reproductive histories were complete and excluding them was not considered appropriate. An alternative approach was therefore sought, in collaboration with a statistician experienced in the analysis of incomplete data. A detailed account of the missing data is given in the next chapter.

4.1 Introduction

The objective of this chapter is to describe the missing data encountered in this study. Specific aims are to summarise potential strategies for dealing with missing data, to examine the characteristics of subjects for whom information was lacking and to describe how analyses were modified to account for the unobserved data.

4.2 Terminology

In epidemiological studies, data are collected to form rectangular data sets in which the rows represent "*units*" (or subjects) of interest and the columns contain data on variables measured for each unit – "*items*". Frequently, this data collection is incomplete. Subjects may not respond or be included at all - "*unit missingness*" - and some may not respond to certain questions - "*item missingness*" (Little, Rubin 1987). Sample sizes are thus reduced and standard complete-data methods of analysis can no longer be applied. In addition, systematic differences between individuals with observed and missing data can lead to biased results.

Different techniques to account for missing data require different assumptions to be met about the "*missing data mechanisms*", or *why* data are missing (Little, Rubin 1987). Rubin (1977) proposed the following terminology. If X and Y are variables (exposures or outcomes) measured during a study, the probability that some values of Y are missing may be:

- Independent of the values of both X, the completely observed variables and Y, the incompletely observed variables;
- Dependant on X but not on Y. That is, the missingness is related to the values of the completely observed variables but NOT to the values of the incompletely observed variables;
- Dependant on Y (and possibly on X). That is, the missingness of Y is related to the values of the missing variables themselves.

In the first case, the data are observed at random and the missing data are missing at random. Missing data of this kind are "*missing completely at random*" (MCAR). For example, in a study of the long-term effects of reproduction (Y) on mortality (X), data

would be MCAR if the probability that reproductive histories were missing was the same for all individuals independent of their reproduction or mortality. In the second case, the data are "*missing at random*" (MAR). The probability that the data are missing is related to the values of other variables, but not to the values of the variable itself. For example, reproductive data (Y) would be MAR if the uneducated (X) were more likely to have missing reproductive data but, in the uneducated (X), the values of the missing data were unrelated to their actual reproductive status. In the third case, the data are neither missing nor observed at random. The missingness is "*nonignorable*", as the probability that a variable is missing depends on the value of the variable itself and the missing values are systematically different from the observed values. This would be the case if, for example, the nulliparous did not provide any data.

It is not usually possible to "prove" whether missing data are MCAR, MAR or nonignorable. Careful consideration of the most plausible mechanism is required however, as the validity of inferences obtained using different missing data techniques depends on the assumptions made about the unobserved data. For example, "*ignoring the missing data implicitly invokes the MCAR assumption, an assumption far more dubious than the MAR or other assumptions*" (Brick, Kalton 1996).

4.3 Strategies for dealing with missing data

Rubin (1987) suggested that a method to account for missing data should have the following properties: "*First, it should allow standard complete-data methods to be used. Second, it should be capable of yielding valid inferences that (a) produce estimates that adjust for observed differences between respondents and nonrespondents and (b) produce standard errors that reflect the reduced sample size...Third, it should display the sensitivity of inferences to various plausible models for nonresponse.*"

This summary will concentrate on methods in relatively widespread use. Other techniques, developed for use with specific methods of analysis such as the EM algorithm, are described in Little and Rubin (1987).

4.3.1 Case deletion

Subjects with missing information are commonly dropped, contributing no information to results obtained. The advantage of this approach is that standard methods of analysis can then be used. However, these will only yield valid inferences if the discarded cases are a random sample of the population of interest and the data are MCAR (Schafer 1999). In addition, significant amounts of data can be lost leading to a reduction in the precision of estimates and *all* information for subjects with *any* missing data is discarded (Little, Rubin 1987). Finally, this method tells us nothing about the subjects with missing information.

4.3.2 Available-case analysis

An alternative approach is available-case analysis, where subjects contribute data where it has been observed. For example, when studying the association of reproduction and mortality, subjects with missing education data can still supply data to the crude analysis of the effects of parity. However, the number of subjects then changes with each analysis. Comparative statistics, such as the mean parity stratified by education and religion, may not be based on the same numbers and more complex analyses such as the comparison of two multivariate statistical models cannot be performed. In addition, this method does not account for differences between observed and missing data. Ignoring this may introduce bias.

4.3.3 Weighted analyses

Weighting is commonly used to account for sampling strategies in survey design but can also be extended to compensate for missing data (Rubin 1987). Weights are assigned to the data acquired from subjects who responded, to represent the nonrespondents. The information on which the weighting is based can be accessible in the original data or can be acquired through additional data collection. An example of weighting was seen in Kitagawa and Hauser's study (1973, see Chapter 1), in which the death certificates of individuals dying soon after the 1960 census were matched to the deceased's census responses. A pilot study had shown that associations between socio-demographic factors and mortality were biased if the subjects for whom the records could not be matched were ignored. A follow-up survey was therefore conducted, in which the relatives of a random sample of the deceased were asked to provide proxy replies for the

information collected in the census. Responses to this survey were obtained for matched and unmatched subjects, and this information was used to weight the standardised mortality ratios for the characteristics of the unmatched individuals.

This method assumes that all bias due to non-response is represented by the variables on which the weighting is carried out (Brick, Kalton 1996). In addition, weighting adjustments are primarily used for unit missingness (Greenland, Finkle 1995; Brick, Kalton 1996). The method's apparent simplicity no longer holds with item missingness where weighting would have to be carried out based on each item that is observed.

4.3.4 Single imputation

Imputation refers to any technique in which missing data are filled-in. The aim is to produce a complete data set that has retained all the recorded data, has missing information filled in with plausible values, and can be analysed using standard statistical methods. Common single imputation procedures include mean imputation, hot deck imputation and regression imputation. A comprehensive review of imputation procedures is given in Little and Rubin (1987).

In mean imputation, the missing data are substituted with the mean of the recorded values. For example in subjects with missing parity data, the unobserved values could be replaced with the mean parity of subjects with observed data. More complex methods have been proposed, to adjust the means for values of other variables using techniques similar to those used for weighting (Little, Rubin 1987). For mean imputation to yield valid inferences, the data must be MCAR (Rubin 1987). In addition, the distribution of the variable in question becomes distorted and relationships between variables, such as correlations, are no longer useful. The number of cases at the extremes is also underestimated. This method would not therefore be suitable if one wished, for example, to examine the association between nulliparity and mortality. More sophisticated single imputation procedures include hot deck and regression imputation. Hot deck imputation involves substituting the missing values with values drawn from subjects belonging to the same "*imputation class*", as defined by one or more variables observed for both (Brick, Kalton 1996). In a simplified example, if a woman with ten years of schooling had

missing data in reproductive variables they could be imputed using data from another woman with the same level of educational attainment. The selection of a "*donor*" can be random or sequential (the next similar subject in the data set is used), and may involve elaborate schemes using many observed variables such as the "*hierarchical*" hot deck used at the United States Census Bureau (Rubin 1987). In regression imputation, the missing values are replaced by estimates predicted by a regression model (such as a multiple linear regression) based on the observed variables. With both hot deck and regression imputation, imputed values should provide reasonable estimates if the missing values are MAR and the classification for the hot deck or the regression models are appropriate (Little, Rubin 1987).

The main advantage of single imputation is that standard complete-data methods can be used to analyse the resulting data sets. These will provide reliable estimates if the proportion of missing data is small (Schafer suggests less than 5%) and the appropriate assumptions about the missing data mechanism are met. However, even when these conditions are fulfilled, analyses based on such data sets will fail to represent the uncertainty that exists about which value to impute (Rubin, Schenker 1991). This leads to estimates that are too precise, with "*standard errors that are too small, p-values that are systematically too significant and confidence intervals that cover less than their nominal coverages*" (Rubin, Solas website).

4.3.5 Multiple imputation

Multiple imputation (MI) attempts to overcome the disadvantages of single imputation by imputing several plausible values for each missing datum. It was first proposed in the 1970's (Rubin 1977). Since then, different techniques have been developed to obtain the imputed values (Rubin 1987; Little, Rubin 1987; Rubin, Schenker 1991; Schafer 1997). Recent publications have discussed its usefulness for missing data in epidemiological research (Crawford *et al* 1995; Freedman, Wolf 1995; Greenland, Finkle 1996; Barnard, Meng 1999).

MI is a technique in which the missing values are replaced by a number (m, where $m > 1$) of simulated values, to form m complete data sets. The variation between these m imputed values represents the uncertainty about the true value of the unobserved data.

Each of the *m* data sets is analysed using standard statistical methods. The results of the *m* analyses are ultimately combined to yield "*repeated-imputation inferences*" and a measure of the additional uncertainty due to the missing data – the "*between-imputation variance*" – is incorporated into the estimates along with a measure of ordinary sampling variability (Rubin 1987). Thus, standard errors and p values are inflated and confidence intervals widened such that they reflect the additional uncertainty that is introduced by the missing data.

To obtain 'proper' imputations, they should be generated under a Bayesian statistical framework[4.1], using the following general scheme (Schafer 1999): "*Specify a parametric model for the complete data (and, if necessary, a model for the mechanism by which data became missing), apply a prior distribution to the unknown model parameters, and simulate* ***m*** *independent draws from the conditional distribution of* Y_{mis} *given* Y_{obs} *by Bayes' theorem.*" Therefore, a model is specified to predict the missing values, given the complete data and a nonresponse mechanism if appropriate. Parameters are randomly and independently drawn from this "*conditional distribution*" (also called the "*posterior predictive density*") to produce the *m* imputed values, to form the *m* complete data sets (van Buuren *et al* 1999). Most techniques for creating multiple imputations assume that the data are MAR. They also function better in the presence of monotone missing data patterns. A monotone pattern occurs when the variables in a data set can be ordered according to the missing data, as shown in Table 4.1. The subjects in the first group always have more observed information than those in the second group and so on. Monotone missing data patterns are beneficial in the generation of multiple imputations as the imputations are reduced to a series of single variable imputations, which allows for greater modelling flexibility (Little, Rubin 1987).

Table 4.1: Monotone missing pattern

	Group 1	**Group 2**	**Group 3**
Variable 1	Complete	Complete	**Missing**
Variable 2	Complete	**Missing**	**Missing**
Variable 3	**Missing**	**Missing**	**Missing**

[4.1] A brief description of Bayesian methods and how they may be applied to missing data problems is given in Appendix 4.1.

MI is therefore useful, as standard methods can be used to analyse the complete data sets. In addition, unlike single imputation, the uncertainty as to which value to impute is incorporated into the results (Barnard, Meng 1999). The main disadvantage of MI is the work and computing power required to create and analyse the imputed data sets. However, unless the rates of missing information are high, there is little gain in the efficiency from producing more than five imputed data sets (Brick, Kalton 1996; Rubin 1996; Schafer 1997). The additional effort needed to use MI is therefore not excessive.

4.3.6 Summary

Missing data are a common problem in epidemiological research that can lead to reduced sample sizes and biased results. Many of the common strategies for dealing with missing data make inappropriate assumptions about the unobserved data. Imputation procedures that make less stringent assumptions have therefore been developed. In particular, multiple imputation has been shown to provide valid estimates whilst incorporating the additional uncertainty that exists due to missing data.

4.4 Patterns of missing data in this study

4.4.1 Introduction

The patterns of missing data are shown in Tables 4.2 (female) and 4.3 (male). 1573 (7.72%) of the women were missing data on childbearing variables. In subjects with missing reproductive information, all of the reproductive variables (living sons, dead sons, living daughters, dead daughters, fetal losses) were unknown. In addition, 302 (1.49%) were missing data on female education, 5120 (25.12%) on male education, and 5150 (25.27%) on male occupation. Reproductive histories were missing for all men married to women with no pregnancy history (861, 5.82%). There were also 189 (1.28%) with data missing on female education, 296 (2.00%) lacking information on male education and 326 (2.20%) with no record of male occupation. There was no missing data on the outcome variable in either sex. Subjects of both sexes migrated during the study period. However, the exact date of migration was known and person-years of follow-up could be calculated accurately. This discussion will focus on the missing reproductive histories as they were the main exposures of interest, were missing in greatest numbers, and were unobserved for a sample that were systematically different to subjects with complete information.

Table 4.2: Patterns Of Missing Data In The Female Data Set (Total Population 20,383)						
Number (%)	**Pregnancy history**	**Female education**	**Male education**	**Husband's occupation**	**Religion**	**Marital status**
13607 (66.76)	Complete	Complete	Complete	Complete	Complete	Complete
1563 (7.67)	Missing	Complete	Complete	Complete	Complete	Complete
1 (0.01)	Missing	Missing	Complete	Complete	Complete	Complete
2 (0.01)	Missing	Complete	Missing	Complete	Complete	Complete
1 (0.01)	Missing	Complete	Complete	Missing	Complete	Complete
6 (0.03)	Missing	Complete	Missing	Missing	Complete	Complete
49 (0.24)	Complete	Missing	Complete	Complete	Complete	Complete
10 (0.05)	Complete	Complete	Missing	Complete	Complete	Complete
38 (0.19)	Complete	Complete	Complete	Missing	Complete	Complete
1 (0.01)	Complete	Missing	Missing	Complete	Complete	Complete
4854 (23.81)	Complete	Complete	Missing	Missing	Complete	Complete
4 (0.02)	Complete	Missing	Complete	Missing	Complete	Complete
247 (1.21)	Complete	Missing	Missing	Missing	Complete	Complete
Variables to be included in the analyses:						
Total number (percentage) of women with missing reproductive histories: 1573 (7.72)						
Total number (percentage) missing female education: 302 (1.49)						
Variables not included in the analyses:[4.2]						
Total number (percentage) missing male education: 5120 (25.12)						
Total number (percentage) missing male occupation: 5150 (25.27)						

Table 4.3: Patterns Of Missing Data In The Male Data Set (Total Population 14,803)						
Number (%)	**Pregnancy history**	**Female education**	**Male education**	**Male's occupation**	**Religion**	**Marital status**
13563 (91.62)	Complete	Complete	Complete	Complete	Complete	Complete
851 (5.75)	Missing	Complete	Complete	Complete	Complete	Complete
1 (0.01)	Missing	Missing	Complete	Complete	Complete	Complete
2 (0.01)	Missing	Complete	Missing	Complete	Complete	Complete
1 (0.01)	Missing	Complete	Complete	Missing	Complete	Complete
6 (0.04)	Missing	Complete	Missing	Missing	Complete	Complete
49 (0.33)	Complete	Missing	Complete	Complete	Complete	Complete
10 (0.07)	Complete	Complete	Missing	Complete	Complete	Complete
38 (0.26)	Complete	Complete	Complete	Missing	Complete	Complete
1 (0.01)	Complete	Missing	Missing	Complete	Complete	Complete
143 (0.70)	Complete	Complete	Missing	Missing	Complete	Complete
4 (0.02)	Complete	Missing	Complete	Missing	Complete	Complete
134 (0.66)	Complete	Missing	Missing	Missing	Complete	Complete
Variables to be included in the analyses:						
Total number (percentage) of men with missing reproductive histories: 861 (5.82)						
Total number (percentage) missing female education: 189 (1.28)						
Total number (percentage) missing male education: 296 (2.00)						
Total number (percentage) missing male occupation: 326 (2.20)						

[4.2] As a high percentage of the male education and occupation data were missing for the females, these variables were not used in any of the further female analyses. However the data was relatively complete for the males.

4.4.2 Factors that affected the measurement of reproductive histories

Pregnancy histories were collected from women who experienced a pregnancy outcome in the study area and from ever-married woman under 55 years of age who migrated into the area after 1982. Women who had no pregnancy outcomes at all, women who had no further pregnancies in the area after the start of data collection (1966), and women who migrated to Matlab before 1982 and experienced no pregnancy outcomes in the area should therefore have no recorded reproductive history.

Women lacking pregnancy histories in this cohort were a biased sample, both in terms of mortality (Table 4.4) and socio-economic status (Table 4.5). In fact, 41% of all deaths occurred in this group (794 of 1939) and they were 14 times more likely to die than the women with complete reproductive histories (crude rate ratio 14.34, 95%CI 13.10-15.70). More of these women also migrated from the surveillance area during the study period.

They were of lower socio-economic status than those with complete reproductive data. They were older at entry and younger at exit from the cohort. There was a higher percentage of Hindu women, a group known to be socially excluded in Bangladesh, (26.38% compared with 13.01%, Pearson's chi squared statistic 213.88, $p < 0.001$) and a greater percentage from the comparison area (53.72% compared with 48.45%, Pearson's chi squared statistic 16.14, $p < 0.001$). Over 30% had received no formal education (compared with less than 20% of women with complete pregnancy histories). Finally, more were widowed or divorced (39.92% widowed on entry compared with 13.85%, 1.59% divorced compared with 0.79%). Similarly, the males with missing reproductive data were different to their counterparts with recorded information. They too had higher mortality, although the relative differences were not as extreme as in the females. They were older at entry and exit, were more frequently Hindu, were more likely to live in the comparison area, were less educated and were less likely to be employed in a job that was skilled. All of these differences were statistically significant.

Table 4.4: Mortality Status Of Women With Missing And Complete Reproductive Histories					
Women with missing pregnancy history			**Women with complete pregnancy history**		
Outcome	**Number**	**%**	**Outcome**	**Number**	**%**
Alive	779	49.51	**Alive**	17665	93.91
Dead	794	50.49	**Dead**	1145	6.09
Total	1573	100.00	**Total**	18810	100.00
Pearson's chi squared for comparing percentages = 3322.89, $p < 0.001$					
Of those alive					
Alive	72	9.24	**Alive**	16188	91.64
Migrated	707	90.76	**Migrated**	1477	8.36
Total	779	100.00	**Total**	17665	100.00
Pearson's chi squared for comparing percentages = 4852.30, $p < 0.001$					

Table 4.5: Characteristics Of Women With Missing And Complete Reproductive Histories					
Age at entry					
Women with missing pregnancy history			**Women with complete pregnancy history**		
Mean age at entry	**Mean age at exit**		**Mean age at entry**	**Mean age at exit**	
49.37	55.30		46.51	56.77	
t test comparing mean age at entry: $t = 40.49$, $p < 0.0001$; t test comparing mean age at exit: $t = 8.30$, $p < 0.0001$					
Religion					
Women with missing pregnancy history			**Women with complete pregnancy history**		
Muslim	1158	73.62	**Muslim**	16362	86.99
Hindu	415	26.38	**Hindu**	2448	13.01
Total	1573	100.00	**Total**	18810	100.00
Pearson's chi squared statistic = 213.88, $p < 0.001$					
Area of residence					
Women with missing pregnancy history			**Women with complete pregnancy history**		
Intervention	728	46.28	**Intervention**	9697	51.55
Comparison	845	53.72	**Comparison**	9113	48.45
Total	1573	100.00	**Total**	18810	100.00
Pearson's chi squared statistic = 16.14, $p < 0.001$					
Female education					
Women with missing pregnancy history			**Women with complete pregnancy history**		
None	528	33.57	**None**	3519	18.71
Maktab	836	53.15	**Maktab**	11146	59.26
Any formal	208	13.22	**Any formal**	3844	20.44
Unknown	1	0.06	**Unknown**	301	1.60
Total	1573	100.00	**Total**	18810	100.00
Pearson's chi squared statistic = 231.75, $p < 0.001$					
Marital status on entry					
Women with missing pregnancy history			**Women with complete pregnancy history**		
Unmarried	0	0.00	**Unmarried**	17	0.09
Married	920	58.49	**Married**	15851	83.27
Widowed	628	39.92	**Widowed**	2794	13.85
Divorced	25	1.59	**Divorced**	148	0.79
Total	1573	100.00	**Total**	18810	100.00
Pearson's chi squared statistic = 673.14, $p < 0.001$					

Table 4.6: Mortality Status Of Men With Missing And Complete Reproductive Histories					
Men with missing pregnancy history			**Men with complete pregnancy history**		
Outcome	**Number**	**%**	**Outcome**	**Number**	**%**
Alive	430	49.94	**Alive**	9979	71.58
Dead	431	50.06	**Dead**	3963	28.42
Total	861	100.00	**Total**	13942	100.00
Pearson's chi squared statistic for comparing percentages = 181.823, $p < 0.001$					
Crude mortality rate ratio = 1.94, 95% CI 1.75-2.14					
Of those alive					
Alive	148	33.42	**Alive**	9187	92.06
Migrated	282	65.58	**Migrated**	792	7.94
Total	430	100.00	**Total**	9979	100.00
Pearson's chi squared statistic for comparing percentages = 6161.79, $p < 0.001$					

Table 4.7: Characteristics Of Men With Missing And Complete Reproductive Histories					
Age at entry					
Men with missing pregnancy history			**Men with complete pregnancy history**		
Mean age at entry	**Mean age at exit**		**Mean age at entry**	**Mean age at exit**	
61.63	69.32		56.98	65.43	
t test comparing mean age at entry: $t = 23.53$, $p < 0.0001$; t test comparing mean age at exit: $t = 13.32$, $p < 0.0001$					
Religion					
Men with missing pregnancy history			**Men with complete pregnancy history**		
Muslim	622	72.24	**Muslim**	12081	86.65
Hindu	239	27.76	**Hindu**	1861	13.35
Total	861	100.00	**Total**	13942	100.00
Pearson's chi squared statistic = 138.32, $p < 0.001$					
Area of residence					
Men with missing pregnancy history			**Men with complete pregnancy history**		
Intervention	417	48.43	**Intervention**	7239	51.92
Comparison	444	51.57	**Comparison**	6703	48.08
Total	861	100.00	**Total**	13942	100.00
Pearson's chi squared statistic = 3.96, $p = 0.047$					
Male education					
Men with missing pregnancy history			**Men with complete pregnancy history**		
None	277	32.17	**None**	2519	18.07
Maktab	453	52.61	**Maktab**	8173	58.62
Any formal	130	15.10	**Any formal**	3062	21.96
Unknown	1	0.12	**Unknown**	188	1.35
Total	861	100.00	**Total**	13942	100.00
Pearson's chi squared statistic = 117.79, $p < 0.001$					
Male occupation					
Men with missing pregnancy history			**Men with complete pregnancy history**		
Unskilled	617	71.66	**Unskilled**	8942	63.14
None	10	1.16	**None**	119	0.85
Skilled	199	23.11	**Skilled**	4399	31.55
Disabled	28	3.25	**Disabled**	163	1.17
Unknown	7	0.81	**Unknown**	319	2.29
Total	861	100.00	**Total**	13942	100.00
Pearson's chi squared statistic = 61.86, $p < 0.001$					

The bias in mortality was particularly worrying and we therefore attempted to obtain detailed descriptions of the data collection from the ICDDR,B. A data manager suggested that when the new reproductive history database was built in 1988 around 7000 women were missing reproductive histories, and that an attempt was made to collect this missing data retrospectively. This could not be confirmed by other sources at the centre. We suspect however, that additional data collection did occur after 1988. Only 1573 women in our cohort were missing reproductive histories. We would expect more missing data than this, as many of the women who were included may not have had pregnancies in the study area. For example, women who were between 45 and 55 years in 1982 (and therefore entered the cohort) were aged 29 to 39 years in 1966 (the date at which data collection commenced). It is likely that a high percentage of these women experienced no pregnancy outcomes after that date, and they should therefore have missing information. In addition, migration to and from the study area is common. It is therefore possible that many females migrated to Matlab before 1982 and experienced no pregnancies in the area.

Women entering the cohort in 1982 were older at the start of the DSS data collection than women who entered after 1982. The older the woman, the less likely it is that she had further pregnancies after 1966. We would therefore expect most of the missing pregnancy histories to occur in women who entered in 1982, and for the percentage missing to increase with age in 1982. Table 4.8 shows that both of these statements are true. More than 80% of women who were missing reproductive data entered in 1982 (1293 of 1573) and the percentage of women with missing reproductive histories increases with age. However, these percentages are smaller than anticipated. Only 25% of women 51 years or older in 1982 (aged 35-39 in 1966) were missing pregnancy histories. This suggests, if no additional data collection occurred, that the remaining 75% experienced a pregnancy outcome after 1966 and therefore, had her reproductive history recorded. This seems unlikely. The earliest reported data in this population shows that the age-specific fertility rate in women older than 35 years in 1983 was 73 births per 1000 women and 48 births per 1000 women in 1990 (ICDDR,B 1985, 1990). Although fertility at all ages was higher in the late 1960's and 1970's, it is doubtful that three-quarters of the women aged between 35 and 39 in 1966 had pregnancies after this date.

Table 4.8: Availability of reproductive history by year and age of entry						
	Missing		Available		Total	
Year & age at entry	Number	Percentage	Number	Percentage	Number	%
1982, 45 years	78	11.24	616	88.76	694	100.00
1982, 46 years	128	13.66	809	86.34	937	100.00
1982, 47 years	163	15.98	857	83.02	1020	100.00
1982, 48 years	104	16.46	528	83.54	632	100.00
1982, 49 years	138	19.38	574	80.62	712	100.00
1982, 50 years	94	17.77	435	82.23	529	100.00
1982, 51 years	160	22.73	544	77.27	704	100.00
1982, 52 years	140	20.38	547	79.62	687	100.00
1982, 53 years	133	26.28	373	73.72	506	100.00
1982, 54 years	153	26.70	420	73.30	573	100.00
1982, 55 years	2	20.00	8	80.00	10	100.00
Sub-total	**1293**	**18.46**	**5711**	**81.54**	**7004**	**100.00**
After 1982, 45 years	280	2.20	12453	97.80	12733	100.00
After 1982, 46 years	-	-	159	100.00	159	100.00
After 1982, 47 years	-	-	109	100.00	109	100.00
After 1982, 48 years	-	-	75	100.00	75	100.00
After 1982, 49 years	-	-	77	100.00	77	100.00
After 1982, 50 years	-	-	83	100.00	83	100.00
After 1982, 51 years	-	-	47	100.00	47	100.00
After 1982, 52 years	-	-	34	100.00	34	100.00
After 1982, 53 years	-	-	31	100.00	31	100.00
After 1982, 54 years	-	-	28	100.00	28	100.00
After 1982, 55 years	-	-	3	100.00	3	100.00
Sub-total	**280**	**2.09**	**13099**	**97.91**	**13379**	**100.00**
Total	**1573**	**7.72**	**18810**	**92.28**	**20383**	**100.00**

Two other, much smaller, groups may also provide some evidence that additional data was collected retrospectively. 84 (33.20%) of the 253 women noted as being nulligravid (no living or dead children and no fetal losses) entered in 1982. The DSS staff confirmed that they were truly nulligravid rather than of unknown pregnancy history. In addition, there were 17 unmarried women with data on reproductive histories in the sample. Neither of these two groups should have recorded pregnancy histories, suggesting that reproductive information may have been obtained from women other than those fitting the specified criteria.

It is therefore possible that some women were missing pregnancy histories as they had simply not been asked to provide the information. It is also possible that if retrospective data collection occurred they died or migrated before the information was collected. If this were true, then one would expect a greater percentage of these women to have died or migrated before or shortly after 1988, when the missing reproductive histories were discovered.

Table 4.9: Availability of reproductive histories by death and migration			
Women with missing pregnancy histories - Year of death			
Year of death	**No.**	**%**	**Cumulative %**
1982	28	3.53	3.53
1983	55	6.93	10.45
1984	68	8.56	19.02
1985	49	6.17	25.19
1986	78	9.82	35.01
1987	65	8.19	43.20
1988	72	9.07	52.27
1989	63	7.93	60.20
1990	74	9.32	69.52
1991	91	11.46	80.98
1992	96	12.09	93.07
1993	48	6.05	99.12
After 1994	7	0.89	100.00
Total	**794**	**100.00**	
Women with pregnancy histories available – Year of death			
Year of death	**No.**	**%**	**Cumulative %**
1982	0	-	-
1983	10	0.88	0.88
1984	7	0.61	1.48
1985	5	0.44	1.92
1986	8	0.70	2.62
1987	17	1.48	3.10
1988	28	2.45	6.55
1989	24	2.10	8.65
1990	24	2.10	10.74
1991	31	2.71	13.45
1992	44	3.84	17.29
1993	90	7.86	25.15
After 1994	857	73.85	100.00
Total	**1145**	**100.00**	
Women with missing pregnancy histories - Year of migration			
Year of migration	**No.**	**%**	**Cumulative %**
1982	22	3.11	3.11
1983	48	6.79	9.9
1984	67	9.48	19.38
1985	60	8.49	27.86
1986	65	9.19	37.06
1987	81	11.46	48.51
1988	60	8.49	57
1989	62	8.77	65.77
1990	60	8.49	73.26
1991	72	10.18	83.44
1992	89	12.59	97.03
1993	14	1.98	99.01
After 1994	7	0.99	100.00
Total	**707**	**100.00**	
Women with pregnancy histories available - Year of migration			
Year of migration	**No.**	**%**	**Cumulative %**
1982	14	0.95	0.95
1983	29	1.96	2.91
1984	57	3.86	6.77
1985	65	3.40	11.17
1986	60	3.06	15.23
1987	90	6.09	21.33
1988	75	5.08	26.40
1989	69	3.67	31.08
1990	91	6.16	37.24
1991	84	5.69	42.92
1992	83	5.62	48.54
1993	105	7.11	55.66
After 1994	655	43.34	100.00
Total	**1477**	**100.00**	

In fact, over half of the deaths in women with missing reproductive histories occurred by the end of 1988, compared with only 7% of the deaths in their counterparts with complete data (Table 4.9). This percentage was higher in women who entered in 1982 (data not shown). This means that a quarter of the 1573 with missing reproductive histories were dead by the end of 1988 compared with only 0.4% of the 18810 women with complete reproductive data. It is therefore possible that these women had no recorded reproductive history as they had died before the additional data collection had occurred. In addition, this pattern continued with time. 99% of the deaths in women with missing reproductive histories had occurred by the end of 1993, compared with only 25% of the deaths in the cohort with recorded pregnancy histories. Similar patterns are seen with migrations.

4.4.3 Summary

The subjects with missing reproductive histories were systematically different from the subjects with complete data in terms of mortality and socio-demographic factors. The missing reproduction data were not therefore MCAR.

There is no formal way to test whether the data were missing at random, but we can speculate about the reproductive histories of the women with missing data and whether the missingness of the reproductive histories was associated with the values of the reproductive histories (Table 4.10). In this summary table, the women are separated according to whether they were missed from the original DSS or the presumed additional data collection.

In the prospective data collection, the reproductive histories of women who experienced no pregnancies at all and women who did not report their fetal losses would not be recorded. Some of the women with missing reproductive histories were therefore nulligravid and nulliparous. The reproductive histories of women who did not experience any pregnancies after 1966, and women who migrated in to the area before 1982, were also not collected. It is likely that many, if not most, of these women were gravid or parous.

We also know the characteristics associated with being missed in the assumed additional data collection. We can therefore make inferences about the reproductive histories of these women, based on the patterns of fertility known to be associated with these traits at the time that the women were having children. It is probable that their reproductive histories varied. Fertility in Matlab has declined since the 1970's (Fauveau, Chakraborty 1994). Older women were therefore likely to be of higher parity. Hindu women in Matlab have lower fertility than Muslim women (Chaudhury 1971, Fauveau 1994). A study published in 1968 also showed that Hindu couples practised more family planning than Muslims (Aitken, Stoeckel 1971)[4.3], particularly older and less educated couples. Fertility in the comparison area has always been higher than in the intervention area (ICDDR,B 1990). Women with more education in Matlab have been shown to have lower fertility (Stoeckel, Choudhury 1969), despite the finding that in the rest of Bangladesh only high levels of educational attainment had a serious impact on fertility behaviour (Cleland et al 1993). Finally, it may be reasonable to assume that widowed and divorced women had lower parity, especially those who were already widowed or divorced by the time they were 45 years of age.

Table 4.10: Women with missing reproductive histories - Characteristics and most likely reproductive history	
Missed from original DSS data collection	
Characteristics	**Most likely reproductive history**
Married, experienced no pregnancies	**Nulligravid**
Married, experienced no live births, experienced fetal loss but not reported	**Nulliparous, Unknown number of fetal losses**
No pregnancies in the study area since 1966	**Unknown gravidity/parity**
Migrated in before 1982, no pregnancies in the study area	**Unknown gravidity/parity**
Unmarried, experienced no pregnancies or experienced fetal loss but not reported	**Nulligravid or nulliparous: NOT included in our study**
Missed from presumed additional data collection	
Characteristics	**Most likely reproductive history**
Older	**Higher gravidity/parity**
More Hindus	**Lower gravidity/parity**
More from comparison area	**Higher gravidity/parity**
Less educated	**Higher gravidity/parity**
More widowed or divorced	**Lower gravidity/parity**

[4.3] It is interesting to note that they also found that "*women who have had no children represent an extreme group for each religion since both religions stress that women must have some children. These childless women in both religions probably do not even consider family planning because of their desire to have at least some children. Thus, the differential practice of family planning is not likely to appear until after several children are born.*"

Were the data therefore missing at random? We know that the data were probably missing because the women were never asked to give their reproductive history. The information may not have been collected, either because the woman did not fit the criteria for collection of reproductive histories from the DSS or because the women had died and migrated or were older, less educated and so on and were therefore missed from the additional data collection. Other data such as education, religion and marital status were available for the women with missing reproductive histories suggesting that they did provide information to both the DSS and census data collection when it was requested. In fact, the education data were missing for a smaller proportion of these women than their counterparts with complete reproductive data. They were not therefore a sample of women who, for instance, suffered from mental illness and were hence unable to provide any data (and also possibly less likely to have had children).

All of these factors suggest that it is unlikely that the missing reproductive histories were systematically different from those in women with observed data. However, there is one important group of women in whom the missingness of the reproductive histories may be related to the values of the reproductive histories. These are the nulligravid women who experienced no pregnancy outcomes at all and would therefore have not been asked to provide a reproductive history during the DSS data collection. Although some (253) were identified, during the presumed additional data collection or if they migrated in after 1982, it is possible that some nulligravid women still had missing reproductive histories. However nulligravid women are a rarity in Matlab, particularly among the ever married. For the purpose of this analysis therefore, we have to assume that they are a small enough percentage of the total group with missing reproductive histories to assume that overall the data is missing at random.

4.5 Missing data strategy

Case deletion was not an appropriate strategy in this cohort. In particular, eliminating the subjects with missing reproductive history would lead to an underestimation of the true mortality in the cohort. Restricting the entry criteria in other ways such as to exclude most of the subjects with missing reproductive histories, for example taking June 30th 1983 as the first day of follow-up, limited the sample size to such a degree that no discrete patterns or statistically significant effects could be

identified. Nor was available-case analysis suitable. They would provide no information to the main analysis and the results may not have represented the true relationship in the population. Weighting the complete reproductive histories for the unobserved data would have been difficult, as information was available on the socio-demographic variables in most subjects. Simple imputation strategies were not thought to be adequate, as they would not reflect the uncertainty about which value to impute.

A sensitivity analysis was conducted to confirm that simple approaches were inadequate (Heitjan 1997). Table 4.11 shows crude results from the female data set in which the missing data were replaced with the mean value, the minimum value and the maximum value for each variable. The range of results obtained is wide, with crude mortality estimates merely indicating where the replacement has taken place. Subjects in each of the other categories have significantly lower mortality than subjects in the category where the missing values have been placed. For example, the mortality rate in subjects with none to two live births is 49.21 (95%CI 46.06-52.58) when the missing reproductive variables are replaced by the minimum value, compared with 9.68 (95%CI 7.80-12.02) in the same group pre-imputation. This mortality rate is significantly higher than that of the other parities.

Table 4.11: Results Of Crude Analysis Following Replacement With *Mean* Values (Parity = 7, Surviving Children = 5 for all with missing childbearing variables)					
Variable	**Number of deaths**	**Death rate (/1000 pyrs)**	**95% CI**	**Crude Rate Ratio**	**95% CI**
Parity:					
0-2	82	**9.68**	7.80-12.02	**0.74**	0.59-0.93
3-5	239	**6.34**	5.58-7.19	**0.48**	0.42-0.56
6-8 (mean)	*1283*	***13.08***	*12.39-13.82*	***1.00***	-
9+	335	**5.77**	5.18-6.42	**0.44**	0.39-0.50
Surviving children:					
0-2	200	**10.33**	8.99-11.87	**0.74**	0.63-0.85
3-5 (mean)	*1320*	***13.04***	*13.30-13.82*	**1.00**	-
6-8	372	**3.77**	3.31-5.28	***0.34***	0.30-0.38
9+	47	**3.28**	3.21-5.69	**0.30**	0.23-0.41
Results Of Crude Analysis Following Replacement With *Minimum* Values (Parity = 0, Surviving Children = 0 for all with missing childbearing variables)					
Variable	**Number of deaths**	**Death rate (/1000 pyrs)**	**95% CI**	**Crude Rate Ratio**	**95% CI**
Parity:					
0-2	*876*	***49.21***	*46.06-52.58*	***8.93***	*7.99-9.97*
3-5	239	**6.34**	5.58-7.19	**1.15**	0.98-1.34
6-8 (mean)	489	**5.51**	5.04-6.02	**1.00**	-
9+	335	**5.77**	5.18-6.42	**1.05**	0.91-1.20
Surviving children:					
0-2	*994*	***33.64***	*32.56-36.87*	***5.58***	*5.02-6.20*
3-5 (mean)	526	**6.21**	5.70-6.77	**1.00**	-
6-8	372	**3.77**	3.31-5.28	**0.77**	0.67-0.88
9+	47	**3.28**	3.21-5.69	**0.69**	0.51-0.93
Results Of Crude Analysis Following Replacement With *Maximum* Values (Parity = 18, Surviving Children = 15 for all with missing childbearing variables)					
Variable	**Number of deaths**	**Death rate (/1000 pyrs)**	**95% CI**	**Crude Rate Ratio**	**95% CI**
Parity:					
0-2	82	**9.68**	7.80-12.02	**1.76**	1.39-2.22
3-5	239	**6.34**	5.58-7.19	**1.15**	0.98-1.34
6-8 (mean)	489	**5.51**	5.04-6.02	**1.00**	-
9+	*1129*	***16.75***	*15.80-17.76*	***3.04***	*2.73-3.38*
Surviving children:					
0-2	200	**10.33**	8.99-11.87	**1.66**	1.41-1.96
3-5 (mean)	526	**6.21**	5.70-6.77	**1.00**	-
6-8	372	**3.77**	3.31-5.28	**0.77**	0.67-0.88
9+	*841*	***41.39***	*38.69-43.29*	***6.66***	*5.98-7.43*

4.6 Multiple imputation

4.6.1 Introduction

MI was therefore a more appropriate strategy for this situation: the missing reproductive histories were assumed to be MAR; data were available for many variables that were associated with the missingness, such that good predictions of the missing values could be obtained; and the additional uncertainty due to the missing data could be represented.

The multiple imputations were generated in Solas 2.0. In this package, ordinary least squares multiple regression is used to predict the missing data from the observed data. The statistical model of the linear regression is given by:

$$y = \beta_0 + \beta_1 \chi_1 + ... + \beta_p \chi_p + \varepsilon,$$

where y is the variable to be predicted, β is the regression coefficient associated with each predictor variable x, p is the number of covariates used in the prediction and ε represents an error term. Each imputation is generated independently by randomly drawing regression model parameters from the Bayesian posterior distribution of the above prediction, using "*noninformative*" priors. Additional variability, to prevent over-smoothing of the imputations, is also added to each imputed value in the form of a randomly drawn error term[4.3] .

4.6.2 Imputation model

There were five reproductive variables to be imputed (number of living sons, number of dead sons, number of living daughters, number of dead daughters, number of fetal losses). Schafer (1997) noted "*to produce high-quality imputations for a particular variable Y_l, the imputation model should include variables that are (a) potentially related to Y_l and (b) potentially related to the missingness of Y_l.*" Rubin and Schenker (1991) added that "*.....it is important to include as predictors as many of the variables that are likely to be used in subsequent analyses as possible. Leaving out such variables, even when they are weak predictors, implies that it is known with certainty that they have no relation with the missing values; the result is that correct uncertainty is not reflected.*"

Also, including as many predictors as possible makes the MAR assumption more plausible (Schafer 1997). Each of the socio-demographic variables including age, year, religion, education, area of residence, marital status, migration and mortality status, was therefore included in the predictive regression models.

[4.3] Full details of the methods used in Solas are given in the Solas Imputation Users Manual (1999).

Imputations were performed separately for the female and male cohorts, as there were significant proportions of missing male education and occupation in the females, and were not therefore used in the prediction models for the women. The variables were imputed under an assumption of joint normality, despite the fact that they were not all normally distributed. Simulation studies have shown that using the normal model for MI works reasonably well when the observed data are non-normal (Schafer 1997). In addition, no interactions between the socio-demographic and reproductive variables were specified to keep the models simple, as overly complex imputation models can lead to poor predictions (Barnard and Meng 1999). As a result however, estimates of interactions in the Poisson regression would be conservative (Schafer 1997).

4.6.3 Hot deck imputation

The missing data patterns in the Matlab samples were not monotone, as there was some missing covariate data[4.4]. However, when only the reproductive variables are taken into account the pattern was monotone, as all subjects with missing reproductive information were lacking data on all reproductive variables. Hot-deck imputation was therefore used to fill in the missing covariate values, thus creating a monotone missing pattern. In Solas, "imputation subsets" are created, containing subjects that have the same values of specified covariates that are highly correlated with the variable that has missing values. Missing values are replaced with values taken from randomly selected "donors" from the same imputation subset. This was adequate as the amounts of missing data in each covariate was small and subjects with missing covariate data were not systematically different from those with observed values.

4.6.4 How many imputations?

The efficiency of an estimate based on m imputations varies according to the rate of missing information[4.5] (Rubin 1987). Schafer (1999) showed that, unless the rates of missing information are unusually high, there is little gain in the efficiency of estimates from producing more than a few (that is, more than five) imputed data sets.

[4.4] Female education in the female data; male and female education and male occupation in the male data.
[4.5] A description of how this rate of missing information is calculated is given in Appendix 4.2.

Table 4.12: The percentage efficiency of an estimate achieved for different rates of missing information by the number of imputations					
	Rate of missing information, γ				
Number of imputations	0.1	0.3	0.5	0.7	0.9
3	97	91	86	81	77
5	98	94	91	88	85
10	99	97	95	93	92
20	100	99	98	97	96

In both sexes, the rate of missing information was less than 0.1 (see Appendix 4.2) and five imputations for each cohort were therefore adequate.

4.7 Summary

Multiple imputation was an appropriate method for dealing with the missing data encountered in this study. Figures 4.1 and 4.2 summarise the schemes used to perform the multiple imputations. In the next chapters, the data obtained from the imputations will be described. Then, the repeated-imputation inferences will be presented. They will be compared with the results obtained from analyses performed with cases missing reproductive histories deleted. An opportunity to compare imputation models also arose in this study as we used different variables to predict the reproductive histories in the females and the males. It was, therefore, possible to obtain five alternative data sets for the men from the female imputations. As we assumed that the women and men had the same reproductive histories, we would expect the association between reproductive history and mortality to be the same whether we use the data from the female or male imputations. Results for the male cohort using data from both sets of imputations will therefore also be compared.

> *"Isn't multiple imputation just making up data? When multiple imputation is presented to a new audience, some may view it as a kind of statistical alchemy in which information is somehow invented or created out of nothing. This objection is quite valid for single-imputation methods, which treat imputed values no differently from observed ones. Multiple imputation, however, is nothing more than a device for representing missing-data uncertainty."* (Schafer 1999)

Figure 4.1: Scheme for the multiple imputations in female data set

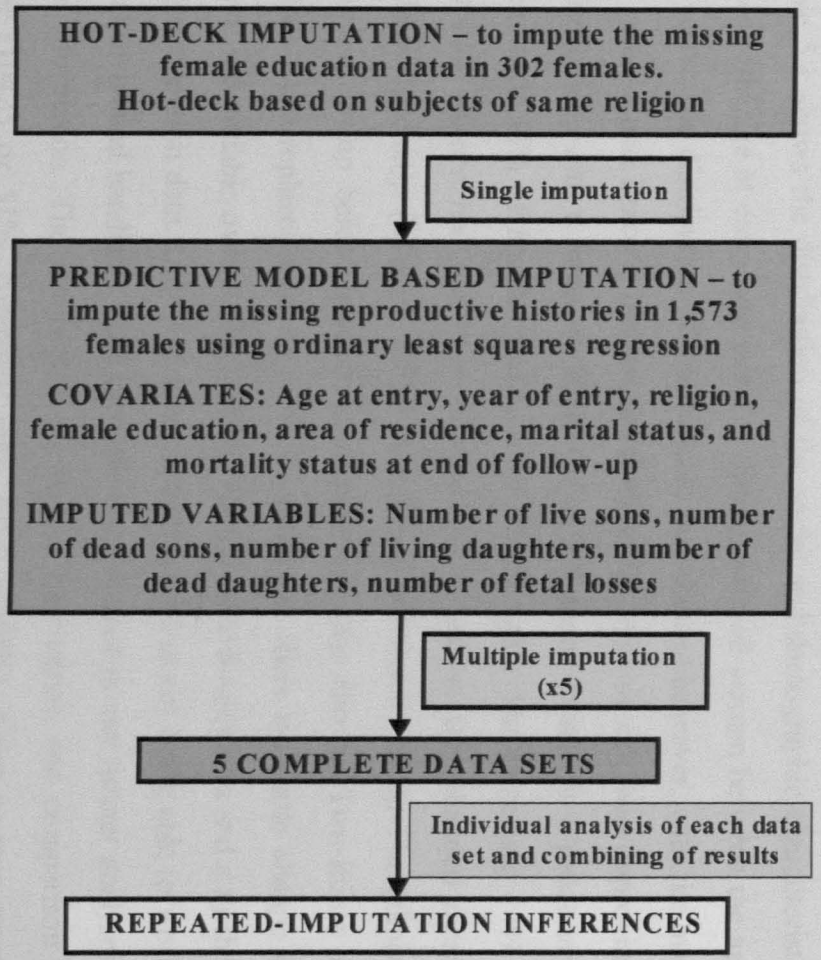
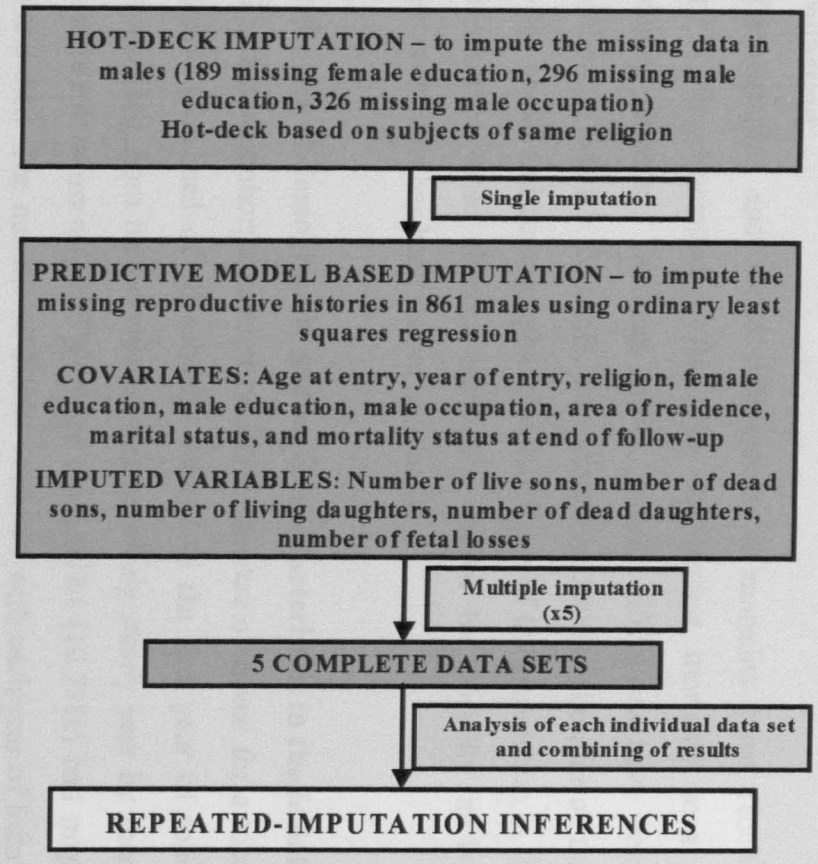


Figure 4.2: Scheme for the multiple imputations in male data set



In addition, 5 alternative complete data sets were obtained for the men using the data acquired from the female imputations. Repeated-imputation inferences were obtained for the men using these 5 data sets and the results compare with those obtained using data from the male imputations

5.1 Introduction

Demographic and social differentials in mortality have received widespread attention in the developed world, with the highest mortality seen in the socially disadvantaged (Preston, Taubman 1994). Similar differences have been shown in an elderly cohort in Matlab (Mostafa, van Ginneken 2000). The aim of this chapter is to describe the social and demographic characteristics of the population in this study and to examine whether these characteristics are related to mortality in both cohorts, in agreement with what has been shown previously.

5.2 Distribution of demographic and social characteristics in the females

The female cohort consisted of 20383 women observed for a total of 202322.20 person-years. One-third of all subjects entered in the first year of follow-up, and the numbers recruited from then onwards were relatively steady year by year. At the end of follow-up, 16260 women (79.77%) were alive, 2184 (10.71%) had migrated and 1939 (9.51%) had died. The number of deaths increased with each year of follow-up, reflecting the fact that women were becoming older. Migrations were relatively constant throughout the study period, with between 115 and 172 women leaving the study area each year.

Table 5.1 shows the distribution of the social and demographic characteristics in the female cohort. Age at entry was fixed by design, with all women between the ages of 45 and 55 years. The distribution of this variable was skewed however, with the majority entering at age 45 and hence a median value of 45.00. Age at exit was approximately normally distributed, with a mean of 56.66 (+/- 6.77) years. Matlab is a predominantly Muslim area, with 86% of females in the study of this faith. The remaining 14% were Hindus. 20% of women had not been educated at all and of the educated more had received Islamic teachings (Maktab, 60%) than formal education (20%). The numbers in each educational group before hotdeck imputation are also shown. Two-thirds of the missing values were replaced into the Maktab group but there was little change in the distribution of the variable overall. 94% of the women were housewives and a further 2% had missing occupation data. Only one woman was classed as not being able to work due to a physical or mental handicap. This variable was not used in any further analyses as it added little information. The numbers living in the intervention and comparison areas were similar (10425 or 51%, compared with 9958 or 49%). Most women were still

married at the start of the study but during follow-up 6334 women became widowed (52% of those originally married). Divorce was less common with 82 of those originally married divorcing by the end of the study, bringing the total number of divorced women to 255 (1.25%).

Table 5.1: The Demographic and Social Characteristics Of The Female Cohort

	Median		**Range**	
Age at entry	45.00		45.00-55.00	
	Mean (standard deviation)		**Range**	
Age at exit	56.66 (6.77)		45.04-71.55	
Religion	**Number**		**Percentage**	
Muslim	17520		85.95	
Hindu	2863		14.05	
Female education	**Number**	**Percentage**	**Number**	**Percentage**
	After hotdeck		**Before hotdeck**	
None	4091	20.07	4047	19.85
Maktab	12185	59.78	11982	58.78
Any formal	4107	20.15	4052	19.88
Unknown	-	-	302	1.48
Female occupation	**Number**		**Percentage**	
Housewife	19161		94.00	
Other	792		3.89	
Unknown	430		2.11	
Area of residence	**Number**		**Percentage**	
Intervention	10425		51.15	
Comparison	9958		48.85	
Marital status at entry	**Number**		**Percentage**	
Unmarried	17		0.08	
Married	16771		82.28	
Widowed	3422		16.79	
Divorced	173		0.85	
Marital status at exit	**Number**		**Percentage**	
Unmarried	17		0.08	
Married	10355		50.80	
Widowed	9756		47.86	
Divorced	255		1.25	
Total	**20383**		**100.00**	

5.3 Demographic and social differentials in mortality of females

Table 5.2 shows the crude female mortality rates and rate ratios by demographic and social factors. Adjusted rate ratios are also presented, in which the estimates have been controlled for all of the other factors in the table. Each of the variables was significantly related to mortality and the results of likelihood ratio tests, conducted to assess the statistical effect of variables on the Poisson regression models, are also presented.

The overall mortality rate was 9.58 deaths per 1000 person-years of follow-up. Mortality increased with age, with similar patterns in the crude and adjusted ratios. For example, the adjusted rate ratio (RR) for mortality in women aged 70 years and above compared with those aged 45 to 49.9 years was 12.24 (95%CI 7.69-19.47). Mortality also appeared to increase with time period in the crude analyses. However, once the estimates were adjusted for the other factors (and age in particular), mortality decreased with each year of follow-up. Hindus had higher mortality than Muslims. Once adjusted, the estimated increase reduced from 35% to 16% and was of borderline statistical significance (adjusted RR 1.16. 95%CI 0.99-1.36). Mortality decreased with increasing educational attainment. The adjusted rate ratio for women who had received Islamic teachings was 0.79 (95%CI 0.69-0.91) compared with women who had not been educated at all, and mortality was lower still in women who had received any formal education (adjusted RR compared with those who had none 0.62, 95% CI 0.52-0.73). Women living in the comparison area had significantly higher mortality than those in the intervention area (adjusted RR 1.13, 95% CI 1.03-1.24). Married women whose husbands were present or absent had similar mortality and were therefore analysed as one group. None of the 17 unmarried women died during follow-up, but both widowed and divorced women had higher mortality than those who remained married did. Widowed women had significantly higher mortality than the married (adjusted RR 1.30, 95%CI 1.18-1.43) although the adjusted estimate was markedly lower than the crude rate ratio. Divorced women had twice the mortality of married females, with no considerable change with adjustment (adjusted RR 2.36, 95% CI 1.68-3.31). Results of the multivariate analyses for the demographic and social variables before hotdeck imputation of female education are not shown. The results did not differ markedly to those presented here.

Table 5.2: Crude Mortality Rates And Crude And Adjusted Rate Ratios In Women Who Have Completed Their Reproduction: Demographic and Social Characteristics

Variable	Deaths	Person-years of follow-up	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj.[1] Rate Ratio	95% CI
Total	1939	202322.20	**9.58**	-	-	-	-
Age groups							
45 to 49.9 years	284	65683.42	**4.32**	**1.00**	-	**1.00**	-
50.0 to 54.9 years	468	61285.54	**7.64**	**1.77**	1.52-2.05	**1.71**	1.48-1.98
55.0 to 59.9 years	485	43710.48	**11.10**	**2.57**	2.22-2.97	**2.46**	2.12-2.86
60.0 to 64.9 years	426	23348.72	**18.25**	**4.21**	3.63-4.90	**4.15**	3.53-4.88
65.0 to 69.9 years	257	7934.91	**32.39**	**7.49**	6.33-8.87	**7.45**	6.16-9.01
70.0 + years	19	359.13	**52.91**	**12.24**	7.69-19.47	**13.32**	8.19-21.67
LR statistic = 534.69, p < 0.001[2]							
Time period:							
30/6/1982-29/6/1987	349	42551.38	**8.20**	**1.00**	-	**1.00**	-
30/6/1987-29/6/1992	504	60309.62	**8.36**	**1.02**	0.89-1.17	**0.82**	0.71-0.94
30/6/1992-31/12/1998	1086	99461.20	**10.92**	**1.33**	1.18-1.50	**0.77**	0.67-0.88
LR statistic = 14.42, p = 0.007							
Religion:							
Muslim	1604	175236.85	**9.15**	**1.00**	-	**1.00**	-
Hindu	335	27085.35	**12.37**	**1.35**	1.20-1.52	***1.16***[3]	*0.99-1.36*
LR statistic = 3.39, p = 0.066							
Female education:							
None	521	40238.92	**12.95**	**1.00**	-	**1.00**	-
Maktab	1178	124874.27	**9.43**	**0.73**	0.66-0.81	**0.79**	0.69-0.91
Any formal	240	37209.01	**6.45**	**0.50**	0.43-0.58	**0.62**	0.52-0.73
LR statistic = 32.07, p < 0.001							
Area of residence:							
Intervention	949	104547.68	**9.08**	**1.00**	-	**1.00**	-
Comparison	990	97774.52	**10.13**	**1.12**	1.02-1.22	**1.13**	1.03-1.24
LR statistic = 6.81, p = 0.009							
Marital status:							
Unmarried	0	81.55	**0.00**	-	-	-	-
Still married	886	125579.81	**7.06**	**1.00**	-	**1.00**	-
Widowed	1018	74727.75	**13.62**	**1.93**	1.76-2.11	**1.30**	1.18-1.43
Divorced	35	1933.09	**18.11**	**2.57**	1.83-3.60	**2.36**	1.68-3.31
LR statistic = 44.44, p = < 0.001							

1. Adjusted for all other factors in the table
2. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
3. *Estimates and confidence intervals in italics not statistically significant*

5.4 Distribution of demographic and social characteristics in the males

Overall, the 14803 men were observed for 124498 person-years. Male age at entry and exit were both approximately normally distributed. The mean male age at entry was 57.25 (+/- 5.74) years, reflecting the tendency of Bangladeshi men to marry women considerably younger than themselves. Age at death ranged from 42.02 to 98.90 years, with a mean of 65.66 (+/- 7.79 years). As the men entered on the same day as their wives, the pattern of male entry into the cohort was similar to that of the females. There were more deaths in the male cohort. 4394 men died during follow-up (29.68%) leaving 9335 men (63.06%) alive in December 1998. 1074 men (7.25%) migrated during the study period, with the numbers migrating relatively constant over the years. As shown in Table 5.3, the distribution of men by religion and area of residence was also similar to the female cohort, as one would expect. More of these men had received some formal education compared with their wives (51% versus 22%) and fewer had not been educated at all (14% versus 19%). Two thirds were employed in "unskilled" professions, with around a third performing work that was considered skilled. There were very few men who did not work or were considered disabled. All men were married at the start of follow-up, with 1024 becoming widowed during the study period and 32 getting divorced.

Table 5.3 also shows how the missing values for male and female education and male occupation were assigned during the hotdeck imputation. Most of the missing male education values were replaced into the educated (Maktab or any formal education groups). Two-thirds of the missing values in female education were replaced into the Maktab group. The replacement into the missing occupation variable followed the distribution of the observed values. There was little change in the distribution of any of the variables overall.

Table 5.3: The Demographic and Social Characteristics Of The Male Cohort

Age at entry	**Mean (standard deviation)**		**Range**	
	57.25 (5.74)		40.11-90.70	
Age at exit	**Mean (standard deviation)**		**Range**	
	65.66 (7.79)		42.02-98.90	
Religion	**Number**		**Percentage**	
Muslim	12703		85.81	
Hindu	2100		14.19	
Area of residence	**Number**		**Percentage**	
Intervention	7656		51.72	
Comparison	7147		48.28	
Male education	**Number**	**Percentage**	**Number**	**Percentage**
	After hotdeck		**Before hotdeck**	
None	2059	13.91	2026	13.69
Maktab	5182	35.01	5074	34.28
Any formal	7562	51.08	7407	50.04
Unknown	-	-	296	2.00
Wife's education	**Number**	**Percentage**	**Number**	**Percentage**
	After hotdeck		**Before hotdeck**	
None	2819	19.04	2796	18.89
Maktab	8750	59.11	8626	58.27
Any formal	3234	21.85	3192	21.56
Unknown	-	-	189	1.28
Male occupation	**Number**	**Percentage**	**Number**	**Percentage**
	After hotdeck		**Before hotdeck**	
None	131	0.88	129	0.87
Unskilled	9780	66.07	9559	64.57
Skilled	4696	31.72	4598	31.06
Disabled	196	1.32	191	1.29
Unknown	-	-	326	2.20
Marital status at exit	**Number**		**Percentage**	
Married	13747		92.87	
Widowed	1024		6.92	
Divorced	32		0.22	
Total	**14803**		**100.00**	

5.5 Demographic and social differentials in mortality of males

Crude mortality rates and rate ratios are shown in Table 5.4, along with rate ratios adjusted for each of the other factors in the table. The mortality rate overall was 35.29 deaths per 1000 person-years of follow-up, confirming that the men died more than the women. As expected, mortality increased with age and decreased between the first time period and the second. However, mortality in the last period was not significantly lower than that in the first. Hindu men had significantly higher rates of mortality than Muslim men did (adjusted RR 1.13, 95% CI 1.01-1.27). Male mortality decreased with the level of both male and female education, but the effect was greatest if the wives had received any formal education (adjusted RR for men whose wives had received any formal education compared with those whose wives had received no education 0.75, 95% CI 0.66-0.85; corresponding RR for male education 0.83, 95% CI 0.74-0.92). There was no significant interaction between male and female education (likelihood ratio test statistic 2.95, p = 0.57). However, on excluding subjects who had received Islamic teachings from the analysis (subjects remaining = 17387), male mortality was significantly lower if both husband and wife had received any formal education than if the husband had received formal education and the wife had not (crude RR 0.85, 95% CI 0.75-0.96; adjusted RR 0.78, 95% CI 0.65-0.95). Men in skilled employment had significantly lower mortality than those in unskilled jobs, whilst the mortality of disabled men was three times higher than in those with unskilled work. Men with no employment did not have significantly different mortality to those in unskilled jobs (adjusted RR 1.07, 95% CI 0.79-1.44). Males living in the comparison area had slightly higher mortality than men in the intervention area (adjusted RR 1.09 95% CI 1.02-1.15). Becoming widowed during the follow-up period conferred a significantly higher mortality on individuals compared with remaining married (adjusted RR 1.26, 95% CI 1.12-1.42). 9 deaths occurred in the 32 men who were divorced but their mortality did not differ significantly from the married men. Crude and adjusted estimates did not differ markedly except for religion and widowhood, for which the rate ratios were reduced in the multivariate models. The results obtained were not notably different from the estimates obtained in a data set in which the unknown values had not been replaced by hotdeck imputation (results not shown).

Table 5.4: Crude mortality rates and rate ratios in the men who had completed their reproduction: Demographic and Social Characteristics

Variable	Deaths	Person-years of follow-up	Mortality Rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj.[1] Rate Ratio	95% CI
Total	4394	124498.00	**35.29**	-	-	-	-
Age groups							
40-49.9 years	11	1119.26	**9.83**	**1.00**	-	**1.00**	-
50-59.9 years	816	45055.40	**18.11**	**1.84**	1.02-3.34	**1.78**	0.98-3.22
60-69.9 years	2010	57298.09	**35.08**	**3.57**	1.97-6.46	**3.37**	1.86-6.10
70-79.9 years	1259	18755.20	**67.13**	**6.83**	3.77-12.37	**6.33**	3.50-11.47
80-89.9 years	284	2190.47	**129.65**	**13.19**	7.22-24.09	**11.72**	6.41-21.42
90+ years	14	79.58	**175.92**	**17.90**	8.13-39.43	**14.34**	6.50-31.66
LR statistic = 1098.88, $p < 0.001$[2]							
Time period:							
30/6/1982-29/6/1987	939	27087.43	**34.67**	**1.00**	-	**1.00**	-
30/6/1987-29/6/1992	1228	37776.41	**32.51**	***0.94***[3]	*0.86-1.02*	**0.91**	0.83-0.99
30/6/1992-31/12/1998	2227	59634.16	**37.34**	**1.08**	1.00-1.16	***0.95***	*0.88-1.03*
LR statistic = 5.04, p = 0.080							
Religion:							
Muslim	3705	108089.18	**34.28**	**1.00**	-	**1.00**	-
Hindu	689	16408.82	**41.99**	**1.22**	1.13-1.33	**1.13**	1.01-1.27
LR statistic = 4.42, p = 0.035							
Male's education:							
None	698	15894.34	**43.91**	**1.00**	-	**1.00**	-
Maktab	1605	43168.64	**37.18**	**0.85**	0.77-0.93	***0.98***	*0.87-1.10*
Any formal	2091	65435.02	**31.95**	**0.73**	0.67-0.79	**0.83**	0.74-0.92
LR statistic = 29.55, $p < 0.001$							
Female education:							
None	980	22382.74	**43.79**	**1.00**	-	**1.00**	-
Maktab	2689	75949.03	**35.41**	**0.81**	0.75-0.87	**0.84**	0.75-0.95
Any formal	725	26166.23	**27.71**	**0.63**	0.57-0.70	**0.75**	0.66-0.85
LR statistic = 20.17, $p < 0.001$							
Male occupation:							
Unskilled	3171	85979.19	**36.88**	**1.00**	-	**1.00**	-
None	43	1011.50	**42.51**	***1.15***	*0.85-1.56*	***1.07***	*0.79-1.44*
Skilled	1034	36540.53	**28.30**	**0.77**	0.72-0.82	**0.89**	0.83-0.95
Disabled	146	966.78	**151.02**	**4.09**	3.46-4.83	**3.21**	2.72-3.80
LR statistic = 146.03, $p < 0.001$							
Area of residence:							
Intervention	2204	64852.78	**33.98**	**1.00**	-	**1.00**	-
Comparison	2190	59645.22	**36.72**	**1.08**	1.02-1.15	**1.09**	1.02-1.15
LR statistic = 7.32, p = 0.009							
Marital status:							
Still married	4100	119622.23	**34.27**	**1.00**	-	**1.00**	-
Widowed	285	4662.47	**61.13**	**1.78**	1.58-2.01	**1.26**	1.12-1.42
Divorced	9	213.30	**42.19**	***1.23***	*0.64-2.37*	***0.96***	*0.50-1.85*
LR statistic = 12.98, p = 0.002							

1. Estimates and confidence intervals from Poisson regression, adjusting for all other factors in the table
2. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
3. *Estimates and confidence intervals in italics not statistically significant*

5.6 Summary

These results confirm that there were significant demographic and social differentials in the mortality of adults who had completed their reproduction in Matlab, with the patterns seen similar to those expected and comparable in women and men. Mortality increased with age, decreased with time period and increased with social disadvantage. A particularly interesting finding was that male mortality decreased more if the man's wife had received any education than if the man himself had done so, and mortality was significantly lower in men when both the husband and wife had received any formal education than when only the man had done so.

6.1 Introduction

The main aim of this study was to examine the association between reproductive variables and mortality in Bangladeshi women who had completed their reproduction. In this chapter, the female reproductive histories acquired by imputation are described. Then, a summary of the relationship between the main reproductive variables of interest and socio-demographic factors is presented. Finally, the results of the Poisson regression analysis to assess the relationship between reproductive history and all-cause mortality are presented.

6.2 Distribution of the female reproductive histories after imputation

The reproductive variables obtained from the female imputations are shown in Table A6.1 to A6.5 in Appendix 6.1. Overall the imputed values were reasonable, with no impossible values such as 100 living sons. The distribution of each variable remained similar to that seen before imputation with the same means, medians and ranges to the original data set. The imputed estimates tended to take the lower values of each variable and there was little, if any, replacement at the higher extremes of each value. For example, most of the missing values in the living sons variable were imputed with a value of between one and four. Only in two imputed data sets was a missing value given a value of eight in the living son variable, and there was no imputation into categories higher than this.

The frequency distributions of the main variables in the five imputed data sets and in the original data set are shown in Table 6.1. The individual numbers are shown rather than a summary (such as a box-and-whisker plot) to illustrate how the imputed data sets differed. The mean parity in each case was approximately seven, with a range of none to 18 live births. Only around 1.4% of women were nulliparous and over 15% of women had experienced ten or more live births in all data sets. The mean number of surviving children on entry into the cohort was five, with a range of none to 15 children alive. The fetal loss variable was positively skewed, with around 66% of women never experiencing a fetal loss. The number of fetal losses experienced ranged from none to 12.

Table 6.1: Reproductive variables from the imputed data sets

	Imputed data set 1		Imputed data set 2		Imputed data set 3		Imputed data set 4		Imputed data set 5	
Parity	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**
0	**290**	1.42	**293**	1.44	**291**	1.43	**293**	1.44	**294**	1.44
1	**268**	1.31	**273**	1.34	**273**	1.34	**273**	1.34	**276**	1.35
2	**393**	1.93	**401**	1.97	**398**	1.95	**399**	1.96	**400**	1.96
3	**788**	3.87	**804**	3.94	**817**	4.01	**810**	3.97	**815**	4.00
4	**1391**	6.82	**1403**	6.88	**1402**	6.88	**1402**	6.88	**1399**	6.86
5	**2282**	11.20	**2315**	11.36	**2307**	11.32	**2291**	11.24	**2302**	11.29
6	**3069**	15.06	**3022**	14.83	**2996**	14.70	**3040**	14.91	**3012**	14.78
7	**3273**	16.06	**3235**	15.87	**3257**	15.98	**3245**	15.92	**3259**	15.99
8	**3055**	14.99	**3013**	14.78	**3028**	14.86	**3024**	14.84	**3023**	14.83
9	**2420**	11.87	**2419**	11.87	**2411**	11.83	**2403**	11.79	**2410**	11.82
10	**1569**	7.70	**1578**	7.74	**1593**	7.82	**1569**	7.70	**1570**	7.70
11	**887**	4.35	**908**	4.45	**892**	4.38	**902**	4.43	**906**	4.44
12	**414**	2.03	**411**	2.02	**422**	2.07	**429**	2.10	**422**	2.07
13	**181**	0.89	**193**	0.95	**187**	0.92	**194**	0.95	**180**	0.88
14+	**103**	0.51	**115**	0.56	**109**	0.53	**109**	0.53	**115**	0.56
Total	**20383**	-	**20383**	-	**20383**	-	**20383**	-	**20383**	-
Mean (SD)	**6.98 (2.57)**		**6.98 (2.60)**		**6.98 (2.59)**		**6.98 (2.59)**		**6.97 (2.59)**	
Range	**0-18**		**0-18**		**0-18**		**0-18**		**0-18**	
Surviving children	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**
0	**432**	2.12	**437**	2.14	**439**	2.15	**433**	2.12	**443**	2.17
1	**597**	2.93	**621**	3.05	**608**	2.98	**617**	3.03	**620**	3.04
2	**1089**	5.34	**1101**	5.40	**1107**	5.43	**1111**	5.45	**1093**	5.36
3	**2015**	9.89	**2050**	10.06	**2052**	10.07	**2055**	10.08	**2037**	9.99
4	**3259**	15.99	**3237**	15.88	**3228**	15.84	**3228**	15.84	**3229**	15.84
5	**4022**	19.73	**3943**	19.34	**3974**	19.50	**3972**	19.49	**3956**	19.41
6	**3689**	18.10	**3683**	18.07	**3665**	17.98	**3678**	18.04	**3695**	18.13
7	**2713**	13.31	**2715**	13.32	**2716**	13.32	**2698**	13.24	**2714**	13.32
8+	**2567**	12.59	**2596**	12.74	**2594**	12.73	**2591**	12.71	**2596**	12.74
Total	**20383**	-	**20383**	-	**20383**	-	**20383**	-	**20383**	-
Mean (SD)	**5.16 (2.12)**		**5.16 (2.13)**		**5.16 (2.13)**		**5.16 (2.13)**		**5.16 (2.13)**	
Range	**0-15**		**0-15**		**0-15**		**0-15**		**0-15**	
Fetal losses	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**
0	**13410**	65.79	**13440**	65.94	**13415**	65.81	**13426**	65.87	**13405**	65.77
1	**4596**	22.55	**4543**	22.29	**4579**	22.46	**4581**	22.47	**4569**	22.42
2	**1534**	7.53	**1563**	7.67	**1551**	7.61	**1542**	7.57	**1566**	7.68
3	**533**	2.61	**527**	2.59	**528**	2.59	**524**	2.57	**534**	2.62
4	**179**	0.88	**179**	0.88	**179**	0.88	**179**	0.88	**178**	0.87
5+	**131**	0.64	**131**	0.64	**131**	0.64	**131**	0.64	**131**	0.64
Total	**20383**	-	**20383**	-	**20383**	-	**20383**	-	**20383**	-
Mean (SD)	**0.53 (0.93)**		**0.53 (0.93)**		**0.53 (0.93)**		**0.53 (0.93)**		**0.53 (0.93)**	
Median	**0**		**0**		**0**		**0**		**0**	
Range	**0-12**		**0-12**		**0-12**		**0-12**		**0-12**	

6.3 The association between reproductive history and the socio-demographic variables

Tables 6.2 to 6.4 summarise the relationships between the three main reproductive variables and socio-demographic status. For parity and number of surviving children, mean values in different demographic and socio-economic groups are compared. When the socio-demographic variable was binary, the means were compared using a t test. It was possible to combine the means and results of the t tests for the five imputed data sets in Solas. These combined statistics are presented. When the socio-demographic variable had more than two categories, the means were compared using analysis-of-variance. No methodology for combining the ANOVA results could be found and the results presented are an example from one of the imputed data sets. ANOVA results from each imputed data sets were similar, but the results presented may not completely reflect the uncertainty due to the missing data. The fetal loss variable was skewed but the median number of fetal losses in different socio-economic groups was not informative as it was always zero. The proportions that had and had not experienced a fetal loss were therefore compared in different socio-economic groups, using a chi-squared test. Once again, no methodology for combining proportions and the results of a chi-squared test could be found and the results presented are an example from one of the imputed data sets. The results from each imputed data set were similar but as with the ANOVA results, the ones presented may not completely reflect the uncertainty due to the missing data.

The reproductive variables all varied significantly with socio-demographic status. Women who were younger at entry had lower mean parity (Table 6.2), but more surviving children on average (Table 6.3). Both mean parity and number of surviving children seemed to decrease with year of entry. Muslim women had significantly higher parity than Hindu women (mean of 7.05 compared with 6.51, p value for t test < 0.0001) and more surviving children (mean of 5.22 compared with 4.83, p value for t test < 0.0001). Parity was higher in the comparison area, as was the mean number of surviving children. Interestingly, the mean parity was lowest in women with no formal education (6.67, SD 2.56). The mean number of surviving children increased with educational attainment. Women who were married at entry had the highest mean parity (7.21, SD 2.49), followed by widowed women (6.09, SD 2.58). The divorced and unmarried had much lower average numbers of live births (2.71, SD 2.22 and 2.41, SD 2.15).

Consequently, women who were married and widowed at entry had most surviving children at entry.

Table 6.2: Relationship of parity with other socio-demographic factors		
Age at entry	**Combined mean (SD)**	**t test for comparison of means**
45.0-49.9	6.93 (2.53)	t value = -6.11
50.0-55.0	7.24 (2.74)	p < 0.001
Year of entry	**Example mean (SD)**	**ANOVA for comparison of means**
1982-1987	7.24 (2.61)	
1988-1992	6.99 (2.47)	F value = 249.43
1993-1998	6.23 (2.43)	p < 0.001
Religion	**Combined mean (SD)**	**t test for comparison of means**
Muslim	7.05 (2.57)	t value = 10.55
Hindu	6.51 (2.52)	p < 0.001
Area of residence	**Combined mean (SD)**	**t test for comparison of means**
Intervention	6.77 (2.53)	t value = -11.71
Comparison	7.19 (2.59)	p < 0.001
Education	**Example mean (SD)**	**ANOVA for comparison of means**
None	6.67 (2.56)	
Maktab	7.09 (2.60)	F value = 40.53
Any	6.95 (2.49)	p < 0.001
Unknown	-	
Marital status at entry	**Example mean (SD)**	**ANOVA for comparison of means**
Unmarried	2.41 (2.15)	
Married	7.21 (2.49)	F value = 376.48
Widowed	6.09 (2.58)	p < 0.001
Divorced	2.71 (2.22)	

Table 6.3: Relationship of surviving children with other socio-demographic factors		
Age at entry	**Combined mean (SD)**	**t test for comparison of means**
45.0-49.9	5.19 (2.08)	t value = 4.14
50.0-55.0	5.01 (2.29)	p < 0.001
Year of entry	**Example mean (SD)**	**ANOVA for comparison of means**
1982-1987	5.18 (2.18)	
1988-1992	5.37 (2.04)	F value = 52.05
1993-1998	4.91 (2.43)	p < 0.001
Religion	**Combined mean (SD)**	**t test for comparison of means**
Muslim	5.22 (2.12)	t value = 9.36
Hindu	4.83 (2.07)	p < 0.001
Area of residence	**Combined mean (SD)**	**t test for comparison of means**
Intervention	5.10 (2.08)	t value = -4.67
Comparison	5.23 (2.16)	p < 0.001
Education	**Example mean (SD)**	**ANOVA for comparison of means**
None	4.81 (2.06)	
Maktab	5.15 (2.12)	F value = 124.89
Any	5.54 (2.09)	p < 0.001
Unknown	-	
Marital status at entry	**Example mean (SD)**	**ANOVA for comparison of means**
Unmarried	1.53 (1.42)	
Married	5.42 (2.04)	F value = 590.00
Widowed	4.13 (2.01)	p < 0.001
Divorced	1.50 (1.49)	

t test: combined estimate for the five imputed data sets.
ANOVA: results for one imputed data set as an example.

There were also significant differences in the reporting of fetal losses by socio-demographic characteristics. The results presented below are an example from one of the imputed data sets. A higher proportion of women who were younger than 50 years on entry reported having ever experienced a fetal loss compared with women who were older than 50 years at entry. Women who entered the cohort later were also more likely to have experienced a fetal loss than women who entered in the first five years. Significantly greater proportions of Muslim women and more women from the comparison area reported having lost a pregnancy. The proportion reporting fetal losses tended to rise with educational attainment, although these differences were not statistically significant. 35 percent of married women had experienced a fetal loss compared with 27 percent of the widowed, 18 percent of the unmarried and 17 percent of the divorced.

Table 6.4: Relationship of fetal losses with other socio-demographic factors (Example from one of the imputed data set)

Age at entry	**Fetal losses**		**Chi squared comparing proportions**
	No	**Yes**	
45.0-49.9	11142 (64.98%)	6006 (35.02%)	X^2 statistic = 31.86
50.0-55.0	2268 (70.11%)	967 (29.89%)	$p < 0.001$
Year of entry	**Fetal losses**		**Chi squared comparing proportions**
	No	**Yes**	
1982-1987	7927 (67.87%)	3759 (32.17%)	X^2 statistic = 51.15
1988-1992	2783 (62.75%)	1652 (37.25%)	$p < 0.001$
1993-1998	2700 (63.35%)	1562 (36.65%)	
Religion	**Fetal losses**		**Chi squared comparing proportions**
	No	**Yes**	
Muslim	11461 (65.42%)	6059 (34.58%)	X^2 statistic = 7.73
Hindu	1949 (68.08%)	914 (31.92%)	$p = 0.005$
Area of residence	**Fetal losses**		**Chi squared comparing proportions**
	No	**Yes**	
Intervention	7065 (67.77%)	3360 (32.23%)	X^2 statistic = 37.16
Comparison	6345 (63.72%)	3613 (36.28%)	$p < 0.001$
Education	**Fetal losses**		**Chi squared comparing proportions**
	No	**Yes**	
None	2725 (66.61%)	1366 (33.39%)	X^2 statistic = 3.46
Maktab	8028 (65.88%)	4157 (34.12%)	$p = 0.177$
Any	2657 (64.69%)	1450 (35.31%)	
Marital status at entry	**Fetal losses**		**Chi squared comparing proportions**
	No	**Yes**	
Unmarried	14 (82.35%)	3 (17.65%)	X^2 statistic = 134.05
Married	10743 (64.06%)	6028 (35.94%)	$p < 0.001$
Widowed	2509 (73.32%)	913 (26.68%)	
Divorced	144 (83.24%)	29 (16.76%)	
Total	13410 (65.79%)	6973 (34.21%)	20383 (100.00%)

6.4 The association between reproductive variables and all-cause mortality

6.4.1 Introduction

The repeated-imputation inferences for the associations of reproductive variables with all-cause mortality are given in Figures 6.1 to 6.12 and Tables 6.5 to 6.22. The average number of deaths and average person-years from the five imputed data sets are presented. Crude mortality rates, crude rate ratios and rate ratios adjusted for the socio-demographic factors are shown, each combined from the results of the five imputed data sets. 95% confidence intervals are also presented, which include a measure of the between-imputation variance. Rate ratios are always presented relative to the largest group in each variable. In addition the results of a combined likelihood ratio test, conducted to examine the statistical significance of each of the reproductive variables on the Poisson regression models in the presence of the socio-demographic variables, are presented. For comparison, the equivalent results for the original data set are given in Appendix 6.2. The similarities and differences in the results are discussed in the final chapter of the thesis.

6.4.2 Parity

The mortality of nulliparous women was not significantly different from that of parous women in the crude or multivariate analyses (adjusted RR 0.97, 95% CI 0.60-1.35, Table 6.5). Nor was there a clear trend in mortality with the number of live births (Figure 6.1). When parity was included in the model as a continuous variable, there was no significant trend in mortality with parity (Wald test statistic 1.78, $p = 0.092$). The adjusted rate ratio per child born was 0.98 (95% CI 0.96-1.01). In the crude analysis, women who had experienced between none and two live births had significantly higher mortality than women of parity three to five. Once the estimates were adjusted for the demographic and social factors, this relationship was no longer significant.

Similar results were obtained when examining the relationship of gravidity (number of pregnancies) with all-cause mortality rather than parity (Table 6.6). There was no significant difference in the mortality of nulligravid and gravid women, and there was no clear or significant trend in mortality with an increasing number of pregnancies.

Figure 6.1: Crude female mortality rates (+ 95% CI) with parity

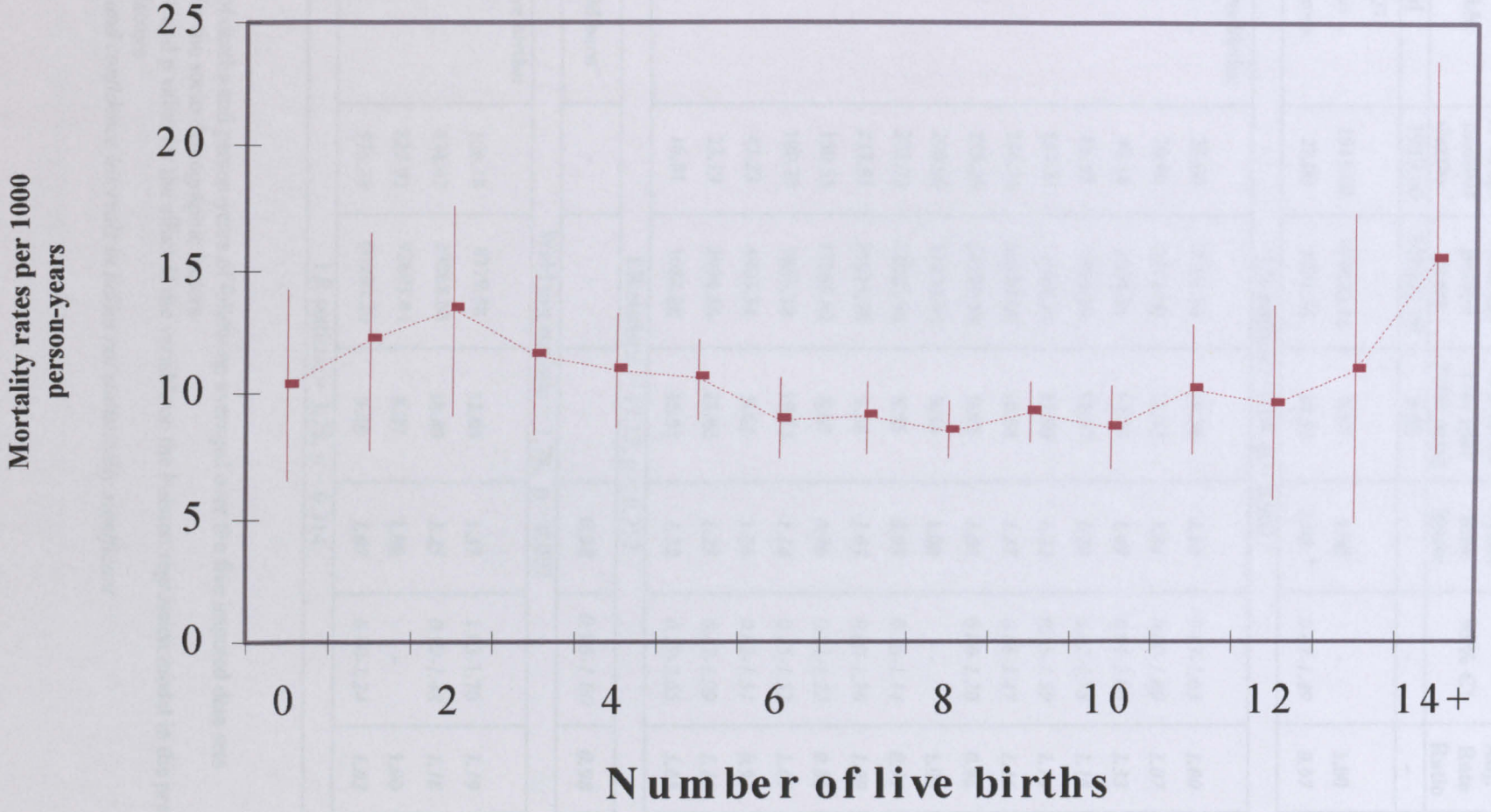


Table 6.5: Mortality In Women Who Have Completed Their Reproduction By Parity

Variable	Average number deaths [1]	Average person years	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj.[2] Rate Ratio	95% CI
Total	1939.00	202322.20	**9.58**	-	-	-	-
Parity:							
Parous	1911.00	199620.46	**9.57**	**1.00**	-	**1.00**	-
Nulliparous	28.00	2701.74	**10.36**	***1.08*** [4]	*0.67-1.49*	***0.97***	*0.60-1.35*
LR statistic = 0.04, p = 0.962 [3]							
Number of live births:							
0	28.00	2701.74	**10.36**	***1.15***	*0.67-1.63*	***1.00***	*0.58-1.42*
1	30.00	2473.90	**12.13**	***1.34***	*0.80-1.89*	***1.07***	*0.62-1.52*
2	48.18	3604.24	**13.37**	***1.49***	*0.91-2.06*	***1.33***	*0.81-1.85*
3	86.45	7460.36	**11.57**	***1.29***	*0.82-1.75*	***1.10***	*0.70-1.50*
4	131.21	11924.32	**11.00**	***1.22***	*0.85-1.59*	***1.14***	*0.79-1.49*
5	216.76	20484.00	**10.58**	***1.17***	*0.88-1.47*	***1.16***	*0.87-1.45*
6	258.29	28599.54	**9.03**	***1.00***	*0.80-1.20*	***0.98***	*0.79-1.18*
7	290.00	32070.94	**9.04**	**1.00**	-	**1.00**	-
8	273.73	32022.96	**8.55**	***0.95***	*0.76-1.14*	***0.91***	*0.73-1.09*
9	237.81	25674.98	**9.26**	***1.03***	*0.80-1.26*	***1.00***	*0.78-1.22*
10	150.55	17365.82	**8.67**	***0.96***	*0.71-1.22*	***0.88***	*0.65-1.11*
11	100.79	9856.32	**10.23**	***1.14***	*0.75-1.52*	***1.09***	*0.72-1.46*
12	47.23	4903.34	**9.62**	***1.06***	*0.62-1.51*	***0.93***	*0.54-1.32*
13	23.19	2094.86	**11.03**	***1.23***	*0.47-1.99*	***1.16***	*0.45-1.86*
14+	16.81	1084.88	**15.51**	***1.72***	*0.79-2.65*	***1.65***	*0.75-2.54*
LR statistic = 17.13, p = 0.257							
RR "per child born"	-	-	-	***0.98***	*0.96-1.00*	***0.98***	*0.96-1.01*
Wald test statistic = 1.78, p = 0.092							
Number of live births:							
0-2	106.18	8779.88	**12.09**	**1.37**	1.03-1.70	***1.19***	*0.89-1.50*
3-5	434.42	39868.68	**10.89**	***1.23***	*0.99-1.48*	***1.18***	*0.95-1.42*
6-8	822.02	92693.44	**8.87**	**1.00**	-	**1.00**	-
9+	576.38	60980.20	**9.45**	***1.07***	*0.90-1.24*	***1.02***	*0.86-1.19*
LR statistic = 3.78, p = 0.314							

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
4. *Estimates and confidence intervals in italics not statistically significant*

Table 6.6: Mortality In Women Who Have Completed Their Reproduction By Gravidity							
Variable	**Average number deaths[1]**	**Average person years**	**Mortality rate (per 1000 pyrs)**	**Crude Rate Ratio**	**95% CI**	**Adj.[2] Rate Ratio**	**95% CI**
Total	1939.00	202322.20	**9.58**	-	-	-	-
Gravidity:							
Gravid	1911.37	199940.42	**9.56**	**1.00**	-	**1.00**	-
Nulligravid	27.63	2381.78	**11.59**	***1.21*** [4]	*0.75-1.67*	***1.07***	*0.66-1.47*
LR statistic = 0.07, p = 0.889[3]							
Number of pregnancies:							
0	27.63	2381.79	**11.59**	***1.25***	*0.75-1.76*	***1.08***	*0.64-1.52*
1	25.32	2283.06	**11.13**	***1.20***	*0.71-1.70*	***0.96***	*0.56-1.37*
2	38.87	3266.31	**11.88**	***1.29***	*0.80-1.77*	***1.15***	*0.71-1.59*
3	63.8	5900.69	**10.81**	***1.17***	*0.74-1.60*	***1.00***	*0.64-1.37*
4	104.39	9822.28	**10.62**	***1.15***	*0.82-1.48*	***1.03***	*0.73-1.33*
5	168.65	16684.54	**10.11**	***1.09***	*0.81-1.38*	***1.09***	*0.81-1.37*
6	234.66	24571.29	**9.54**	***1.03***	*0.81-1.26*	***1.01***	*0.79-1.23*
7	259.57	29404.93	**8.83**	***0.96***	*0.75-1.16*	***0.97***	*0.77-1.18*
8	287.39	31057.53	**9.25**	**1.00**	-	**1.00**	-
9	249.79	26909.71	**9.28**	***1.00***	*0.82-1.19*	***1.01***	*0.82-1.19*
10	189.03	21749.42	**8.70**	***0.94***	*0.74-1.14*	***0.90***	*0.71-1.09*
11	134.22	13026.22	**10.32**	***1.12***	*0.87-1.36*	***1.11***	*0.87-1.35*
12	68.35	7705.98	**8.82**	***0.96***	*0.59-1.32*	***0.94***	*0.59-1.29*
13	50.18	4350.08	**11.53**	***1.25***	*0.80-1.69*	***1.25***	*0.81-1.69*
14+	37.15	3208.37	**11.59**	***1.26***	*0.73-1.78*	***1.25***	*0.72-1.78*
LR statistic = 11.35, p = 0.682							
RR "per pregnancy"	-	-	-	***0.99***	*0.97-1.01*	***1.00***	*0.98-1.02*
Wald test statistic = 0.30, p = 0.857							
Number of pregnancies:							
0-2	91.82	7931.16	**11.57**	***1.26***	*0.96-1.56*	***1.08***	*0.81-1.34*
3-5	336.84	32407.51	**10.40**	***1.13***	*0.89-1.38*	***1.06***	*0.83-1.29*
6-8	781.62	85033.75	**9.19**	**1.00**	-	**1.00**	-
9+	728.72	76949.78	**9.47**	***1.03***	*0.91-1.15*	***1.01***	*0.90-1.13*
LR statistic = 1.87, p = 0.798							

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
4. *Estimates and confidence intervals in italics not statistically significant*

6.4.3 Surviving children

In the crude analysis, women with any surviving children on entry had significantly lower mortality than women with no surviving children (crude RR 0.72, 95% CI 0.51-0.94, Table 6.7). In the adjusted analysis, women with any surviving children appeared to have 15% lower mortality, although the estimate was no longer statistically significant (adjusted RR 0.85, 95% CI 0.59-1.11). Mortality decreased as the number of surviving children increased (Figure 6.2). This trend was statistically significant (Wald test statistic 5.33, $p < 0.001$). The adjusted reduction in mortality rate per surviving child was 0.91 (95% CI 0.89-0.93). When the surviving children variable was grouped, women with between zero and two surviving children had 35% higher mortality than women with three to five surviving children (adjusted RR 1.35, 95% CI 1.10-1.61). Women with between six and eight or more than nine surviving children both had significantly lower mortality than with women with between three and five (adjusted RR 0.78, 95% CI 0.67-0.87 and 0.74, 95% CI 0.54-0.94). Women in whom less than a quarter of their live births had survived had almost twice the mortality of women with between three-quarters and all of their children still alive (crude RR 2.26, 95% CI 1.72-2.81, adjusted RR 1.78, 95% CI 1.34-2.22).

The magnitude of the associations reduced when other variables (notably age, female education and marital status) were added to the models, suggesting that there was some confounding by these variables.

Parity and surviving children are closely related: a woman has to be of high parity to have a high number of surviving children. Due to this potential 'interaction', the relationship between these two variables was examined in two ways. The trends in mortality with parity were examined in women with each number of surviving children, and vice versa. The variables were also combined into one summary variable that noted the parity and surviving children of a woman.

When the crude rates were examined, the trends noted above seemed to persist (Figure 6.3). However, when examining trends by parity in each surviving children group, there appeared to be a trend of increasing mortality with increasing parity in the crude analysis (Table 6.9). For example, in women with three to five surviving children, there

was a 7% increase in mortality per live birth (95% CI 1.03-1.12, Wald test p value = 0.034). After adjusting for socio-demographic variables, the rate ratio per live birth decreased in each for each surviving children group, and none of the estimates or trends were still significant. For example, in women with three to five surviving children, the adjusted rate ratio per live birth was 1.05 (95% CI 0.97-1.09, Wald test p value = 0.096). On examining trends in mortality with surviving children in parity groups, mortality rates decreased significantly per surviving child. The estimates and trends were all statistically significant, but decreased slightly in magnitude on adjusting for socio-demographic factors. For example, in women who had experienced six to eight live births, there was a 22 percent decrease in mortality rates per surviving child in the crude analysis (95% CI 0.73-0.83, Wald test p value < 0.001) that reduced when adjusted to a 17 percent decrease in mortality rates per surviving child (95% CI 0.78-0.88, Wald test p value < 0.001).

These patterns were the same when examining the effects of parity and surviving children in combination (Table 6.10), with a slight increase in mortality with parity and a tendency for mortality to decrease with the number of surviving children. Again, these trends appeared to be confounded by socio-economic status as for example the excess risk among those with between none and two surviving children reduced substantially and lost significance among women of parity six to eight. Even after adjusting for socio-economic status, lowest relative mortality rates were still observed among those of parity six to eight and parity nine in whom all of their children had survived.

Figure 6.2: Crude female mortality rates (+95% CI) by number of surviving children

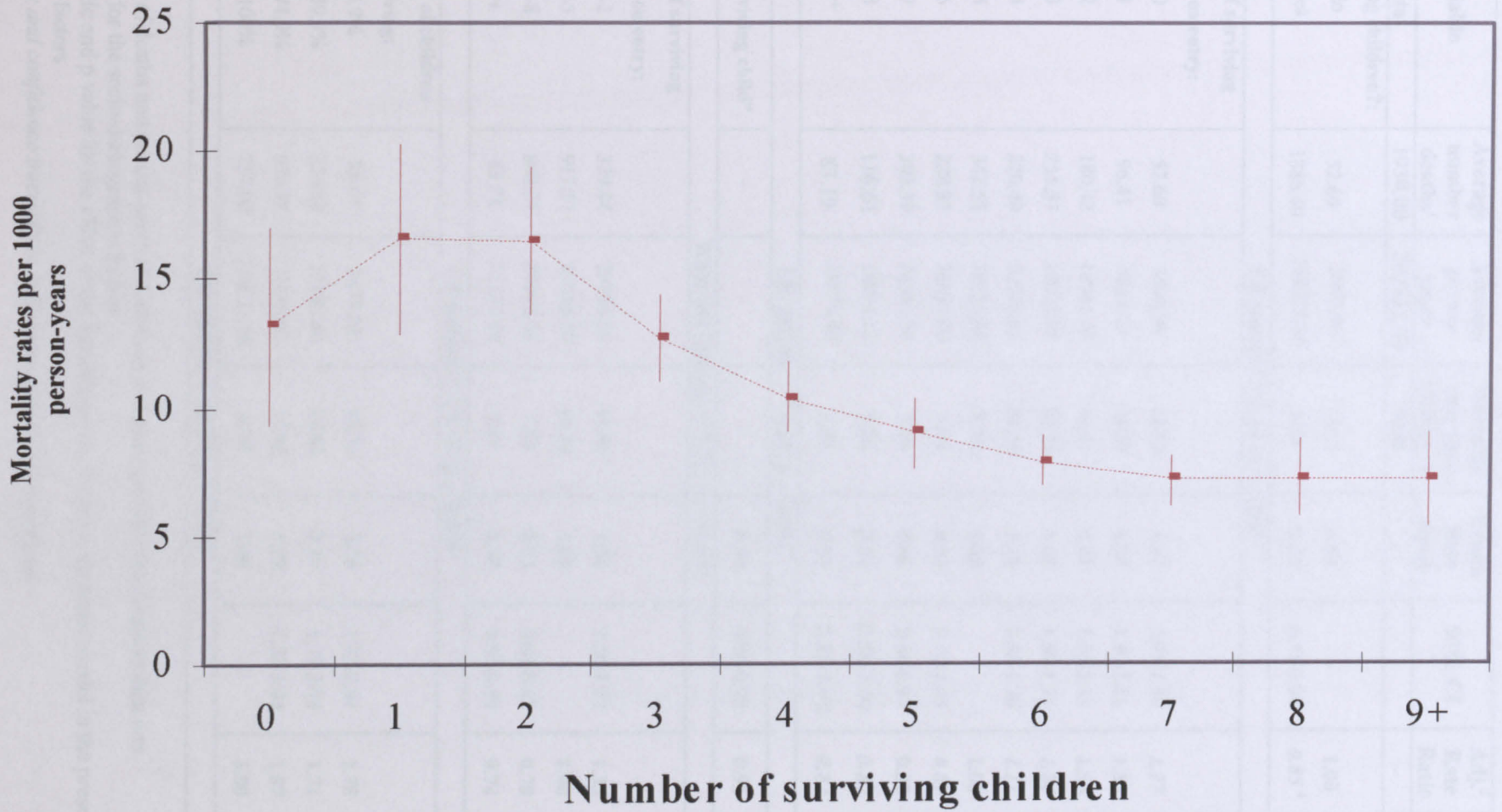


Table 6.7: Mortality In Women Who Have Completed Their Reproduction By Surviving Children							
Variable	**Average number deaths[1]**	**Average person years**	**Mortality rate (per 1000 pyrs)**	**Crude Rate Ratio**	**95% CI**	**Adj.[2] Rate Ratio**	**95% CI**
Total	1939.00	202322.20	**9.58**	-	-	-	-
Any surviving children?:							
No	52.60	3992.96	**13.17**	**1.00**	-	**1.00**	-
Yes	1886.40	198329.24	**9.51**	**0.72**	0.51-0.94	***0.85*** [4]	*0.59-1.11*
LR statistic = 1.14, p = 0.546[3]							
Number of surviving children on entry:							
0	52.60	3992.96	**13.17**	***1.47***	*0.95-1.99*	***1.27***	*0.81-1.73*
1	96.41	5814.79	**16.57**	**1.85**	1.30-2.41	**1.53**	1.06-2.00
2	180.42	10947.50	**16.47**	**1.84**	1.35-2.33	**1.55**	1.13-1.97
3	254.57	20033.28	**12.71**	**1.42**	1.09-1.75	***1.24***	*0.95-1.52*
4	320.40	30870.62	**10.38**	***1.16***	*0.95-1.36*	***1.11***	*0.91-1.31*
5	342.58	38126.80	**8.98**	**1.00**	-	**1.00**	-
6	288.83	36631.00	**7.88**	***0.88***	*0.71-1.05*	***0.89***	*0.72-1.06*
7	203.39	28307.73	**7.19**	**0.80**	0.64-0.97	**0.82**	0.65-0.99
8	116.61	16058.12	**7.26**	***0.81***	*0.58-1.04*	***0.82***	*0.59-1.06*
9+	83.19	11539.40	**7.21**	***0.81***	*0.55-1.06*	***0.81***	*0.55-1.06*
LR statistic = 71.48, p < 0.001							
RR "per surviving child"	-	-	-	**0.88**	0.86-0.90	**0.91**	0.89-0.93
Wald test statistic = 5.33, p < 0.001							
Number of surviving children on entry:							
0-2	329.44	20755.25	**15.87**	**1.54**	1.26-1.82	**1.35**	1.10-1.61
3-5	917.57	89030.70	**10.31**	**1.00**	-	**1.00**	-
6-8	608.21	80996.86	**7.52**	**0.73**	0.64-0.82	**0.78**	0.69-0.87
9+	83.78	11539.39	**7.21**	**0.70**	0.51-0.89	**0.74**	0.54-0.94
LR statistic = 65.38, p < 0.001							
Percentage of children surviving:							
0-24.9%	85.04	5477.83	**18.93**	**2.26**	1.72-2.81	**1.78**	1.34-2.22
25.0-49.9%	226.18	15182.46	**14.83**	**2.17**	1.77-2.58	**1.71**	1.38-2.03
50.0-74.9%	870.78	71428.93	**11.02**	**1.78**	1.52-2.04	**1.57**	1.34-1.81
75.0-100%	757.00	110232.98	**6.74**	**1.00**	-	**1.00**	-
LR statistic = 92.90, p < 0.001							

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
4. *Estimates and confidence intervals in italics not statistically significant*

Figure 6.3: Crude female mortality rates by number of surviving children, in parity groups

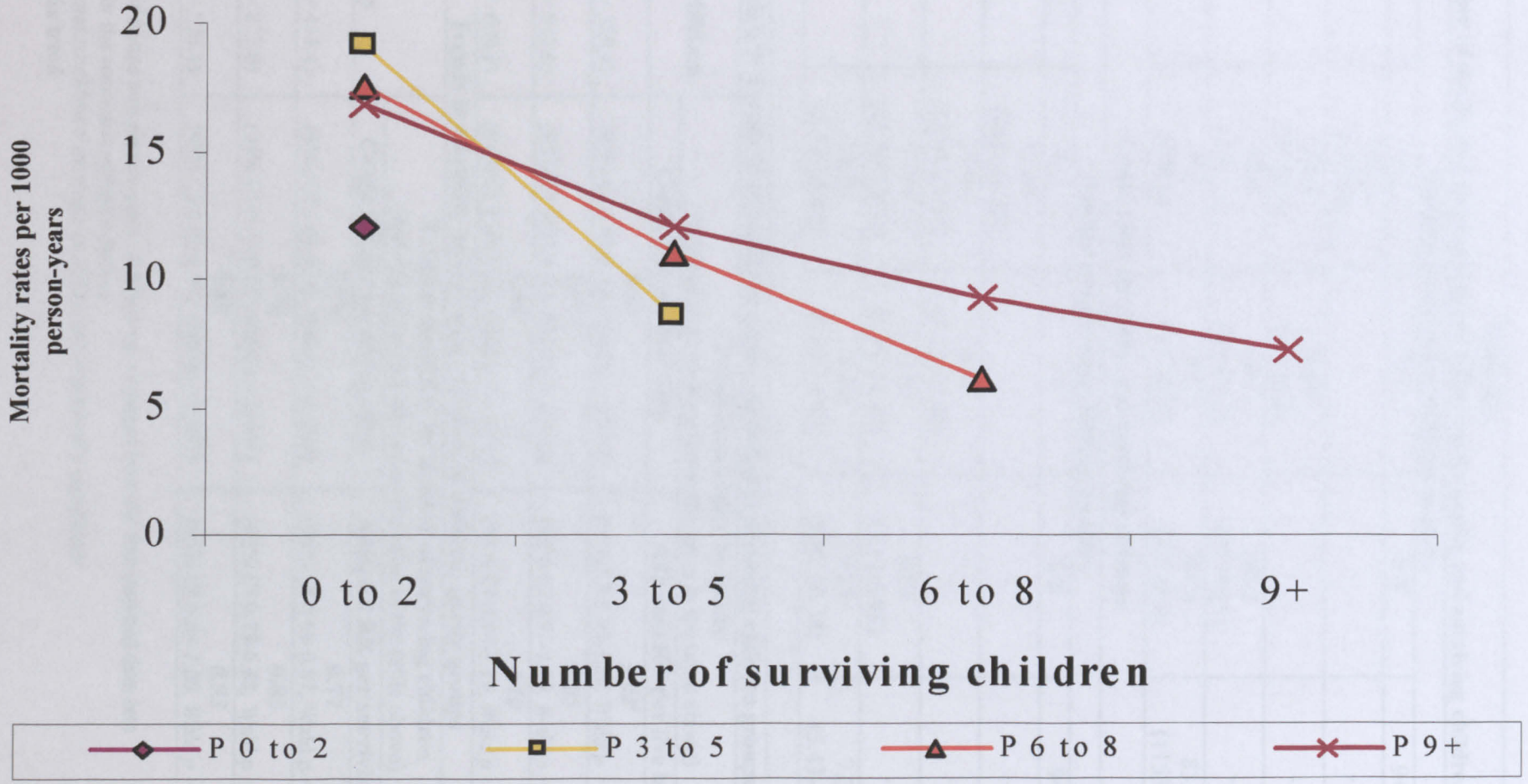


Table 6.8: Number of deaths and person-years of follow-up for parity and surviving children[1]				
Number of surviving children on entry				
Parity	0-2	3-5	6-8	9+
0-2	106.2 (8779.9)	-	-	-
3-5	166.4 (8723.9)	268.0 (31144.8)	-	-
6-8	48.6 (2761.5)	509.2 (46183.5)	264.2 (43748.5)	-
9+	8.2 (490.0)	140.4 (11702.3)	344.6 (37248.4)	83.2 (11539.4)
Crude rates for parity and surviving children				
Number of surviving children on entry				
Parity	0-2	3-5	6-8	9+
0-2	12.09 (9.63-14.56)	-	-	-
3-5	19.06 (14.97-23.15)	8.60 (7.21-10.00)	-	-
6-8	17.59 (11.50-23.67)	11.02 (9.62-12.43)	6.04 (5.11-6.98)	-
9+	16.73 (5.14-28.32)	12.00 (9.91-14.09)	9.25 (8.02-10.48)	7.21 (5.43-8.99)

Table 6.9: Trends in mortality by parity, in different surviving children groups		
Surviving children	**Trend in mortality by parity** (equivalent to looking down the rates in the table above)	
	Crude RR per live birth	**Adjusted RR per live birth[2]**
0-2 (no. deaths = 329.4)	**1.03** (95% CI 1.01-1.12, Wald p = 0.034)	***1.02***[3] (95% CI *0.98-1.09, Wald p = 0.164*[4])
3-5 (no. deaths = 917.6)	**1.07** (95% CI 1.03-1.12, Wald p = 0.012)	***1.05*** (95% CI *0.97-1.09, Wald p = 0.096*)
6-8 (no. deaths = 608.8)	**1.14** (95% CI 1.06-1.22, Wald p = 0.027)	***1.10*** (95% CI *0.98-1.19, Wald p = 0.129*)
Trends in mortality by surviving children, in different parity groups		
Parity	**Trend in mortality by number of surviving children** (equivalent to looking across the rates in the table above)	
	Crude RR per surviving child	**Adjusted RR per surviving child**
3-5 (no. deaths = 434.4)	**0.70** (95% CI 0.61-0.78, Wald p < 0.001)	**0.77** (95% CI 0.66-0.87, Wald p < 0.001)
6-8 (no. deaths = 822.0)	**0.78** (95% CI 0.73-0.83, Wald p < 0.001)	**0.83** (95% CI 0.78-0.88, Wald p < 0.001)
9+ (no. deaths = 576.4)	**0.89** (95% CI 0.83-0.95, Wald p = 0.007)	***0.93*** (95% CI *0.86-1.00, Wald p = 0.083*)

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. *Estimates and confidence intervals in italics not statistically significant*
4. Wald test for trend

Table 6.10:
Crude Rate Ratios for Parity and Surviving Children

	Number of surviving children on entry			
Parity	0-2	3-5	6-8	9+
0-2	*1.10 (0.81-1.39)*[1]	-	-	-
3-5	1.74 (1.24-2.23)	0.78 (0.60-0.97)	-	-
6-8	1.60 (1.03-2.16)	**1.00 (reference)**	0.55 (0.45-0.65)	-
9+	*1.52 (0.47-2.57)*	*1.09 (0.87-1.31)*	*0.84 (0.67-1.01)*	0.66 (0.47-0.84)

Adjusted Rate Ratios for Parity and Surviving Children[2]

	Number of surviving children on entry			
Parity	0-2	3-5	6-8	9+
0-2	*1.08 (0.80-1.36)*	-	-	-
3-5	1.53 (1.10-1.97)	*0.85 (0.65-1.04)*	-	-
6-8	*1.30 (0.85-1.76)*	**1.00 (reference)**	0.63 (0.52-0.75)	-
9+	*1.36 (0.42-2.31)*	*1.02 (0.81-1.23)*	*0.86 (0.69-1.04)*	0.71 (0.50-0.91)

1. *Results in italics not statistically significant*
2. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors: LR statistic = 96.95, $p < 0.001$
   Adjusted for the socio-demographic factors

6.5.4 Surviving sons

Table 6.11 shows the relationship between surviving sons and mortality. Women who had any surviving sons on entry had significantly lower mortality than those with no sons alive in the crude (RR 0.69, 95% CI 0.59-0.79) and adjusted (RR 0.78, 95% CI 0.68-0.87) estimates. Mortality decreased with the number of surviving sons (Figure 6.4). There was a reduction in mortality rates of 9% per surviving son (adjusted, 95% CI 0.88-0.94). When the surviving children variable was grouped, women with few (0-2) surviving sons had a 23% higher adjusted mortality (95% CI 1.10-1.38) than women with three to five surviving sons. There was no association between the percentage of all live births who were male and female all-cause mortality. Mortality was higher if only a small percentage of the surviving children were male however. When up to a quarter of the surviving children were male, women had a significant 20% increased mortality (adjusted RR 1.20, 95% CI 1.04-1.36). All of the above results appeared to be confounded by socio-demographic status, with the largest changes in estimates with age, female education and changes in marital status.

As with parity and surviving children, the number of surviving children and number of surviving sons were examined in combination in an attempt to ascertain whether it was surviving children or surviving sons that had the largest influence on mortality. Crude mortality rates suggest that mortality decreased with the number of surviving children, although the differences were most apparent when there were only between none and two surviving sons (Figure 6.5). When trends were examined, mortality tended to reduce with the number of surviving children in each surviving sons group, but mortality only reduced with the number of surviving sons in women with only three to five surviving children (Table 6.12). This trend of reducing mortality with surviving children was confirmed when the two variables were examined in combination, although again it was most apparent when there were only none to two surviving sons (Table 6.13).

Figure 6.4: Crude female mortality rates (+95% CI) by number of surviving sons

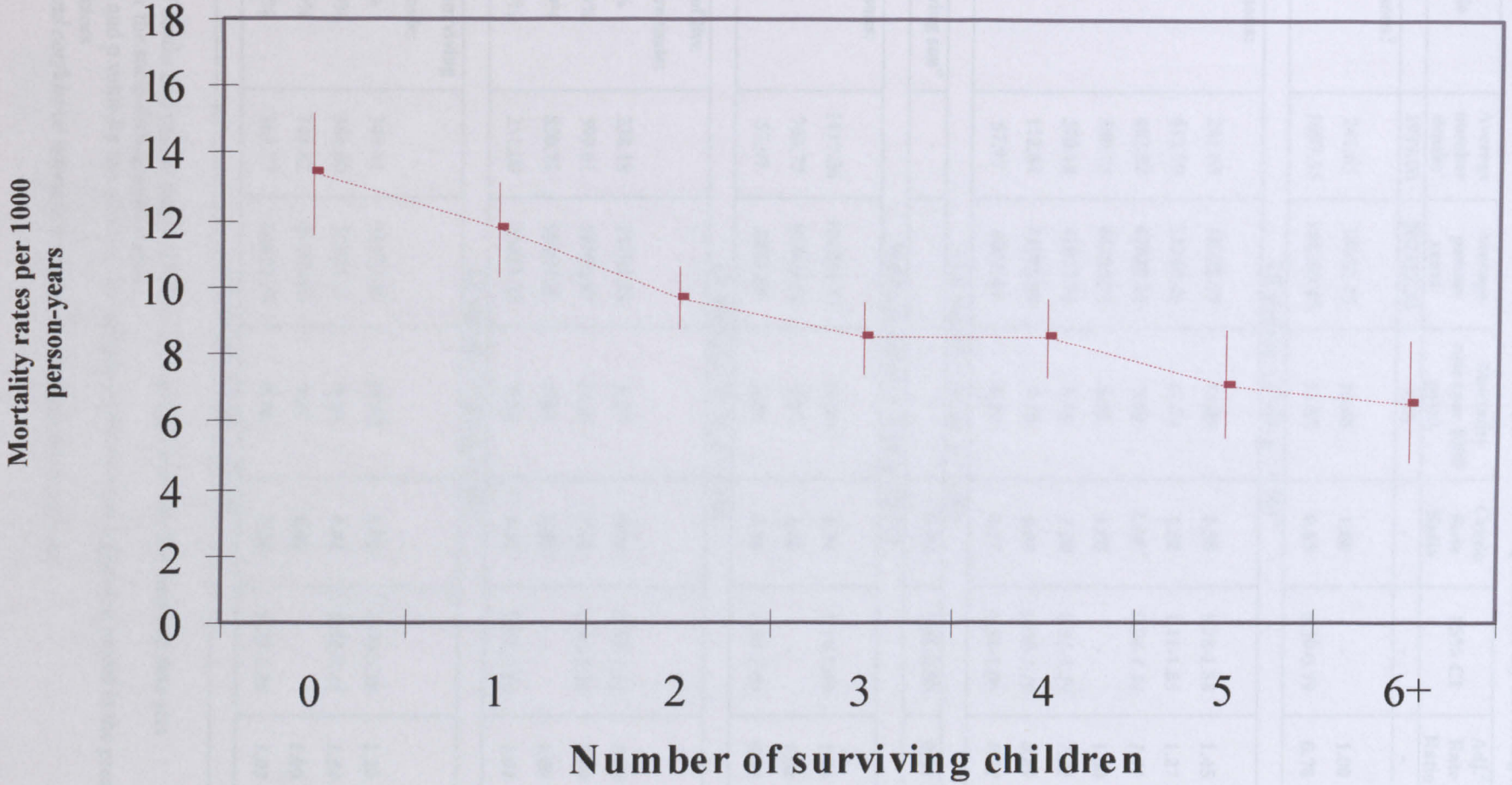


Table 6.11: Mortality In Women Who Have Completed Their Reproduction By Surviving Sons							
Variable	**Average number deaths[1]**	**Average person years**	**Mortality rate (per 1000 pyrs)**	**Crude Rate Ratio**	**95% CI**	**Adj.[2] Rate Ratio**	**95% CI**
Total	1939.00	202322.20	**9.58**	-	-	-	-
Surviving sons?							
No	241.65	18022.75	**13.40**	**1.00**	-	**1.00**	-
Yes	1697.35	184299.45	**11.57**	**0.69**	0.59-0.79	**0.78**	0.68-0.87
LR statistic = 17.04, $p < 0.001$[3]							
Surviving sons:							
0	241.65	18022.75	**13.40**	**1.58**	1.28-1.88	**1.45**	1.17-1.73
1	412.79	35240.46	**11.71**	**1.38**	1.11-1.65	**1.27**	1.03-1.52
2	462.82	47828.36	**9.68**	***1.14***[4]	*0.94-1.34*	***1.11***	*0.91-1.30*
3	380.75	44705.53	**8.52**	**1.00**	-	**1.00**	-
4	270.18	31817.76	**8.49**	***1.00***	*0.81-1.19*	***1.02***	*0.83-1.21*
5	112.84	15885.89	**7.10**	***0.84***	*0.60-1.19*	***0.89***	*0.63-1.14*
6+	57.97	8821.45	**6.57**	**0.77**	0.54-1.00	***0.82***	*0.58-1.05*
LR statistic = 42.24, $p < 0.001$							
RR "per surviving son"	-	-	-	0.89	0.86-0.90	**0.91**	0.88-0.94
Wald test statistic = 3.58, $p = 0.018$							
Surviving sons:							
0-2	1117.26	101091.57	**11.05**	**1.34**	1.19-1.49	**1.23**	1.10-1.38
3-5	763.77	92409.18	**8.27**	**1.00**	-	**1.00**	-
6+	57.97	8821.45	**6.57**	***0.80***	*0.58-1.01*	***0.83***	*0.60-1.05*
LR statistic = 26.78, $p = 0.001$							
Percentage of live births that were male:							
0-24.9%	238.18	25705.23	**9.27**	***0.99***	*0.83-1.14*	***1.02***	*0.86-1.18*
25.0-49.9%	599.61	59896.62	**10.01**	***1.06***	*0.90-1.23*	***1.09***	*0.92-1.26*
50.0-74.9%	850.21	90397.00	**9.41**	**1.00**	-	**1.00**	-
75.0-100%	251.00	26323.35	**9.54**	***1.01***	*0.87-1.16*	***1.01***	*0.86-1.16*
LR statistic = 0.87, $p = 0.984$							
% of children surviving who were male:							
0-24.9%	345.41	31112.40	**11.10**	**1.22**	1.06-1.38	**1.20**	1.04-1.36
25.0-49.9%	484.00	52597.21	**9.20**	***1.01***	*0.89-1.14*	***1.04***	*0.91-1.17*
50.0-74.9%	743.82	81975.00	**9.07**	**1.00**	-	**1.00**	-
75.0-100%	365.77	36637.59	**9.98**	***1.10***	*0.92-1.28*	***1.08***	*0.91-1.26*
LR statistic = 8.50, $p = 0.025$							

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
4. *Estimates and confidence intervals in italics not statistically significant*

Figure 6.5: Crude female mortality rates by number of surviving children, in surviving sons groups

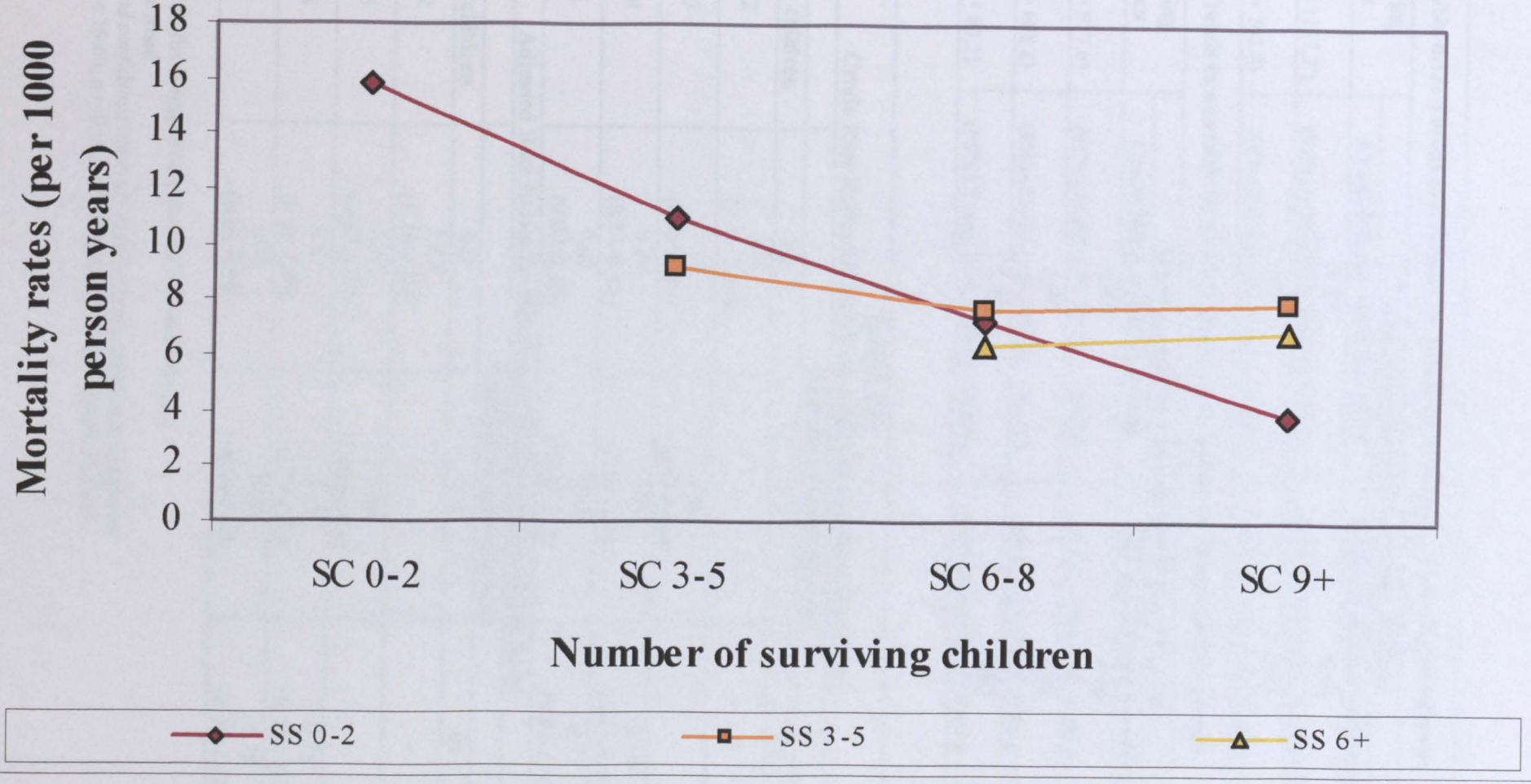


Table 6.12: Trends in mortality by surviving children, in surviving son groups		
Surviving sons	**Trend in mortality by surviving children**	
	Crude RR per surviving child	**Adjusted RR per surviving child**
0-2 (no. deaths = 1117.2[1])	**0.88** (95% CI 0.84-0.91, Wald p = 0.013)	**0.91** (95% CI 0.87-0.94, Wald p = 0.027[2])
3-5 (no. deaths = 763.8)	**0.93** (95% CI 0.86-0.99, Wald p < 0.001)	***0.95*** [3] (95% CI *0.88-1.02, Wald p = 0.173*)
Trends in mortality by surviving sons, in different surviving children groups		
Surviving children	**Trend in mortality by number of surviving sons**	
	Crude RR per surviving sons	**Adjusted RR per surviving sons**
3-5 (no. deaths = 917.6)	**0.89** (95% CI 0.84-0.95, Wald p = 0.008)	**0.90** (95% CI 0.84-0.96, Wald p = 0.012)
6-8 (no. deaths = 608.8)	***1.00*** (95% CI *0.95-1.06, Wald p = 0.213*)	***1.01*** (95% CI *0.95-1.07, Wald p = 0.275*)
9+ (no. deaths = 83.2)	***1.01*** (95% CI *0.88-1.14, Wald p = 0.427*)	***1.03*** (95% CI *0.89-1.17, Wald p = 0.555*)

Table 6.13: **Crude Rate Ratios for Surviving Children and Surviving Sons**			
	Number of surviving sons		
Surviving children	0-2	3-5	6+
0-2	1.72 (1.31-2.14)	-	-
3-5	*1.19* *(0.99-1.39)*	**1.00** **(reference)**	-
6-8	0.79 (0.61-0.98)	0.84 (0.69-0.99)	0.69 (0.43-0.94)
9+	0.42 (0.02-0.85)	*0.86* *(0.53-1.19)*	*0.75* *(0.41-1.08)*
Adjusted Rate Ratios for Surviving Children and Surviving Sons[4]			
	Number of surviving sons		
Surviving children	0-2	3-5	6+
0-2	1.53 (1.16-1.90)	-	-
3-5	*1.17* *(0.97-1.36)*	**1.00** **(reference)**	-
6-8	*0.83* *(0.63-1.03)*	*0.89* *(0.73-1.05)*	*0.75* *(0.47-1.02)*
9+	0.44 (0.02-0.89)	*0.90* *(0.56-1.24)*	*0.79* *(0.43-1.14)*

1. Numbers of deaths averaged over the five imputed data sets
2. Wald test for trend
3. *Estimates and confidence intervals in italics not statistically significant*
4. LR statistic = 16.60, p = 0.002, adjusted for socio-demographic factors

6.4.6 Surviving daughters

Having any surviving daughters was also associated with lower mortality in both the crude (RR 0.66, 95% CI 0.56-0.76) and adjusted (RR 0.75, 95% CI 0.64-0.87) analyses, as shown in Table 6.14. The trend was for decreasing mortality with an increasing number of surviving daughters (Figure 6.6), with an adjusted decrease of 6% per surviving daughter (95% CI 0.91-0.97, Wald test statistic 3.78, $p < 0.001$). When the surviving daughter variable was grouped, women with six or more surviving daughters had significantly lower mortality than women with between three and five surviving daughters (adjusted RR 0.64, 95% CI 0.47-0.81). This estimate did not change between the crude and multivariate analyses.

As with surviving children and surviving sons, the number of surviving children and number of surviving daughters were examined in combination in an attempt to ascertain whether it was surviving children or surviving daughters that had the most influence on mortality. As with the surviving sons, crude mortality rates confirm that mortality decreased with the number of surviving children, with the decrease greatest when there were less surviving daughters (Figure 6.6). Mortality reduced with the number of surviving children in each surviving daughter group (estimates and trends significant), but there was no trend of reducing mortality by surviving daughters in surviving children groups (Table 6.15). This trend of reducing mortality with surviving children, regardless of the number of surviving daughters, was confirmed when the two variables were examined in combination (Table 6.16).

Figure 6.6: Crude female mortality rates (+95% CI) by number of surviving daughters

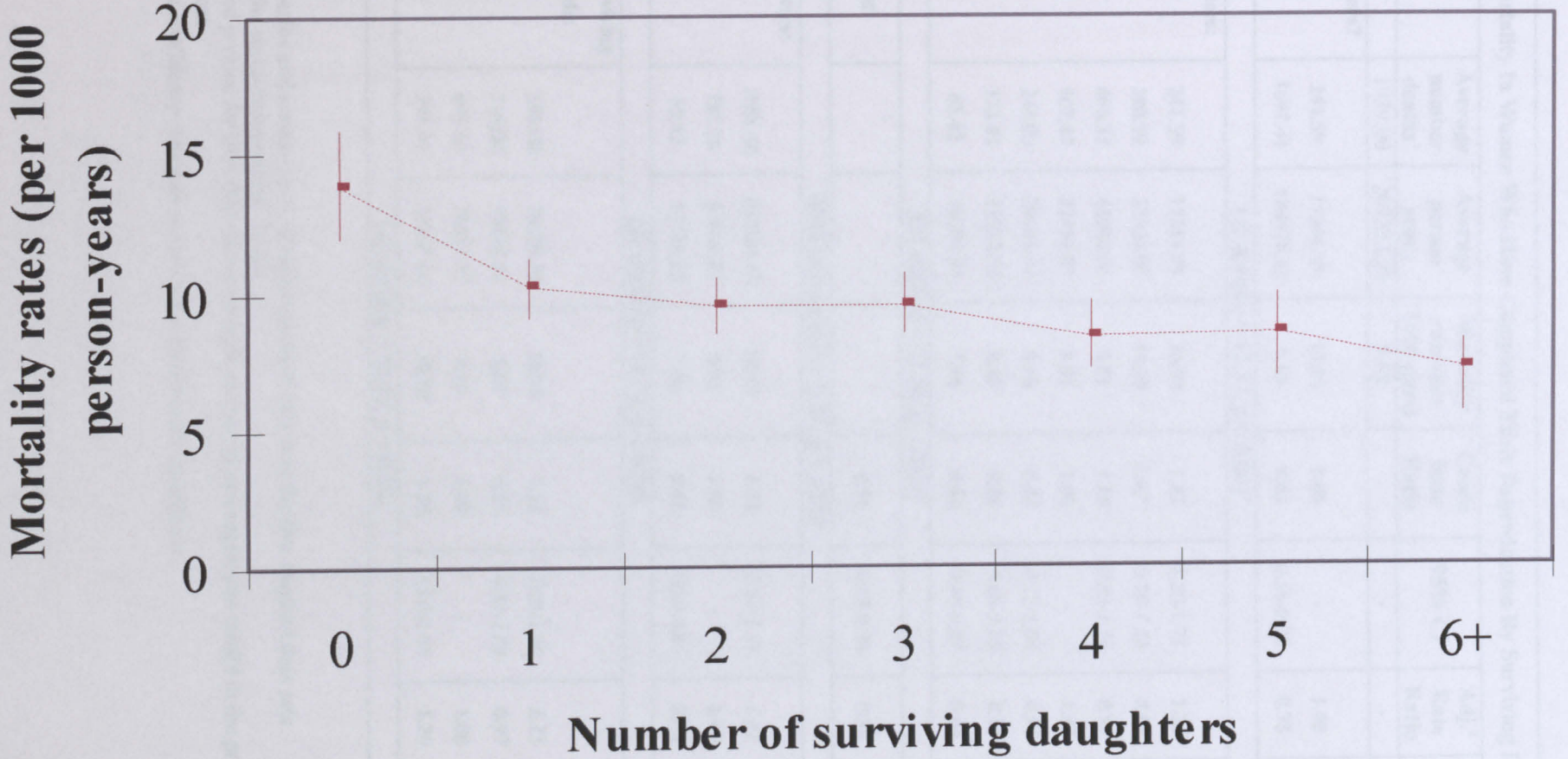


Table 6.14: Mortality In Women Who Have Completed Their Reproduction By Surviving Daughters							
Variable	**Average number deaths[1]**	**Average person years**	**Mortality rate (per 1000 pyrs)**	**Crude Rate Ratio**	**95% CI**	**Adj.[2] Rate Ratio**	**95% CI**
Total	1939.00	202322.20	**9.58**	-	-	-	-
Surviving daughters?							
No	241.59	17344.39	**13.93**	**1.00**	-	**1.00**	-
Yes	1697.41	184978.81	**9.18**	**0.66**	0.56-0.76	**0.75**	0.64-0.87
LR statistic = 15.37, $p < 0.001$[3]							
Surviving daughters:							
0	241.59	17344.39	**13.93**	**1.47**	1.20-1.73	**1.25**	1.02-1.48
1	380.39	37304.00	**10.20**	***1.07***[4]	*0.90-1.25*	***0.99***	*0.83-1.15*
2	466.32	48998.04	**9.52**	***1.00***	*0.83-1.18*	***0.94***	*0.78-1.11*
3	407.47	42856.83	**9.51**	**1.00**	-	**1.00**	-
4	244.00	29101.01	**8.38**	***0.88***	*0.72-1.04*	***0.91***	*0.74-1.07*
5	133.81	15932.98	**8.40**	***0.88***	*0.68-1.09*	***0.88***	*0.68-1.08*
6+	65.42	10784.95	**7.16**	**0.64**	0.46-0.81	**0.64**	0.47-0.81
LR statistic = 32.50, $p < 0.001$							
Per "surviving daughter"	-	-	-	**0.91**	0.88-0.94	**0.94**	0.91-0.97
Wald test statistic = 3.78, $p < 0.001$							
Surviving daughters:							
0-2	1088.30	103646.43	**10.50**	***1.18***	*1.04-1.31*	***1.07***	*0.95-1.19*
3-5	785.28	87890.82	**8.93**	**1.00**	-	**1.00**	-
6+	65.42	10784.95	**7.16**	**0.68**	0.50-0.86	**0.68**	0.49-0.86
LR statistic = 19.37, $p < 0.001$							
% of children surviving who were female:							
0-24.9%	336.00	30583.58	**10.99**	**1.21**	1.02-1.40	***1.15***	*0.97-1.33*
25.0-49.9%	516.00	59429.41	**8.68**	***0.95***	*0.83-1.08*	***0.97***	*0.84-1.10*
50.0-74.9%	695.59	76453.37	**9.10**	**1.00**	-	**1.00**	-
75.0-100%	391.41	35855.84	**10.92**	**1.20**	1.05-1.35	**1.20**	1.05-1.36
LR statistic = 15.05, $p = 0.001$							

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
4. *Estimates and confidence intervals in italics not statistically significant*

Figure 6.7: Crude female mortality rates by number of surviving children, in surviving daughter groups

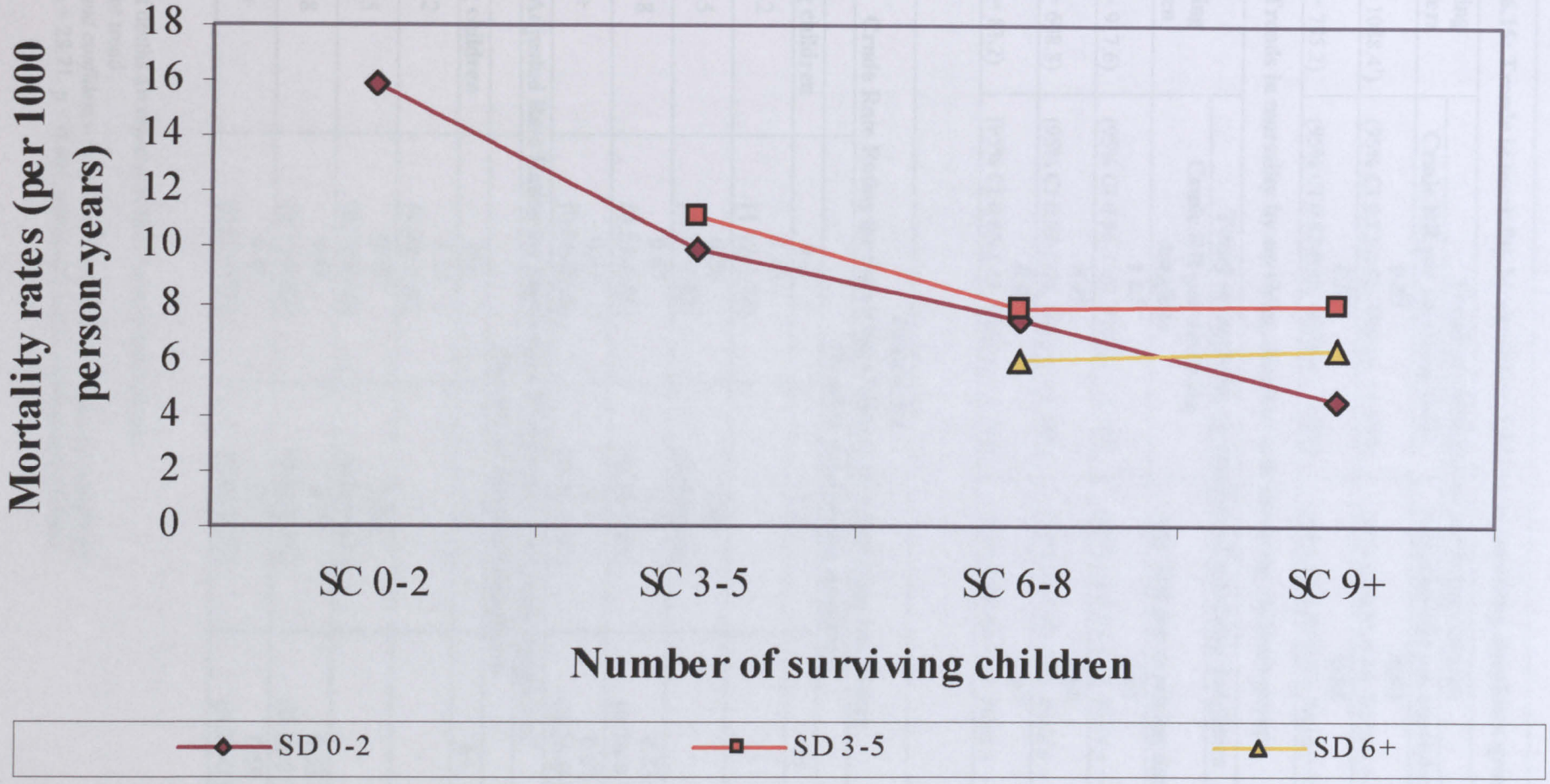


Table 6.15: Trends in mortality by surviving children, in surviving daughters groups		
Surviving daughters	**Trend in mortality by surviving children**	
	Crude RR per surviving child	**Adjusted RR per surviving child**
0-2 (no. deaths = 1088.4[1])	**0.87** (95% CI 0.83-0.90, Wald p = 0.024)	**0.89** (95% CI 0.85-0.93, Wald p = 0.033[2])
3-5 (no. deaths = 785.2)	**0.87** (95% CI 0.82-0.92, Wald p = 0.028)	**0.88** (95% CI 0.83-0.93, Wald p = 0.032)
Trends in mortality by surviving daughters, in surviving children groups		
Surviving children	**Trend in mortality by number of surviving daughters**	
	Crude RR per surviving daughter	**Adj. RR per surviving daughter**
3-5 (no. deaths = 917.6)	***1.02***[3] (95% CI *0.96-1.09, Wald p = 0.492*)	***1.05*** (95% CI *0.98-1.12, Wald p = 0.507*)
6-8 (no. deaths = 608.8)	***0.99*** (95% CI *0.93-1.04, Wald p = 0.366*)	***0.98*** (95% CI *0.92-1.04, Wald p = 0.422*)
9+ (no. deaths = 83.2)	***0.99*** (95% CI *0.85-1.13, Wald p = 0.793*)	***0.97*** (95% CI *0.83-1.11, Wald p = 0.828*)

Table 6.16: **Crude Rate Ratios for Surviving Children and Surviving Daughters**			
	Number of surviving daughters		
Surviving children	0-2	3-5	6+
0-2	1.43 (1.12-1.74)	-	-
3-5	*0.89* *(0.75-1.03)*	**1.00** **(reference)**	-
6-8	0.67 (0.53-0.81)	0.70 (0.58-0.82)	0.53 (0.36-0.71)
9+	0.41 (0.06-0.88)	0.71 (0.46-0.97)	0.57 (0.26-0.89)
Adjusted Rate Ratios for Surviving Children and Surviving Daughters[4]			
	Number of surviving daughters		
Surviving children	0-2	3-5	6+
0-2	*1.22* *(0.96-1.49)*	-	-
3-5	0.83 (0.70-0.96)	**1.00** **(reference)**	-
6-8	0.68 (0.54-0.82)	0.72 (0.60-0.85)	0.53 (0.36-0.71)
9+	0.45 (0.07-0.97)	0.71 (0.46-0.96)	0.59 (0.27-0.91)

1. Numbers of deaths averaged over the five imputed data sets
2. Wald test for trend
3. *Estimates and confidence intervals in italics not statistically significant*
4. LR statistic = 28.71, p < 0.001, adjusted for socio-demographic factors

6.4.7 Fetal losses

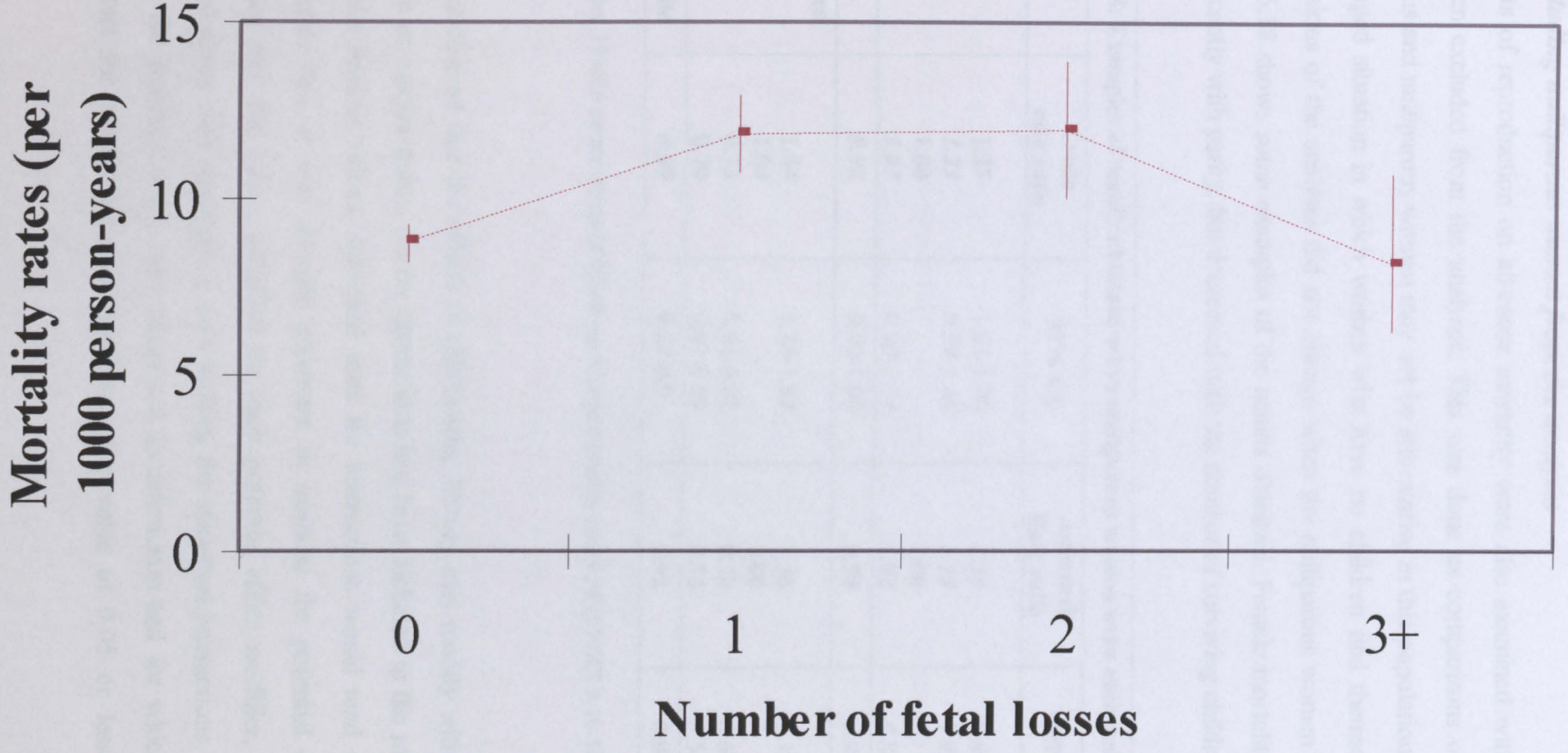
Women who had experienced any fetal losses had a significant 50% adjusted increase in mortality compared with those who had none (adjusted RR 1.47, 95% CI 1.31-1.63, Table 6.17). Mortality by number of fetal losses formed an inverted u-shaped trend (Figure 6.8), with an increased mortality of 50% in women with one or two losses than in women with no losses and mortality lower than women with no losses (crude) or only slightly higher than women with no losses (adjusted) in women who had lost three of more pregnancies. The only differences that were statistically significant were the comparison between those who had suffered none and those who had experienced one or two losses. These differences persisted when the nulligravid women (those who had experienced no pregnancies) were examined as a separate group. These estimates all increased on adjusting for the socio-demographic factors, particularly when the age, religion and education variables were added to the models.

Table 6.17: Mortality In Women Who Have Completed Their Reproduction By Fetal Losses

Variable	Average number deaths[1]	Person-years of follow-up	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj.[2] Rate Ratio	95% CI
Total	1939.00	202322.20	**9.58**	-	-	-	-
Fetal loss?:							
No	1196.58	137171.44	**8.72**	**1.00**	-	**1.00**	-
Yes	742.42	65150.76	**11.40**	**1.31**	1.16-1.45	**1.47**	1.31-1.63
LR statistic = 65.25, $p < 0.001$[3]							
Fetal losses:							
0	1196.58	137171.44	**8.72**	**1.00**	-	**1.00**	-
1	508.20	43025.51	**11.81**	**1.35**	1.20-1.51	**1.51**	1.34-1.68
2	169.61	14220.16	**11.93**	**1.37**	1.12-1.62	**1.55**	1.27-1.83
3+	64.61	7905.09	**8.17**	***0.94***[4]	*0.65-1.22*	***1.09***	*0.76-1.42*
LR statistic = 73.67, $p < 0.001$							
Fetal losses:							
No fetal losses	1169.00	134789.66	**8.67**	**1.00**	-	**1.00**	-
Nulligravid	27.58	2381.78	**11.59**	***1.34***	*0.83-1.85*	***1.21***	*0.75-1.67*
1-2 fetal losses	677.81	57245.67	**11.84**	**1.37**	1.23-1.51	**1.53**	1.36-1.69
3+ fetal losses	64.61	7905.09	**8.17**	***0.94***	*0.66-1.23*	***1.09***	*0.76-1.42*
LR statistic = 73.55, $p < 0.001$							

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
4. *Estimates and confidence intervals in italics not statistically significant*

Figure 6.8: Crude female mortality rates (+95% CI) by number of fetal losses



6.4.8 Results excluding nulliparous women from the analyses

The effects of reproduction on all-cause mortality were also examined with the nulliparous women excluded from the analyses. This was done as comparisons of the mortality of parous and nulliparous women may not be informative in this population, due to the disadvantaged situation in which women who have no children find themselves. The main conclusions of the analyses did not change when the nulliparous women were excluded. Table 6.18 shows some examples of the results obtained. Female mortality did not change significantly with parity, but decreased with the number of surviving children.

Table 6.18: Examples of results obtained when nulliparous women were excluded*

Characteristic	Crude rate ratio	95% CI	Adjusted Rate ratio	95% CI
Parity				
1-2	**1.37**	1.03-1.70	***1.19***	*0.89-1.50*
3-5	***1.23***	*0.99-1.48*	***1.18***	*0.95-1.42*
6-8	**1.00**	-	**1.00**	-
9+	***1.07***	*0.90-1.24*	***1.02***	*0.86-1.19*
Per child born	***0.98***	*0.96-1.00*	***0.98***	*0.96-1.00*
Surviving children				
0-2	**1.54**	1.26-1.82	**1.36**	1.10-1.61
3-5	**1.00**	-	**1.00**	-
6-8	**0.73**	0.64-0.82	**0.78**	0.69-0.87
9+	**0.70**	0.51-0.89	**0.74**	0.54-0.94
Per surviving child	**0.89**	0.87-0.91	**0.92**	0.90-0.94

*Based on 1912 deaths, 199626 person-years of follow-up. Crude mortality rate 9.58 (95%CI 9.16-10.02).

6.5 Interactions

It was hypothesised that the effects of childbearing history may modify with age, education, religion or marital status. As no interactions had been included in the models used to impute the missing values, statistical tests for interactions would tend to be conservative. Despite this, it was thought important to examine for potential effect modification. Rates and rate ratios, stratified for each potential effect modifier, were therefore examined along with significance tests looking for statistical interactions. Only results for which the patterns in the rates suggested an interaction and for which the likelihood ratio test for interaction was significant (a p value of 0.05 or less) are presented.

6.5.1 Interactions with age

Some effects of reproductive history on all-cause mortality modified with age in the females. Age was grouped in ten-year bands to ensure adequate numbers in each group. Reproductive exposures were grouped as previously.

There were some statistically significant interactions in the effects of age and surviving children but the trends need to be interpreted with caution. The results suggest that mortality decreases with the number of surviving children in each age group but that in older women, the effects seem to be confined to having any surviving children rather than a consistent trend in decreasing mortality with the number of surviving children (Figure 6.9, Table 6.18, LR statistic for interaction 16.36, p = 0.038). For example, there is a slight decrease in mortality with surviving children in women aged between 45 and 55, with no significant estimates after adjustment. The effects in women aged 55 to 65 years are also slight with more significant effects. However, in women over the age of 65 years, the effects were confined to women who had few surviving children. These women had twice the mortality of women with three to five surviving children (adjusted RR 1.98, 95% CI 1.37-2.59). Similar patterns were seen when examining mortality by parity and number of surviving children (Figures 6.10-6.12, Tables 6.19-6.21: LR test statistic for interaction of age with combined parity and surviving children variable 54.78, p = 0.030). In the youngest women, there was a tendency for mortality to be lower in women with more surviving children. In women over 65 however, the effects were confined to women of high parity with few surviving children. For example, the adjusted RR in women of parity six to eight with none to two surviving children was 2.40 compared with women of parity six to eight with three to five surviving children (95% CI 1.02-3.78). The corresponding RR in women of parity 9+ with 0-2 surviving children was 2.73 (95% CI 1.11-5.57).

6.5.2 Other interactions

The effects of reproductive history on mortality did not modify with education, religion or marital status in the females. There were no patterns seen on examining the stratified mortality rates and rate ratios, or any statistically significant interactions

Figure 6.9: Crude female mortality rates by number of surviving children, in age groups

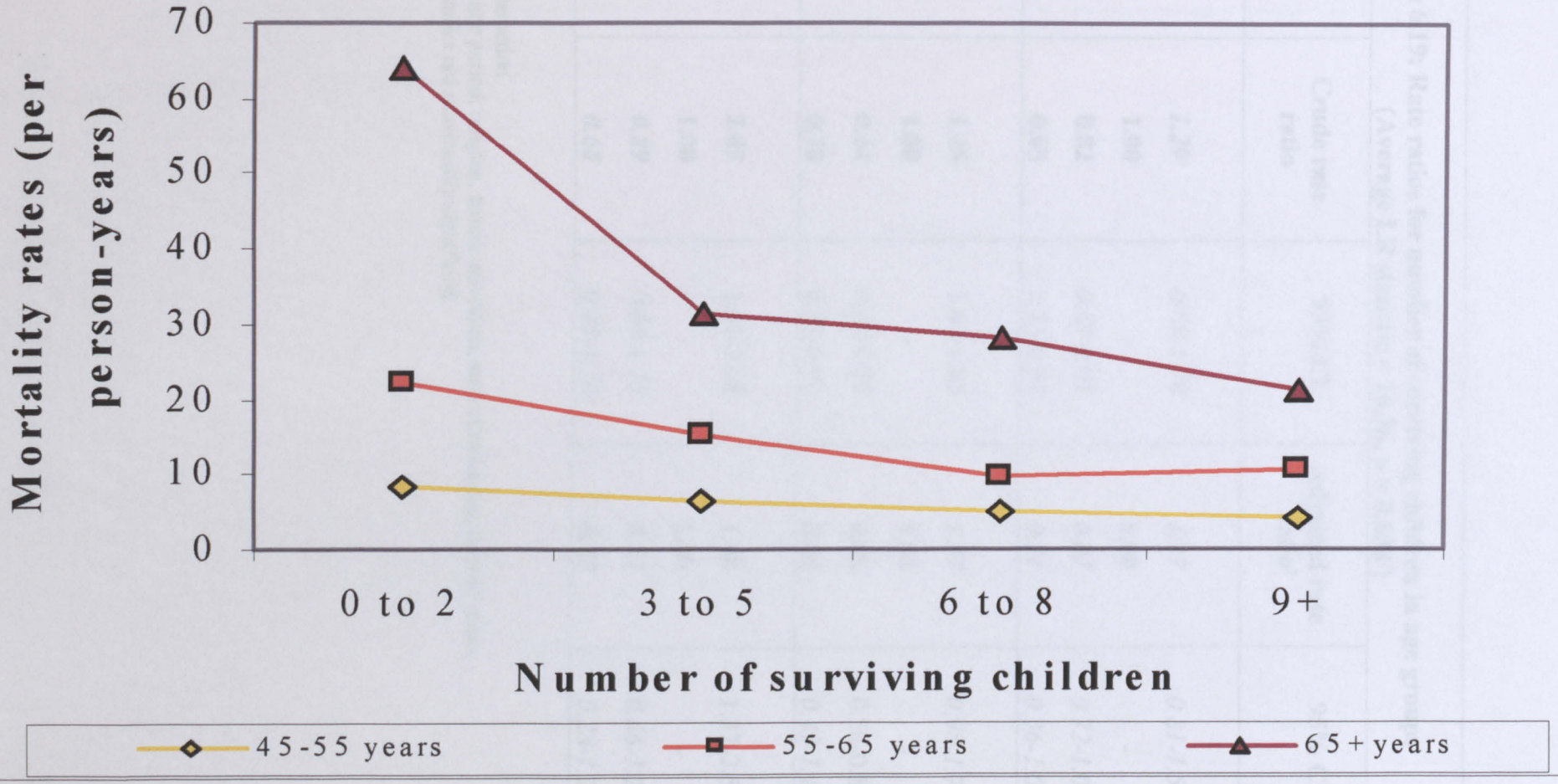


Table 6.19: Rate ratios for number of surviving children in age groups (Average LR statistic = 16.36, p = 0.038[1])

	Crude rate ratio	95% CI	Adjusted rate ratio[2]	95% CI
Age 45-55:				
0-2	***1.29***[3]	*0.88-1.70*	***1.17***	*0.81-1.55*
3-5	**1.00**	-	**1.00**	-
6-8	**0.82**	0.67-0.97	***0.87***	*0.72-1.03*
9+	**0.65**	0.33-0.97	***0.71***	*0.36-1.06*
Age 55-65:				
0-2	**1.45**	1.04-1.85	***1.37***	*0.98-1.76*
3-5	**1.00**	-	**1.00**	-
6-8	**0.64**	0.53-0.75	**0.68**	0.56-0.80
9+	**0.70**	0.43-0.97	***0.80***	*0.49-1.10*
Age 65+:				
0-2	**2.05**	1.41-2.68	**1.98**	1.37-2.59
3-5	**1.00**	-	**1.00**	-
6-8	***0.89***	*0.64-1.15*	***0.93***	*0.66-1.20*
9+	***0.68***	*0.25-1.10*	***0.77***	*0.28-1.26*

1. LR test for interaction
2. Adjusted for time period, religion, female education, area of residence, marital status
3. *Estimates in italics not statistically significant*

Figure 6.10: Crude female mortality rates by number of surviving children, in parity groups (45-55 years)

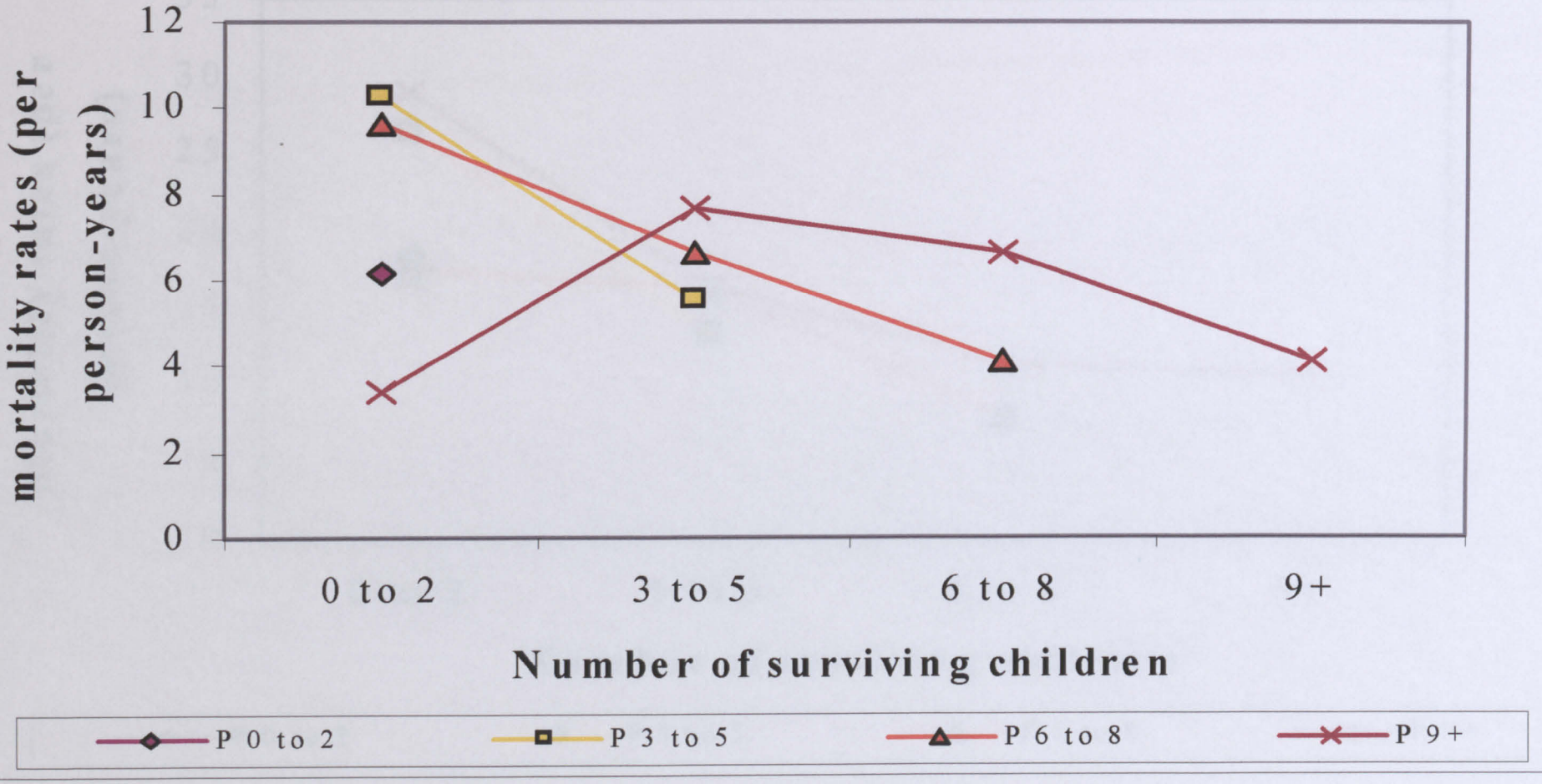


Figure 6.11: Crude female mortality rates by number of surviving children, in parity group (55-65 years)

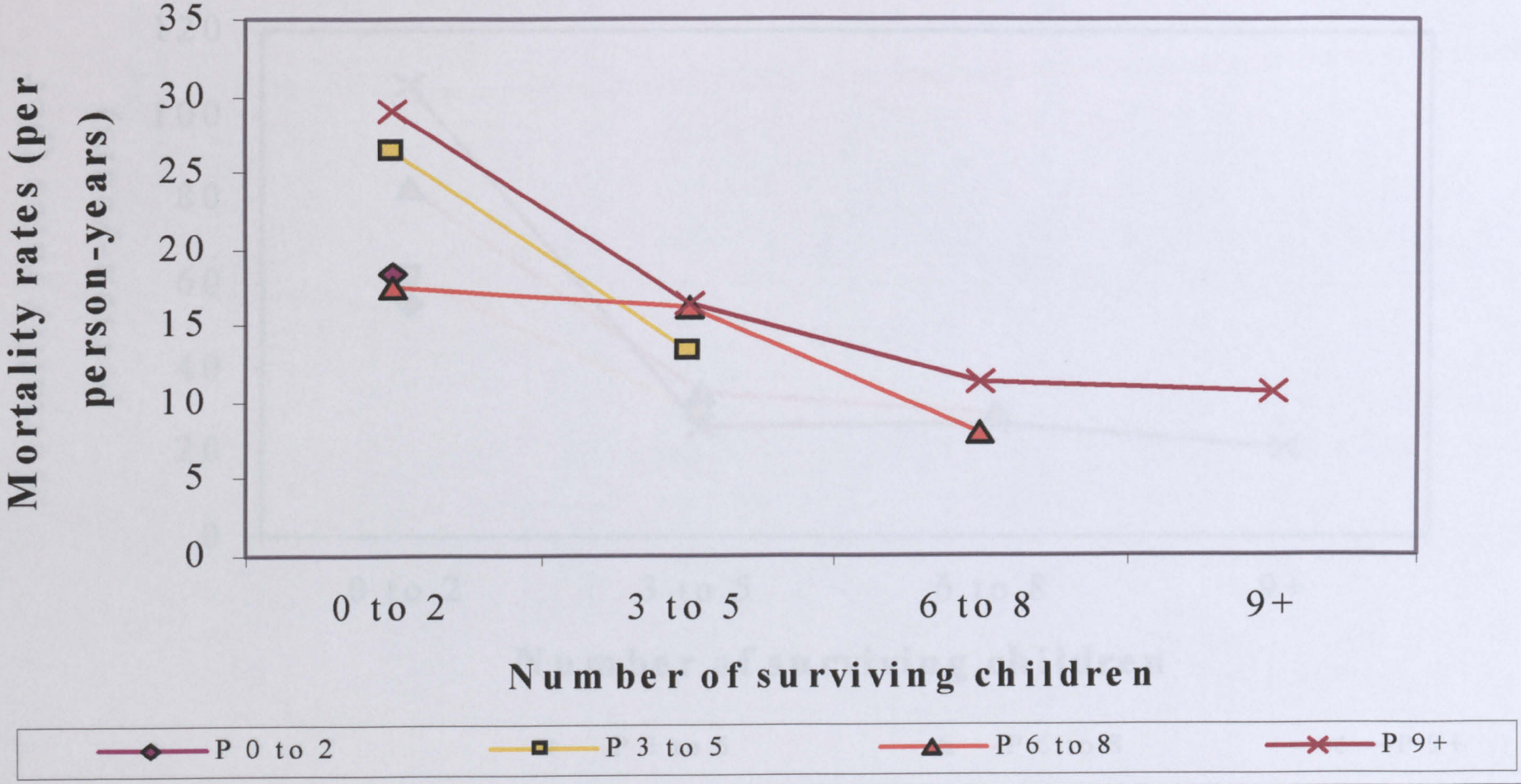


Figure 6.12: Crude female mortality rates by number of surviving children, in parity groups (65+ years)

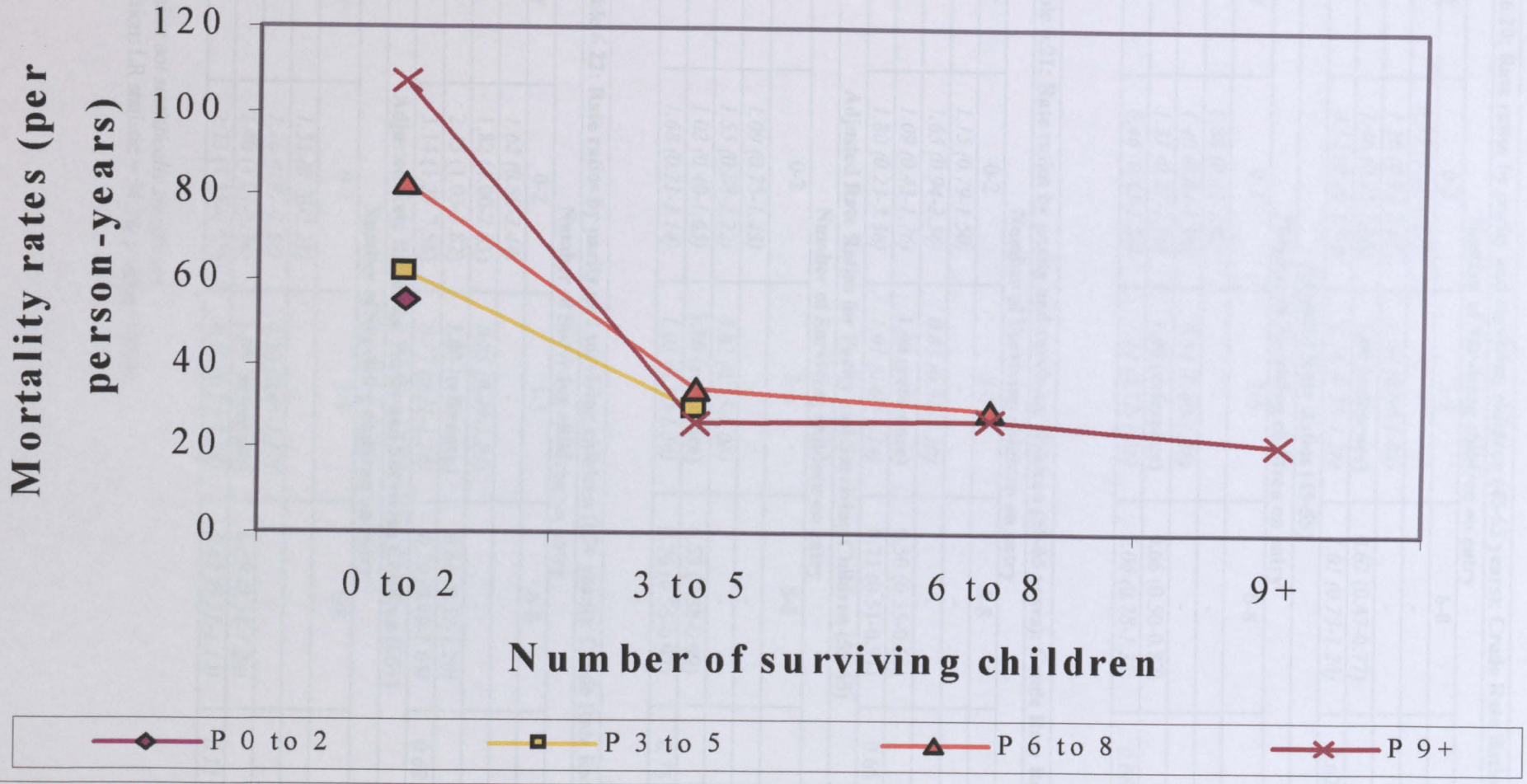


Table 6.20: Rate ratios by parity and surviving children (45-55 years): Crude Rate Ratios (45-55)				
Number of Surviving children on entry				
Parity	0-2	3-5	6-8	9+
0-2	*0.93 (0.44-1.42)* [1]	-	-	-
3-5	*1.56 (0.93-2.18)*	*0.84 (0.60-1.08)*	-	-
6-8	*1.46 (0.25-2.66)*	**1.00 (reference)**	0.62 (0.47-0.77)	-
9+	*0.52 (0.49-1.54)*	*1.16 (0.73-1.28)*	*1.01 (0.73-1.28)*	0.62 (0.29-0.96)
Adjusted Rate Ratios (45-55)				
Number of Surviving children on entry				
Parity	0-2	3-5	6-8	9+
0-2	*0.86 (0.41-1.32)*	-	-	-
3-5	*1.40 (0.84-1.96)*	*0.84 (0.60-1.08)*	-	-
6-8	*1.31 (0.22-2.39)*	**1.00 (reference)**	0.66 (0.50-0.82)	-
9+	*0.46 (0.43-1.38)*	*1.14 (0.72-1.56)*	*1.06 (0.78-1.35)*	*0.68 (0.32-1.05)*

Table 6.21: Rate ratios by parity and surviving children (55-65 years): Crude Rate Ratios				
Number of Surviving children on entry				
Parity	0-2	3-5	6-8	9+
0-2	*1.15 (0.79-1.50)*	-	-	-
3-5	*1.65 (0.94-2.36)*	*0.83 (0.56-1.10)*	-	-
6-8	*1.09 (0.43-1.76)*	**1.00 (reference)**	0.50 (0.35-0.65)	-
9+	*1.80 (0.23-3.38)*	*1.01 (0.69-1.34)*	0.71 (0.51-0.91)	0.66 (0.42-0.91)
Adjusted Rate Ratios for Parity and Surviving Children (55-65)				
Number of Surviving children on entry				
Parity	0-2	3-5	6-8	9+
0-2	*1.09 (0.75-1.43)*	-	-	-
3-5	*1.55 (0.88-2.22)*	*0.82 (0.55-1.08)*	-	-
6-8	*1.02 (0.40-1.65)*	**1.00 (reference)**	0.53 (0.38-0.69)	-
9+	*1.68 (0.21-3.14)*	*1.03 (0.70-1.36)*	0.76 (0.55-0.97)	*0.75 (0.47-1.03)*

Table 6.22: Rate ratios by parity and surviving children (65+ years): Crude Rate Ratios				
Number of Surviving children on entry				
Parity	0-2	3-5	6-8	9+
0-2	*1.62 (0.80-2.44)*	-	-	-
3-5	1.82 (1.00-2.63)	*0.85 (0.49-1.21)*	-	-
6-8	2.43 (1.03-3.82)	**1.00 (reference)**	*0.86 (0.52-1.20)*	-
9+	3.14 (1.27-7.56)	*0.77 (0.31-1.23)*	*0.79 (0.49-1.08)*	*0.62 (0.21-1.03)*
Adjusted Rate Ratios for Parity and Surviving Children (65+)				
Number of Surviving children on entry				
Parity	0-2	3-5	6-8	9+
0-2	*1.55 (0.76-2.33)*	-	-	-
3-5	*1.76 (0.97-2.54)*	*0.82 (0.47-1.17)*	-	-
6-8	2.40 (1.02-3.78)	**1.00 (reference)**	*0.89 (0.54-1.24)*	-
9+	2.73 (1.11-6.57)	*0.80 (0.33-1.28)*	*0.82 (0.51-1.13)*	*0.71 (0.25-1.17)*

Estimates in italics not statistically significant
Test for interaction: LR statistic = 54.78, p value = 0.040

6.6 Summary

The mortality of nulliparous women or women of high parities was not different to that of women who had experienced a few live births. Mortality decreased with the number of surviving children however, whatever the parity of the woman and whether the surviving children were female or male. There was some suggestion that this effect modified with age, with the highest mortality in women over the age of 65 who had no surviving children. Mortality was also higher in females who had suffered fetal losses.

Table 6.23 (below and next page) summarises the main findings from the female cohort, including the effects of both the socio-demographic and reproductive variables. It is clear that, in females in Matlab, socio-demographic factors (age, time period, religion, area of residence, marital status, and including the number of surviving children) have an important effect on all-cause mortality after age 45. Factors directly linked to the reproductive process such as parity and gravidity do not influence mortality in this cohort.

Table 6.23: Summary table of the effects seen in the females

Characteristic	Crude rate ratio	95% CI	Adjusted Rate ratio	95% CI
Age groups				
45 to 49.9 years	**1.00**	-	**1.00**	-
50.0 to 54.9 years	**1.77**	1.52-2.05	**1.71**	1.48-1.98
55.0 to 59.9 years	**2.57**	2.22-2.97	**2.46**	2.12-2.86
60.0 to 64.9 years	**4.21**	3.63-4.90	**4.15**	3.53-4.88
65.0 to 69.9 years	**7.49**	6.33-8.87	**7.45**	6.16-9.01
70.0 + years	**12.24**	7.69-19.47	**13.32**	8.19-21.67
Time period:				
30/6/1982-29/6/1987	**1.00**	-	**1.00**	-
30/6/1987-29/6/1992	**1.02**	0.89-1.17	**0.82**	0.71-0.94
30/6/1992-31/12/1998	**1.33**	1.18-1.50	**0.77**	0.67-0.88
Religion:				
Muslim	**1.00**	-	**1.00**	-
Hindu	**1.35**	1.20-1.52	***1.16***	*0.99-1.36*
Female education:				
None	**1.00**	-	**1.00**	-
Maktab	**0.73**	0.66-0.81	**0.79**	0.69-0.91
Any formal	**0.50**	0.43-0.58	**0.62**	0.52-0.73

Table 6.23: Summary table of the effects seen in the females (continued)				
Characteristic	**Crude rate ratio**	**95% CI**	**Adjusted rate ratio**	**95% CI**
Area of residence:				
Intervention	**1.00**	-	**1.00**	-
Comparison	**1.12**	1.02-1.22	**1.13**	1.03-1.24
Marital status:				
Unmarried	-	-	-	-
Still married	**1.00**	-	**1.00**	-
Widowed	**1.93**	1.76-2.11	**1.30**	1.18-1.43
Divorced	**2.57**	1.83-3.60	**2.36**	1.68-3.31
Parity:				
0-2	**1.37**	1.03-1.70	***1.19***	*0.89-1.50*
3-5	***1.23***	*0.99-1.48*	***1.18***	*0.95-1.42*
6-8	**1.00**	-	**1.00**	-
9+	***1.07***	*0.90-1.24*	***1.02***	*0.86-1.19*
Gravidity:				
0-2	***1.26***	*0.96-1.56*	***1.08***	*0.81-1.34*
3-5	***1.13***	*0.89-1.38*	***1.06***	*0.83-1.29*
6-8	**1.00**	-	**1.00**	-
9+	***1.03***	*0.91-1.15*	***1.01***	*0.90-1.13*
Surviving children:				
0-2	**1.54**	1.26-1.82	**1.35**	1.10-1.61
3-5	**1.00**	-	**1.00**	-
6-8	**0.73**	0.64-0.82	**0.78**	0.69-0.87
9+	**0.70**	0.51-0.89	**0.74**	0.54-0.94
Parity and surviving children:				
P 0-2, SC 0-2	***1.10***	*0.81-1.39*	***1.08***	*0.80-1.36*
P 3-5, SC 0-2	**1.74**	1.24-2.23	**1.53**	1.10-1.97
P 3-5, SC 3-5	**0.78**	0.60-0.97	***0.85***	*0.65-1.04*
P 6-8, SC 0-2	**1.60**	1.03-2.16	***1.30***	*0.85-1.76*
P 6-8, SC 3-5	**1.00**	-	**1.00**	-
P 6-8, SC 6-8	**0.55**	0.45-0.65	**0.63**	0.52-0.75
P 9+, SC 0-2	***1.52***	*0.47-2.57*	***1.36***	*0.42-2.31*
P 9+, SC 3-5	***1.09***	*0.87-1.31*	***1.02***	*0.81-1.23*
P 9+, SC 6-8	***0.84***	*0.67-1.01*	***0.86***	*0.69-1.04*
P 9+, SC 9+	**0.66**	0.47-0.84	**0.71**	0.50-0.91
Fetal losses:				
0	**1.00**	-	**1.00**	-
1	**1.35**	1.20-1.51	**1.51**	1.34-1.68
2	**1.37**	1.12-1.62	**1.55**	1.27-1.83
3+	***0.94***	*0.65-1.22*	***1.09***	*0.76-1.42*

7.1 Introduction

The purpose of examining the associations between reproductive history and all-cause mortality in the males was to provide a comparison to the female results, which may help to unravel the potential mechanisms behind any association seen. The results for the males follow the same structure as in the previous chapter.

7.2 Distribution of the male reproductive histories after imputation and their relation with the socio-demographic factors

The results of the male imputations are given in Tables A7.1 to A7.5 in Appendix 7.1 As for the females, the simulated values seemed reasonable, with the distribution of the resulting variables similar to that seen before imputation. The imputations tended to result in values that were clustered at the lower values of each variable and there was little if any replacement at the higher extremes of each value. The frequency distributions of the main variables of interest are given in Table 7.1. The means, medians and ranges of each variable were similar in each data set and the same as in the original data set.

The number of live births experienced by the wives of these men was 7.35 (SD 2.47), which is slightly higher than that seen in the female cohort (Table 7.2). The range of live births was the same. The average number of surviving children was also higher, at 5.52 (SD 2.03, Table 7.3). The reproductive variables varied significantly with male socio-demographic status (Table 7.2-7.4). There was no clear pattern in wife's parity with age at entry, but the number of surviving children decreased with the man's age. Wife's parity decreased with time of entry, and the men who entered the cohort latest had the least average number of surviving children (5.18, SD 1.90). The wives of Muslim men had experienced more live births and had more surviving children. All means were higher in men living in the comparison area. All men were married on entry, therefore reproductive variables were compared by men's marital status on exit. The wives of divorced men had the lowest parity and divorced men also had less surviving children. There were no clear patterns in parity with male or female education, but the mean number of surviving children increased with the educational attainment of both husband and wife. The wives of men in unskilled occupations had the highest parity, with the wives of disabled men having the lowest mean parity. These men also had the lowest number of surviving children.

Table 7.1: Reproductive variables from the imputed data sets

	Imputed Data set 1		Imputed data set 2		Imputed data set 3		Imputed data set 4		Imputed data set 5	
Parity	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**
0	**154**	1.04	**154**	1.04	**153**	1.03	**153**	1.03	**153**	1.03
1	**107**	0.72	**109**	0.74	**108**	0.73	**111**	0.75	**108**	0.73
2	**148**	1.00	**153**	1.03	**151**	1.02	**153**	1.03	**151**	1.02
3	**390**	2.63	**403**	2.72	**388**	2.62	**405**	2.74	**392**	2.65
4	**796**	5.38	**794**	5.36	**807**	5.45	**799**	5.40	**799**	5.40
5	**1500**	10.13	**1492**	10.08	**1505**	10.17	**1497**	10.11	**1513**	10.22
6	**2214**	14.96	**2196**	14.83	**2212**	14.94	**2193**	14.81	**2194**	14.82
7	**2475**	16.72	**2456**	16.59	**2456**	16.59	**2452**	16.56	**2473**	16.71
8	**2381**	16.08	**2372**	16.02	**2382**	16.09	**2381**	16.08	**2358**	15.93
9	**1943**	13.13	**1945**	13.14	**1931**	13.04	**1958**	13.23	**1937**	13.09
10	**1313**	8.87	**1329**	8.98	**1320**	8.92	**1308**	8.84	**1320**	8.92
11	**765**	5.17	**769**	5.19	**763**	5.15	**758**	5.12	**774**	5.23
12	**359**	2.43	**363**	2.45	**364**	2.46	**355**	2.40	**359**	2.43
13	**169**	1.14	**170**	1.15	**174**	1.18	**175**	1.18	**178**	1.20
141	**89**	0.60	**98**	0.66	**89**	0.60	**105**	0.71	**94**	0.64
Total	**14803**	-	**14803**	-	**14803**	-	**14803**	-	**14803**	-
Mean (SD)	**7.35 (2.46)**		**7.35 (2.47)**		**7.35 (2.46)**		**7.35 (2.48)**		**7.35 (2.47)**	
Range	**0-18**		**0-18**		**0-18**		**0-18**		**0-18**	
Surviving children	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**
0	**206**	1.39	**211**	1.43	**208**	1.41	**210**	1.42	**205**	1.38
1	**223**	1.51	**231**	1.56	**234**	1.58	**226**	1.53	**230**	1.55
2	**499**	3.37	**514**	3.47	**499**	3.37	**527**	3.56	**512**	3.46
3	**1204**	8.13	**1212**	8.19	**1207**	8.15	**1204**	8.13	**1207**	8.15
4	**2228**	15.05	**2206**	14.9	**2238**	15.12	**2213**	14.95	**2212**	14.94
5	**3001**	20.27	**2968**	20.05	**2981**	20.14	**2978**	20.12	**2993**	20.22
6	**2935**	19.83	**2917**	19.71	**2897**	19.57	**2895**	19.56	**2899**	19.58
7	**2258**	15.25	**2257**	15.25	**2261**	15.27	**2272**	15.35	**2266**	15.31
81	**2249**	15.19	**2287**	15.45	**2278**	15.39	**2278**	15.39	**2279**	15.40
Total	**14803**	-	**14803**	-	**14803**	-	**14803**	-	**14803**	-
Mean (SD)	**5.51 (2.02)**		**5.52 (2.04)**		**5.51 (2.03)**		**5.52 (2.04)**		**5.52 (2.03)**	
Range	**0-15**		**0-15**		**0-15**		**0-15**		**0-15**	
Fetal losses	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**
0	**9397**	63.48	**9402**	63.51	**9397**	63.48	**9403**	63.52	**9385**	63.40
1	**3519**	23.77	**3505**	23.68	**3515**	23.75	**3489**	23.57	**3525**	23.81
2	**1202**	8.12	**1207**	8.15	**1206**	8.15	**1235**	8.34	**1214**	8.20
3	**426**	2.88	**429**	2.90	**423**	2.86	**417**	2.82	**418**	2.82
4	**148**	1.00	**149**	1.01	**151**	1.02	**148**	1.00	**150**	1.01
51	**111**	0.75	**111**	0.75	**111**	0.75	**111**	0.75	**111**	0.75
Total	**14803**	-	**14803**	-	**14803**	-	**14803**	-	**14803**	-
Median	**0**		**0**		**0**		**0**		**0**	
Range	**0-12**		**0-12**		**0-12**		**0-12**		**0-12**	

Table 7.2: Relationship of parity with other socio-demographic factors		
Age at entry	**Combined mean (SD)**	**t test for comparison of means**
40.0-54.9	7.25 (2.35)	
55.0-69.9	7.44 (2.40)	F value = 16.21
70.0-max	6.95 (2.80)	p < 0.0001
Year of entry	**Example mean (SD)**	**ANOVA for comparison of means**
1982-1987	7.69 (2.48)	
1988-1992	7.32 (2.34)	F value = 264.76
1993-1998	6.53 (2.33)	p < 0.0001
Religion	**Combined mean (SD)**	**t test for comparison of means**
Muslim	7.43 (2.47)	t value = 11.01
Hindu	6.83 (2.31)	p < 0.0001
Area of residence	**Combined mean (SD)**	**t test for comparison of means**
Intervention	7.12 (2.42)	t value = -11.40
Comparison	7.58 (2.48)	p < 0.0001
Male Education	**Example mean (SD)**	**ANOVA for comparison of means**
None	7.05 (2.31)	
Maktab	7.46 (2.47)	F value = 20.27
Any	7.35 (2.48)	p < 0.0001
Unknown	-	
Female Education	**Example mean (SD)**	**ANOVA for comparison of means**
None	7.05 (2.31)	
Maktab	7.51 (2.50)	F value = 47.48
Any	7.17 (2.43)	p < 0.0001
Unknown	-	
Male Occupation	**Example mean (SD)**	**ANOVA for comparison of means**
None	6.94 (2.67)	
Unskilled	7.44 (2.45)	F value = 17.34
Skilled	7.18 (2.43)	p < 0.0001
Disabled	6.74 (2.84)	
Unknown	-	
Marital status at exit	**Example mean (SD)**	**ANOVA for comparison of means**
Married	7.34 (2.45)	
Widowed	7.51 (2.52)	F value = 3.35
Divorced	6.75 (3.57)	p = 0.03

Table 7.3: Relationship of surviving children with other socio-demographic factors		
Age at entry	**Combined mean (SD)**	**t test for comparison of means**
40.0-54.9	5.59 (1.92)	
55.0-69.9	5.49 (2.06)	F value = 24.23
70.0-max	4.94 (2.30)	p < 0.0001
Year of entry	**Example mean (SD)**	**ANOVA for comparison of means**
1982-1987	5.58 (2.08)	
1988-1992	5.68 (1.93)	F value = 59.77
1993-1998	5.18 (1.90)	p < 0.0001
Religion	**Combined mean (SD)**	**t test for comparison of means**
Muslim	5.57 (2.02)	t value = 9.43
Hindu	5.14 (1.93)	p < 0.0001
Area of residence	**Combined mean (SD)**	**t test for comparison of means**
Intervention	5.43 (1.98)	t value = -5.24
Comparison	5.60 (2.05)	p < 0.0001
Male Education	**Example mean (SD)**	**ANOVA for comparison of means**
None	5.12 (1.86)	
Maktab	5.46 (2.00)	F value = 59.07
Any	5.65 (2.05)	p < 0.0001
Unknown	-	
Female Education	**Example mean (SD)**	**ANOVA for comparison of means**
None	5.18 (1.88)	
Maktab	5.53 (2.03)	F value = 63.17
Any	5.75 (2.04)	p < 0.0001
Unknown	-	
Male Occupation	**Example mean (SD)**	**ANOVA for comparison of means**
None	4.96 (2.39)	
Unskilled	5.51 (2.00)	F value = 9.62
Skilled	5.56 (2.01)	p < 0.0001
Disabled	4.93 (2.31)	
Unknown	-	
Marital status at exit	**Example mean (SD)**	**ANOVA for comparison of means**
Married	5.54 (2.01)	
Widowed	5.17 (2.07)	F value = 16.73
Divorced	5.13 (3.06)	p < 0.0001

In Table 7.4 are presented the proportions of men whose wives reported fetal losses in one of the imputed data sets. The results from the other data sets were similar, but these results are an example and may underestimate the uncertainty due to missing data. A higher proportion of women had reported fetal losses in men who were younger on entry into the cohort or if the men entered the cohort later. A greater proportion of wives of Muslim men or wives living in the comparison area had reported losing a pregnancy. The proportion of fetal losses experienced by wives did not change with male or female education in this cohort of men. In the occupation category, wives of unskilled workers reported the highest proportion of fetal losses and wives of disabled men reported the lowest proportion. The wives of 43 percent of men who became widowed during the study reported experiencing a fetal loss, compared with 36 percent of men who remained married and 31 percent of men who became divorced.

Table 7.4: Relationship of fetal losses with other socio-demographic factors (Example)

	Fetal losses		Chi squared comparing proportions
Age at entry	**No**	**Yes**	
40.0-54.9	3548 (61.65%)	2207 (38.35%)	
55.0-69.9	5515 (64.52%)	3033 (35.48%)	X^2 statistic = 14.6569
70.0-max	334 (66.80%)	166 (33.20%)	p = 0.001
	Fetal losses		**Chi squared comparing proportions**
Year of entry	**No**	**Yes**	
1982-1987	5298 (65.58%)	2781 (34.42%)	
1988-1992	2086 (60.10%)	1385 (39.90%)	X^2 statistic = 36.04
1993-1998	2013 (61.88%)	1240 (38.12%)	p < 0.001
	Fetal losses		**Chi squared comparing proportions**
Religion	**No**	**Yes**	
Muslim	8008 (63.04%)	4695 (36.96%)	X^2 statistic = 7.48
Hindu	1389 (66.14%)	711 (33.86%)	p = 0.006
Area	**Fetal losses**		**Chi squared comparing proportions**
of residence	**No**	**Yes**	
Intervention	5006 (65.39%)	2650 (34.61%)	X^2 statistic = 24.86
Comparison	4391 (61.44%)	2756 (38.56%)	p < 0.001
Male	**Fetal losses**		**Chi squared comparing proportions**
Education	**No**	**Yes**	
None	1317 (63.96%)	742 (36.04%)	
Maktab	3302 (63.72%)	1880 (36.28%)	X^2 statistic = 0.62
Any	4778 (63.18%)	2784 (36.82%)	p = 0.733
Female	**Fetal losses**		**Chi squared comparing proportions**
Education	**No**	**Yes**	
None	1810 (64.21%)	1009 (35.79%)	
Maktab	5548 (63.41%)	3202 (36.59%)	X^2 statistic = 0.92
Any	2039 (63.05%)	1195 (36.95%)	p = 0.63
Male	**Fetal losses**		**Chi squared comparing proportions**
Occupation	**No**	**Yes**	
None	83 (63.36%)	48 (36.64%)	
Unskilled	6154 (62.92%)	3626 (37.08%)	X^2 statistic = 8.04
Skilled	3020 (64.31%)	1676 (35.69%)	p = 0.05
Disabled	140 (71.43%)	56 (28.57%)	
Marital status at exit	**Fetal losses**		**Chi squared comparing proportions**
	No	**Yes**	
Married	8788 (63.93%)	4959 (36.07%)	
Widowed	587 (57.32%)	437 (42.68%)	X^2 statistic = 18.30
Divorced	22 (68.75%)	10 (31.25%)	p < 0.001
Total			

7.3 The association between reproductive variables and all-cause mortality

7.3.1 Introduction

The repeated-imputation inferences for the associations of reproductive variables with all-cause mortality are summarized in Figures 7.1-7.8 and Tables 7.5-7.18. Crude mortality rates, crude mortality rate ratios and rate ratios adjusted for the socio-demographic factors, each with their 95% confidence intervals, are presented. As in the females, the rate ratios are always relative to the largest group in each variable.

7.3.2 Wife's parity

Men whose wives were nulliparous or nulligravid did not have significantly different mortality from those men whose wives were parous or gravid (Table 7.5). For example, the adjusted rate ratio comparing the mortality of men whose wives were nulliparous with those whose wives were parous was 0.87 (95% CI 0.61-1.13). The overall pattern was for mortality to decrease with wife's parity (Figure 7.1), and there was a significant trend of decreasing mortality per child born. The magnitude of this change was small however (adjusted RR per child born 0.97, 95% CI 0.96-0.98, Wald test statistic 3.01, $p = 0.029$). In addition, men whose wives had experienced nine or more live births had significantly lower mortality than those whose wives had between six and eight live births although the relative difference was only 9% (adjusted RR 0.91, 95% CI 0.85-0.98).

The patterns in male mortality by wife's gravidity were very similar to those seen with parity (Table 7.6).

Figure 7.1: Crude male mortality rates (+95% CI) by wife's parity

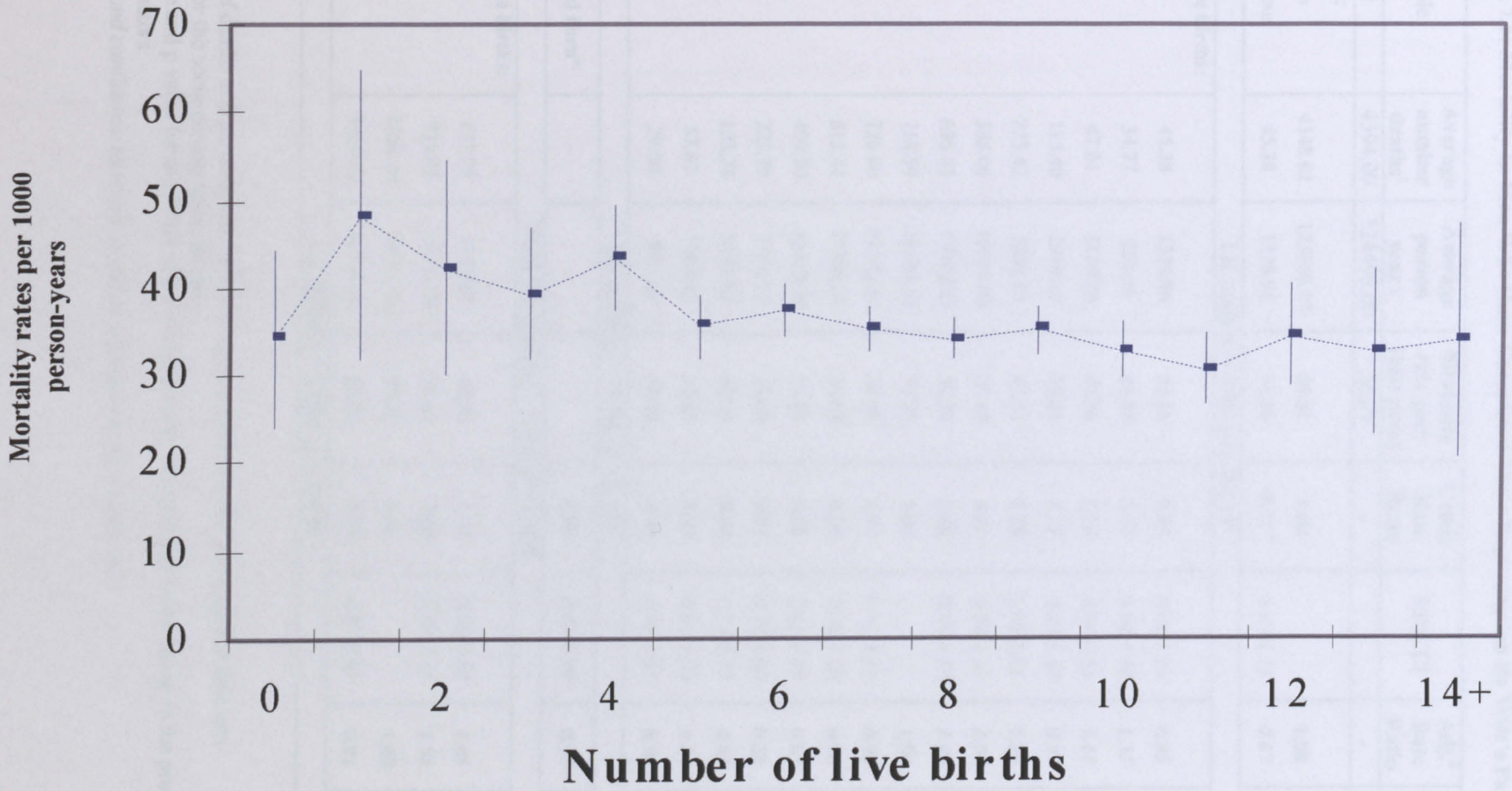


Table 7.5: Mortality In Men Who Have Completed Their Reproduction By Wife's Parity

Variable	Average number deaths[1]	Average person years	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj.[2] Rate Ratio	95% CI
Total	4394.00	124498.00	**35.29**	-	-	-	-
Parity:							
Parous	4348.62	123169.04	**35.31**	**1.00**	-	**1.00**	-
Nulliparous	45.38	1328.96	**34.16**	***0.97***[4]	*0.68-1.25*	***0.87***	*0.61-1.13*
LR statistic = 0.90, p = 0.513[3]							
Number of live births:							
0	45.38	1328.96	**34.16**	***0.97***	*0.68-1.26*	***0.85***	*0.60-1.11*
1	34.77	720.65	**48.29**	***1.37***	*0.90-1.84*	***1.35***	*0.88-1.82*
2	47.61	1129.26	**42.16**	***1.20***	*0.84-1.55*	***1.11***	*0.77-1.45*
3	115.40	2940.73	**39.22**	***1.11***	*0.89-1.34*	***0.97***	*0.77-1.17*
4	225.42	5202.13	**43.33**	**1.23**	1.04-1.42	**1.25**	1.06-1.44
5	385.00	10859.90	**35.45**	***1.01***	*0.88-1.13*	***1.04***	*0.91-1.17*
6	636.81	17090.45	**37.26**	***1.06***	*0.94-1.17*	***1.06***	*0.94-1.17*
7	718.59	20380.64	**35.26**	**1.00**	-	**1.00**	-
8	726.00	21300.67	**34.08**	***0.97***	*0.87-1.07*	***0.95***	*0.85-1.06*
9	613.44	17500.61	**35.05**	***0.99***	*0.88-1.10*	***0.98***	*0.87-1.09*
10	409.20	12460.70	**32.84**	***0.93***	*0.81-1.05*	**0.87**	0.76-0.98
11	225.79	7365.71	**30.65**	***0.87***	*0.74-1.00*	**0.84**	0.71-0.97
12	123.78	3595.05	**34.45**	***0.98***	*0.78-1.17*	***0.85***	*0.66-1.03*
13	57.81	1769.42	**32.65**	***0.93***	*0.65-1.20*	***0.84***	*0.60-1.09*
14+	29.00	853.12	**33.90**	***0.96***	*0.58-1.35*	***0.90***	*0.54-1.25*
LR statistic = 38.40, p = 0.273							
RR "per child born"	-	-	-	**0.98**	0.97-0.99	**0.97**	0.96-0.98
Wald test statistic = 3.01, p = 0.029							
Number of live births:							
0-2	127.76	3178.87	**40.20**	***1.14***	*0.93-1.34*	***1.05***	*0.86-1.24*
3-5	725.82	19002.76	**38.19**	***1.08***	*0.98-1.18*	***1.08***	*0.99-1.18*
6-8	2081.40	58771.76	**35.42**	**1.00**	-	**1.00**	-
9+	1459.02	43544.61	**33.51**	***0.95***	*0.88-1.01*	**0.91**	0.85-0.98
LR statistic = 16.86, p = 0.084							

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
4. *Estimates and confidence intervals in italics not statistically significant*

Table 7.6: Mortality In Women Who Have Completed Their Reproduction By Gravidity

Variable	Average number deaths[1]	Average person years	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj.[2] Rate Ratio	95% CI
Total	4394.00	124498.00	**35.29**	-	-	-	-
Gravidity:							
Gravid	4356.8	123357.54	**35.32**	**1.00**	-	**1.00**	-
Nulligravid	37.2	1140.64	**32.61**	***0.92***[4]	*0.62-1.22*	***0.83***	*0.56-1.10*
LR statistic = 1.09, p = 0.450[3]							
Pregnancies:							
0	37.2	1140.61	**32.61**	***0.95***	*0.64-1.26*	***0.84***	*0.56-1.12*
1	37.4	716.72	**52.19**	**1.52**	1.02-2.02	***1.45***	*0.96-1.93*
2	38.8	898.35	**43.17**	***1.26***	*0.84-1.68*	***1.22***	*0.81-1.63*
3	84	2195.98	**38.25**	***1.11***	*0.85-1.38*	***0.99***	*0.73-1.24*
4	191.4	3972.83	**48.19**	**1.40**	1.17-1.64	**1.42**	1.16-1.67
5	305	8200.35	**37.19**	***1.08***	*0.93-1.23*	***1.10***	*0.95-1.25*
6	536.8	13838.40	**38.79**	**1.13**	1.00-1.26	**1.14**	1.01-1.27
7	639	18191.016	**35.13**	***1.02***	*0.91-1.14*	***1.02***	*0.90-1.13*
8	700.8	20406.706	**34.34**	**1.00**	-	**1.00**	-
9	657.6	18308.516	**35.92**	***1.05***	*0.93-1.16*	***1.05***	*0.94-1.17*
10	488.4	15050.656	**32.45**	***0.95***	*0.83-1.06*	***0.91***	*0.80-1.02*
11	299.4	9750.41	**30.70**	***0.89***	*0.77-1.02*	**0.86**	0.73-0.99
12	186.8	5654.91	**33.03**	***0.96***	*0.80-1.12*	***0.93***	*0.78-1.09*
13	101.6	3547.02	**28.64**	***0.83***	*0.64-1.03*	**0.78**	0.60-0.95
14+	89.8	2625.65	**34.19**	***1.00***	*0.75-1.24*	***0.93***	*0.70-1.15*
LR statistic = 37.42, p = 0.189							
RR "per pregnancy"	-	-	-	**0.97**	0.96-0.98	**0.97**	0.96-0.98
Wald test statistic = 3.35, p = 0.023							
Pregnancies:							
0-2	113.4	2755.7	**41.15**	***1.15***	*0.93-1.37*	***1.07***	*0.86-1.28*
3-5	580.4	14369.16	**40.39**	**1.13**	1.02-1.24	**1.12**	1.01-1.22
6-8	1876.6	52436.16	**35.79**	**1.00**	-	**1.00**	-
9+	1823.6	54937.18	**33.20**	**0.93**	0.87-0.99	**0.90**	0.84-0.96
LR statistic = 13.81, p = 0.108							

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
4. *Estimates and confidence intervals in italics not statistically significant*

7.3.3 Surviving children

Men with any surviving children on entry into the cohort did not have lower mortality than those who had any surviving children in the crude (RR 1.00, 95% CI 0.75-1.25) or adjusted (RR 1.14, 95% CI 0.85-1.43, Table 7.7) estimates. Mortality rates tended to decrease as the number of surviving children increased (Figure 7.2). There was a significant decrease in mortality per surviving child (adjusted RR per surviving child 0.95, 95% CI 0.94-0.97, Wald test statistic 5.46, $p < 0.001$). Men who had six to eight surviving children had a 14% lower mortality than men who had three to five surviving children (adjusted RR 0.86, 95% CI 0.80-0.92). The same comparison for men with nine or more surviving children showed that they had an almost 30% reduction in mortality (adjusted RR 0.72, 95% CI 0.62-0.83). The effects on mortality were not as strong as those seen in the repeated-imputation inferences for the women. Mortality tended to decrease with an increase in the percentage of children surviving but the differences were not large and generally not statistically significant.

As for the women, the trends in mortality with parity were examined in each surviving children group, and vice versa. The variables were also combined into one summary variable that noted the parity and surviving children. The trends noted above seemed to persist when the crude rates were examined (Figure 7.3). There was no trend of increasing mortality with increasing parity in surviving children groups in the crude or adjusted analysis (Table 7.9). In the same table however, mortality rates are seen to decrease significantly per surviving child in each of the parity groups. The estimates and trends were all statistically significant, and decreased slightly in magnitude on adjusting for socio-demographic factors. These patterns were the same when examining the effects of parity and surviving children in combination (Table 7.10), with mortality decreasing with the number of surviving children. Again, these trends appeared to be confounded by socio-economic status.

Figure 7.2: Crude male mortality rates (+95% CI) by number of surviving children

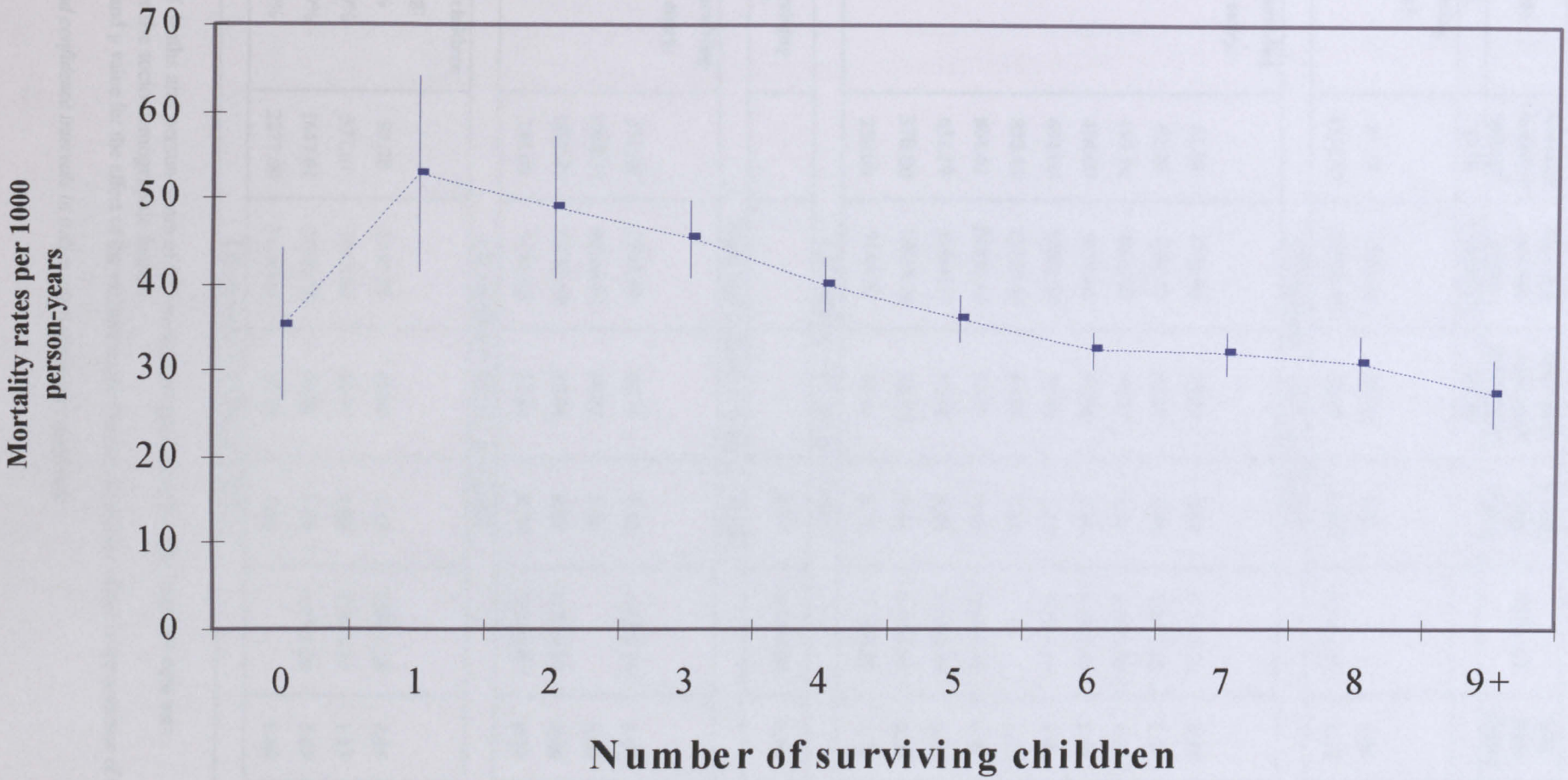


Table 7.7: Mortality In Men Who Have Completed Their Reproduction By Surviving Children

Variable	Average number deaths[1]	Average person years	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj.[2] Rate Ratio	95% CI
Total	4394	124498.00	**35.29**	-	-	-	-
Any surviving children?:							
No	61.38	1738.44	**35.32**	**1.00**	-	**1.00**	-
Yes	4332.62	122759.56	**35.29**	***1.00***[4]	*0.75-1.25*	***1.14***	*0.85-1.43*
LR statistic = 1.07, p = 0.395[3]							
Number of surviving children on entry:							
0	61.38	1738.44	**35.32**	***0.99***	*0.73-1.24*	***0.85***	*0.63-1.08*
1	92.20	1741.11	**52.95**	**1.48**	1.14-1.82	***1.26***	*0.96-1.56*
2	199.16	4065.92	**48.97**	**1.37**	1.12-1.60	***1.11***	*0.91-1.30*
3	424.00	9377.62	**45.22**	**1.26**	1.09-1.43	**1.16**	1.01-1.32
4	694.00	17461.87	**39.74**	***1.11***	*0.99-1.23*	***1.06***	*0.94-1.18*
5	850.45	23727.56	**35.90**	**1.00**	-	**1.00**	-
6	801.42	24835.63	**32.27**	**0.90**	0.81-0.99	***0.91***	*0.81-1.00*
7	651.39	20368.77	**31.98**	**0.89**	0.80-0.99	***0.91***	*0.81-1.00*
8	370.00	12038.76	**30.73**	**0.86**	0.75-0.96	**0.88**	0.77-0.99
9+	250.00	9144.32	**27.34**	**0.76**	0.64-0.89	**0.76**	0.64-0.89
LR statistic = 62.46, p < 0.001							
RR "per surviving child"	-	-	-	**0.93**	0.91-0.94	**0.95**	0.94-0.97
Wald test statistic = 5.46, p < 0.001							
Number of surviving children on entry:							
0-2	352.74	7545.50	**46.75**	**1.20**	1.05-1.35	***1.03***	*0.89-1.16*
3-5	1968.45	50566.10	**38.93**	**1.00**	-	**1.00**	-
6-8	1822.81	57242.08	**31.84**	**0.82**	0.77-0.87	**0.86**	0.80-0.92
9+	250.00	9144.32	**27.34**	**0.70**	0.60-0.81	**0.72**	0.62-0.83
LR statistic = 42.33, p < 0.001							
Percentage of children surviving:							
0-24.9%	97.78	2332.38	**41.93**	**1.31**	1.04-1.58	***1.05***	*0.83-1.28*
25.0-49.9%	371.61	7619.04	**48.77**	**1.53**	1.34-1.71	**1.23**	1.07-1.38
50.0-74.9%	1647.61	43341.92	**38.01**	**1.19**	1.11-1.26	***1.05***	*0.98-1.12*
75.0-100%	2277.00	71204.66	**31.98**	**1.00**	-	**1.00**	-
LR statistic = 13.09, p = 0.013							

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
4. *Estimates and confidence intervals in italics not statistically significant*

Figure 7.3: Crude male mortality rates by number of surviving children, in parity groups

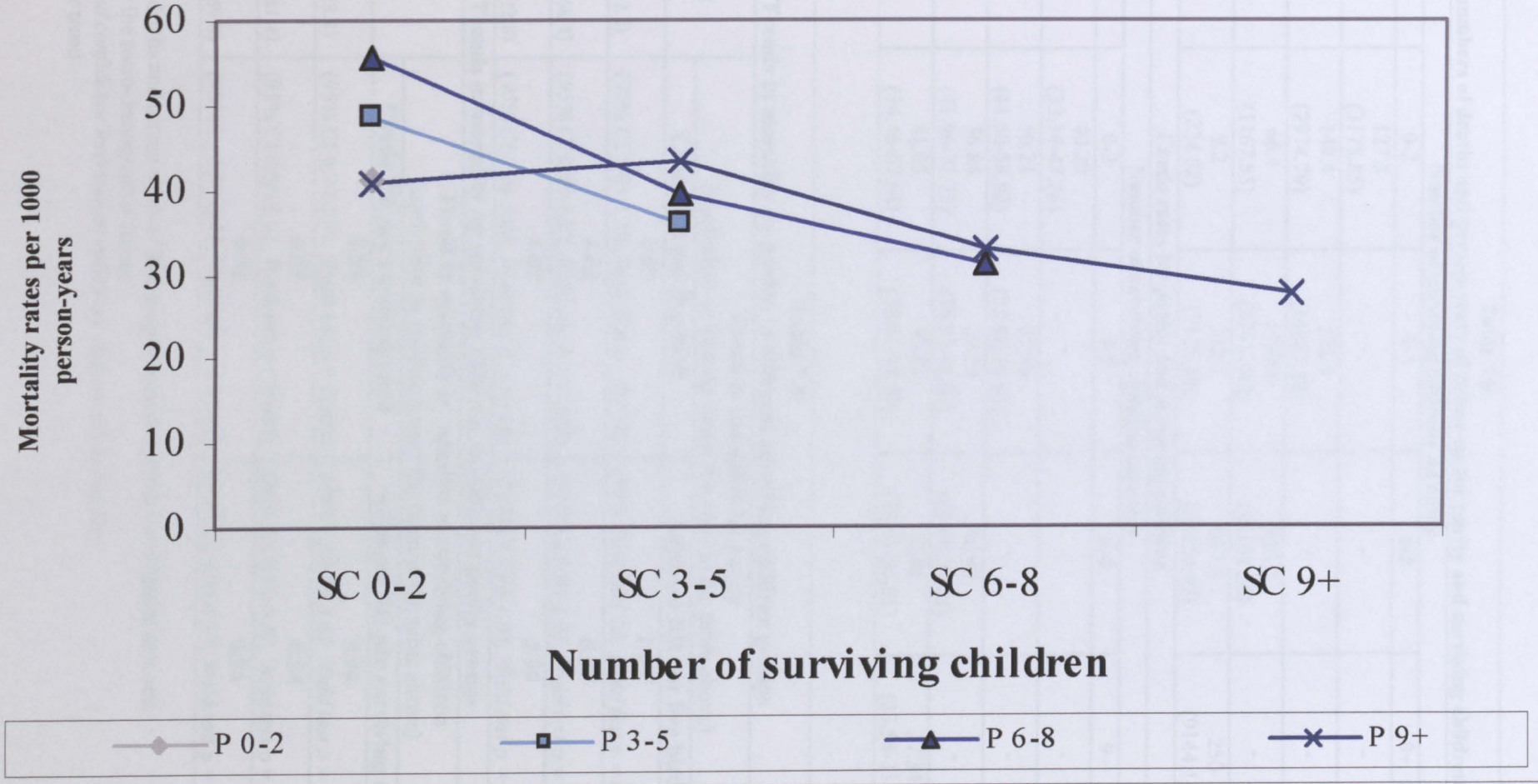


Table 7.8: Average numbers of deaths and person-years of follow-up for parity and surviving children[1]				
Number of surviving children on entry				
Parity	0-2	3-5	6-8	9+
0-2	127.8 (3178.85)	-	-	-
3-5	149.4 (2974.79)	576.4 (16027.98)	-	-
6-8	66.4 (1167.85)	1079.8 (27412.62)	935.2 (30191.26)	-
9+	9.2 (224.02)	312.2 (7125.49)	887.6 (27050.97)	250 (9144.11)
Crude rates for parity and surviving children				
Number of surviving children on entry				
Parity	0-2	3-5	6-8	9+
0-2	40.20 (33.14-47.26)	-	-	-
3-5	50.21 (41.60-58.82)	35.96 (32.92-39.01)	-	-
6-8	56.84 (41.96-71.73)	39.39 (36.97-41.81)	30.98 (28.94-33.01)	-
9+	41.05 (14.46-67.64)	43.81 (38.65-48.97)	32.81 (30.61-35.01)	27.34 (23.54-31.13)

Table 7.9: Trends in mortality by parity, in different surviving children groups		
Surviving children	**Trend in mortality by parity** (equivalent to looking down the rates in the table above)	
	Crude RR per live birth	**Adjusted RR per live birth[2]**
0-2 (no. deaths =352.8)	**1.05** (95% CI 1.01-1.10, Wald test p = 0.015)	***1.03***[3] *(95% CI 0.98-1.08, Wald test p = 0.213*[4]*)*
3-5 (no. deaths = 1968.4)	***1.02*** *(95% CI 0.99-1.05, Wald test p = 0.103)*	***0.99*** *(95% CI 0.96-1.02, Wald test p = 0.096)*
6-8 (no. deaths = 1822.8)	***1.02*** *(95% CI 0.98-1.05, Wald test p = 0.118)*	***0.99*** *(95% CI 0.96-1.03, Wald test p = 0.114)*
Trends in mortality by surviving children, in different parity groups		
Parity	**Trend in mortality by number of surviving children** (equivalent to looking across the rates in the table above)	
	Crude RR per surviving child	**Adjusted RR per surviving child**
3-5 (no. deaths = 725.8)	**0.85** (95% CI 0.79-0.91, Wald test p = 0.009)	***0.96*** *(95% CI 0.89-1.03, Wald test p = 0.345)*
6-8 (no. deaths = 2081.4)	**0.89** (95% CI 0.86-0.92, Wald test p < 0.001)	**0.94** (95% CI 0.91-0.97, Wald test p = 0.020)
9+ (no. deaths = 1459.0)	**0.91** (95% CI 0.87-0.94, Wald test p < 0.001)	**0.94** (95% CI 0.90-0.97, Wald test p = 0.018)

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. *Estimates and confidence intervals in italics not statistically significant*
4. Wald test for trend

Table 7.10:
Crude Rate Ratios for Parity and Surviving Children

	Number of surviving children on entry			
Parity	0-2	3-5	6-8	9+
0-2	*1.03* *(0.83-1.21)*[1]	-	-	-
3-5	1.27 (1.04-1.51)	*0.91* *(0.82-1.01)*	-	-
6-8	1.44 (1.05-1.84)	**1.00** **(reference)**	0.79 (0.72-0.86)	-
9+	*1.04* *(0.36-1.72)*	*1.11* *(0.96-1.26)*	0.83 (0.76-0.91)	0.69 (0.59-0.80)

Adjusted Rate Ratios for Parity and Surviving Children[2]

	Number of surviving children on entry			
Parity	0-2	3-5	6-8	9+
0-2	*0.99* *(0.81-1.18)*	-	-	-
3-5	*1.05* *(0.84-1.26)*	*1.02* *(0.91-1.13)*	-	-
6-8	*1.13* *(0.81-1.44)*	**1.00** **(reference)**	0.88 (0.80-0.96)	-
9+	*1.01* *(0.35-1.67)*	*1.04* *(0.90-1.19)*	0.85 (0.77-0.93)	0.73 (0.62-0.85)

1. *Results in italics not statistically significant*
2. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors: LR statistic = 44.58, $p < 0.001$
   Adjusted for the socio-demographic factors

7.3.4 Surviving sons

There was no significant difference in the mortality of men with no surviving sons compared with men who had any surviving sons (adjusted RR 0.94, 95% CI 0.84-1.05, Table 7.11). Mortality decreased slightly per surviving son (Figure 7.4, adjusted RR per surviving son 0.96, 95% CI 0.94-0.907, Wald test statistic 4.33, $p < 0.001$). There were no trends in mortality with the percentage of live births that were male or with the percentage of surviving children who were male. The number of surviving children and number of surviving sons were examined in combination in an attempt to ascertain whether it was surviving children or surviving sons that had the largest influence on mortality. Crude mortality rates suggest that mortality decreased with the number of surviving children, regardless of the number of surviving sons (Figure 7.5). Mortality reduced with the number of surviving children in each surviving sons group (estimates and trends significant), but not with surviving sons in surviving children groups (Table 7.12). This trend of reducing mortality with surviving children regardless of the number of surviving sons, was confirmed when the two variables were examined in combination (Table 7.13).

7.3.5 Surviving daughters

The mortality of men who had any surviving daughters was lower than that of men with no surviving daughters in the crude analysis (RR 0.85, 95% CI 0.75-0.95) but not when the estimates were adjusted (RR 0.96, 95% CI 0.85-1.07, Table 7.14). Mortality did decrease significantly per surviving daughter (Figure 7.6), but the relative difference was small (adjusted RR per surviving daughter 0.97, 95% CI 0.95-0.99, Wald test statistic 3.01, $p = 0.001$). Men with between none and two surviving daughters had significantly higher mortality than those with between three and five surviving daughters but the relative differences were small (adjusted RR 1.08, 95% CI 1.01-1.15). There were no differences in male mortality with the percentage of children surviving who were daughters. As with surviving sons, mortality reduced with the number of surviving children in each surviving daughter group (estimates and trends significant), but not with surviving daughters in surviving children groups (Figure 7.7, Table 7.15). This trend was confirmed when the two variables were examined in combination (Table 7.16).

Figure 7.4: Crude male mortality rates (+95% CI) by number of surviving sons

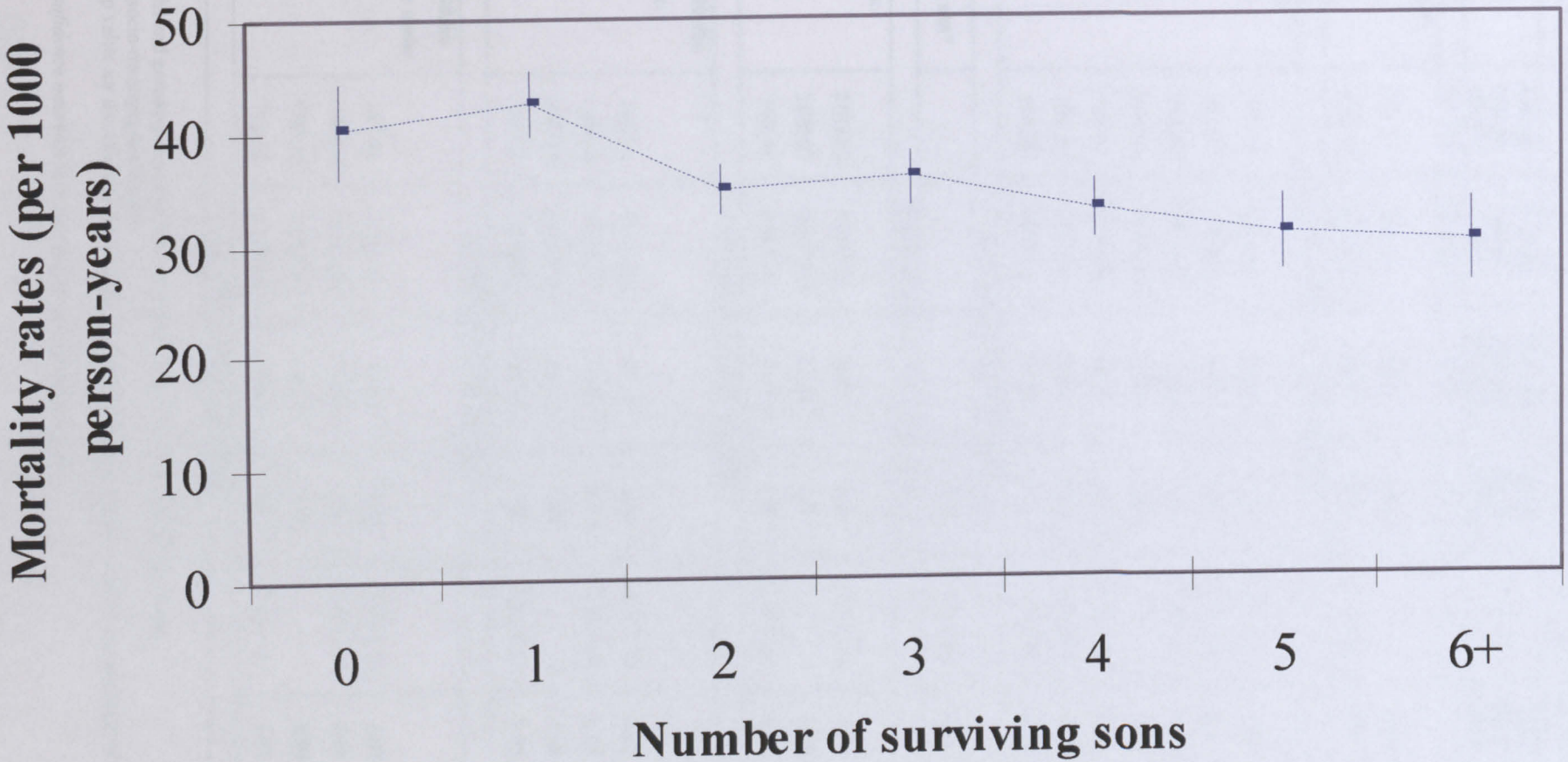


Table 7.11: Mortality In Men Who Have Completed Their Reproduction By Surviving Sons

Variable	Average number deaths[1]	Average person years	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj.[2] Rate Ratio	95% CI
Total	4394.00	124498.00	**35.29**	-	-	-	-
Any surviving sons?:							
No	372.57	9265.87	**40.21**	**1.00**	-	**1.00**	-
Yes	4021.43	115232.13	**34.90**	**0.86**	0.77-0.96	***0.94***[4]	*0.84-1.05*
LR statistic = 1.23, p = 0.554[3]							
Surviving sons:							
0	372.57	9265.87	**40.21**	***1.13***	*0.99-1.27*	***1.02***	*0.88-1.15*
1	761.36	17949.50	**42.42**	**1.19**	1.08-1.30	**1.11**	1.00-1.22
2	970.00	28046.84	**34.58**	***0.97***	*0.88-1.06*	***0.93***	*0.85-1.02*
3	1012.43	28403.48	**35.64**	**1.00**	-	**1.00**	-
4	731.44	22304.80	**32.79**	***0.92***	*0.83-1.01*	***0.90***	*0.81-1.00*
5	356.20	11640.35	**30.60**	**0.86**	0.75-0.96	**0.86**	0.75-0.96
6+	190.00	6887.16	**27.59**	**0.77**	0.65-0.90	**0.79**	0.66-0.92
LR statistic = 38.55, p < 0.001							
RR "per surviving son"	-	-	-	**0.94**	0.92-0.96	**0.96**	0.94-0.97
Wald test statistic = 4.33, p < 0.001							
Surviving sons:							
0-2	2103.93	55262.21	**38.07**	**1.13**	1.06-1.20	**1.07**	1.00-1.14
3-5	2100.07	62348.63	**33.68**	**1.00**	-	**1.00**	-
6+	190.00	6887.16	**27.59**	**0.82**	0.69-0.95	**0.84**	0.71-0.98
LR statistic = 12.88, p = 0.004							
Percentage of live births that were male:							
0-24.9%	563.15	15340.35	**36.71**	***1.04***	*0.94-1.14*	**1.03**	0.93-1.13
25.0-49.9%	1309.58	38149.17	**34.33**	***0.97***	*0.90-1.04*	**0.98**	0.91-1.06
50.0-74.9%	1987.69	56068.48	**35.45**	**1.00**	-	**1.00**	-
75.0-100%	533.58	14940.00	**35.72**	***1.01***	*0.91-1.11*	**1.03**	0.92-1.13
LR statistic = 1.53, p = 0.438							
Percentage of children surviving who were male:							
0-24.9%	657.56	17811.63	**36.92**	***1.06***	*0.96-1.16*	***1.04***	*0.94-1.13*
25.0-49.9%	1190.65	33932.20	**35.09**	***1.01***	*0.94-1.09*	***1.03***	*0.95-1.11*
50.0-74.9%	1783.21	51350.64	**34.73**	**1.00**	-	**1.00**	-
75.0-100%	762.58	21403.53	**35.63**	***1.03***	*0.94-1.12*	***1.02***	*0.93-1.11*
LR statistic = 2.85, p = 0.301							

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
4. *Estimates and confidence intervals in italics not statistically significant*

Figure 7.5: Crude male mortality rates by number of surviving children, in surviving son groups

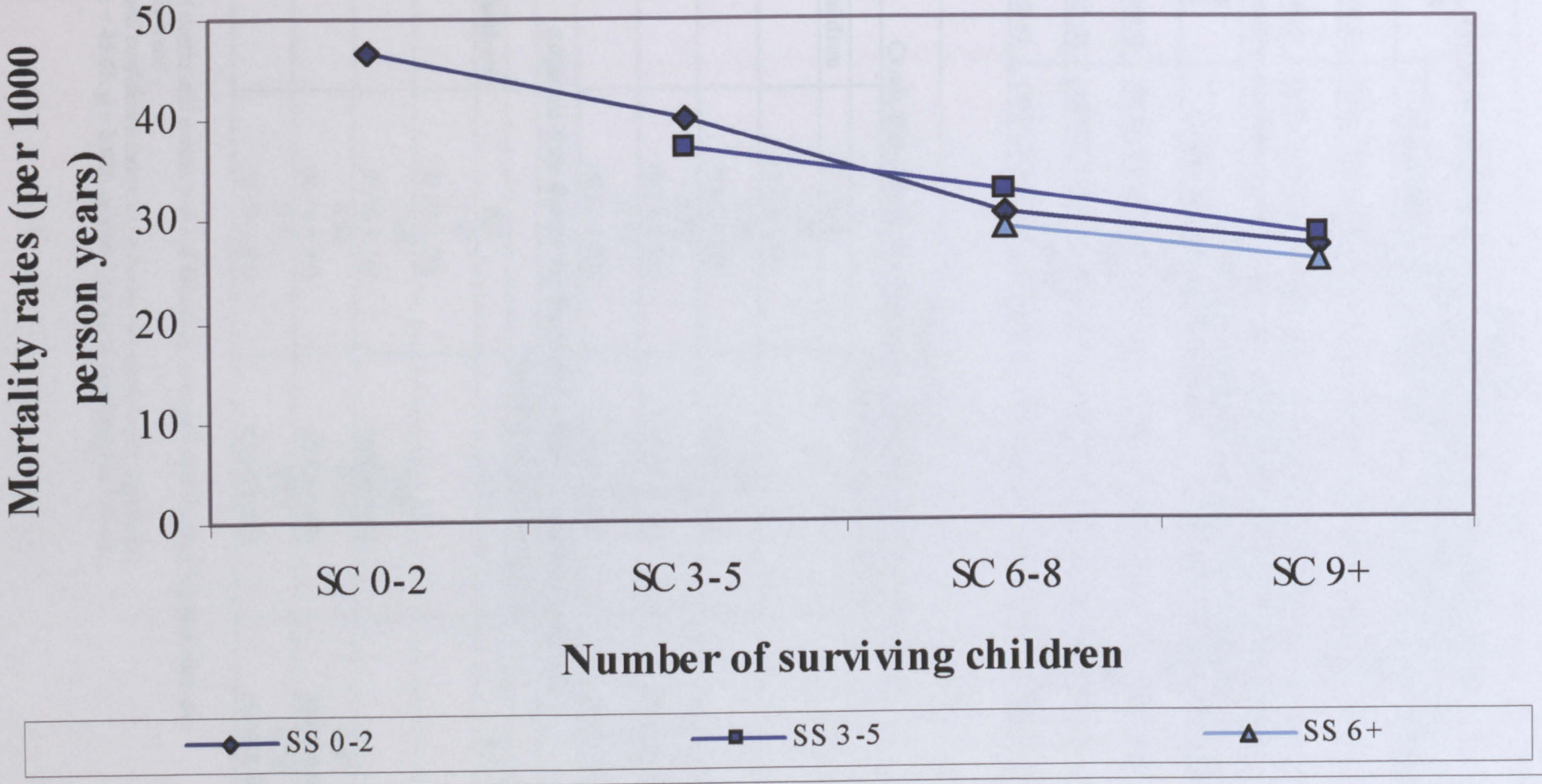


Table 7.12: Trends in mortality by surviving children, in surviving son groups		
Surviving Sons	**Trend in mortality by surviving children**	
	Crude RR per surviving child	**Adjusted RR per surviving child**
0-2 (no. deaths = 2104.0[1])	**0.93** (95% CI 0.90-0.95, Wald test p < 0.001)	**0.96** (95% CI 0.93-0.98, Wald test p = 0.013[2])
3-5 (no. deaths = 2100.0)	**0.94** (95% CI 0.91-0.97, Wald test p = 0.026)	**0.95** (95% CI 0.92-0.99, Wald test p = 0.041)
Trends in mortality by surviving sons, in different surviving children groups		
Surviving Children	**Trend in mortality by number of surviving sons**	
	Crude RR per surviving sons	**Adjusted RR per surviving sons**
3-5 (no. deaths = 1968.4)	**0.95** (95% CI 0.91-0.99, Wald test p = 0.048)	***0.96***[3] *(95% CI 0.92-1.00, Wald test p = 0.092)*
6-8 (no. deaths = 1822.8)	***0.99*** *(95% CI 0.96-1.02, Wald test p = 0.126)*	***0.99*** *(95% CI 0.96-1.02, Wald test p = 0.117)*
9+ (no. deaths = 250.0)	***0.94*** *(95% CI 0.87-1.01, Wald test p = 0.341)*	***0.95*** *(95% CI 0.87-1.02, Wald test p = 0.400)*

Table 7.13: Crude Rate Ratios for Surviving Children and Surviving Sons			
	Number of surviving sons		
Surviving children	0-2	3-5	6+
0-2	1.26 (1.08-1.44)	-	-
3-5	*1.08 (0.98-1.18)*[1]	**1.00 (reference)**	-
6-8	0.82 (0.73-0.92)	0.88 (0.80-0.97)	0.78 (0.62-0.94)
9+	*0.73 (0.41-1.05)*	0.76 (0.61-0.91)	0.70 (0.53-0.86)
Adjusted Rate Ratios for Surviving Children and Surviving Sons[4]			
	Number of surviving sons		
Surviving children	0-2	3-5	6+
0-2	*1.07 (0.91-1.23)*	-	-
3-5	*1.06 (0.96-1.16)*	**1.00 (reference)**	-
6-8	0.84 (0.74-0.94)	*0.91 (0.83-1.00)*	0.82 (0.65-0.98)
9+	*0.70 (0.40-1.01)*	0.77 (0.61-0.92)	0.74 (0.56-0.92)

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Wald test for trend
3. *Estimates and confidence intervals in italics not statistically significant*
4. LR statistic = 45.45, p = 0.026, adjusted for socio-demographic factors

Figure 7.6: Crude male mortality rates (+95% CI) by number of surviving daughters

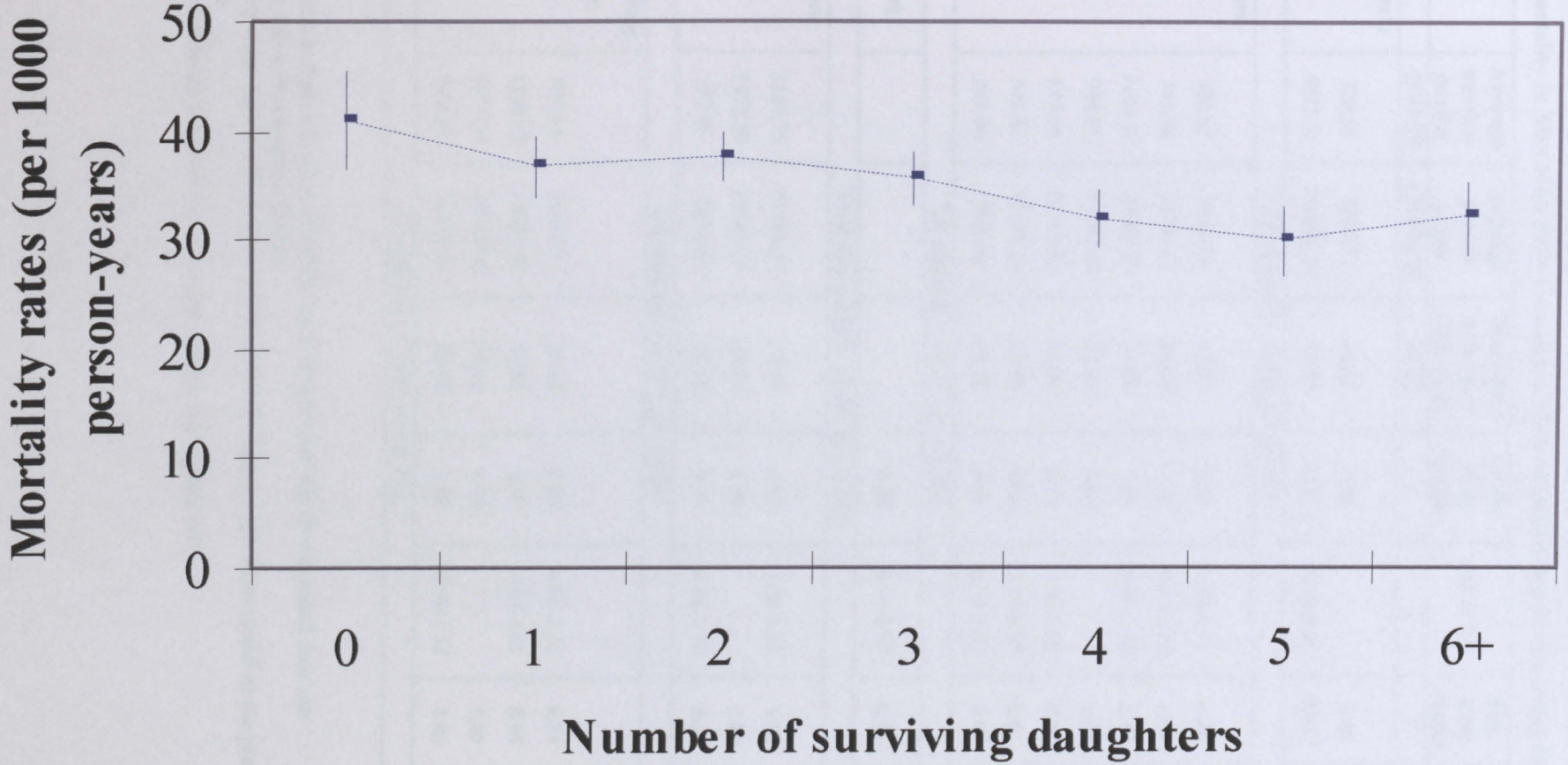


Table 7.14: Mortality In Men Who Have Completed Their Reproduction By Surviving Daughters							
Variable	**Average number deaths[1]**	**Average person years**	**Mortality rate (per 1000 pyrs)**	**Crude Rate Ratio**	**95% CI**	**Adj.[2] Rate Ratio**	**95% CI**
Total	4394.00	124498.00	**35.29**	-	-	-	-
Surviving daughters?:							
No	320.55	7815.73	**41.02**	**1.00**	-	**1.00**	-
Yes	4073.45	116682.27	**34.91**	**0.85**	0.75-0.95	***0.96***[4]	*0.85-1.07*
LR statistic = 0.48, p = 0.791[3]							
Surviving daughters:							
0	320.55	7815.73	**41.02**	**1.15**	1.00-1.30	***1.01***	*0.88-1.14*
1	743.78	20290.41	**36.66**	***1.03***	*0.92-1.13*	***1.00***	*0.89-1.10*
2	1103.42	29282.45	**37.68**	***1.06***	*0.96-1.15*	***1.02***	*0.93-1.12*
3	984.81	27652.74	**35.61**	**1.00**	-	**1.00**	-
4	645.66	20195.80	**31.96**	***0.90***	*0.80-1.00*	***0.91***	*0.80-1.01*
5	341.82	11401.21	**29.98**	**0.84**	0.74-0.95	**0.84**	0.73-0.94
6+	253.96	7859.66	**32.32**	***0.91***	*0.78-1.04*	***0.92***	*0.78-1.05*
LR statistic = 19.17, p = 0.006							
RR "per surviving daughter"	-	-	-	**0.96**	0.94-0.97	**0.97**	0.95-0.99
Wald test statistic =3.01 p = 0.001							
Surviving daughters:							
0-2	2167.75	57388.59	**37.78**	**1.13**	1.06-1.21	**1.08**	1.01-1.15
3-5	1972.29	59249.75	**33.29**	**1.00**	-	**1.00**	-
6+	253.96	7859.66	**32.32**	***0.97***	*0.84-1.10*	***0.84***	*0.84-1.12*
LR statistic = 7.27, p = 0.049							
% of children surviving who were female:							
0-24.9%	612.16	16956.37	**36.10**	***1.03***	*0.93-1.12*	***0.99***	*0.90-1.08*
25.0-49.9%	1298.23	38699.19	**33.55**	***0.95***	*0.88-1.03*	***0.96***	*0.89-1.03*
50.0-74.9%	1671.39	47519.00	**35.17**	**1.00**	-	**1.00**	-
75.0-100%	812.22	21323.44	**38.09**	***1.08***	*0.99-1.18*	***1.06***	*0.97-1.15*
LR statistic = 2.99, p = 0.332							

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
4. *Estimates and confidence intervals in italics not statistically significant*

Figure 7.7: Crude male mortality rates by number of surviving children, in surviving daughter groups

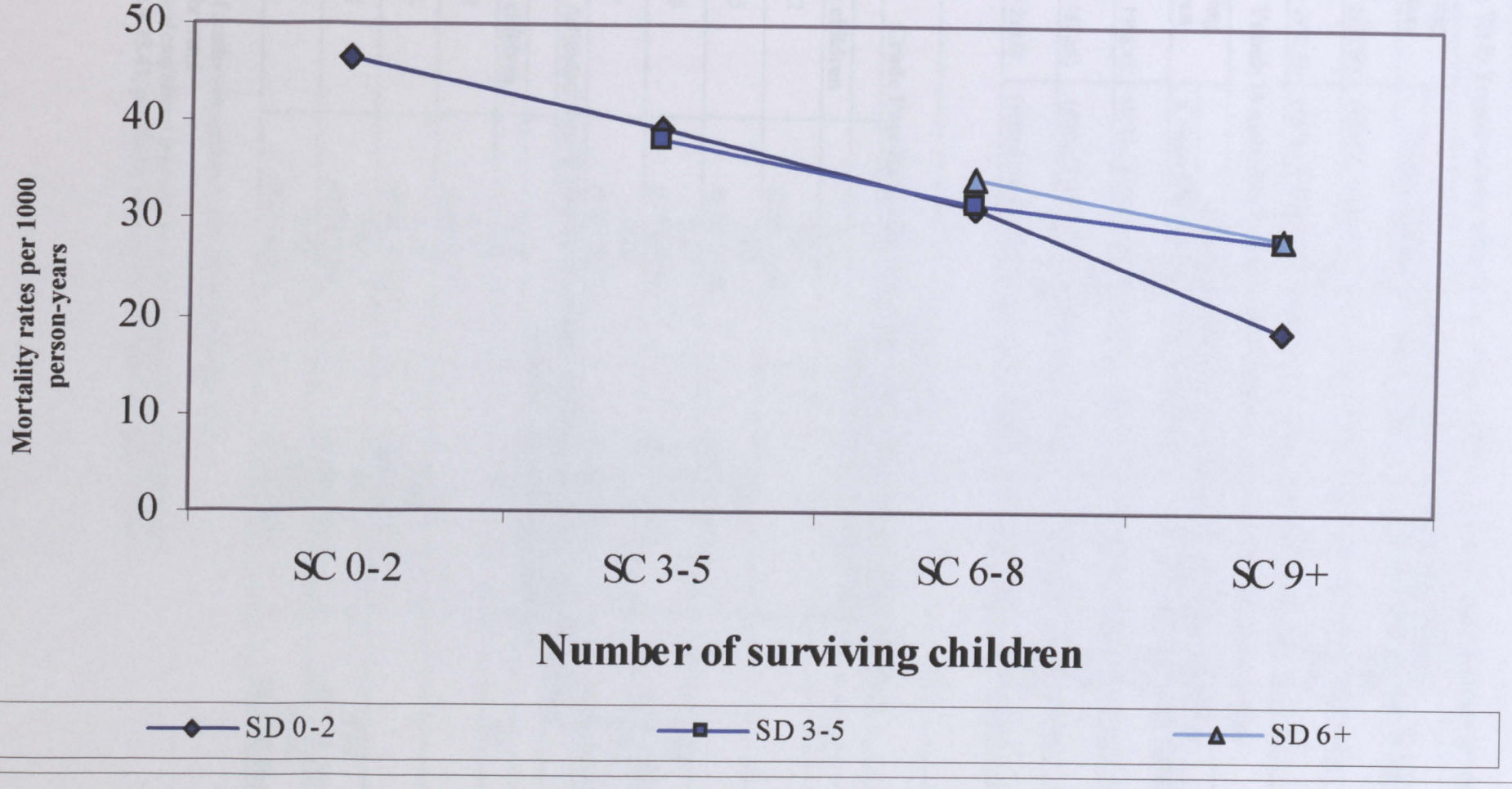


Table 7.15: Trends in mortality by surviving children, in surviving daughters groups		
Surviving Daughters	**Trend in mortality by surviving children**	
	Crude RR per surviving child	**Adjusted RR per surviving child**
0-2 (no. deaths = 2167.8[1])	**0.92** (95% CI 0.90-0.95, Wald test p < 0.001)	**0.96** (95% CI 0.93-0.98, Wald test p = 0.007[2])
3-5 (no. deaths = 1972.2)	**0.93** (95% CI 0.90-0.96, Wald test p < 0.001)	**0.94** (95% CI 0.91-0.97, Wald test p < 0.001)
Trends in mortality by surviving daughters, in surviving children groups		
Surviving Children	**Trend in mortality by number of surviving daughters**	
	Crude RR per surviving daughters	**Adj. RR per surviving daughters**
3-5 (no. deaths = 1968.4)	***1.00***[3] *(95% CI 0.96-1.04, Wald test p =0.268)*	***1.01*** *(95% CI 0.96-1.05, Wald test p =0.298)*
6-8 (no. deaths = 1822.8)	***1.00*** *(95% CI 0.97-1.03, Wald test p =0.115)*	***1.00*** *(95% CI 0.97-1.03, Wald test p =0.128)*
9+ (no. deaths = 250.0)	***1.04*** *(95% CI 0.97-1.12, Wald test p =0.477)*	***1.04*** *(95% CI 0.96-1.12, Wald test p =0.437)*

Table 7.16: Crude Rate Ratios for Surviving Children and Surviving Daughters			
	Number of surviving daughters		
Surviving children	0-2	3-5	6+
0-2	1.23 (1.05-1.40)	-	-
3-5	*1.03 (0.93-1.13)*[1]	**1.00 (reference)**	-
6-8	0.82 (0.73-0.92)	0.83 (0.75-0.91)	*0.90 (0.75-1.05)*
9+	0.49 (0.21-0.76)	0.73 (0.59-0.87)	0.74 (0.55-0.93)
Adjusted Rate Ratios for Surviving Children and Surviving Daughters[4]			
	Number of surviving daughters		
Surviving children	0-2	3-5	6+
0-2	*1.05 (0.89-1.19)*	-	-
3-5	*1.02 (0.92-1.12)*	**1.00 (reference)**	-
6-8	0.84 (0.74-0.94)	0.87 (0.78-0.95)	*0.94 (0.77-1.10)*
9+	0.58 (0.25-0.91)	0.74 (0.59-0.88)	0.76 (0.57-0.96)

1. Numbers of deaths averaged over the five imputed data sets
2. Wald test for trend
3. *Estimates and confidence intervals in italics not statistically significant*
4. LR statistic = 38.43, p = 0.012, adjusted for socio-demographic factors

7.3.6 Fetal losses

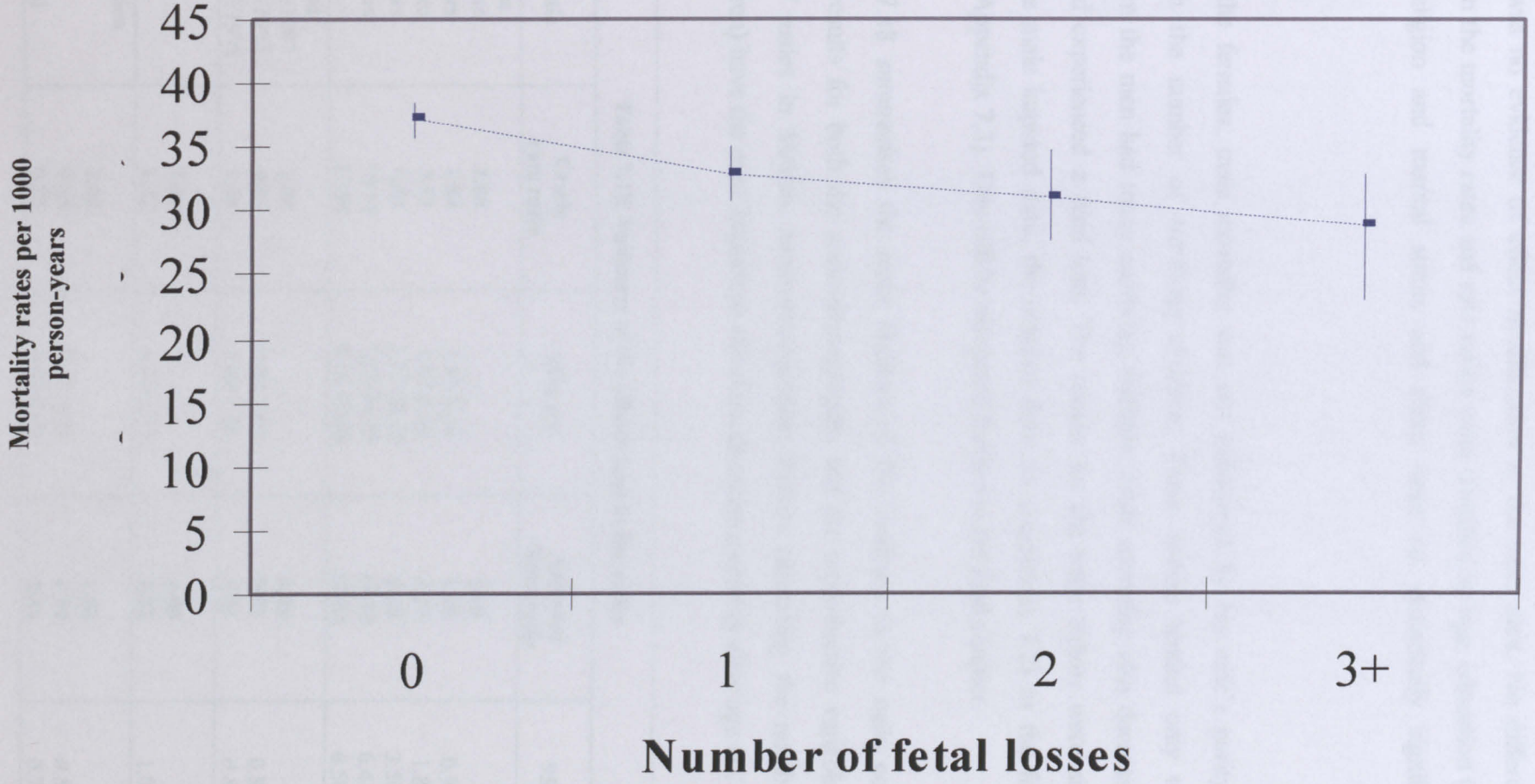
Perplexingly, men whose wives had suffered fetal losses had significantly lower mortality than men whose wives had not experienced a pregnancy loss, no matter how the data was grouped (Figure 7.8, Table 7.17). For example, the adjusted rate ratio for men whose wives had suffered any fetal losses compared with those whose wives had not suffered any was 0.89 (95% CI 0.83-0.95).

Table 7.17: Mortality In Men Who Have Completed Their Reproduction By Wife's Fetal Losses

Variable	Average number deaths[1]	Average person years	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj.[2] Rate Ratio	95% CI
Total	4394.00	124498.00	**35.29**	-	-	-	-
Fetal loss?:							
No	2949.44	79422.03	**37.14**	**1.00**	-	**1.00**	-
Yes	1444.56	45075.97	**32.05**	**0.86**	0.81-0.92	**0.89**	0.83-0.95
LR statistic = 13.91, $p < 0.001$[3]							
Fetal losses:							
0	2949.44	79422.03	**37.14**	**1.00**	-	**1.00**	-
1	967.00	29439.50	**32.85**	**0.88**	0.82-0.95	**0.91**	0.84-0.98
2	309.39	9929.45	**31.16**	**0.84**	0.74-0.94	**0.85**	0.75-0.96
3+ fetal losses	168.17	5707.02	**29.47**	**0.79**	0.67-0.92	**0.84**	0.71-0.97
LR statistic = 25.70, $p < 0.001$							
RR "per fetal loss"	-	-	-	**0.93**	0.89-0.96	**0.94**	0.91-0.97
Wald test statistic = 3.46, $p < 0.001$							
Fetal losses:							
No fetal losses	2912.20	78281.42	**37.20**	**1.00**	-	**1.00**	-
Nulligravid	37.24	1140.61	**32.61**	***0.88***[4]	*0.59-1.16*	***0.80***	*0.54-1.05*
1-2 fetal losses	1276.39	39368.95	**32.42**	**0.87**	0.81-0.93	**0.89**	0.83-0.95
3+ fetal losses	168.17	5707.02	**29.47**	**0.79**	0.67-0.92	**0.83**	0.70-0.97
LR statistic = 16.64, $p = 0.009$							

1. Numbers of deaths and person-years of follow-up averaged over the five imputed data sets
2. Adjusted for the socio-demographic factors
3. LR statistic and p value for the effect of the variable on the Poisson regression model in the presence of the other factors
4. *Estimates and confidence intervals in italics not statistically significant*

Figure 7.8: Crude male mortality rates (+95% CI) by number of fetal losses experienced by wife



7.4 Interactions

There was no evidence of effect modification in the male data. No differences were seen when the mortality rates and rate ratios were stratified by age, education (male or female), religion and marital status and there were no statistically significant interactions.

7.5 Summary

As in the females, male mortality was not influenced by his wife's parity but decreased with the number of surviving children. These results tended only to be significant when the men had many surviving children. Male mortality also decreased if their wives had experienced a fetal loss. The results for the male cohort were similar when using the male imputed data, the original data set (Appendix 7.2) or the female imputed data (Appendix 7.3). This will be discussed further in the final chapter.

Table 7.18 summarises the main findings of the analyses in the male cohort, including the results for both the socio-demographic and the reproductive variables. In this cohort of males in Matlab, socio-demographic factors (including the number of surviving children) have the most important effect on all-cause mortality after age 40.

Table 7.18: Summary of the effects seen in the males

Characteristic	Crude rate ratio	95% CI	Adjusted Rate ratio	95% CI
Age groups				
40-49.9 years	**1.00**	-	**1.00**	-
50-59.9 years	**1.84**	1.02-3.34	**1.78**	0.98-3.22
60-69.9 years	**3.57**	1.97-6.46	**3.37**	1.86-6.10
70-79.9 years	**6.83**	3.77-12.37	**6.33**	3.50-11.47
80-89.9 years	**13.19**	7.22-24.09	**11.72**	6.41-21.42
90+ years	**17.90**	8.13-39.43	**14.34**	6.50-31.66
Time period				
30/6/1982-29/6/1987	**1.00**	-	**1.00**	-
30/6/1987-29/6/1992	***0.94***	*0.86-1.02*	**0.91**	0.83-0.99
30/6/1992-31/12/1998	**1.08**	1.00-1.16	***0.95***	*0.88-1.03*
Religion				
Muslim	**1.00**	-	**1.00**	-
Hindu	**1.22**	1.13-1.33	**1.13**	1.01-1.27
Male education				
None	**1.00**	-	**1.00**	-
Maktab	**0.85**	0.77-0.93	***0.98***	*0.87-1.10*
Any formal	**0.73**	0.67-0.79	**0.83**	0.74-0.92

Summary table of the effects seen in the males (continued)				
Characteristic	**Crude rate ratio**	**95% CI**	**Adjusted rate ratio**	**95% CI**
Female education				
None	**1.00**	-	**1.00**	-
Maktab	**0.81**	0.75-0.87	**0.84**	0.75-0.95
Any formal	**0.63**	0.57-0.70	**0.75**	0.66-0.85
Male occupation				
Unskilled	**1.00**	-	**1.00**	-
None	***1.15***	*0.85-1.56*	***1.07***	*0.79-1.44*
Skilled	**0.77**	0.72-0.82	**0.89**	0.83-0.95
Disabled	**4.09**	3.46-4.83	**3.21**	2.72-3.80
Area of residence				
Intervention	**1.00**	-	**1.00**	-
Comparison	**1.08**	1.02-1.15	**1.09**	1.02-1.15
Marital status				
Still married	**1.00**	-	**1.00**	-
Widowed	**1.78**	1.58-2.01	**1.26**	1.12-1.42
Divorced	***1.23***	*0.64-2.37*	***0.96***	*0.50-1.85*
Parity				
0-2	***1.14***	*0.93-1.34*	***1.05***	*0.86-1.24*
3-5	***1.08***	*0.98-1.18*	***1.08***	*0.99-1.18*
6-8	**1.00**	-	**1.00**	-
9+	***0.95***	*0.88-1.01*	**0.91**	0.85-0.98
Gravidity				
0-2	***1.15***	*0.93-1.37*	***1.07***	*0.86-1.28*
3-5	**1.13**	1.02-1.24	**1.12**	1.01-1.22
6-8	**1.00**	-	**1.00**	-
9+	**0.93**	0.87-0.99	**0.90**	0.84-0.96
Surviving children				
0-2	**1.20**	1.05-1.35	***1.03***	*0.89-1.16*
3-5	**1.00**	-	**1.00**	-
6-8	**0.82**	0.77-0.87	**0.86**	0.80-0.92
9+	**0.70**	0.60-0.81	**0.72**	0.62-0.83
Parity and surviving children				
P 0-2, SC 0-2	***1.03***	*0.83-1.21*	***0.99***	*0.81-1.18*
P 3-5, SC 0-2	**1.27**	1.04-1.51	***1.05***	*0.84-1.26*
P 3-5, SC 3-5	***0.91***	*0.82-1.01*	***1.02***	*0.91-1.13*
P 6-8, SC 0-2	**1.44**	1.05-1.84	***1.13***	*0.81-1.44*
P 6-8, SC 3-5	**1.00**	-	**1.00**	-
P 6-8, SC 6-8	**0.79**	0.72-0.86	**0.88**	0.80-0.96
P 9+, SC 0-2	***1.04***	*0.36-1.72*	***1.01***	*0.35-1.67*
P 9+, SC 3-5	***1.11***	*0.96-1.26*	***1.04***	*0.90-1.19*
P 9+, SC 6-8	**0.83**	0.76-0.91	**0.85**	0.77-0.93
P 9+, SC 9+	**0.69**	0.59-0.80	**0.73**	0.62-0.85
Fetal losses				
0	**1.00**	-	**1.00**	-
1	**0.88**	0.82-0.95	**0.91**	0.84-0.98
2	**0.84**	0.74-0.94	**0.85**	0.75-0.96
3+	**0.79**	0.67-0.92	**0.84**	0.71-0.97

8.1 The principal findings

There was no evidence of an association between parity and all-cause mortality in women who had completed their reproduction in Matlab, Bangladesh. In particular, there was no evidence of increased mortality at the extremes of parity. These conclusions did not change when looking at gravidity (number of pregnancies) rather than parity (number of live births) or after adjusting for age, time period and socio-economic factors. However, female mortality decreased with an increasing number of surviving children, regardless of parity. These associations also persisted after adjusting for potential confounders, although the magnitude of the estimates reduced. The patterns were relatively consistent whether the surviving children were boys or girls. There was also some evidence that the effect of surviving children may modify with age, with mortality highest in women over the age of 65 with none or few surviving children. Women who had experienced a fetal loss had significantly higher mortality than those who had not.

The effects in the male cohort were strikingly similar, if a little weaker. There was no effect of wife's parity on male survival, but mortality decreased with the number of surviving children, regardless of their sex. Puzzlingly, male mortality was significantly lower if the man's wife had suffered a fetal loss. All of the patterns seen persisted after adjusting for potential confounders and there were no significant interactions.

In addition, the socio-demographic determinants of adult mortality were consistent with patterns previously observed. Mortality reduced over time and was higher in Hindus and in individuals living in the comparison area. Mortality decreased significantly with educational attainment, with mortality lowest in adults who had attended any formal education. An interesting finding was that female education appeared to be an independent predictor of male mortality, a finding not reported in earlier studies. In addition, subjects who had received Islamic teachings (Maktab) had lower mortality than those who had not attended any form of education. This is also a finding that has not previously been discussed. Subjects who remained married had lower mortality than those who were divorced or widowed. In females, mortality was greatest in subjects who became divorced whereas widowed men had the highest mortality. In fact, the effect of divorce disappeared in the men after adjusting for socio-economic factors.

8.2 Are there alternative explanations for the results?

8.2.1 The role of chance

Sample size calculations showed that there were enough eligible subjects under surveillance at Matlab to detect statistically significant differences in the mortality of parous and nulliparous subjects with 80% power and 95% confidence. However, the actual numbers of nulliparous women and men without children in the sample were lower than expected. The sample size calculations were therefore re-estimated using these lower percentages. The person-years of follow-up available remained adequate to rule out chance as an alternative explanation for the findings[8.1]. The person-years of observation were also sufficient to analyse the effects of parity and surviving children over a wider range of exposures than in previous studies. Poisson regression was used for the comparison of mortality rates. This is suitable for the analysis of cohort data and is appropriate when the event of interest is rare (Preston 1998). Appropriate statistical tests were therefore performed to assess the role of chance in the estimation of relative rates.

8.2.2 Misclassification of outcome

The prospective DSS data (that includes demographic data on births, deaths and marriages) are thought to be relatively accurate and complete (Fauveau 1994). The CHWs who collect the information receive six weeks of training when first employed, regular educational sessions throughout their tenure and supervision throughout their fieldwork. Many are very experienced. In 1994, 70% of the CHWs had worked for the project for around 20 years (Fauveau *et al* 1994). They also live in the village or area in which they work and, as a result, are unlikely to miss many events.

[8.1] Assuming that 1% of women were nulliparous (smaller percentage than in our sample), 1937 nulliparous women-years and 193700 parous women-years were required to detect a relative mortality rate of 1.5 in the nulliparous compared with the parous, with 1444 nulliparous women-years and 1444400 parous women-years necessary to detect a halving of the risk. In the data there were 2702 women-years of observation in nulliparous women and 199621 for parous women. For the men, assuming that 1% were 'nulliparous', a sample of 1307 childless men-years and 130700 'men with children' years was required to detect a relative mortality rate of 1.5 in the childless men compared with men with children, with 977 childless men-years and 97700 'men with children' years necessary to detect a halving of the risk. In the data, there were 1329 childless men-years of observation and 123169 'men with children' years.

When I accompanied a CHW on her data collection rounds, the women in the villages were awaiting her arrival and had prepared food for her. This enthusiasm and continuing co-operation is another essential feature of the data collection system. The community is also aware of the many benefits of the ICDDR, B presence in the area. For example, locals can remember a time when a severe case of cholera was almost always fatal. They therefore know that the free treatment, offered in the Matlab field hospital to all residents under surveillance, saves lives.

The data undergo frequent validation. Senior field assistants visit the villages monthly to verify that an event has occurred. Senior managers also perform random checks on the quality and completeness of the fieldwork (D'Souza 1981). In addition, the computer package used to enter the data is programmed to detect impossible and inconsistent information, which can then be checked in the field. Further verification occurs during the census data collection and specific validation studies have also been conducted (Becker, Mahmud 1984; Mahmud, Becker 1987). In this current study, the data were extracted in collaboration with an experienced data manager and consistency checks performed with his help. Several discrepancies were corrected in this way. The outcome data in this study are therefore thought to be reasonably accurate and complete.

Other advantages of the DSS data include the availability of an accurate count of the population that gives accurate denominator data (D'Souza 1981), comparable data collection for each subject as structured forms are used to collect the information (Fauveau *et al* 1989), and the presence of an identification number that is "*unique, permanent, universal and available*" (Sorensen *et al* 1996). This allows individuals to be followed throughout their life-course and for linkage between different data collection systems and different individuals.

8.2.3 Misclassification of exposure

Reproductive histories are collected in the DSS when a woman experiences a birth or, after 1982, when women under the age of 55 migrate into the Matlab surveillance area. They are based on retrospective recall, other than in women who have experienced all of their pregnancies whilst living under surveillance. Despite this reliance on recall, they are thought to be relatively accurate. A validation study was conducted to assess the

quality of reproductive data collected in Matlab between 1966 and 1979 (Becker, Mahmud 1984). When interviewed, only 3.2 percent of women reported a different number of children ever borne to that recorded in the DSS and 3.6 percent reported a different number of child deaths. It is therefore possible that there was some random misclassification of parity and number of surviving children in the data, but that it would have little impact on the results. In addition there was more reproductive data available in this current study than had been used in previous studies. This included data on the sex of the children, number of surviving children and fetal losses.

Reproductive histories may have changed after entry into the cohort. Pregnancy records were therefore checked for any additional pregnancies, and altered accordingly. Data on the number of surviving children could not be updated however, in part as many children had migrated out of the surveillance area. The number of surviving children may therefore have been overestimated. In most cases, this misclassification would be unrelated to the parents' mortality, leading to an underestimation of the association between number of surviving children and the mortality of their parents. It is possible to conceive of a situation in which a child's death was related to parents' mortality. For example, they may have both died of the same infectious disease or grief may have had a negative effect on parental mortality. It is not possible to assess how often this happened in the DSS data. If this led to non-random misclassification of the number of surviving children, however, it is probable that the error would have resulted in a further underestimation of the effect of surviving children on adult mortality.

Fetal losses are probably underestimated by the DSS, as they are in most populations (Fauveau, Chakraborty 1994). Individuals in Matlab are particularly wary of discussing fetal losses, as local beliefs assert that women who miscarry may have misbehaved in such a way as to attract evil spirits (Yunus *et al* 1994). In this data, there is evidence to suggest that women who were older, less educated, Hindu and living in the comparison area reported less fetal losses (see Table 6.4, Chapter 6). This lends weight to the intimation that cultural and educational factors may have influenced the way in which individuals reported past losses. There was also no information of induced abortions, as they are illegal and therefore not asked about in the DSS data collection. The finding that male mortality decreased with the number of fetal losses experienced by the wife arouses

further suspicion about the quality of the fetal loss data, as I cannot think of any biological or social phenomena that could explain this result. Therefore, the conclusions that can be drawn about the effect of gravidity and fetal losses on long-term survival in this study are limited.

Finally, male reproductive histories were obtained by linkage with the wife's data. It was assumed that the linkage between husband and wife was accurate. In addition, a male's reproductive history was presumed to be the same as their wife's. This is a reasonable assumption as polygamy is rare and extramarital sexual activity discouraged in this society. However, it is possible that the male reproductive histories did not always represent the man's true history. Any such errors are unlikely to be related to male mortality, and would lead to an underestimation of the effects of reproductive history on male mortality.

8.2.4 Selection bias

"Missing data bias"

Reproductive histories were missing for 1573 females. Excluding these women would have been akin to introducing a selection bias, as they differed systematically from the subjects with complete data. In particular, mortality would be underestimated. Attempts to modify the cohort, by moving the entry date forward for example, depleted the sample to such a degree that the study no longer had the power to detect significant differences in mortality and did not produce any meaningful results (results not shown). Other strategies for dealing with missing data, such as weighted analyses, were not appropriate for this pattern of missing data, as explained in Chapter 4.

Multiple imputation (MI) was therefore used to obtain a range of "*'reasonable' hypothetical responses*" (Rubin 1997) for the missing reproductive variables, based on the information available for all subjects in the cohort. However, MI is not without its' flaws. Most notably, the imputed values are based on the data that is available. The predicted values will only be satisfactory if the models used for the imputations are adequate and the assumptions made are reasonable.

All of the variables associated with the reproductive histories and the missingness of reproductive histories were used in the predictive imputation models. These variables were thought to be relatively accurate, were measured in the same way for those with missing and recorded reproductive histories and were assumed to account for all of the bias introduced by the missing values. They were also the variables to be used in the Poisson regression models. This is important as, after imputation, an association between a variable and reproductive history will be underestimated if that variable had not been included as a predictor in the imputation models.

The variables were imputed under an assumption of joint normality. The values obtained in this way were compared with those obtained with the skewed variables (number of dead sons, number of dead daughters, number of fetal losses) transformed using log and reciprocal transformations. The models assuming joint normality produced the most plausible values for the missing data. For example, when the skewed variables were transformed using natural logarithms, a significant proportion of the women with imputed data had apparently experienced more pregnancies that biologically plausible. With one reciprocal transformation (1/x), all of the women with imputed data had only an even number of surviving children. A further check was performed, comparing the data obtained for the male reproductive histories using data from both the male and female imputations. The values for the reproductive histories obtained from both sets of imputations were similar, assuring us that two different models imputing under an assumption of joint normality gave consistent results.

We also assumed that the reproductive data were missing at random. But was this a fair assumption? In truth, we can only guess. It is not obvious from the discussion in Chapter 4 (for example, Table 4.10) that the women with missing data were more likely to have one reproductive history or another. One way to assess the quality of the imputations may be to compare the estimates of parity obtained in the female imputed data with estimates from other Bangladeshi sources, as shown in Table 8.1 (next page).

Table 8.1: Comparing female imputed data with data from other Bangladeshi sources

Average data from the five imputations 1982-1997 (ever-married women, aged 45-55) n = 20 383		NIS 1968-69 (ever-married, 45-49 yrs) n = 179		RSFM 1974 (ever-married, 45-55 yrs) n = 2 174 605	
Parity	**Percentage**	**Parity**	**Percentage**	**Parity**	**Percentage**
0	1.4	0	4	0	3.7
1	1.3	1	2	1	4.9
2	2.0	2	5	2	6.7
3	4.0	3	7	3	7.8
4	6.9	4	10	4	10.6
5	11.3	5	9	5	11.6
6	14.9	6	11	6	10.9
(4-6)	(33.1)	(4-6)	(30)	(4-6)	(33.1)
7	16.0	7	12	7	11.1
(7+)	(57.4)	(7+)	(52)	(7+)	(42.6)
8	14.9	8	12	8	10.3
9	11.8	9	11	9	7.9
10+	15.7	10+	17	10+	13.3
Missing	0.0	Missing	Unknown	Missing	0.2
Mean parity	**6.98**	**Mean parity**	**6.55**	**Mean parity**	-
BFS 1975 (ever-married, aged 45+) n = 495		**BDHS 1993-1994 (ever-married, 45-49 yrs) n = 656**		**BDHS 1996-1997 (ever-married, 45-49 yrs) n = 658**	
Parity	**Percentage**	**Parity**	**Percentage**	**Parity**	**Percentage**
0	2.7	0	0.7	0	1.3
1	3.4	1	1.4	1	1.6
2	4.5	2	3.5	2	3.7
3	6.8	3	4.8	3	6.3
4	-	4	7.1	4	7.7
5	-	5	11.3	5	14.3
6	-	6	13.7	6	16.3
4-6	26.6	(4-6)	(33.1)	(4-6)	(39.3)
7	-	7	16.1	7	14.3
7+	56.1	(7+)	(56.7)	(7+)	(47.8)
8	-	8	13.6	8	11.7
9	-	9	11.4	9	10.3
10+	-	10+	15.6	10+	11.5
Missing	Unknown	Missing	Unknown	Missing	Unknown
Mean parity	-	**Mean parity**	**6.86**	**Mean parity**	**6.44**

NIS = National Impact Survey, Bangladesh; RSFM = Retrospective Survey of Fertility and Mortality, Bangladesh; BFS = Bangladesh Fertility Survey; BHDS = Bangladesh Demographic and Health Survey

These sources include a post-enumeration survey conducted after the 1974 census (RSFM, Anon 1977), the Bangladesh Fertility Survey (BFS, World Fertility Survey 1975) that was part of the World Fertility Survey programme and two recent Demographic and Health Surveys (1993-1994, 1996-1997). All consist of cross-sectional surveys. Their samples vary in size from only 179 women in the National Impact Survey (NIS, Sirageldin *et al* 1975) to over two million women in the RSFM. The parity estimates are all based on ever-married women and, although the figures all come from women over the age of 45, the age range included is not always the same.

The percentage nulliparous varies from 4% (NIS 1968-1969) to 0.7% (BDHS 1993-1994). The estimate of the percentage nulliparous in the imputed data seems low at 1.4%, although it is higher than both estimates from the BDHS. The imputed data also have slightly lower numbers at low parities and slightly higher numbers at high parities (with higher mean parity overall). Thus, the estimates obtained from the imputations do not correspond exactly with any of the other sources, although they are more comparable with some (for example the 1993-1994 BDHS) than others. It is important to note however that the parity estimates also vary considerably between all sources and that only one of the studies reported the percentage of missing data in their samples. In addition, the imputed estimates are based on a sample of women spanning sixteen years of follow-up whereas the other estimates are all based on snapshot surveys.

What can we therefore conclude about the results based on the imputed data? Although it is possible that levels of nulliparity have decreased over the years with better healthcare and nutrition (Kiernan 1989), they are unlikely to have decreased as much as suggested by both the BDHS and the imputed data. It is therefore possible that nulliparous women are under-represented in the imputed data. We know that there was a group of nulligravid or nulliparous women who were never asked about their reproductive history in the Matlab data. It is likely that the data obtained from the imputations did not adequately account for these women. As the mortality of the women with missing data was high, the mortality of nulligravid and nulliparous women may therefore have been underestimated in this study. It is unlikely however that all of the women with missing reproductive histories were nulligravid or nulliparous, as this would mean that over 9% of

ever-married women in Matlab had not experienced any pregnancies or live births. This estimate is much higher than in any of the studies shown in Table 8.1.

There are also less women of low parity (one and two live births) in the imputed data and, by the same token, more women of higher parity. Thus, it is possible that the mortality of low parity women was underestimated and that the mortality of high parity women was overestimated in this study. The case for stating that women of high parity do not have higher mortality than women of low parity in Matlab may therefore be even stronger than we demonstrated.

If the number of women of low parity was underestimated in the imputed data then so may be women with few surviving children, as women would have to be of low parity to have a low number of surviving children. If this is the case the effects of surviving children may also have been underestimated. Thus, in reality, there may be a more dramatic decline in mortality with the number of surviving children than we have shown.

It is not possible to perform similar comparisons for the number of fetal losses. After imputation, women who had experienced fetal losses had higher mortality than women who had never lost a pregnancy. This is the result that we expected to see. We may therefore have made up for the underreporting of fetal losses in the imputed data. However, the peculiarity of the male results makes this less likely, as the results in the males do not change after imputation and remain difficult to explain.

It is possible to get further clues about the results of which we are uncertain by looking at the associations seen in the original data set (Appendix 6.2, 7.2). In fact, in the original female data set, the mortality of nulliparous women and women with only one or two live births was higher than women of higher parities (Table A6.6). There was no change in mortality at higher parities however. Moreover, mortality reduced with an increasing number of surviving children (Table A6.7). Finally in the original female data, the number of fetal losses was not associated with mortality (Table A6.13). The male results are the same no matter what data is used (Tables A7.6-A7.21). Therefore, the inconsistencies between the imputed and original results may help to confirm our

suspicions about the imputed data. It would not be correct to draw inferences from the original data as the mortality in these cohorts is grossly underestimated when the subjects with missing data are not included. Nevertheless, the contradictions in the results help us to conclude that the effects of nulliparity, low parity and fetal losses cannot be adequately described in this study.

In conclusion it remains better to ensure that the risk of missing data is minimised, if not eliminated, by good study design. However, when such data are unavoidable, multiple imputation is a tool that can assist epidemiologists to make inferences from data sets that would otherwise be unusable, provided that the assumptions made are examined in detail and the imputation models constructed with caution.

Other selection biases

Loss to follow-up can introduce bias in a cohort study, as the individuals who are lost continue to contribute person-years of follow-up whilst it is no longer possible that they contribute data towards the outcome of interest (Breslow, Day 1987). In Matlab, the main source of loss to follow-up is out-migration. Migration to and from Matlab is common and similar proportions migrated in and out during this study period. For example, in the female cohort 1988 (9.75%) females migrated in during the follow-up period and 2184 (10.71%) migrated out. Due to the monthly data collection, the exact date of migration is known and the person-years can thus be calculated exactly.

However, an underestimation of mortality may have occurred if every subject who migrated died very soon after migration. There are no data available that describe the reasons why individuals migrate out of Matlab or their mortality status once they leave. Nonetheless, it is probable that individuals who migrate out are similar to those who migrate in. In Table 8.2, the characteristics of women over the age of 45 who migrated in to Matlab in 1990 are given. None of these characteristics suggest that women who migrate have unusual mortality. For example, only eight of the 122 moved in for health or old age care. In fact, women who migrated in to Matlab during the study period contributed an average of 9.25 person-years of follow-up after entering this cohort.

Table 8.2: Causes of in-migration in women older than 45 years, 1990	
Cause	**Number (%)**
Acquired a job in the area	7 (6)
To acquire education in the area	1 (1)
Acquired new house/land in the area	20 (16)
Had to move from old residence due to river erosion	2 (2)
Marriage	5 (4)
Became separated/divorce/widowed	4 (3)
Moved with or to join spouse or parents	59 (48)
For health or old age care	8 (7)
Other	16 (13)
Total	122 (100)

The loss to follow-up will only cause a differential bias if the subjects who migrated out were not representative of the remainder of the cohort. Both the females and males who migrated out were not systematically different from those who remained in terms of reproductive history or most socio-demographic factors. However, in accordance with national trends, a higher proportion of Hindus than Muslims migrated out during the study period. Hindus in Matlab have significantly higher mortality than Muslims. This is thought to be due in part to the social exclusion faced by Hindus, who are in the minority in the area. We do not know what happens to their mortality once they have migrated out of Matlab.

8.2.5 Confounding and effect modification

We were able to adjust for more potential confounders in this study than in previous studies. The estimates did change in the multivariate analysis particularly when age, education and marital status were included in the models, suggesting that the associations were confounded by these variables. This is important, as the relationship between surviving children and mortality may be due to the fact that relatively affluent parents and their children both die less than poorer parents and children. If we did not control for socio-economic variables, the association between surviving children and reduced mortality could be due to the confounding effects of social status. It remains possible that there was some residual confounding in this study, if socio-economic status or wealth were not represented well enough by the variables available. However, this is unlikely to explain all of the effects seen.

No interactions were included in the imputation models and therefore all estimates of effect modification in this study were conservative. There was a suggestion in the female cohort that some effects modified with age but it is difficult to draw any firm conclusions due to the missing data. As the main finding in the study was a decrease in mortality with an increasing number of surviving children, the inability to examine for effect modification is a major shortcoming. For example, it is disappointing that we could not properly assess whether the effects of surviving children modified with other factors such as marital status, as we would expect the associations to be stronger in widowed or divorced individuals.

8.2.6 Generalisability

The demographic data of the DSS are thought to be generalisable to other rural areas in Bangladesh (D'Souza 1981). Fauveau (1994) noted that "*many of the lessons learned in Matlab about the epidemiology of maternal and child health can reasonably be extended to the major part of Bangladesh, but it is not the case for the 'interventions' or operational approaches to deliver family planning, child survival and maternal health services.*" However, the results may not be generalisable to subjects outside Bangladesh, as the population studied is relatively unique in terms of their poor nutritional status, fertility patterns and culture. In addition, in common with many of the studies previously conducted, we restricted our data to the ever married. The results cannot therefore be generalised to the unmarried, as in Bangladesh they are systematically different to the married in terms of both fertility and mortality (Rahman 1993).

8.3 Plausibility of the results

No association between nulligravidity or nulliparity and mortality was seen in this study. This is in contrast to the studies reviewed, in which nulliparous women tended to have higher mortality. It is also contrary to the hypothesised relationship in this population, where the nulliparous were expected to be a relatively homogenous and disadvantaged group. Few women remain nulliparous voluntarily (Aziz 1994), infertility may be linked to the presence of severe illnesses such as tuberculosis (Parikh *et al* 1997) and divorce rates (and hence mortality rates) have a strong link with childlessness (Ahmed 1987). It is possible, as discussed, that no effects were seen as nulliparous women may have been underestimated in the data collection and hence in the imputed

data. Thus, we can draw no firm conclusions about the mortality of nulliparous women in this study.

There was no reverse-j or u-shaped trend in mortality with parity. The finding that female mortality did not increase at high parities is consistent with conclusions drawn from previous studies. The finding that male mortality did not change with female parity was also consistent with the studies that had examined this relationship in men. However, we would expect a relationship between high parity and mortality, should one exist, to be clearest in a population such as this. They were a natural fertility population, in which marriage was almost universal and contraceptive use limited. They had therefore experienced more pregnancies and births than any cohort previously studied. They were also chronically malnourished, such that any depleting or evolutionary effects of reproduction that may exist might be more apparent. This study therefore provides relatively convincing evidence to refute the existence of a trade-off between reproduction and survival in adults who have completed their reproduction in Matlab.

It is possible that no relationship between parity and mortality was seen due to the "healthy pregnant woman" effect. That is, women who bear many children are healthier or are, in some way, inherently stronger than those who do not. In fact Mace (2000) suggested that such an effect may interact with the potential negative effects of reproduction, and no overall effect of parity should be expected: "*if individual women are reproducing up to their own capacity, then healthier women have larger families and potentially greater longevity, but if that additional reproduction shortens life span, then no correlation between family size and longevity will emerge.*" However, such an effect should have less influence on the mortality of women who have completed their reproduction. For example, if a woman was suffering from an illness that was severe enough to lower her fertility, then we would expect it to also increase her mortality earlier in life. In addition, it is possible that any negative effects of reproduction are only apparent during the reproductive years. For example, maternal mortality is known to have parity specific patterns but it is not known how long into the postpartum period these risks extend. The lack of a parity effect in this study may therefore reflect the fact that the risks associated with reproduction are confined to the reproductive years. This is

supported by the evidence from the studies in the literature review that showed that the effects of reproductive history reduced with age.

The association between reproductive factors and mortality in more affluent nations is thought to reflect the aetiological significance of reproduction in the development of specific diseases. However, infectious diseases remain the commonest causes of mortality in Bangladesh (Strong 1992) and it is thus not clear how mortality might relate to reproduction under these circumstances. In addition, women in developing countries may not live long enough to incur the chronic effects of childbearing, whatever they may be. In Bangladesh, the average expectation of life from birth in females is 58 years (BHDS 1997), which is below the peak age for the diagnosis of many cancers for example.

It has also been suggested that "*deviance from social norms*" rather than the biological effects of reproduction may mediate the relationship between childbearing and mortality (Fox, Goldblatt 1982). This theory is also put forward to explain the higher mortality of lone mothers (Martikainen 1995). Highly parous women in Bangladesh may therefore not have higher mortality, as this is 'normal' behaviour in this cultural context. However, if this were the case, we would also expect a strong effect of nulligravidity and nulliparity in this population as childless women are socially ostracised in Bangladesh.

None of the studies reviewed looked at the effect of surviving children on mortality. However, two previous studies in Matlab have found similar trends in mortality with surviving children in elderly (60 years and over) cohorts. The first study showed that women and men with two surviving sons had significantly lower mortality, but that there was no significant benefit of having more than two sons. They also found no significant effect of having surviving daughters (Rahman 1999, 2000). The second study showed that women who lived in the same household as a son or a daughter had significantly lower mortality and men who lived in the same household as a daughter had significantly lower mortality (Mostafa, van Ginneken 2000). Both of these studies looked at the associations in populations that were older than in this current study. They also had fewer subjects and less follow-up than this study, which may explain why they did not find significant effects for all of the relationships under study. In addition, the second used a different

definition of surviving children than this current study and the results are not therefore directly comparable.

In other developing country populations, Draper and Buchanan (1992) showed that members of the !Kung population of South Africa were more likely to have living parents if two or more of their own siblings (that is, the parents' children) were still alive. These results applied equally to parents of both sexes. Hill and Hurtado (1996) found that men in the Ache ethnic group of Paraguay who had more surviving children had longer survival, but no effect in the women. However their sample was small and adjusting for the potential confounding effects of factors such as age was not possible.

The finding that mortality decreases with the number of surviving children is consistent with the theory that the elderly rely on their children for old-age support, particularly in countries where no aid is provided by the state (Martin, Kinsella 1994). For example, there is perception in Bangladesh that bearing many children is a necessity, both for "*replacement*" of children who die during infancy and "*insurance*" for old age support (Rahman 1998). In Matlab, it has also been found that females expect to gain power, authority and honour by bearing more children (Aziz 1994). Therefore it is plausible that adults in Matlab who have more surviving children have lower mortality.

It may also be that adults with more surviving children have a better network of carers should they fall ill, hence improving their survival. In affluent societies, the likelihood of receiving care from children increases with the number of children (Spitze, Logan 1990) and the total hours of care received increase with the total number of living children (Wolf 1994). In the developing world, having more living children is associated with a higher probability that the elderly parent is living with one or more of them, with approximately three-quarters of elderly Asians living with one or more of their adult children (Martin, Kinsella 1994). This study therefore supports this data. In addition, a series of surveys in Asia found that 34 percent of males received care from their spouse compared with only 8 percent of the females, whereas 48 percent of males received care from their children compared with 72 percent of women (Chen, Jones 1989). This is supported in the Matlab data, as the effect of surviving children seems stronger in women than in men. The men in Matlab are considerably older than their wives and they may

therefore rely on their spouse until their own death, after which the woman becomes reliant on her children.

No previous studies of the effect of fetal losses on female or male mortality were found. This is regrettable, as other studies may have helped to unravel the perplexing male findings. The relationship between fetal losses and mortality is still not clear. It is plausible that women who suffer many fetal losses have higher mortality, either because they miscarry due to an illness or because the loss is traumatic, both physically and mentally. It is not however credible that a wife's fetal loss protects the husband from death. The conclusions that can be drawn about the effects of fetal losses on adult mortality are therefore limited.

8.4 Unanswered questions and future research

Data on other reproductive factors such as age at first birth, birth spacing and breast-feeding were not available for this study, such that their effects could not be examined. This is an important omission and, as a result, the picture of the effects of reproduction on mortality may still be incomplete. For example, we were not able to assess whether the mortality of women who had their children in rapid succession differed from the mortality of women of the same parity whose pregnancies were not closely spaced. In addition, a later age at first birth was consistently associated with lower mortality in the studied reviewed but there was no data to examine its effects in this study. However, this was a population in which most women married young and it is unlikely that many would have chosen to delay their childbearing. Thus, there may not be enough variation in the age at first birth in Matlab for an effect to be seen.

As discussed, an effect of parity on mortality may not have been seen as the influence of this factor may only be important during the reproductive years, whilst the women are still having children. In this study, the women included had completed their reproduction and the outcome of interest was mortality after age 45. Women between the ages of 15 and 44 were not studied, in an attempt to separate the long-term effects of reproduction from the short-term sequelae of pregnancy. For example, if women of reproductive age had been included there may have been an apparent u-shaped pattern in all-cause mortality with parity, as first births and births of high parity are known to affect

the risk of maternal mortality. The immediate effects of parity on pregnancy-related mortality have been well documented, although the length of the postpartum period during which women experience pregnancy-associated mortality risks is less well known. It would have been useful to study mortality in women by duration since childbirth, adjusting for reproductive variables. At the time of writing this thesis however, such data were not available.

More information about the living arrangements of the adults would have been useful, to examine how the effect of the number of surviving children is mediated. It would also have been helpful to know the ages of the surviving children. If the surviving children in subjects who had lower mortality were older, this would support the theory that they may be providing support to their parents, hence reducing their mortality. If those surviving were still in their childhood however, this may suggest that the relationship seen is due to residual confounding by socio-economic status. Further qualitative work examining the relationship between children and their parents may be useful to gain further insight into this association.

8.5 Conclusion

The results of this study therefore suggest that there are few negative long-term biological consequences of bearing children in women who have completed their reproduction in Matlab, Bangladesh. Even if they exist, they may be outweighed by the social advantages of having a family and, possibly, a healthy pregnant woman effect. These conclusions are strengthened by the fact that the reduction in mortality with the number of surviving children persisted after adjusting for potential confounders. In addition, they are supported by the remarkable consistency in the associations in the females and their husbands.

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Useful pages from the World Wide Web

1. http://www.stat.psu.edu/~jls/mifaq.html (Joseph Schafer's multiple imputation website)

2. http://www.stata.com (Stata statistical package website, with frequently asked questions section and new downloadable programmes)

3. http://www.statsol.ie/solas/solas.htm (SOLAS statistical package website, with frequently asked questions section and passage by Donald Rubin on multiple imputation and the use of SOLAS for multiple imputation)

4. http://www.virtualbangladesh.com (Information about Bangladesh online)

APPENDIX 2.1:
ADDITIONAL DATA FOR LITERATURE REVIEW

Table A2.1: A Summary Of The Literature Review Results
Studies using CENSUS data for exposure
Kitagawa, Hauser 1973 (see Figure A2.1): *(No statistical comparisons performed)* ▪ **J-shaped** pattern in mortality with parity in women aged 45-64 at death ▪ **No clear pattern** in mortality with parity in women who died aged 65 or older
Fox and Goldblatt 1982 (OPCS, see Figures A2.2 & A2.3): ▪ Nulliparous women have **higher** mortality than the parous (no comparisons performed) ▪ **U-shaped trend** in mortality with parity in women who died younger than 50 years of age ▪ **No pattern** in the women who died between 50 and 59 years of age ▪ Mortality may be **lower** in women who had their first birth at 25-29 years compared with those 20-24 years ▪ No pattern in mortality of women whose first birth was before age 20 or after age 30 ▪ No clear patterns in mortality by length of reproductive life
Green, Beral, Moser 1988 (OPCS, see Figure A2.4): ▪ Nulliparous women had **higher** mortality than parous (RR **1.16**, p<0.01) ▪ U-shaped trend in mortality with number of children, which is most pronounced in manual social classes
Lund, Arnesen, Borgan 1990 (see Figure A2.5): ▪ Nulliparous women had significantly **higher** mortality than parous women: Age-adjusted relative risk (RR) for women aged 25-84 yrs **1.66** (95%CI 1.63-1.68) ▪ The effect **reduced with age**: RR 35-44 yrs **1.60** (95%CI 1.48-1.74); RR 75-84 yrs **1.03** (95%CI 0.99-1.08) ▪ Women with 4+ children may also have an **increased** risk of mortality (results shown in graphical form only) ▪ Women with a higher age at first birth had **lower** mortality ▪ **Lowest risk of mortality** relative to the nulliparous was in women with 3 children whose first birth was between 25 and 29 years (RR **0.65**, 95%CI 0.63-0.68)
Moser, Pugh, Goldblatt 1990 (OPCS): ▪ Nulliparous women may have **higher** mortality then parous women: SMR for nulliparous women **101** (95% CI 87-117), parous women whose youngest child was 0-16 **89** (95% CI 82-97), and women whose youngest child was 17+ **94** (95%CI 84-104) - no statistical comparisons but CIs overlap ▪ The patterns of mortality with parity **modified** with occupation, although no consistent pattern was discernible
Weatherall, Joshi, Macran 1994 (see Figure A2.6): ▪ Nulliparous women had **higher** mortality than parous women ▪ Relative differences in mortality **changed with age of youngest child**: Women whose youngest child was 0-4 had lowest mortality compared with the nulliparous (multiply-adjusted OR 0.**63**, 95%CI 0.54-0.74), with mortality increasing as the age of the youngest child increased (youngest child 5-9 OR **0.75**, 95%CI 0.65-0.85, youngest child 10-14 OR **0.88**, 95%CI 0.79-0.99). ▪ Mortality of women whose youngest child was 15+ **no different** to that of nulliparous women (OR 0.95, 95%CI 0.88-1.03).
Costa, Luzza, Mattace 2000: ▪ 4 of the 88 (**4.5%**) women in their series were childless, and the median number of children they had was 5 (range 1-12)

Table A2.1: A Summary Of The Literature Review Results (continued)
Studies using CENSUS data for exposure (continued)
Doblhammer 2000 (see Figures A2.7 & A2.8): ▪ In both populations mortality was **highest** in nulliparous women, **lowest** in women with 1 or 2 children and **increased** again at higher parities ▪ Giving birth before age 20 years **increased** the risk of mortality (OPCS data RR 1.26, p<0.01; Austrian data RR 1.09 p<0.01. ▪ Giving birth after age 40 may **reduce** the risk of death (OPCS RR 0.95, p<0.10; Austria RR 0.95, p<0.05)
Manor, Eisenbach, Israeli, Friedlander 2000 (see Figure A2.9): ▪ **Reverse j-shaped** trend in mortality with parity, with less of an effect in older women
Studies using OTHER SOURCES OF ROUTINELY COLLECTED DATA for exposure
Powys 1905 (see Figure A2.10): Mean family size increases with age at death until age 70, and may then decrease
Arvay, Takacs 1966: (*No statistical comparisons performed*) ▪ Nulliparous women had **lower life expectancy** that parous women, with their mortality **4%** lower than that of women with 6+ children
Beral 1985: ▪ Nulliparous women had significantly **lower** mortality than parous women: Age-standardised mortality ratio **0.83** (p<0.05)
Studies using DATA FROM ONGOING STUDIES for exposure
Kotler, Wingard 1989 (see Figure A2.11): ▪ Number of children was **not associated** with mortality in working women: Adjusted odds ratio comparing women with 4+ children to women with 0-3 children **1.1** (95%CI 0.5-2.4) ▪ Housewives with 4 or more children had **higher** mortality than housewives with none to three children: Adjusted odds ratio for the same comparison **1.9** (95%CI 1.1-3.3)
Kvale, Heuch, Nilssen 1994 (see Figure A2.12): ▪ In women <50 at entry, nulliparous had **higher** mortality than parous women with a **reverse j-shaped** pattern in mortality with number of full-term deliveries ▪ In the women ≥50 at entry, **no clear patterns** were observed
Friedlander 1996: ▪ Nulliparous women had significantly **lower** mortality than parous women: Adjusted hazard ratio (HR) **0.70** (95%CI 0.55-0.89) ▪ **A statistically significant linear trend** *"per child born"* among all women (HR per child born **1.09**, 95%CI 1.01-1.17) and those born 1880-1904 (HR **1.15**, 95%CI 1.04-1.28), but not in those born 1905-1929 (HR **1.00**, 95%CI 0.89-1.13).
Studies using DATA FROM NEXT-OF-KIN for exposure
Perls, Alpert, Fretts 1997: ▪ Women who lived to be 100 years old had **significantly greater odds of having given birth after the age of 40** Odds ratio for having given birth after age 40 for the centenarians compared with the women who died aged 73 **4.0** (95%CI 1.02-18.7).
Cooper, Baird, Weinberg, Ephross, Sandler 2000 (see Figure A2.13): ▪ There was **no significant difference** in the mortality of nulliparous and parous women: Adjusted RR for nulliparous compared with parous **1.22**, 95%CI 0.79-1.89 ▪ **Reverse-j shaped** pattern in mortality by number of children, although none of the estimates differed significantly from the nulliparous ▪ Women whose last birth was aged 40-48 had **twice** the mortality of women whose last birth was aged 30-34 (adjusted RR **2.14**, 95%CI 1.05-4.38)

Table A2.1: A Summary Of The Literature Review Results (continued)
Studies using HISTORICAL DEMOGRAPHIC RECORDS for exposure
Phillipe and Yelle 1976 (see Figure A2.14): ▪ **No clear pattern** in mean age at death by number of children. The authors report statistically significant differences in mean age at death of women with 8 children (**67.4** years) compared with women with 1-5 children (**79.3** years) or women with 11 children (**79.3** years)
Voland, Engel 1988: ▪ **No clear pattern** in life expectancy from age 47 with number of pregnancies, births or live births (*no statistical comparison presented*) ▪ Life expectancy **increased** linearly with an increasing number of children surviving to age 15 ▪ Age at death **increased** with an increasing age at last birth, especially if the last child born survives (Pearson's correlation coefficient for age at death and age birth of last child **0.07**, p 0.028; Pearson's correlation coefficient for age at death and age birth of last surviving child **0.11**, p 0.001)
Le Bourg, Thon, Legare, Charbonneau, Desjardins, 1993: ▪ **No clear relationship** between reproductive variables and woman's age at death
Westendorp, Kirkwood 1998 (see Figures A2.15-A2.17): ▪ **U-shaped** pattern of the proportion childless with age at death ▪ Mean number of children **rises** with age at death until age 70 and then decreased in women who died at older ages – differences **not** statistically significant ▪ Mean age at first childbirth **increases** with age at death, with some statistically significant differences ▪ Trends are exaggerated when only women over the age of 60 or women born before 1700 are included
Korpelainen 2000: ▪ Women who died aged 50-79 had significantly higher mean values for number of children, number of children surviving to age 18, age at first and last child, length of reproductive life than women who died <50 ▪ Women who died >80 years had significantly more surviving children (mean of 3.40 compared with 2.61), age at first birth (mean of 25.0 compared with 22.7) and age at last birth (mean of 35.6 compared with 32.8) than women who died <50, and significantly lower mean number of children (4.34 compared with 5.40) and length of reproductive life (mean of 10.5 compared with 12.4 years) than women who died aged 50-79
Lycett, Dunbar, Voland 2000 (see Figure A2.18 – graph of equivalent analyses to Westendorp and Kirkwood Figure A2.17): ▪ Proportion childless **does not vary** with age at death ▪ Mean number of children **rose** with age at death until age 50 after which it remained constant ▪ **No significant correlation** between the number of live births and female age at death in the total population or by socio-economic group (p=0.847) ▪ Associations changed when duration of fecund marriage (the time from their marriage until they were 50 years of age) was included in the models. In farmers (high social status), there was a **weak significant positive relationship** between number of children and age at death (partial regression coefficient=0.099, p=0.043, n=73) and in the landless (low social status), there was a **weak significant negative relationship** (r=-0.074, p=0.005, n=276) ▪ **No effect** of age at marriage, age at first birth and age at last birth.

Table A2.2: All-Cause Mortality Of Nulliparous Women Compared With The Parous
Suggestive of higher mortality in the nulliparous
Studies finding significantly higher mortality in the nulliparous: **Green *et al* 1989, Lund *et al* 1990**
Studies finding higher mortality in the nulliparous but not statistically significant: **Cooper *et al* 2000**
Studies showing higher mortality in the nulliparous but no statistical comparisons performed: **Arvay & Takacs 1966** *(lower comparative life expectancy)*, **Fox & Goldblatt 1982**, **Kvale *et al* 1994** (<50 years), **Moser *et al* 1994**
Studies finding a low percentage of childless women living to an old age but no statistical comparison performed: **Costa *et al* 2000**
Suggestive of lower mortality in the nulliparous
Studies finding significantly lower mortality in the nulliparous: **Beral 1985**, **Friedlander 1996**
Studies finding lower mortality in the nulliparous but not statistically significant: **None**
Studies demonstrating lower mortality in the nulliparous but no statistical comparisons performed: **None**
Studies finding a high percentage of childless women living to an old age but no statistical comparison performed: **Westendorp & Kirkwood 1998** (women who were older than 90 years at death)
Studies finding no clear pattern
Phillipe & Yelle 1976, **Lycett *et al* 2000**

Table A2.3: All-Cause Mortality By The Number Of Children
U or reverse-j shaped trend in mortality with number of children
10 cohorts: **Fox & Goldblatt 1982** (women <35 years and aged 35-49), **Kitagawa & Hauser 1973** (women aged 45-64), **Green *et al* 1989**, **Lund *et al* 1990**, **Kvale *et al* 1994** (women <50 years), **Manor *et al* 2000** (women aged 45-69 and women aged 70+), **Doblhammer 2000** (Austrian and British)
Linear trend in mortality with number of children
Increasing mortality with number of children: **Friedlander 1996** (significant in total cohort and those born 1880-1905, but not significant in those born 1905-1929), **Lycett *et al* 2000** (in land owners, significant) ***Decreasing mortality or increasing life expectancy with number of children*:** **Arvay & Tacaks 1966** (non-significant), **Lycett *et al* 2000** (in landless, significant)
No trend in mortality with number of children
3 cohorts: **Fox & Goldblatt 1982** (women aged 50-59), **Kitagawa & Hauser 1973** (women aged 65+), **Kvale 1994** (women >50 years),
Mortality higher at higher parities than in the nulliparous
4 cohorts: **Kitagawa & Hauser 1973** (women aged 65+), **Fox & Goldblatt 1982** (women <35 years and aged 50-59), **Kvale *et al* 1994** (women >50 years)

Table A2.4: All-Cause Mortality With Other Reproductive Characteristics
Mortality decreased or age at death increased with increasing age at first birth
5 studies: **Fox and Goldblatt 1982, Lund *et al* 1990, Westendorp and Kirkwood 1998, Doblhammer 2000** (Austrian and British data), **Korpelainen 2000**
Mortality decreased or age at death increased with older births
3 studies: **Voland & Engel 1989** (weak but significant positive correlation between age at last birth and age at death), **Perls *et al* 1997, Doblhammer 2000** (only significant in Austrian data)
Mortality increased or age at death decreased with age at last birth
1 study: **Cooper *et al* 2000** (significant)
Relationship of mortality with length of reproductive life span
No association: **Fox & Goldblatt 1982** *Women who died at older ages had shorter mean reproductive life spans*: **Korpelainen 2000**

Figure A2.1: Relative risk of mortality by number of live births, relative to nulliparous (Kitagawa, Hauser 1973)

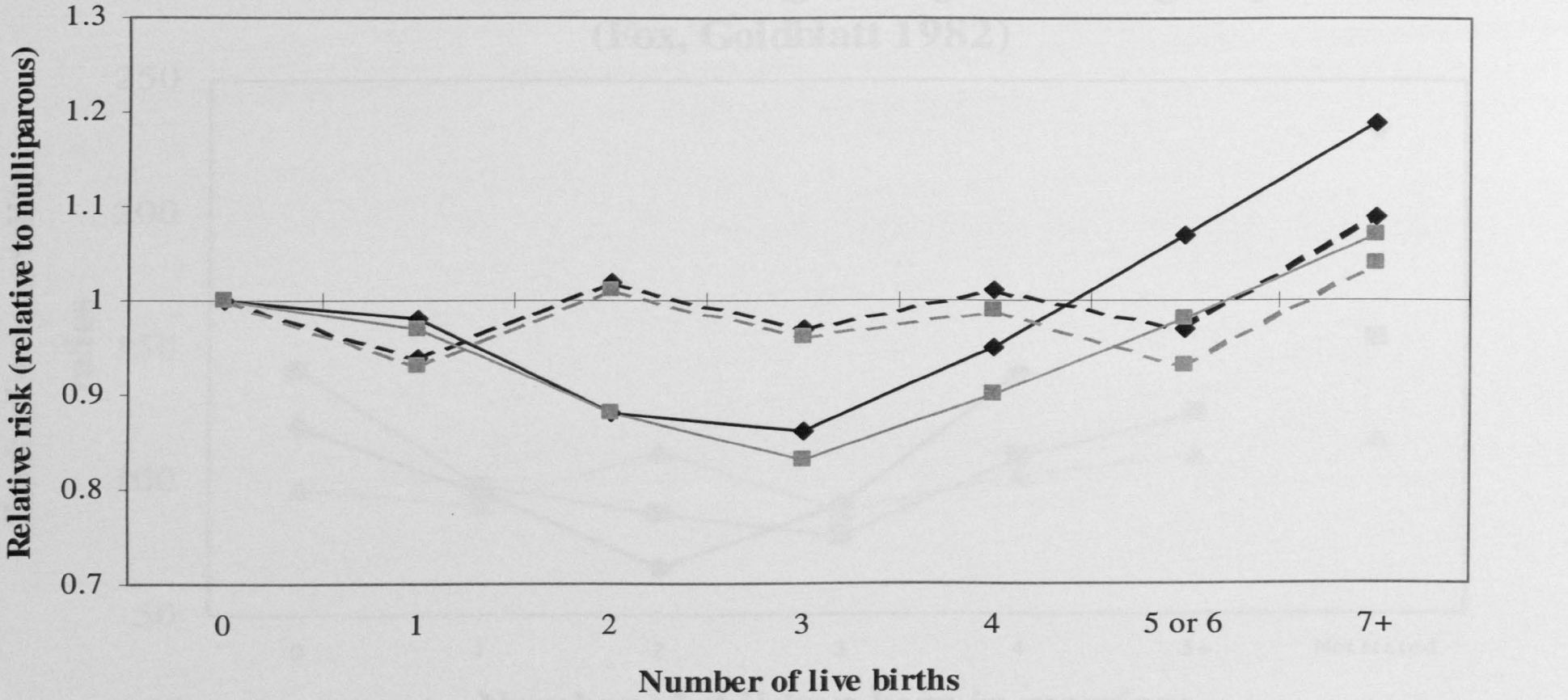


Figure A2.2: Standardised mortality ratios by number of children born in marriage, in age at death groups (Fox, Goldblatt 1982)

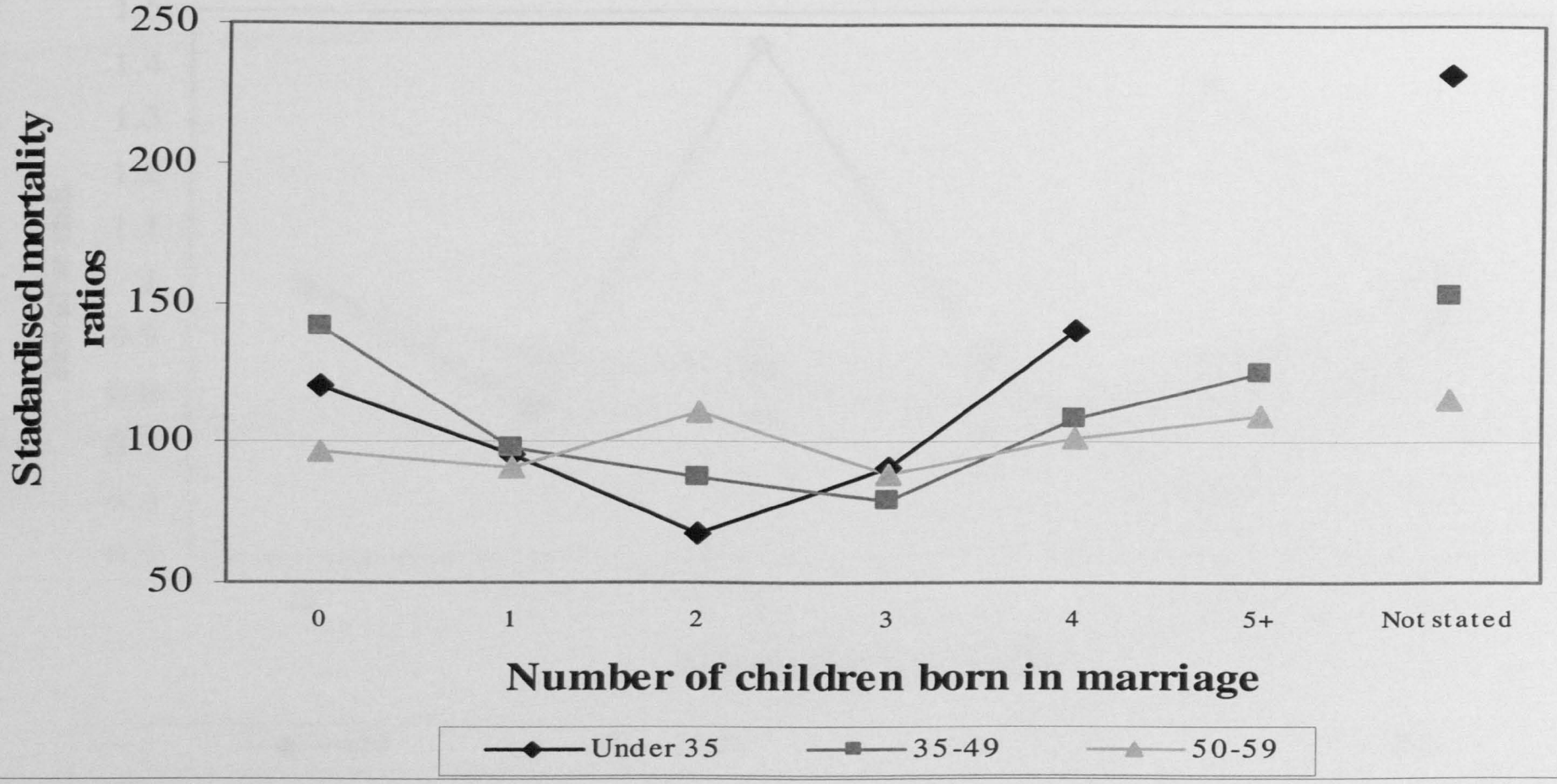


Figure A2.3: Risk of mortality relative to the nulliparous by number of live births in age at first birth groups (women who died age 35-64, Fox and Goldblatt 1982)

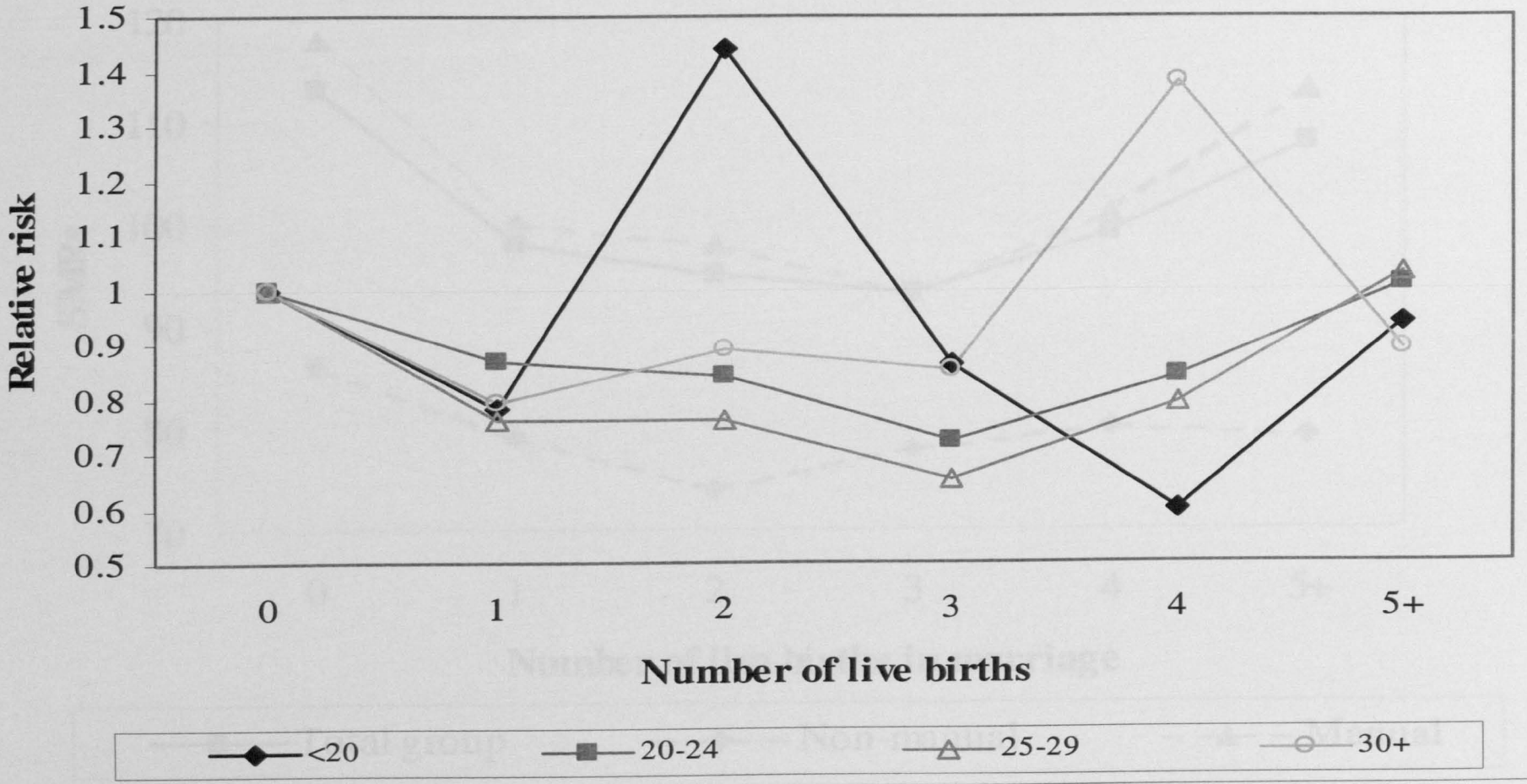


Figure A2.4: Standardised mortality ratios by live births in marriage in the different social classes (Green et al 1988)

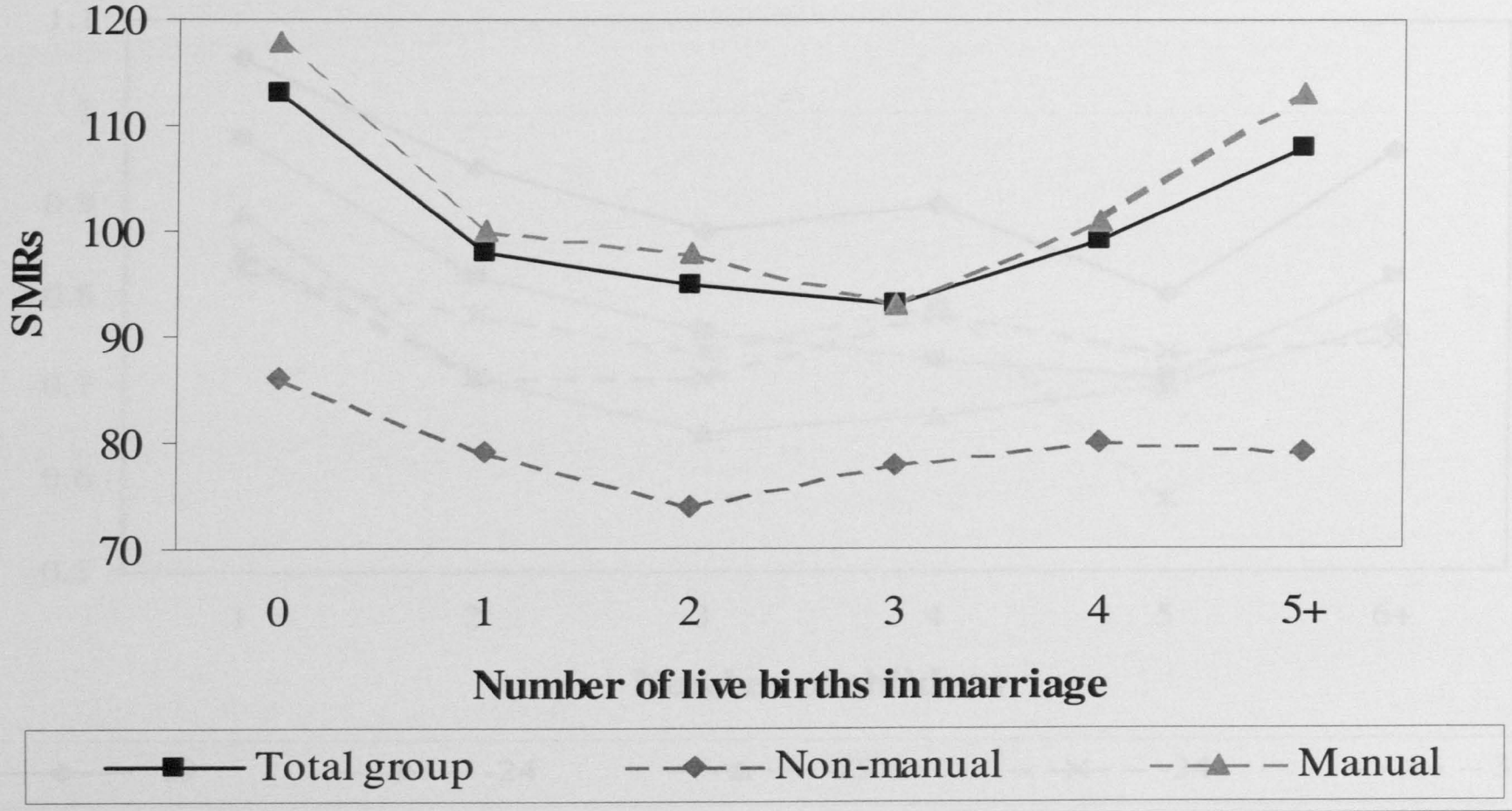


Figure A2.5: Relative risk of mortality compared with the nulliparous by number of children, according to the age at first birth (Lund et al 1990)

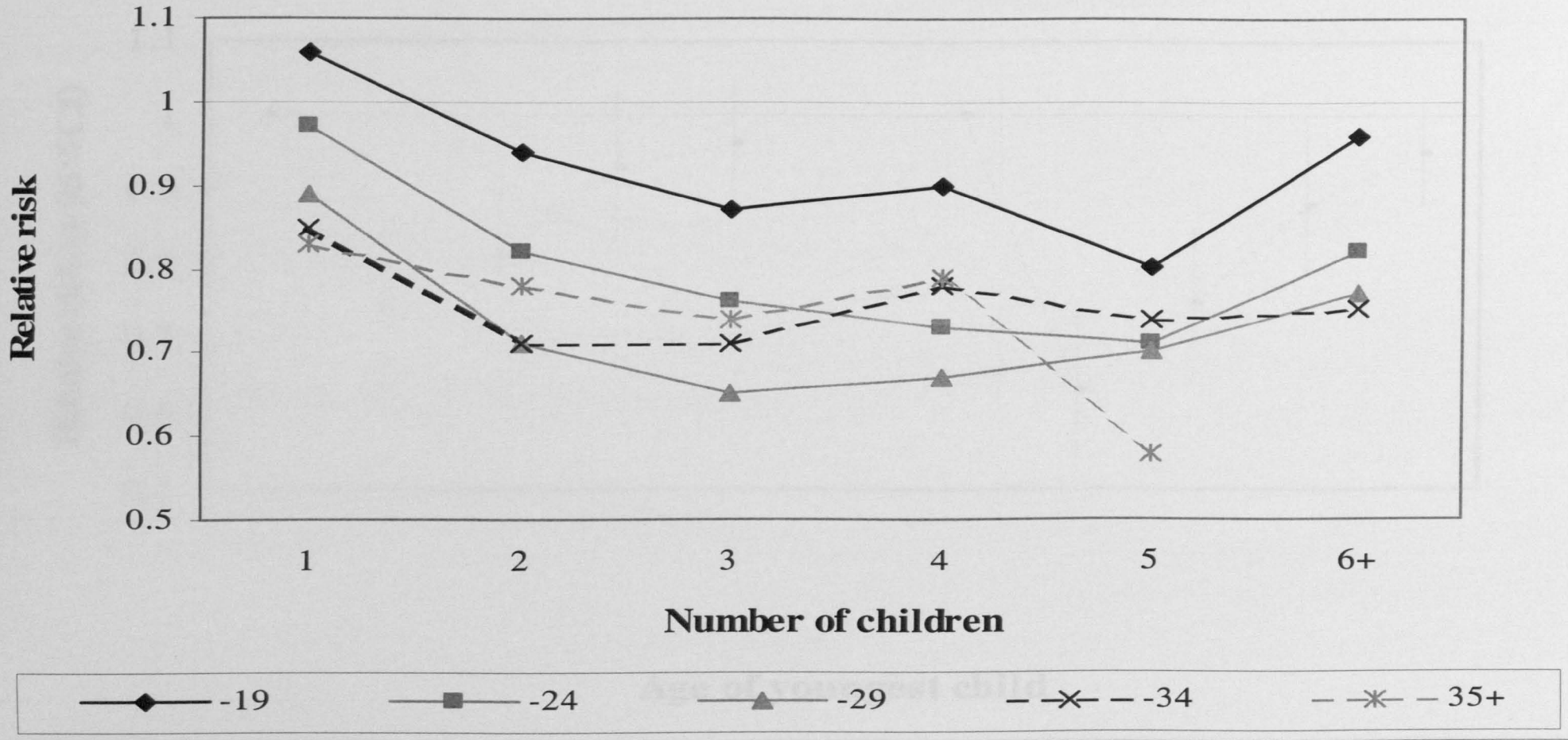


Figure A2.6: Risk of mortality, relative to the nulliparous, according to age of youngest child adjusted for age and year (left) and multiple variables (right) (Weatherall et al 1994)

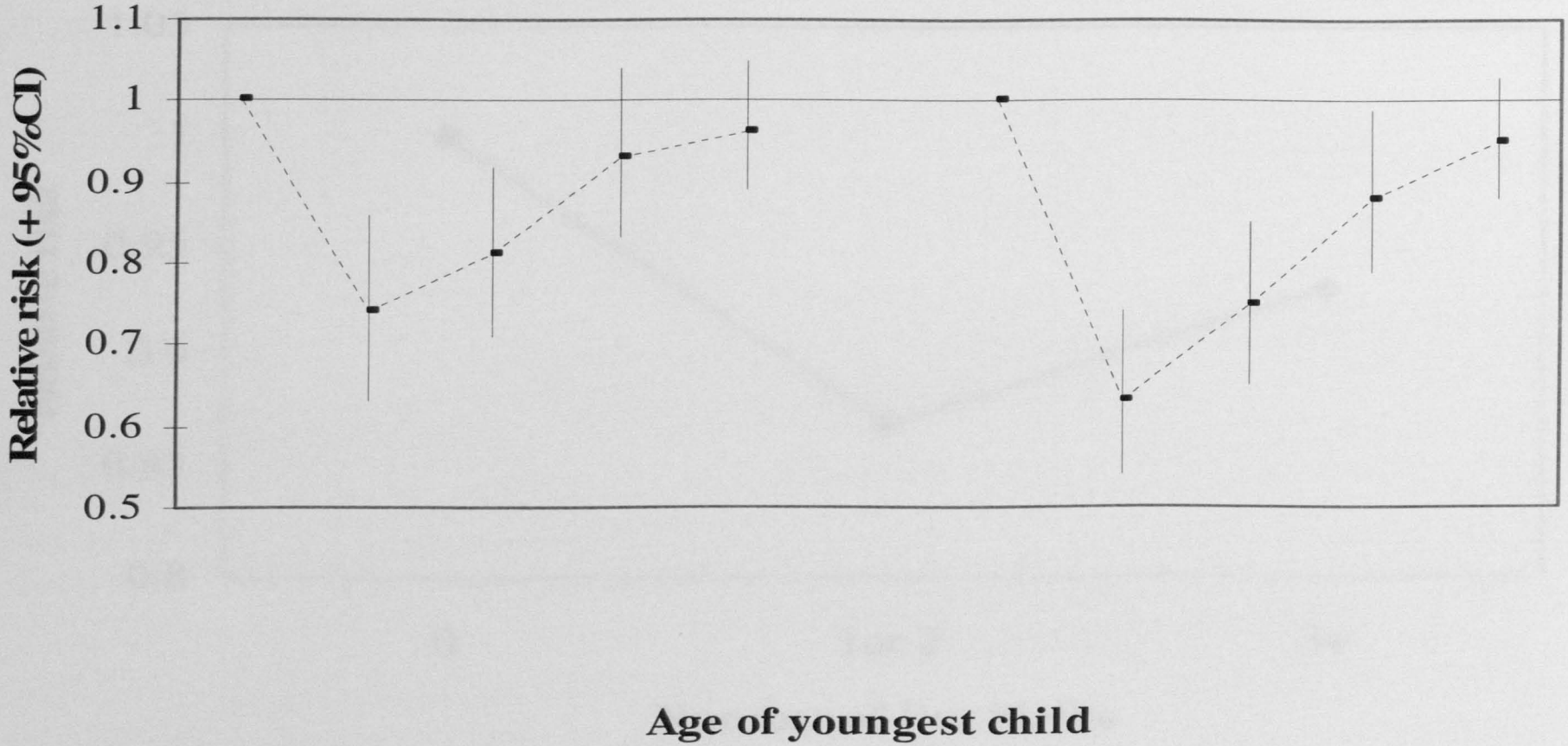


Figure A2.7: Risk of mortality by parity, relative to the nulliparous (Doblhammer, England and Wales, 2000)

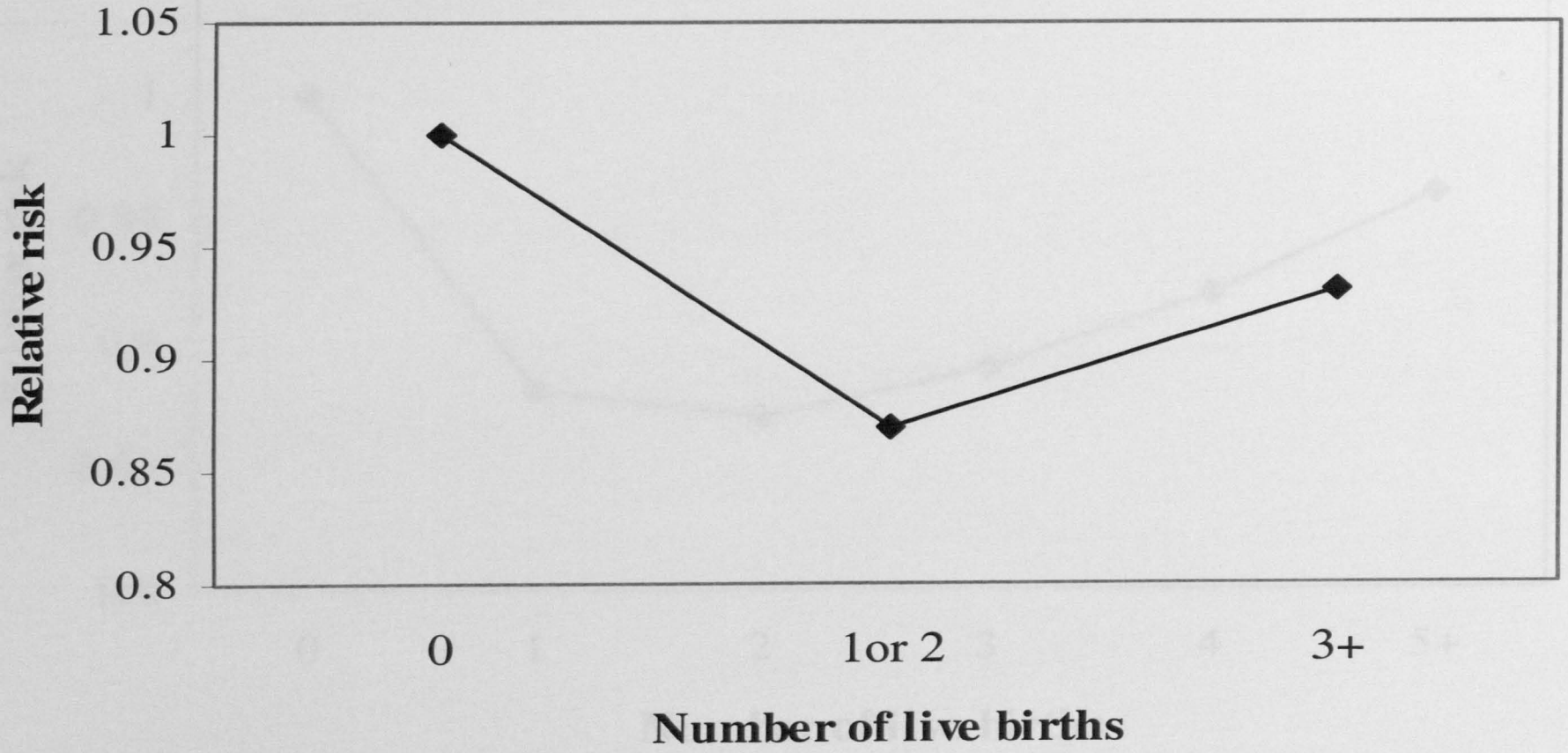


Figure A2.8: Risk of mortality by parity, relative to nulliparous (Doblhammer, Austria, 2000)

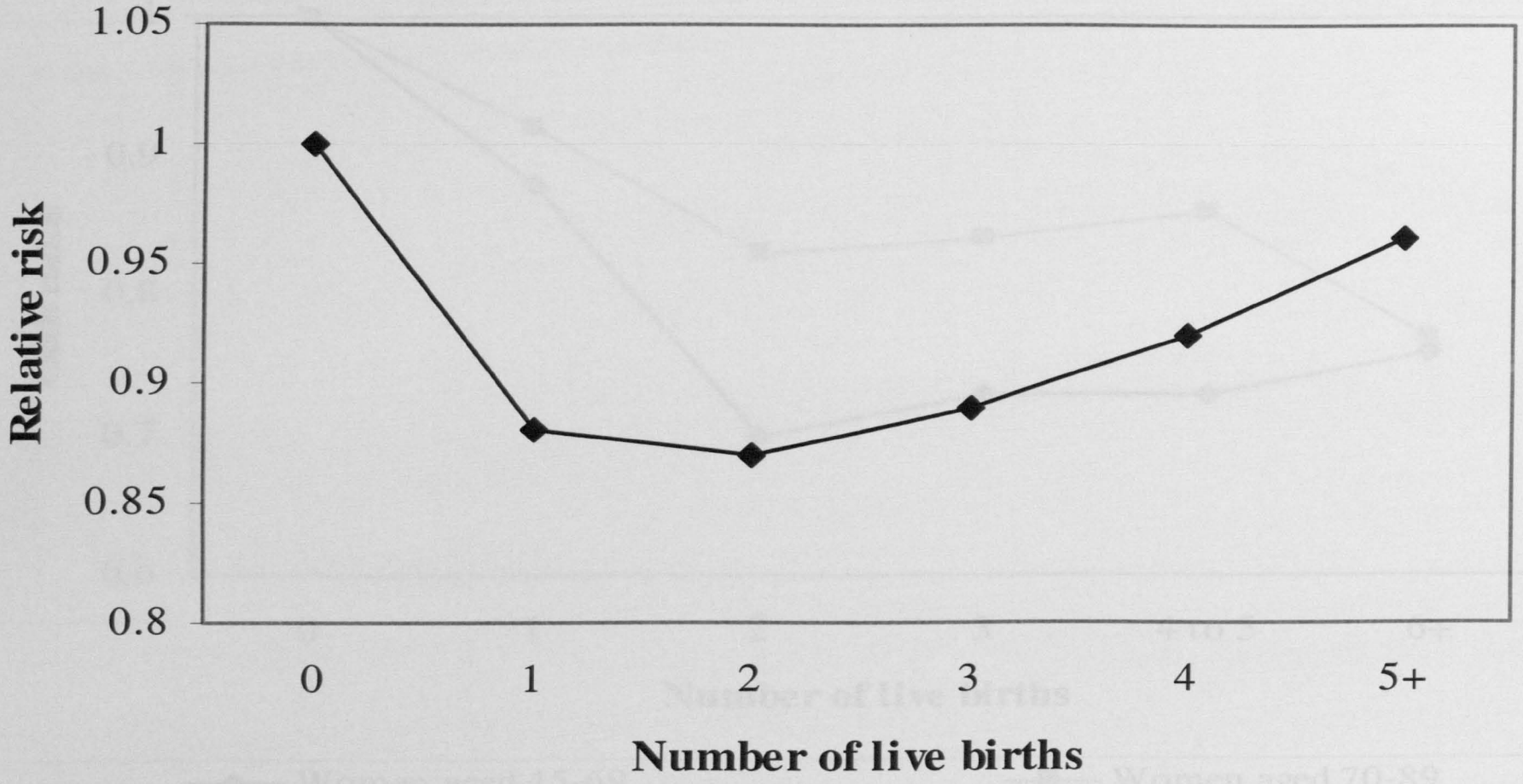


Figure A2.9: Adjusted odds ratios of death by number of live births with nulliparous as the reference (Manor et al 2000)

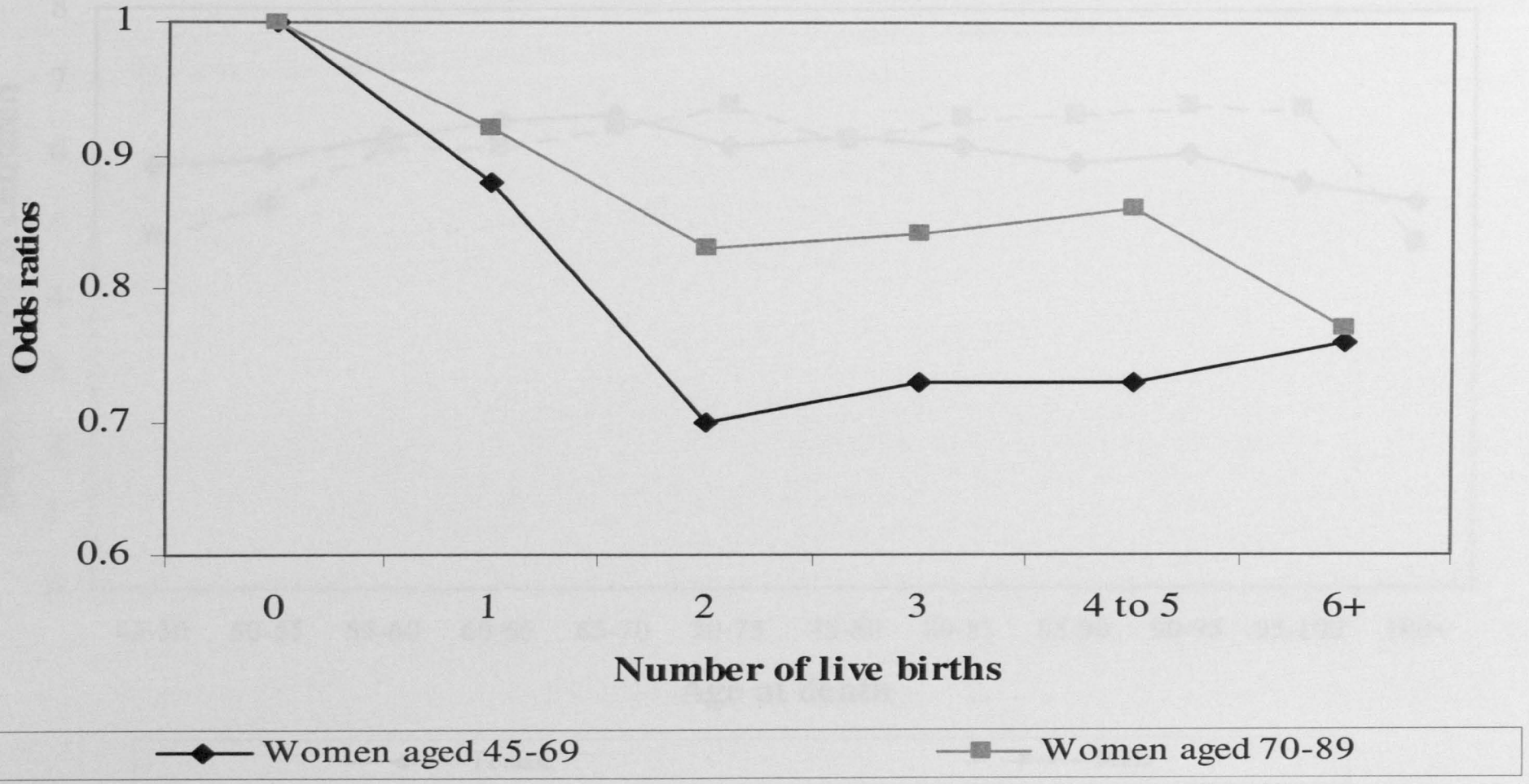


Figure A2.10: Mean number of children by age at death (Powys 1905)

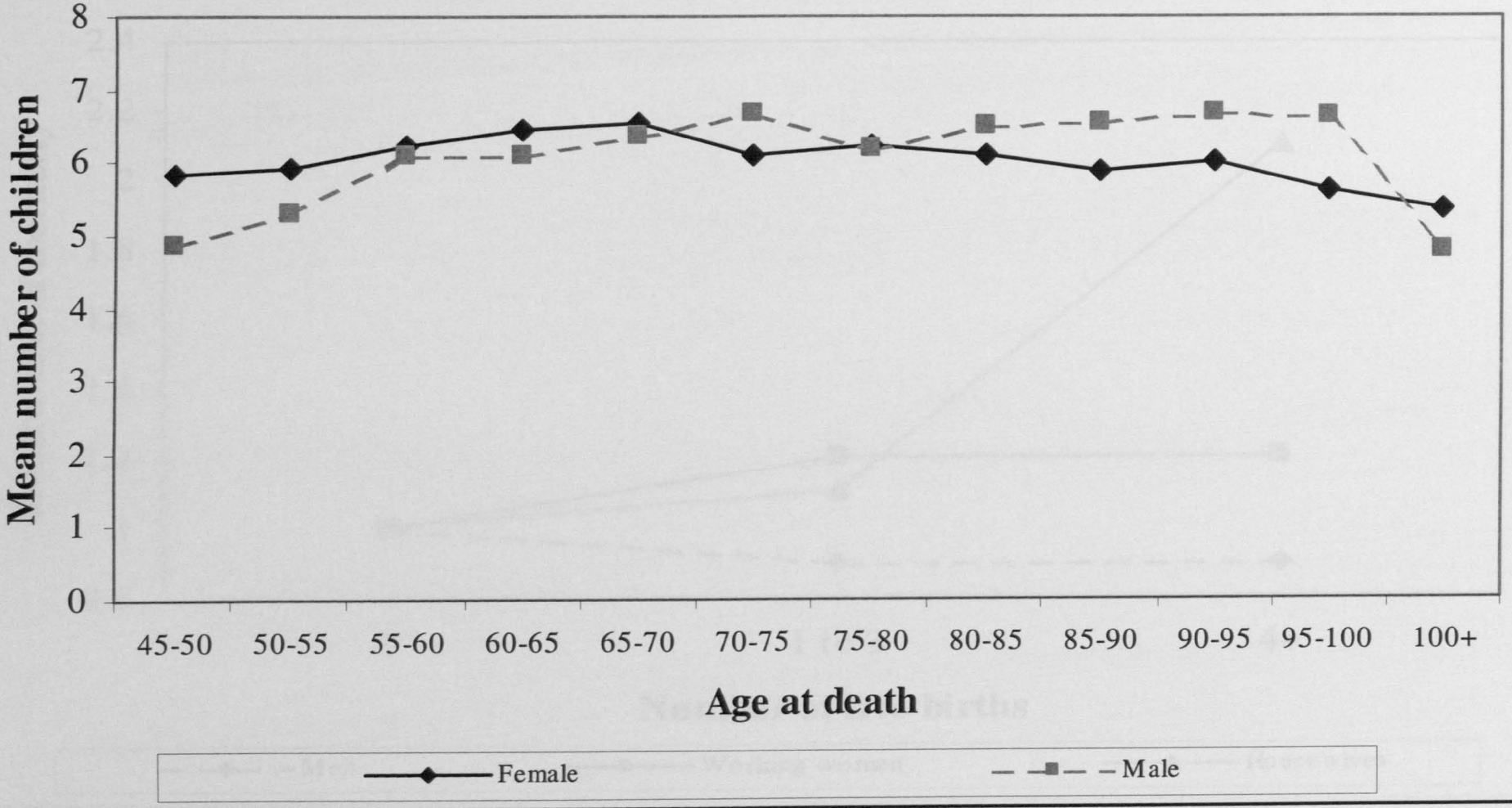


Figure A2.11: Age-adjusted relative risk of mortality in each parity group, by sex and occupation (Kotler, Wingard 1989)

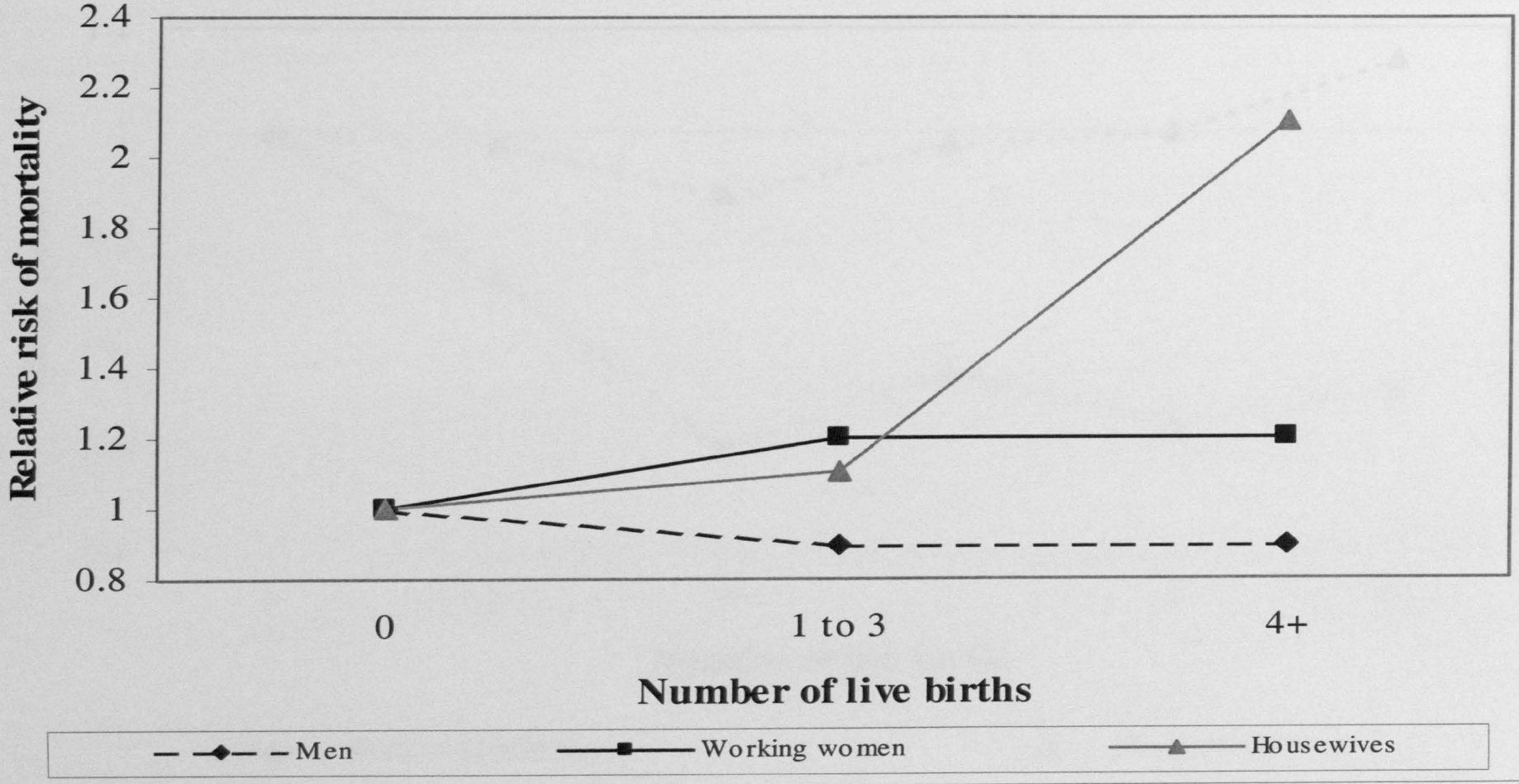


Figure A2.12: Risk of mortality in parous relative to the nulliparous (Kvale et al 1994)

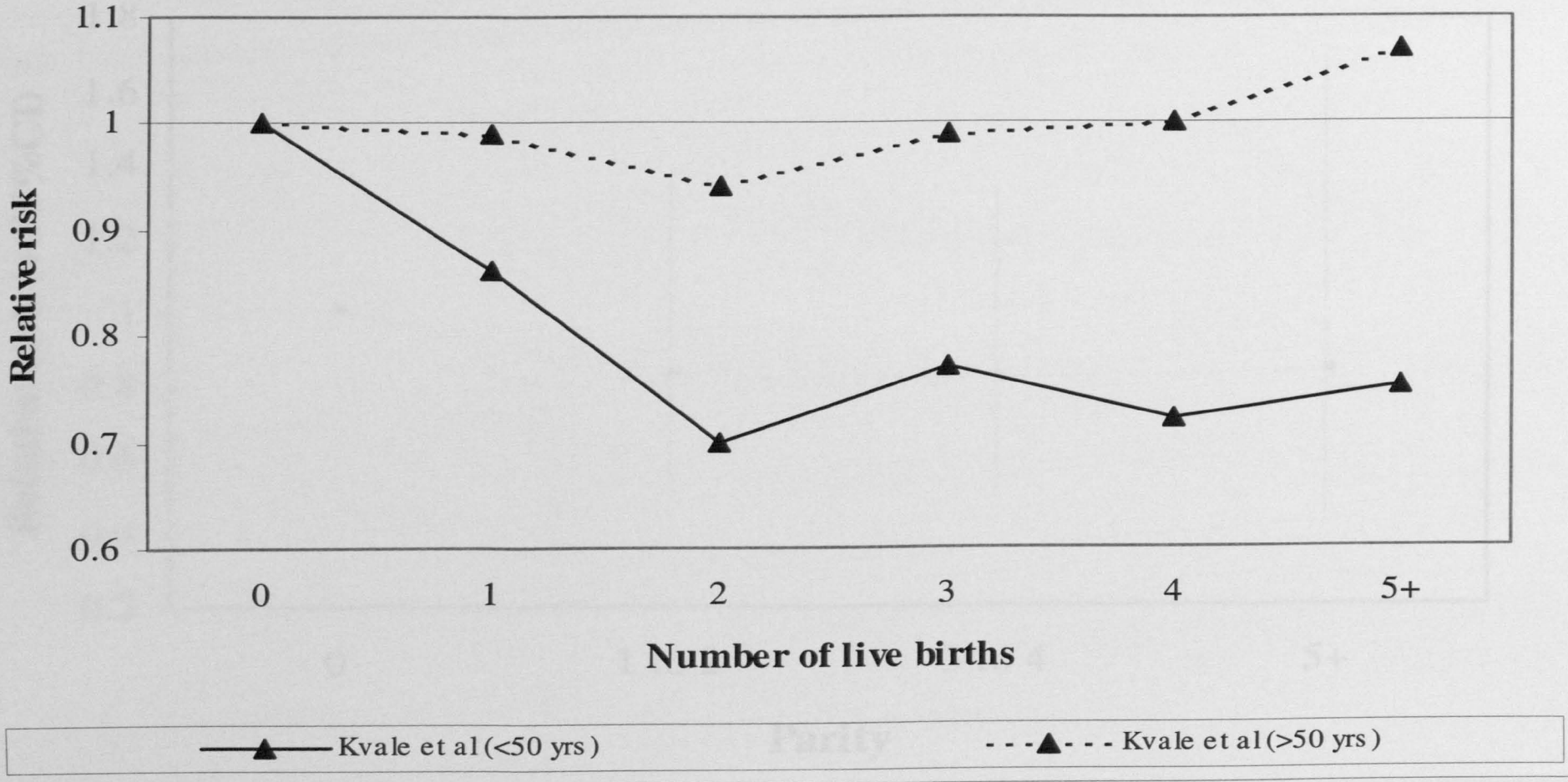


Figure A2.13: Risk of mortality by parity, relative to the nulliparous (Cooper et al 2000)

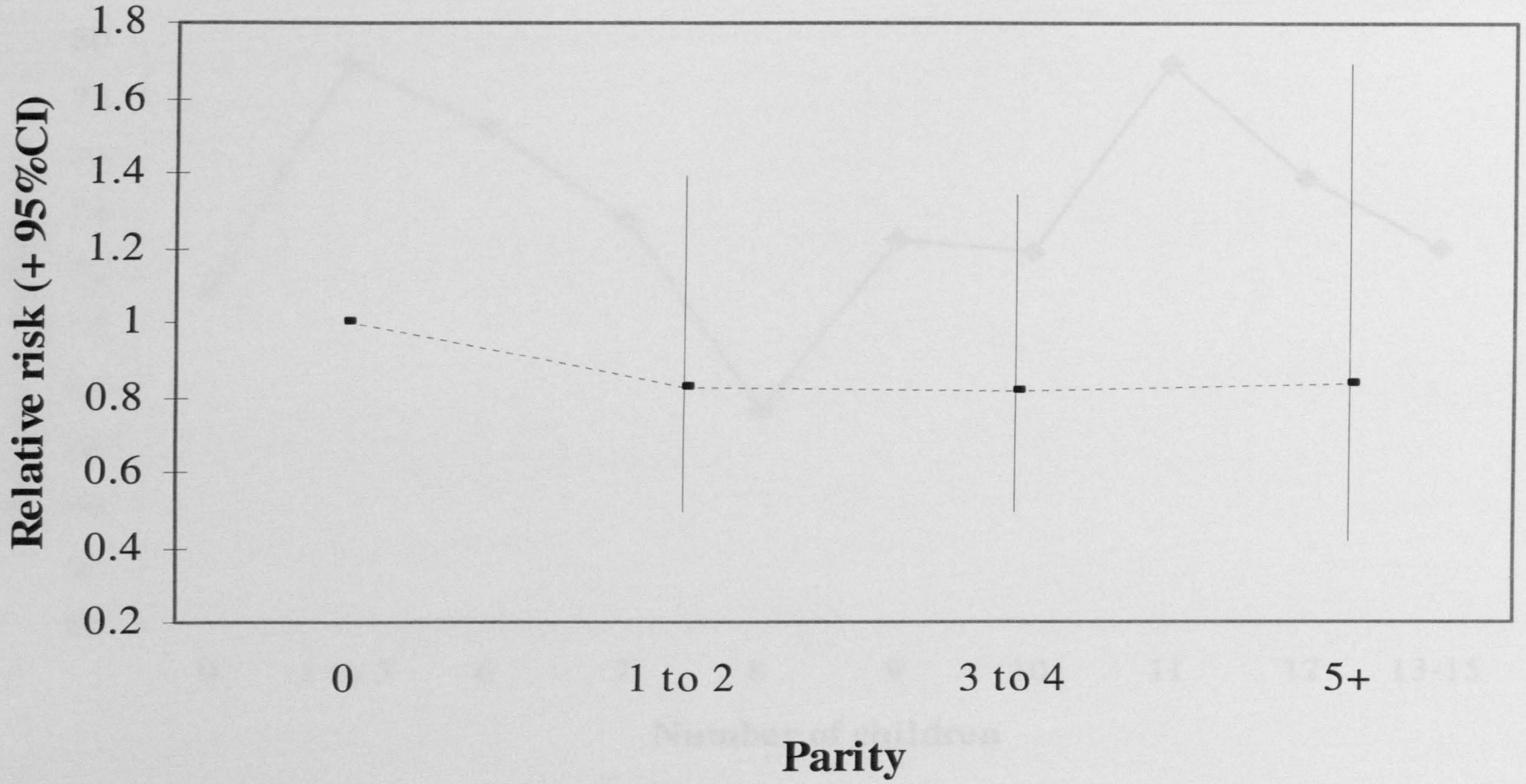


Figure A2.14: Mean age at death by number of children (Phillipe and Yelle 1976)

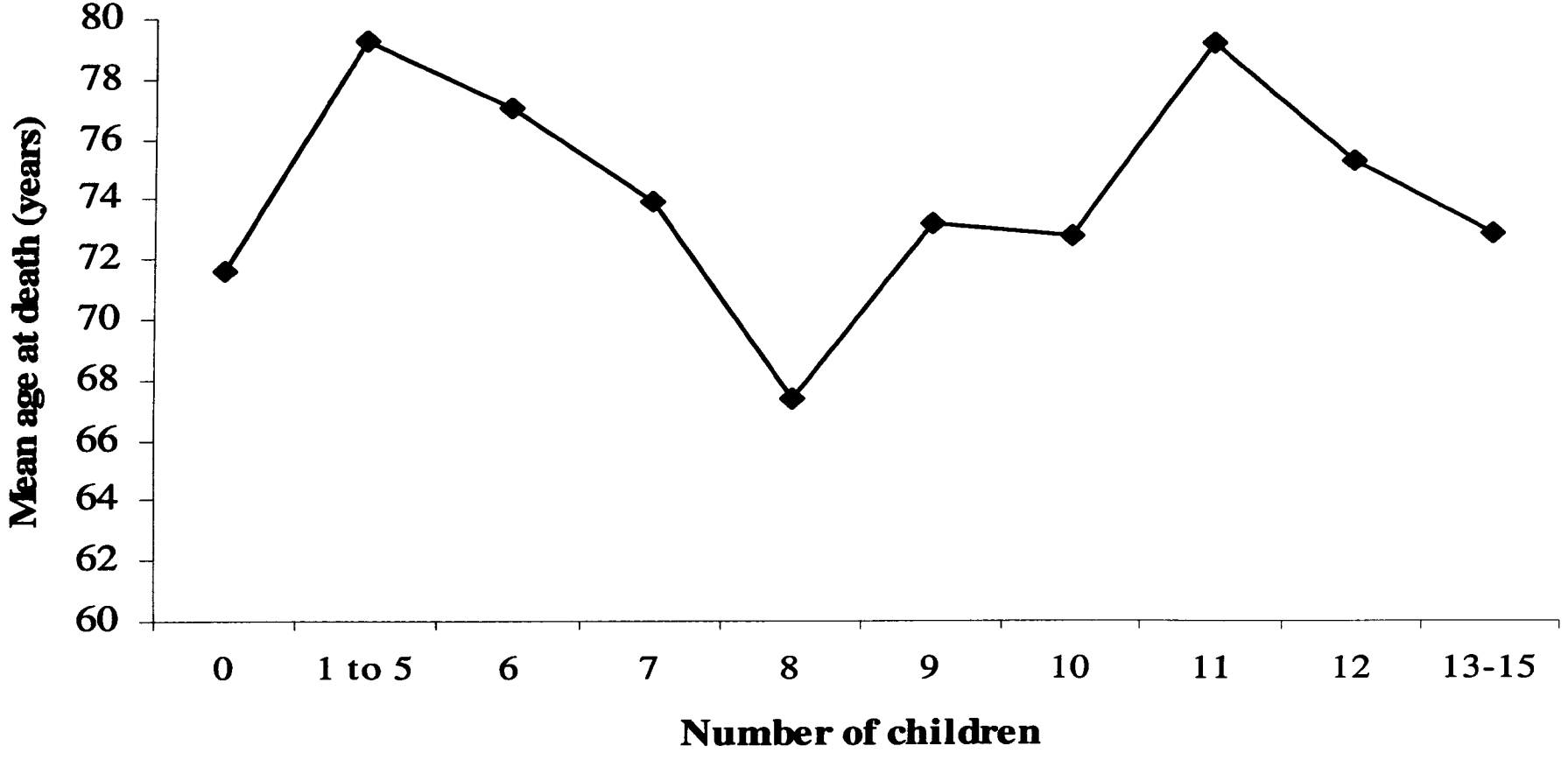


Figure A2.15: Mean number of children by age at death with 95% confidence intervals in females (Westendorp, Kirkwood 1998)

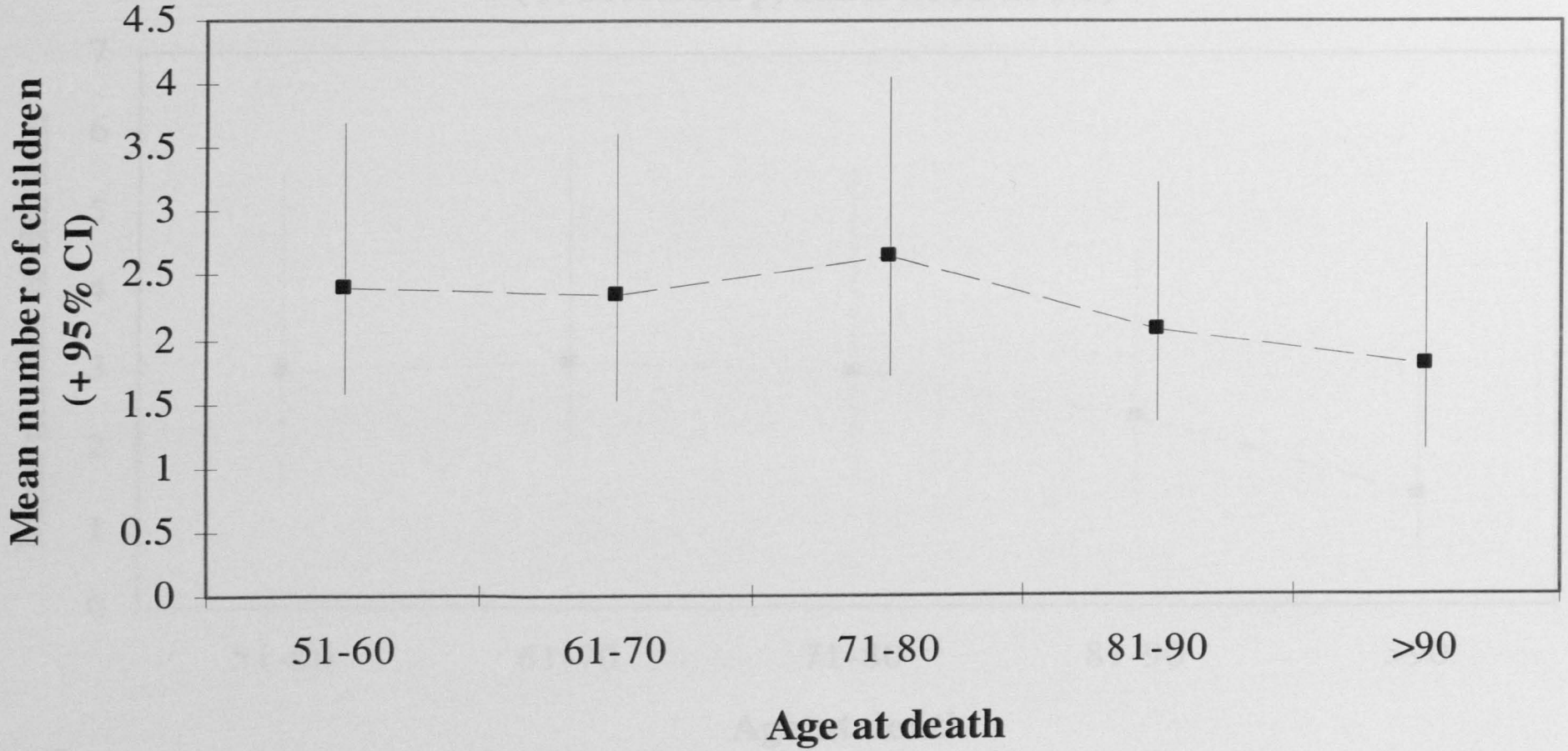


Figure A2.16: Mean number of children by age at death with 95% confidence intervals in men born pre-1700 (Westendorp, Kirkwood 1998)

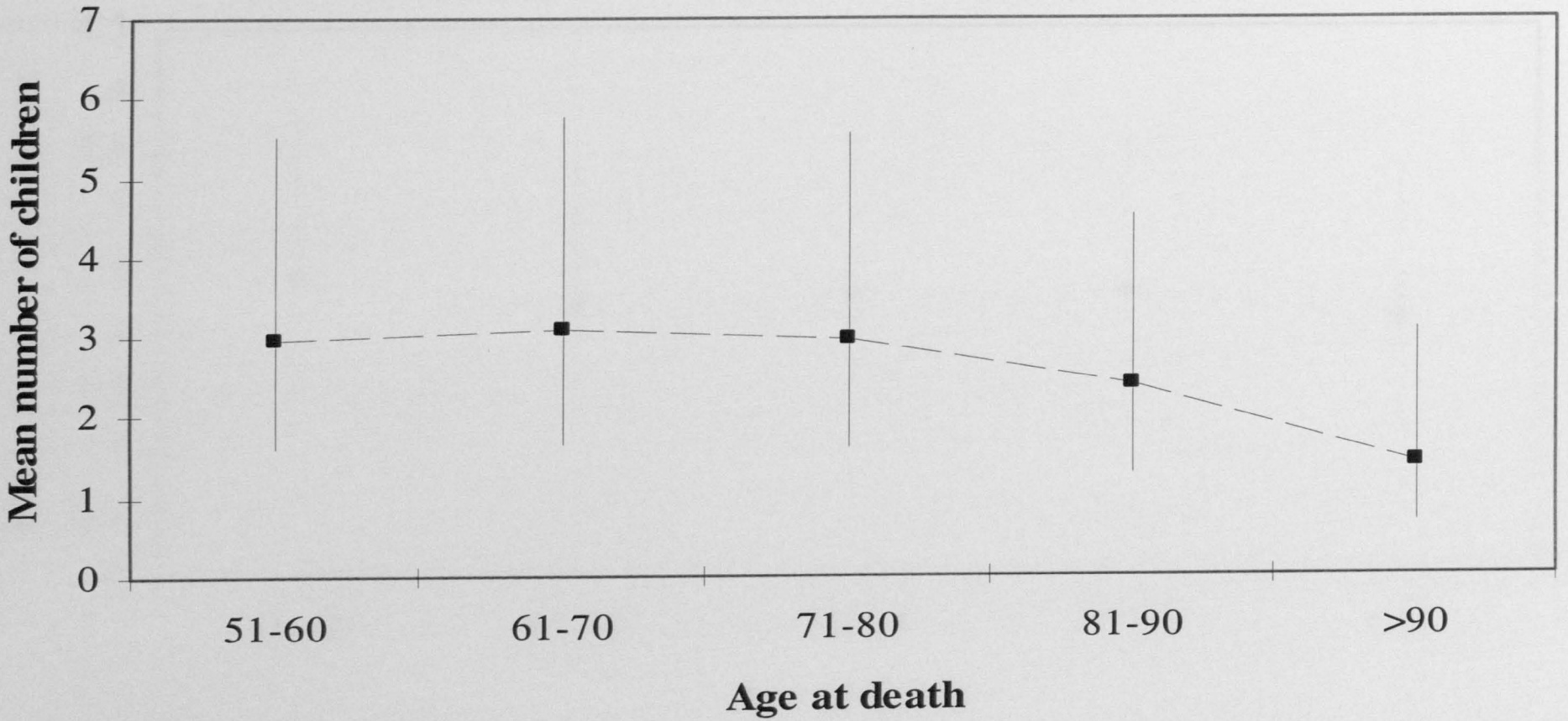


Figure A2.17: Mean number of children by age at death with 95% confidence intervals in men born 1700-1875 (Westendorp, Kirkwood 1998)

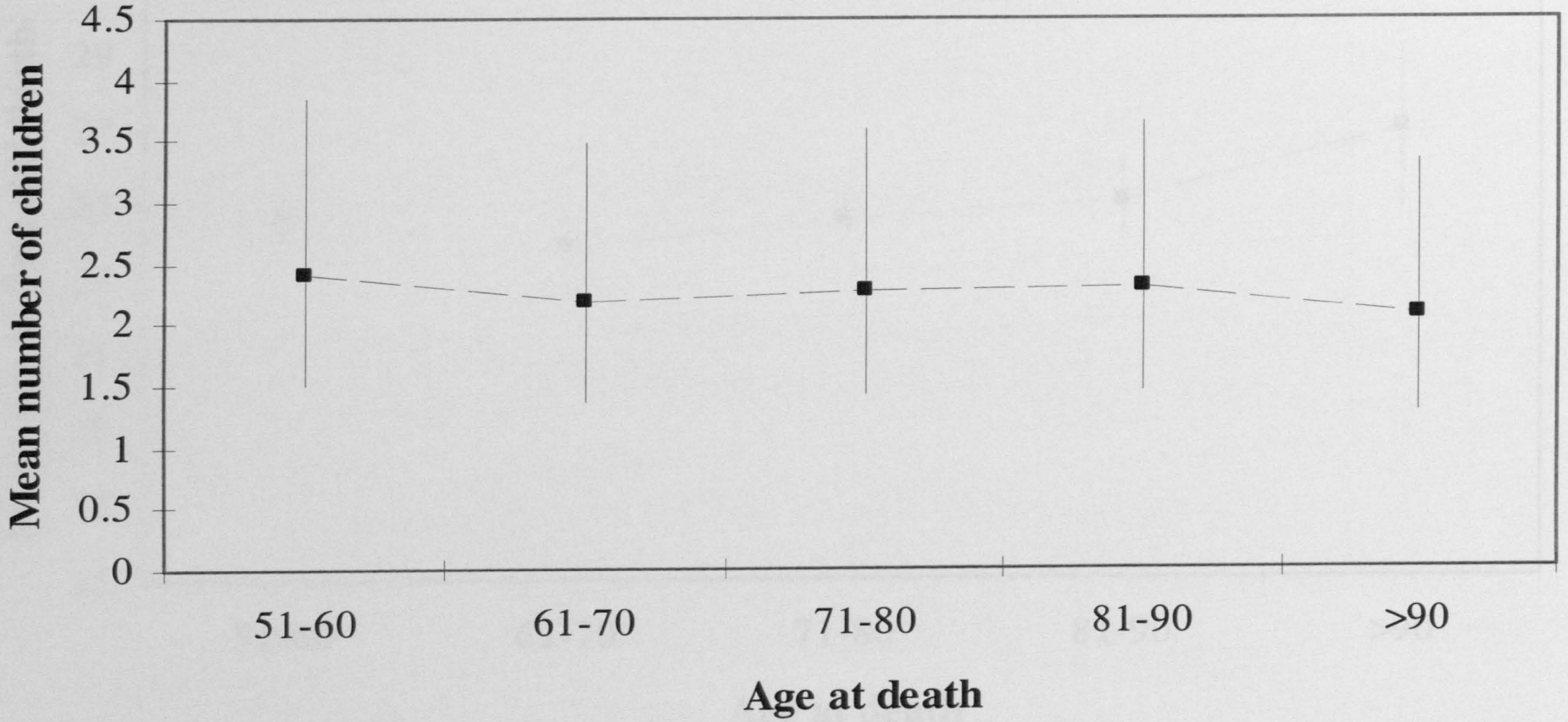


Figure A2.18: Mean age at first childbirth by age at death with 95% confidence intervals in females (Westendorp, Kirkwood 1998)

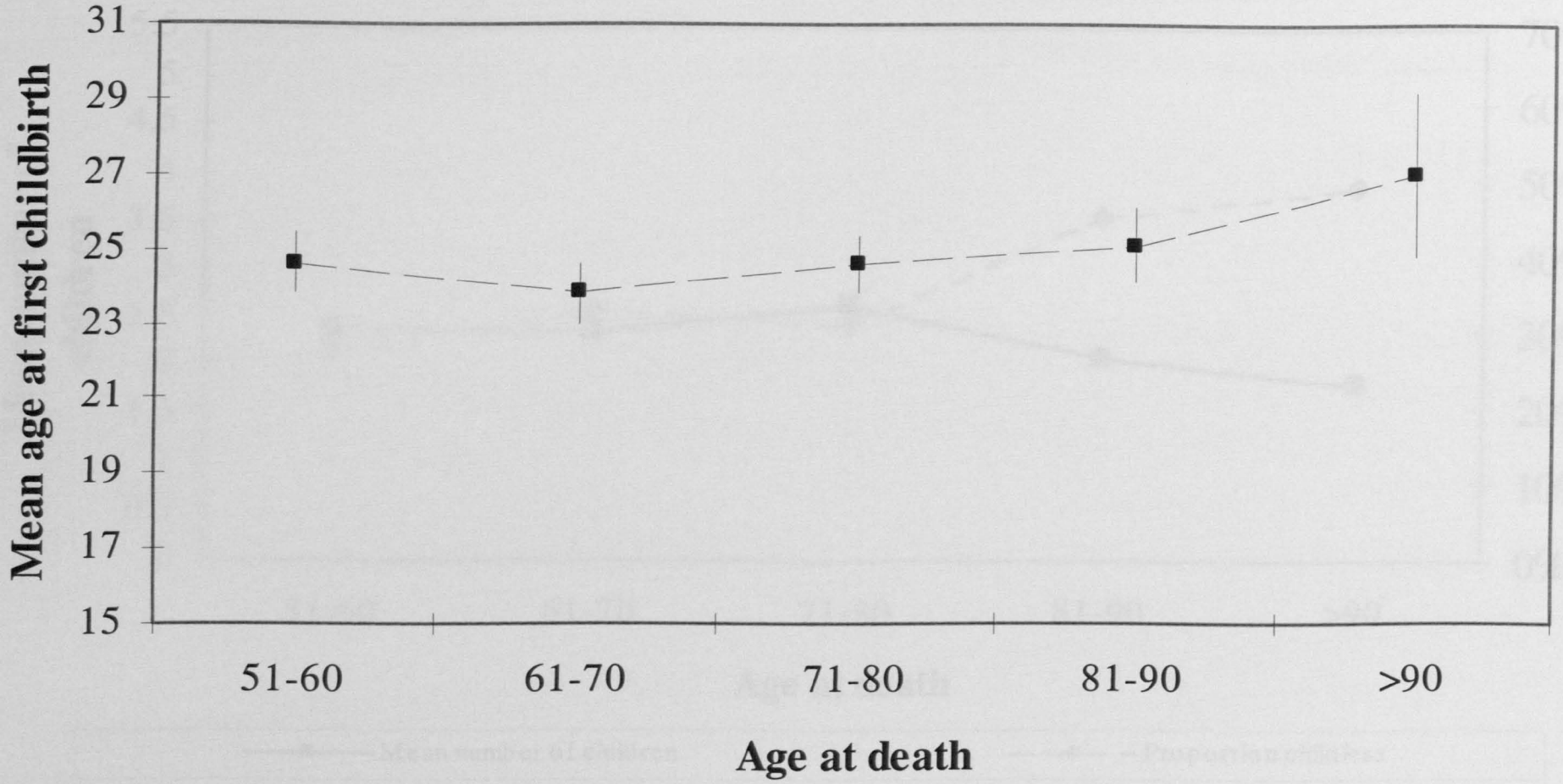


Figure A2.19: Mean number of children and proportion childless by age at death (Westendorp, Kirkwood 1998)

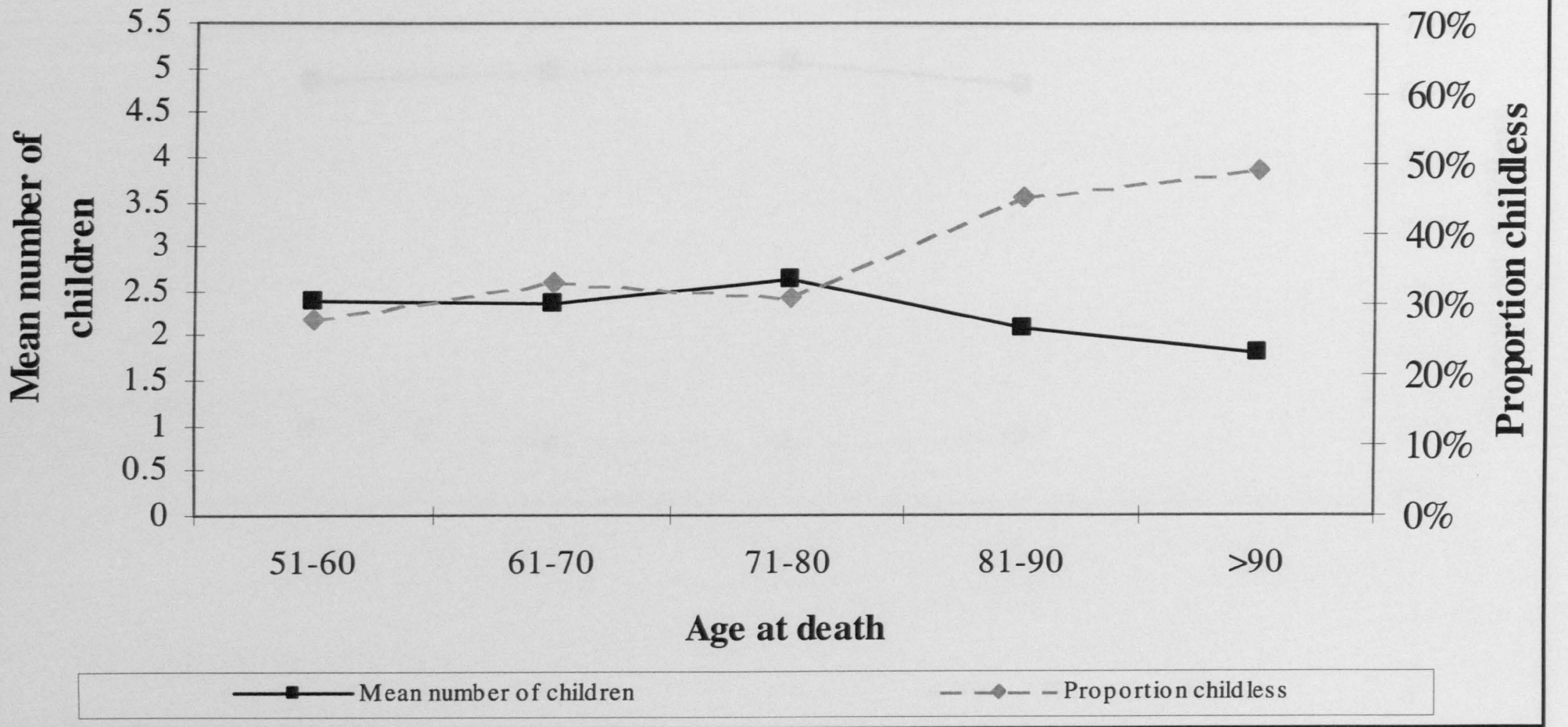
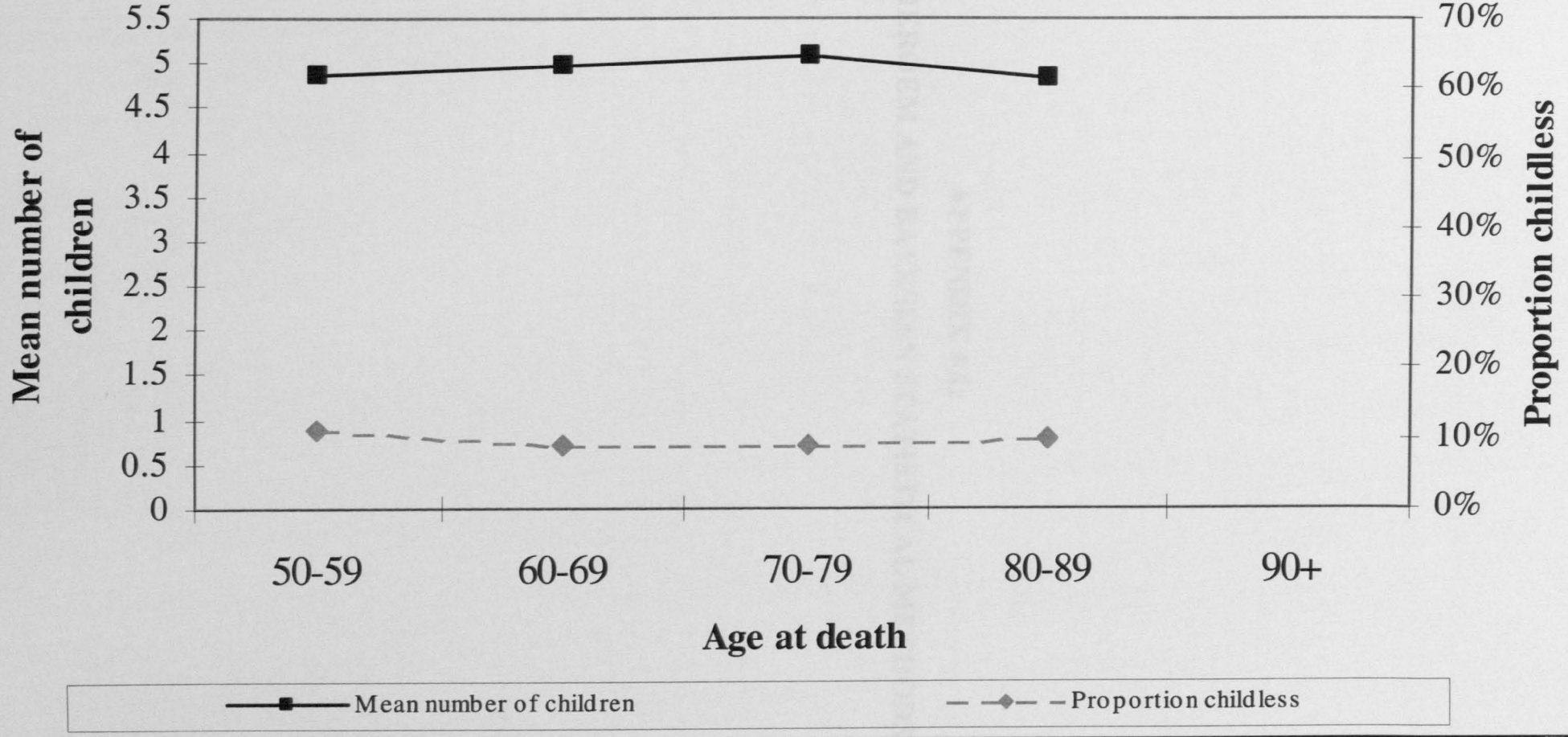


Figure A 2.20: Mean number of children and proportion childless by age at death (Lycett et al 2000)



APPENDIX 4.1:
BAYES' THEROEM AND BAYESIAN STATISTICAL METHODS

Bayes theorem:

Bayes' theorem is a theory in probability theory, and is named after an English clergyman and mathematician, Thomas Bayes (1702-1761). This definition is given in Last's Dictionary of Epidemiology (1995):

> *"In epidemiology, [Bayes' theorem] is used to obtain the probability of disease in a group of people with some characteristic on the basis of the overall rate of the disease (the prior probability of disease) and of the likelihoods of that characteristic in healthy and diseased individuals... A simplified version of the theorem is*
>
> $$P(D|S) = \frac{P(S|D).P(D)}{P(S|D).P(D) + P(S|D_0).P(D_0)}$$
>
> *where D = disease, S = symptom, and D_0 = no disease. The formula emphasises what clinical intuition often overlooks, namely, that the probability of disease given this symptom depends not only on how characteristic that symptom is of the disease but also on how frequent the disease is among the population being served.*
> *Some of the terms in the theorem are named. The probability of disease given the symptom is the* ***posterior probability****. It is an estimate of the probability of disease posterior to knowing whether or not the symptom was present. The overall probability of disease among the population or our guess of the probability of disease before knowing of the presence or absence of the symptom is the* ***prior probability****."*

It can also be shown that the posterior probability is proportional to the likelihood function times the prior probability. In the words of Berry and Stangl (1996):

> *"The prior represents what was thought before seeing the data, the likelihood represents the data now available, and the posterior represents what is thought given both prior information and the data just seen."*

The central idea in Bayesian methods therefore is to use data collected in a study to update the state of our knowledge about the quantity of interest. The use of Bayesian principles is well demonstrated in diagnostic testing (Dunson 2001). A patient presents with a symptom. A doctor will have an idea of the probability of disease - that is, the prior probability of disease - given that symptom. A diagnostic test is then performed to look for evidence of disease. The results of the diagnostic test will change the doctor's ideas of how likely it is that the patient is suffering from a disease – this is the posterior probability. Physicians will usually order more tests (that is, collect more data) until the posterior probability of disease is either 0 (no disease) or 1 (disease). Dunson (2001) describes how this Bayesian framework can be extended for the analysis of epidemiological data:

> *"There is no fundamental conceptual difference between the use of Bayes' theorem to obtain a posterior probability of disease for a patient and the general application of Bayesian methods to the analysis of epidemiological data. In diagnostic settings one wishes to predict the unknown disease status of an individual, while in analyzing data one wishes to perform inferences on a set of unknowns, which may consist of both latent variables*[A4.1] *and population parameters (e.g. the regression coefficients in a logistic regression model.....the investigator first chooses a* ***prior probability distribution*** *for the unknowns in the model (i.e. the parameters and latent variables)*[A4.2] *and then updates this prior distribution to obtain a* ***posterior distribution*** *for the unknowns by plugging the prior and the likelihood of the data (conditional on the unknowns) into Bayes' theorem.....Bayesians base inferences about exposure-disease relations and other hypotheses of interest on the posterior distribution and not on the maximum likelihood or a p value."*

A major source of controversy in Bayesian inference is in the choice of a prior, as this choice is seen as being 'subjective'. Etzioni and Kadane (1995) state that

> *"the use of a prior distribution may be viewed as a strength, rather than a weakness.....The prior provides the mechanism for expressing explicitly some of the possible subjective assumptions that are present but not usually acknowledged in classical statistical analyses."*

The use of noninformative priors, that is when the prior beliefs specify that all possible values are equally likely, is relatively more objective (Berry, Stangl 1996).

In multiple imputation Bayesian statistical are used in the following way (Schafer 1999):

> *"Specify a parametric model for the complete data (and, if necessary, a model for the mechanism by which data became missing), apply a prior distribution to the unknown model parameters, and simulate* ***m*** *independent draws from the conditional distribution of Y_{mis} given Y_{obs} by Bayes' theorem."*

[A4.1] Latent variables are variables that are not observed directly, for example the true disease status in an individual in the presence of diagnostic error or the true blood pressure in the presence of measurement error.

[A4.2] Can also include missing data

APPENDIX 4.2:
RULES FOR COMBINING THE RESULTS OF ANALYSES PERFORMED ON THE IMPUTED DATA SETS AND TO CALCULATE THE RATE OF MISSING INFORMATION

Imputation in Solas

In Solas predictive model based methods are used to impute continuous or ordinal variables, using ordinary least squares regression. The methods used in Solas are given in the Solas Imputation User's Manual (1999).

Combining the estimates

The methods for combining the estimates are described by Rubin (1987, 1996) and Schafer (1997) and are as follows:

The repeated-imputation estimate is the average of the estimates obtained from the imputations. For example in my data, the estimate of interest was the rate ratio and the number of imputations was 5. Therefore,

Repeated-imputation rate ratio = Σ (rate ratio from each imputed data set) / 5

The total variability associated with the estimate T (from which confidence intervals can be calculated) is

$$T = U + (1 + m^{-1}).B$$

where U is the *within-imputation variance* and is the average of the imputed complete-data estimates' variance given by

$$U = \Sigma (\text{variance for each imputed estimate}) / 5$$

B is the *between-imputation variance* that provides a measure of extra inferential uncertainty due to the missing data (that is, accounts for the fact that missing values are not observed but are estimated with uncertainty). It is calculated as

$$B = (\Sigma (\text{Imputation estimate} - \text{Average estimate})^2) / (m - 1)$$

$(1 + m^{-1})$ is the *inflation factor* and it accounts for the additional variability due to using a finite number of imputations (Barnard and Meng 1999).

The *pooled standard error* of a point estimate therefore is $\sqrt{T_m}$

Confidence intervals can then be calculated using the formulae

Repeated imputation estimate +/- ($t_{v,\,1\,-\,\alpha/2}$ x Pooled standard error)

Degrees of freedom, given by

$$(m-1).[1+(U/(1+m^{-1}).B)]^2$$

were sufficiently large in these samples to use 1.96 for $t_{v,\,1\,-\,\alpha/2}$.

The Stata do-file, written to perform the calculations automatically once the estimates from the five imputed data sets were obtained, is shown below:

Stata do file for combining rates

```
capture log close
capture set more off

use c:\stata\rates, replace
log using rates, replace

gen para=(para1 + para2 + para3 + para4 + para5)/5

gen loglow1=log(lowci1)
gen loghigh1=log(highci1)
gen int1=(loghigh1)-(loglow1)
gen divide1=int1/(2*1.96)
gen se1=para1*divide1

gen loglow2=log(lowci2)
gen loghigh2=log(highci2)
gen int2=(loghigh2)-(loglow2)
gen divide2=int2/(2*1.96)
gen se2=para2*divide2

gen loglow3=log(lowci3)
gen loghigh3=log(highci3)
gen int3=(loghigh3)-(loglow3)
gen divide3=int3/(2*1.96)
gen se3=para3*divide3

gen loglow4=log(lowci4)
gen loghigh4=log(highci4)
gen int4=(loghigh4)-(loglow4)
gen divide4=int4/(2*1.96)
gen se4=para4*divide4

gen loglow5=log(lowci5)
gen loghigh5=log(highci5)
gen int5=(loghigh5)-(loglow5)
gen divide5=int5/(2*1.96)
gen se5=para5*divide5

gen var1=(se1)*(se1)
gen var2=(se2)*(se2)
gen var3=(se3)*(se3)
gen var4=(se4)*(se4)
```

Stata does not automatically provide standard errors for rates – these formulae are therefore to obtain the required standard errors

```
gen var5=(se5)*(se5)

gen U=(var1 + var2 + var3 + var4 + var5)/5

gen wvar1=(para1-para)*(para1-para)
gen wvar2=(para2-para)*(para2-para)
gen wvar3=(para3-para)*(para3-para)
gen wvar4=(para4-para)*(para4-para)
gen wvar5=(para5-para)*(para5-para)

gen B=(wvar1 + wvar2 + wvar3 + wvar4 + wvar5)/4

gen T=U + ((1.2)*B)

gen SE=sqrt(T)

gen v= 4* ( (1+(U/(1.2*B)) )^2 )

gen lowerci= para - (1.96*SE)
gen upperci= para + (1.96*SE)

save c:\stata\rates, replace
log close
exit
```

Stata do file for combining rate ratios

```
capture log close
capture set more off

use c:\stata\ratios, replace
log using ratios, replace

gen para=(para1 + para2 + para3 + para4 + para5)/5

gen var1=(se1)*(se1)
gen var2=(se2)*(se2)
gen var3=(se3)*(se3)
gen var4=(se4)*(se4)
gen var5=(se5)*(se5)

gen U=(var1 + var2 + var3 + var4 + var5)/5

gen wvar1=(para1-para)*(para1-para)
gen wvar2=(para2-para)*(para2-para)
gen wvar3=(para3-para)*(para3-para)
gen wvar4=(para4-para)*(para4-para)
gen wvar5=(para5-para)*(para5-para)

gen B=(wvar1 + wvar2 + wvar3 + wvar4 + wvar5)/4

gen T=U + ((1.2)*B)

gen SE=sqrt(T)

gen v= 4* ( (1+(U/(1.2*B)) )^2 )

gen lowerci= para - (1.96*SE)
gen upperci= para + (1.96*SE)
```

```
assert para>=lowerci
assert para<=upperci

save c:\stata\ratios, replace
log close
exit
```

Rate of missing information

Rate of missing information, γ is calculated by

$$\frac{(r+2)/(v+3)}{r+1}$$

where r is the "*relative increase in variance due to nonresponse*" (Rubin 1987), and is calculated by

$$\frac{(1+m^{-1}).B}{U}$$

In the female data set, U and B vary according to the association being assessed (for example, parity and mortality or number of surviving children and mortality). The relative increase in variance due to nonresponse r, the degrees of freedom v and rate of missing information γ were calculated for the minimum and maximum values of U and B obtained to give the range of values for both.

With the minimum values of U and B:

$$r = 0.015788,\ v = 16557.548070,\ \gamma = 0.000120$$

With the maximum values of U and B:

$$r = 0.855967,\ v = 18.805572,\ \gamma = 0.070569$$

APPENDIX 6.1:
IMPUTED REPRODUCTIVE HISTORY VARIABLES - FEMALE

Table A6.1: Number of surviving sons – Original data set and imputed data sets

Original Data Set				First Imputed Data Set					Second Imputed Data Set				
Living sons	Number	Percentage	Cumulative percentage	Living sons	Number	%	Number imputed	%	Living sons	Number	%	Number imputed	%
0	1615	8.59	8.59	0	1818	8.92	203	12.91	0	1807	8.87	192	12.21
1	3228	17.16	25.75	1	3474	17.04	246	15.64	1	3515	17.24	287	18.25
2	4568	24.28	50.03	2	4952	24.29	384	24.41	2	4940	24.24	372	23.65
3	4265	22.67	72.71	3	4623	22.68	358	22.76	3	4596	22.55	331	21.04
4	2895	16.39	88.10	4	3141	15.41	246	15.64	4	3135	15.38	240	15.26
5	1458	7.75	95.85	5	1551	7.61	93	5.91	5	1570	7.70	112	7.12
6	557	2.96	98.81	6	592	2.90	35	2.23	6	587	2.88	30	1.91
7	173	0.92	99.73	7	180	0.88	7	0.45	7	178	0.87	5	0.32
8	38	0.20	99.93	8	39	0.18	1	0.06	8	42	0.21	4	0.25
9	10	0.05	99.98	9	10	0.05	0	0.00	9	10	0.05	0	0.00
10	0	0.00	99.98	10	0	0.00	0	0.00	10	0	0.00	0	0.00
11	2	0.01	99.99	11	2	0.01	0	0.00	11	2	0.01	0	0.00
12	1	0.01	100.00	12	1	0.00	0	0.00	12	1	0.00	0	0.00
Total	18810[1]	100.00		Total	20383[2]	100.00	1573	100.00	Total	20383	100.00	1573	100.00
Mean (Standard Deviation) = 2.61 (1.58) Median = 2				Mean (Standard Deviation) = 2.59 (1.58) Median = 2					Mean (Standard Deviation) = 2.59 (1.58) Median = 2				

Third Imputed Data Set					Fourth Imputed Data Set					Fifth Imputed Data Set				
Living sons	Number	%	Number imputed	%	Living sons	Number	%	Number imputed	%	Living sons	Number	%	Number imputed	%
0	1812	8.89	197	12.52	0	1816	8.91	201	12.78	0	1804	8.85	189	12.02
1	3509	17.22	281	17.86	1	3518	17.26	290	18.44	1	3505	17.20	277	17.61
2	4923	24.15	355	22.57	2	4941	24.24	373	23.71	2	4921	24.14	353	22.44
3	4631	22.72	366	23.27	3	4597	22.55	332	21.11	3	4622	22.68	357	22.70
4	3132	15.37	237	15.07	4	3109	15.25	214	13.60	4	3139	15.40	244	15.51
5	1560	7.65	102	5.48	5	1579	7.75	121	7.69	5	1565	7.68	107	6.80
6	586	2.87	29	1.84	6	590	2.89	33	2.10	6	591	2.90	34	2.16
7	179	0.88	6	0.38	7	182	0.89	9	0.57	7	184	0.90	11	0.70
8	38	0.19	0	0.00	8	38	0.19	0	0.00	8	39	0.19	1	0.06
9	10	0.05	0	0.00	9	10	0.05	0	0.00	9	10	0.05	0	0.00
10	0	0.00	0	0.00	10	0	0.00	0	0.00	10	0	0.00	0	0.00
11	2	0.01	0	0.00	11	2	0.01	0	0.00	11	2	0.01	0	0.00
12	1	0.00	0	0.00	12	1	0.00	0	0.00	12	1	0.00	0	0.00
Total	20383	100.00	1573	100.00	Total	20383	100.00	1573	100.00	Total	20383	100.00	1573	100.00
Mean (Standard Deviation) = 2.59 (1.58) Median = 2					Mean (Standard Deviation) = 2.59 (1.58) Median = 2					Mean (Standard Deviation) = 2.59 (1.58) Median = 2				

1. Missing data not included 2. Imputed data included

Table A6.2: Number of dead sons – Original data set and imputed data sets

Original Data Set				First Imputed Data Set					Second Imputed Data Set				
Dead sons	Number	Percentage	Cumulative percentage	Dead sons	Number	%	Number imputed	%	Dead sons	Number	%	Number imputed	%
0	9137	48.58	48.58	0	9613	47.16	476	30.26	0	9572	46.96	435	27.65
1	5668	30.13	78.71	1	6225	30.54	557	35.41	1	6241	30.62	573	36.43
2	2534	13.47	92.18	2	2919	14.32	385	24.48	2	2955	14.50	421	26.76
3	981	5.22	97.40	3	1118	5.48	137	8.71	3	1106	5.43	125	7.95
4	334	1.78	99.17	4	350	1.72	16	1.02	4	351	1.72	17	1.08
5	110	0.58	99.76	5	112	0.55	2	0.13	5	112	0.55	2	0.13
6	34	0.18	99.94	6	34	0.17	0	0.00	6	34	0.17	0	0.00
7	8	0.04	99.98	7	8	0.04	0	0.00	7	8	0.04	0	0.00
8	4	0.02	100.00	8	4	0.02	0	0.00	8	4	0.02	0	0.00
Total	18810[1]	100.00		Total	20383[2]	100.00	1573	100.00	Total	20383	100.00	1573	100.00
Mean (Standard Deviation) = 0.84 (1.06) Median = 1				Mean (Standard Deviation) = 0.86 (1.06) Median = 1					Mean (Standard Deviation) = 0.87 (1.06) Median = 1				

Third Imputed Data Set					Fourth Imputed Data Set					Fifth Imputed Data Set				
Dead sons	Number	%	Number imputed	%	Dead sons	Number	%	Number imputed	%	Dead sons	Number	%	Number imputed	%
0	9611	47.15	474	30.13	0	9577	46.99	440	27.97	0	9601	47.10	464	29.50
1	6227	30.55	559	35.54	1	6238	30.60	570	36.24	1	6267	30.75	599	38.08
2	2932	14.38	398	25.30	2	2950	14.47	416	26.45	2	2914	14.30	380	24.16
3	1106	5.43	125	7.95	3	1109	5.44	128	8.14	3	1096	5.38	115	7.31
4	348	1.71	14	0.89	4	352	1.73	18	1.14	4	348	1.71	14	0.89
5	113	0.55	3	0.19	5	111	0.54	1	0.06	5	110	0.54	0	0.00
6	34	0.17	0	0.00	6	34	0.17	0	0.00	6	35	0.17	1	0.06
7	8	0.04	0	0.00	7	8	0.04	0	0.00	7	8	0.04	0	0.00
8	4	0.02	0	0.00	8	4	0.02	0	0.00	8	4	0.02	0	0.00
Total	20383	100.00	1573	100.00	Total	20383	100.00	1573	100.00	Total	20383	100.00	1573	100.00
Mean (Standard Deviation) = 0.87 (1.06) Median = 1					Mean (Standard Deviation) = 0.87 (1.06) Median = 1					Mean (Standard Deviation) = 0.86 (1.06) Median = 1				

1. Missing data not included 2. Imputed data included

Table A6.3: Number of surviving daughters – Original data set and imputed data sets

Original Data Set				First Imputed Data Set					Second Imputed Data Set				
Living daughters	Number	Percentage	Cumulative percentage	Living dau	Number	%	Number imputed	%	Living dau	Number	%	Number imputed	%
0	1614	8.58	8.58	0	1802	8.84	188	11.95	0	1814	8.90	200	12.71
1	3608	19.18	27.76	1	3874	19.01	266	16.91	1	3860	18.94	252	16.02
2	4602	24.47	52.23	2	4953	24.30	351	22.31	2	4974	24.40	372	23.65
3	3966	21.08	73.31	3	4305	21.12	339	21.55	3	4321	21.20	355	22.57
4	2685	14.27	87.59	4	2947	14.46	262	16.66	4	2911	14.28	226	14.37
5	1428	7.59	95.18	5	1558	7.64	130	8.26	5	1553	7.62	125	7.95
6	579	3.08	98.26	6	610	2.99	31	1.97	6	617	3.03	38	2.42
7	218	1.16	99.42	7	222	1.09	4	0.25	7	223	1.09	5	0.32
8	84	0.45	99.86	8	86	0.42	2	0.13	8	84	0.41	0	0.00
9	23	0.12	99.98	9	23	0.10	0	0.00	9	23	0.11	0	0.00
10	2	0.01	99.99	10	2	0.01	0	0.00	10	2	0.01	0	0.00
11	0	0.00	99.99	11	0	0.00	0	0.00	11	0	0.00	0	0.00
12	1	0.01	100.00	12	1	0.01	0	0.00	12	1	0.00	0	0.00
Total	18810[1]	100.00		Total	20383[2]	100.00	1573	100.00	Total	20383	100.00	1573	100.00
Mean (Standard Deviation) = 2.58 (1.64) Median = 2				Mean (Standard Deviation) = 2.57 (1.63) Median = 2					Mean (Standard Deviation) = 2.57 (1.63) Median = 2				

Third Imputed Data Set					Fourth Imputed Data Set					Fifth Imputed Data Set				
Living dau	Number	%	Number imputed	%	Living dau	Number	%	Number imputed	%	Living dau	Number	%	Number imputed	%
0	1821	8.93	207	13.16	0	1805	8.86	191	12.14	0	1810	8.88	196	12.46
1	3869	18.98	261	16.59	1	3872	19.00	264	16.78	1	3881	19.04	273	17.36
2	4931	24.19	329	20.92	2	4983	24.45	381	24.22	2	4976	24.41	374	23.78
3	4350	21.34	384	24.41	3	4308	21.14	342	21.74	3	4308	21.14	342	21.74
4	2918	14.32	233	14.81	4	2924	14.35	239	15.19	4	2913	14.29	228	14.49
5	1537	7.54	109	6.93	5	1539	7.55	111	7.06	5	1540	7.56	112	7.12
6	613	3.01	12	0.76	6	614	3.01	35	2.23	6	613	3.01	34	2.16
7	230	1.13	34	2.16	7	227	1.11	9	0.57	7	231	1.13	13	0.83
8	88	0.43	4	0.25	8	85	0.42	1	0.06	8	85	0.42	1	0.06
9	23	0.11	0	0.00	9	23	0.11	0	0.00	9	23	0.11	0	0.00
10	2	0.01	0	0.00	10	2	0.01	0	0.00	10	2	0.01	0	0.00
11	0	0.00	0	0.00	11	0	0.00	0	0.00	11	0	0.00	0	0.00
12	1	0.00	0	0.00	12	1	0.00	0	0.00	12	1	0.00	0	0.00
Total	20383	100.00	1573	100.00	Total	20383	100.00	1573	100.00	Total	20383	100.00	1573	100.00
Mean (Standard Deviation) = 2.57 (1.63) Median = 2					Mean (Standard Deviation) = 2.57 (1.63) Median = 2					Mean (Standard Deviation) = 2.57 (1.63) Median = 2				

1. Missing data not included 2. Imputed data included

Table A6.4: Number of dead daughters – Original data set and imputed data sets

Original Data Set				First Imputed Data Set					Second Imputed Data Set				
Dead daughters	Number	Percentage	Cumulative percentage	Dead dau	Number	%	Number imputed	%	Dead dau	Number	%	Number imputed	%
0	8329	44.28	44.28	0	8776	43.06	447	28.42	0	8787	43.11	458	29.12
1	5996	31.88	76.16	1	6577	32.27	581	36.94	1	6538	32.08	542	34.46
2	2817	14.98	91.13	2	3214	15.77	397	25.24	2	3231	15.85	414	26.32
3	1104	5.87	97.00	3	1234	6.05	130	8.26	3	1242	6.09	138	8.77
4	388	2.06	99.06	4	404	1.98	16	1.02	4	409	2.01	21	1.34
5	118	0.63	99.69	5	119	0.58	1	0.06	5	118	0.58	0	0.00
6	36	0.19	99.88	6	37	0.18	1	0.06	6	36	0.18	0	0.00
7	16	0.09	99.97	7	16	0.08	0	0.00	7	16	0.08	0	0.00
8	5	0.03	99.99	8	5	0.02	0	0.00	8	5	0.02	0	0.00
9	1	0.01	100.00	9	1	0.01	0	0.00	9	1	0.00	0	0.00
Total	18810[1]	100.00		Total	20383[2]	100.00	1573	100.00	Total	20383	100.00	1573	100.00
Mean (Standard Deviation) = 0.93 (1.11) Median = 1				Mean (Standard Deviation) = 0.95 (1.09) Median = 1					Mean (Standard Deviation) = 0.95 (1.09) Median = 1				

Third Imputed Data Set					Fourth Imputed Data Set					Fifth Imputed Data Set				
Dead dau	Number	%	Number imputed	%	Dead dau	Number	%	Number imputed	%	Dead dau	Number	%	Number imputed	%
0	8760	42.98	431	27.40	0	8760	42.98	431	27.40	0	8802	43.18	473	30.07
1	6545	32.11	549	34.90	1	6565	32.21	569	36.17	1	6535	32.06	539	34.27
2	3247	15.93	430	27.34	2	3216	15.78	399	25.37	2	3213	15.76	396	25.17
3	1247	6.12	143	9.09	3	1254	6.15	150	9.54	3	1239	6.08	135	8.58
4	408	2.00	20	1.27	4	411	2.02	23	1.46	4	417	2.05	29	1.84
5	118	0.58	0	0.00	5	119	0.58	1	0.06	5	119	0.58	1	0.06
6	36	0.18	0	0.00	6	36	0.18	0	0.00	6	36	0.18	0	0.00
7	16	0.08	0	0.00	7	16	0.08	0	0.00	7	16	0.08	0	0.00
8	5	0.02	0	0.00	8	5	0.02	0	0.00	8	5	0.02	0	0.00
9	1	0.00	0	0.00	9	1	0.00	0	0.00	9	1	0.00	0	0.00
Total	20383	100.00	1573	100.00	Total	20383	100.00	1573	100.00	Total	20383	100.00	1573	100.00
Mean (Standard Deviation) = 0.95 (1.09) Median = 1					Mean (Standard Deviation) = 0.95 (1.09) Median = 1					Mean (Standard Deviation) = 0.95 (1.09) Median = 1				

1. Missing data not included 2. Imputed data included

Table A6.5: Number of fetal losses – Original data set and imputed data sets

Original Data Set			
Fetal losses	Number	Percentage	Cumulative percentage
0	12589	66.93	66.93
1	4046	21.51	88.44
2	1362	7.24	95.68
3	504	2.68	98.36
4	178	0.95	99.30
5	66	0.35	99.65
6	30	0.16	99.81
7	20	0.11	99.92
8	9	0.05	99.97
9	4	0.02	99.99
10	1	0.01	99.99
11	0	0.00	99.99
12	1	0.01	100.00
Total	18810[1]	100.00	
Mean (Standard Deviation) = 0.52 (0.94) Median = 0			

First Imputed Data Set				
Fetal losses	Number	%	Number imputed	%
0	13410	65.79	821	52.19
1	4596	22.55	550	34.97
2	1534	7.53	172	10.93
3	533	2.61	29	1.84
4	179	0.88	1	0.06
5	66	0.32	0	0.00
6	30	0.15	0	0.00
7	20	0.10	0	0.00
8	9	0.04	0	0.00
9	4	0.02	0	0.00
10	1	0.00	0	0.00
11	0	0.00	0	0.00
12	1	0.00	0	0.00
Total	20383[2]	100.00	1573	100.00
Mean (Standard Deviation) = 0.53 (0.93) Median = 0				

Second Imputed Data Set				
Fetal losses	Number	%	Number imputed	%
0	13440	65.94	851	54.10
1	4543	22.29	497	31.60
2	1563	7.67	201	12.78
3	527	2.59	23	1.46
4	179	0.88	1	0.06
5	66	0.32	0	0.00
6	30	0.15	0	0.00
7	20	0.10	0	0.00
8	9	0.04	0	0.00
9	4	0.02	0	0.00
10	1	0.00	0	0.00
11	0	0.00	0	0.00
12	1	0.00	0	0.00
Total	20383	100.00	1573	100.00
Mean (Standard Deviation) = 0.53 (0.93) Median = 0				

Third Imputed Data Set				
Fetal losses	Number	%	Number imputed	%
0	13415	65.81	826	52.51
1	4579	22.46	533	33.88
2	1551	7.61	189	12.02
3	528	2.59	24	1.53
4	179	0.88	1	0.06
5	66	0.32	0	0.00
6	30	0.15	0	0.00
7	20	0.10	0	0.00
8	9	0.04	0	0.00
9	4	0.02	0	0.00
10	1	0.00	0	0.00
11	0	0.00	0	0.00
12	1	0.00	0	0.00
Total	20383	100.00	1573	100.00
Mean (Standard Deviation) = 0.53 (0.93) Median = 0				

Fourth Imputed Data Set				
Fetal losses	Number	%	Number imputed	%
0	13426	65.87	837	53.21
1	4581	22.47	535	34.01
2	1542	7.57	180	11.44
3	524	2.57	20	1.27
4	179	0.88	1	0.06
5	66	0.32	0	0.00
6	30	0.15	0	0.00
7	20	0.10	0	0.00
8	9	0.04	0	0.00
9	4	0.02	0	0.00
10	1	0.00	0	0.00
11	0	0.00	0	0.00
12	1	0.00	0	0.00
Total	20383	100.00	1573	100.00
Mean (Standard Deviation) = 0.53 (0.93) Median = 0				

Fifth Imputed Data Set				
Fetal losses	Number	%	Number imputed	%
0	13405	65.77	816	51.88
1	4569	22.42	523	33.25
2	1566	7.68	204	12.97
3	534	2.62	30	1.91
4	178	0.87	0	0.00
5	66	0.32	0	0.00
6	30	0.15	0	0.00
7	20	0.10	0	0.00
8	9	0.04	0	0.00
9	4	0.02	0	0.00
10	1	0.00	0	0.00
11	0	0.00	0	0.00
12	1	0.00	0	0.00
Total	20383	100.00	1573	100.00
Mean (Standard Deviation) = 0.53 (0.93) Median = 0				

1. Missing data not included
2. Imputed data included

APPENDIX 6.2:
REPRODUCTION AND MORTALITY: THE EFFECTS IN THE ORIGINAL FEMALE DATA SET

Figure A6.1: Crude female mortality rates (+ 95% CI) with parity

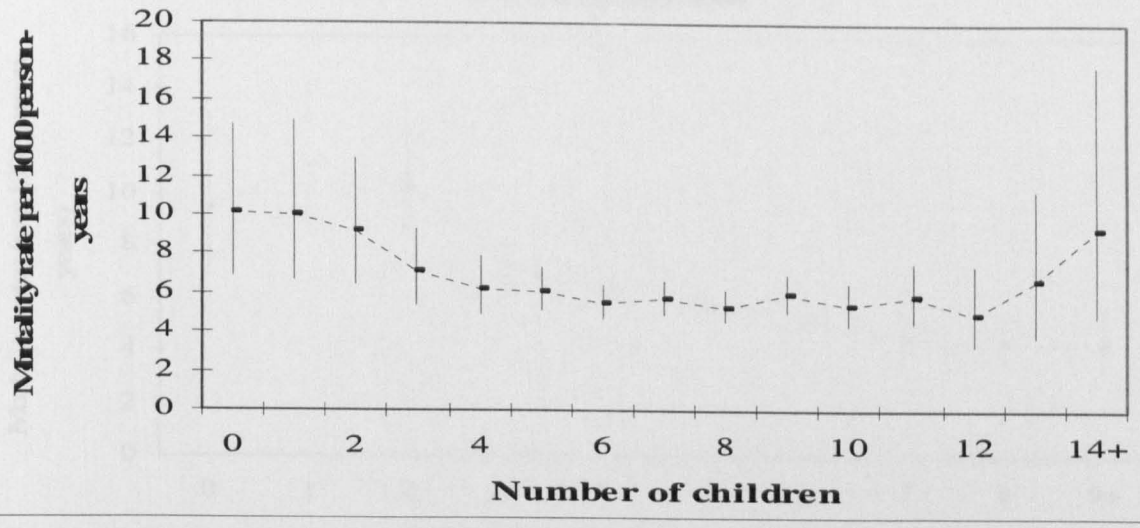


Table A6.6: Mortality In Women Who Have Completed Their Reproduction By Parity

Variable	Number of deaths	Person-years of follow-up	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	1939	202322.20	**9.58**	-	-	-	-
Parity:							
Parous	1118	190310.27	**5.88**	**1.00**	-	**1.00**	-
Nulliparous	27	2681.42	**10.07**	**1.71**	1.17-2.51	**1.69**	1.15-2.48
Unknown	794	9330.51	**85.10**	**14.49**	13.23-15.87	**25.80**	23.06-28.86
LR statistic = 2652.11, p < 0.001							
Number of live births:							
0	27	2681.42	**10.07**	**1.76**	1.18-2.65	**1.71**	1.14-2.58
1	24	2397.14	**10.01**	**1.75**	1.15-2.69	**1.61**	1.04-2.47
2	31	3391.78	**9.14**	**1.60**	1.09-2.35	**1.61**	1.10-2.36
3	50	7054.70	**7.09**	***1.24***	*0.91-1.70*	***1.16***	*0.84-1.59*
4	70	11230.68	**6.23**	***1.09***	*0.83-1.44*	***1.08***	*0.82-1.43*
5	119	19436.00	**6.12**	***1.07***	*0.85-1.35*	***1.08***	*0.85-1.36*
6	151	27347.59	**5.52**	***0.97***	*0.79-1.20*	***0.96***	*0.77-1.19*
7	175	30665.94	**5.71**	**1.00**	-	**1.00**	-
8	163	30720.62	**5.31**	***0.93***	*0.75-1.15*	***0.90***	*0.73-1.12*
9	147	24554.71	**5.99**	***1.05***	*0.84-1.31*	***1.02***	*0.82-1.27*
10	89	16636.07	**5.35**	***0.94***	*0.73-1.21*	***0.86***	*0.67-1.11*
11	54	9301.56	**5.81**	***1.02***	*0.75-1.38*	***0.98***	*0.72-1.33*
12	23	4641.78	**4.96**	***0.87***	*0.56-1.34*	***0.78***	*0.50-1.21*
13	13	1962.64	**6.62**	***1.16***	*0.66-2.04*	***1.07***	*0.61-1.88*
14+	9	969.06	**9.29**	***1.63***	*0.83-3.18*	***1.55***	*0.79-3.04*
Unknown	794	9330.51	**85.10**	**14.91**	12.66-17.56	**25.93**	21.72-30.96
LR statistic = 2671.66, p < 0.001							
Number of live births:							
0-2	82	8470.34	**9.68**	**1.76**	1.39-2.22	***1.72***	*0.98-1.34*
3-5	239	37721.38	**6.34**	***1.15***	*0.98-1.34*	***1.15***	*0.87-1.16*
6-8	489	88734.15	**5.51**	**1.00**	-	**1.00**	-
9+	335	58065.82	**5.77**	***1.05***	*0.91-1.20*	***1.01***	*0.87-1.16*
Unknown	794	9330.51	**85.10**	**15.44**	13.80-17.28	**27.24**	23.89-31.06
LR statistic = 2665.93, p < 0.001							

Figure A6.2: Crude female mortality rates (+95% CI) by number of surviving children

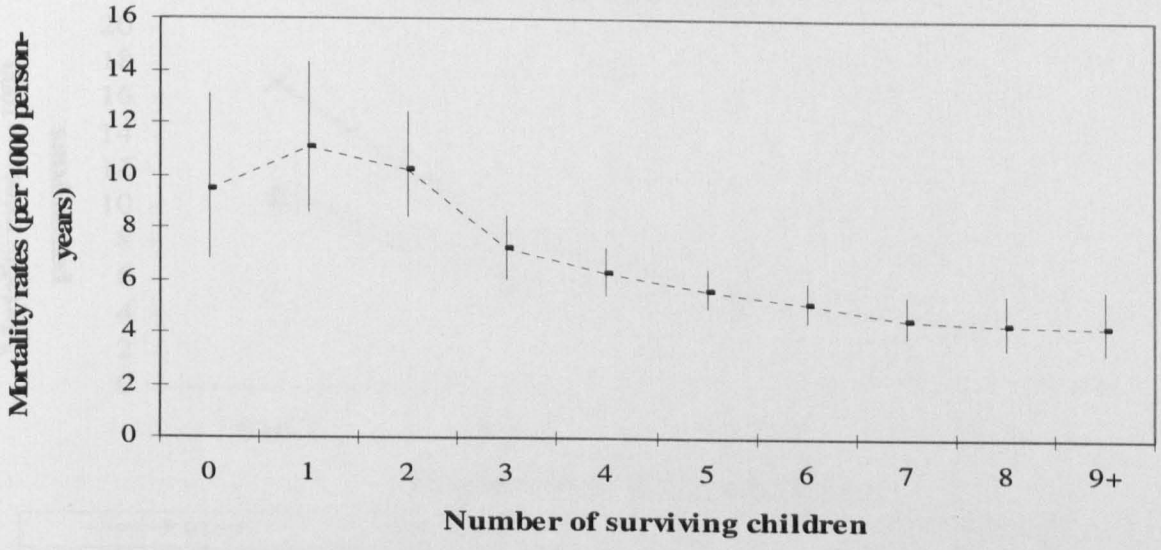


Table A6.7: Mortality In Women Who Have Completed Their Reproduction By Surviving Children

Variable	Number of deaths	Person-years of follow-up	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	1939	202322.20	**9.58**	-	-	-	-
Any surviving children?:							
No	36	3801.39	**9.47**	**1.00**	-	**1.00**	-
Yes	1109	189190.30	**5.86**	**0.62**	0.44-0.86	**0.65**	0.46-0.91
Unknown	794	9330.51	**85.10**	**8.97**	6.43-12.55	**16.78**	11.90-23.66
LR statistic = 2651.60, p < 0.001							
Number of surviving children on entry:							
0	36	3801.39	**9.47**	**1.69**	1.18-2.40	**1.64**	1.14-2.34
1	60	5405.16	**11.10**	**1.98**	1.48-2.64	**1.85**	1.39-2.48
2	104	10155.63	**10.24**	**1.82**	1.44-2.31	**1.72**	1.36-2.18
3	135	18745.29	**7.20**	**1.28**	1.03-1.59	***1.21***	*0.97-1.50*
4	185	29412.22	**6.32**	***1.13***	*0.92-1.37*	***1.12***	*0.92-1.36*
5	205	36518.69	**5.61**	**1.00**	-	**1.00**	-
6	181	35248.47	**5.14**	***0.91***	*0.75-1.12*	***0.92***	*0.75-1.12*
7	124	27252.61	**4.55**	***0.81***	*0.65-1.01*	***0.82***	*0.66-1.02*
8	67	15464.73	**4.33**	***0.77***	*0.59-1.02*	***0.77***	*0.58-1.01*
9+	47	10987.50	**4.28**	***0.76***	*0.56-1.05*	***0.75***	*0.55-1.03*
Unknown	794	9330.51	**85.10**	**15.16**	13.00-17.68	**27.22**	23.01-32.20
LR statistic = 2714.42, p < 0.001							
Number of surviving children on entry:							
0-2	200	19362.2	**10.33**	**1.66**	1.41-1.96	**1.60**	1.35-1.88
3-5	526	84676.2	**6.21**	**1.00**	-	**1.00**	-
6-8	372	77965.8	**4.77**	**0.77**	0.67-0.88	**0.78**	0.69-0.90
9+	47	10987.5	**4.28**	**0.69**	0.51-0.93	**0.69**	0.51-0.93
Unknown	794	9330.51	**85.10**	**13.70**	12.27-15.29	**24.96**	21.97-28.37
LR statistic = 2709.14, p < 0.001							
Percentage of children surviving:							
0-24.9%	58	5185.46	**11.19**	**2.39**	1.82-3.13	**2.17**	1.65-2.87
25.0-49.9%	130	14197.19	**9.16**	**1.95**	1.61-2.37	**1.71**	1.40-2.07
50.0-74.9%	457	66873.66	**6.83**	**1.46**	1.29-1.66	**1.36**	1.20-1.55
75.0-100%	500	106735.38	**4.68**	**1.00**	-	**1.00**	-
Unknown	794	9330.51	**85.10**	**18.17**	16.24-20.32	**31.61**	27.70-36.07
LR statistic = 2700.12 , p < 0.001							

Figure A6.3: Crude female mortality rates by number of surviving children in parity groups

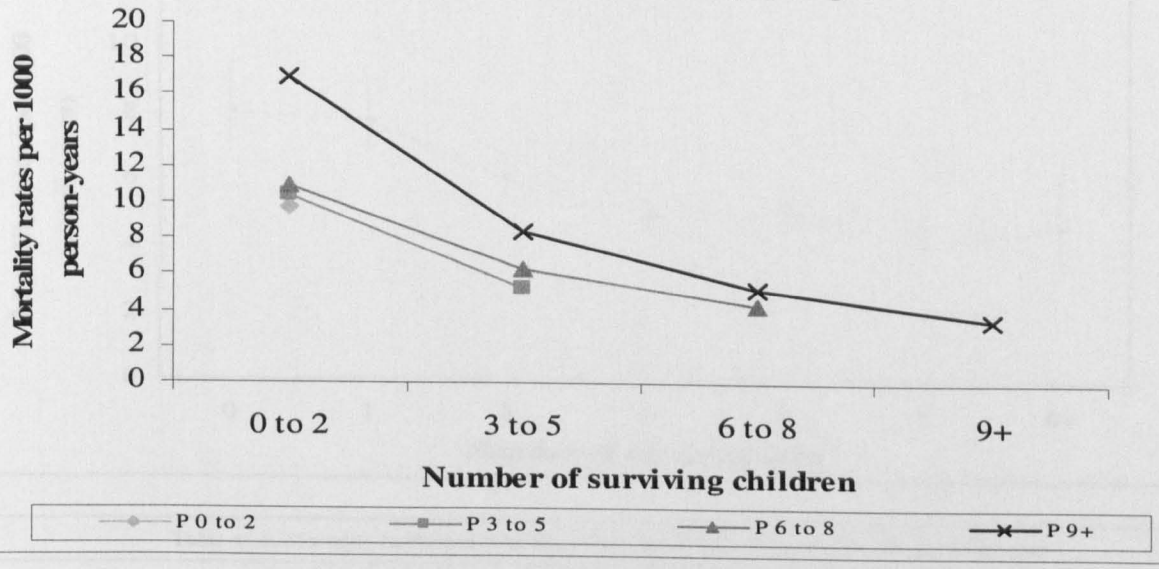


Table A6.8: Crude Rate Ratios for Parity and Surviving Children				
	Number of surviving children on entry			
Parity	0-2	3-5	6-8	9+
0-2	1.53 (1.20-1.96)	-	-	-
3-5	1.66 (1.29-2.12)	*0.83 (0.68-1.01)*	-	-
6-8	1.74 (1.18-2.56)	**1.00 (reference)**	0.69 (0.57-0.83)	-
9+	2.59 (1.28-5.24)	1.33 (1.05-1.68)	*0.83 (0.69-1.00)*	0.68 (0.50-0.92)
Unknown	-	-	-	13.49 (11.76-15.47)
Adjusted Rate Ratios for Parity and Surviving Children *				
	Number of surviving children on entry			
Parity	0-2	3-5	6-8	9+
0-2	1.58 (1.23-2.02)	-	-	-
3-5	1.58 (1.23-2.02)	*0.88 (0.73-1.08)*	-	-
6-8	1.55 (1.05-2.28)	**1.00 (reference)**	0.75 (0.62-0.90)	-
9+	2.42 (1.20-4.91)	1.27 (1.00-1.61)	*0.83 (0.69-1.00)*	0.69 (0.51-0.94)
Unknown	-	-	-	24.92 (21.42-29.00)

* LR test statistic = 2718.76, $p < 0.001$

Figure A6.4: Crude female mortality rates (+95% CI) by number of surviving sons

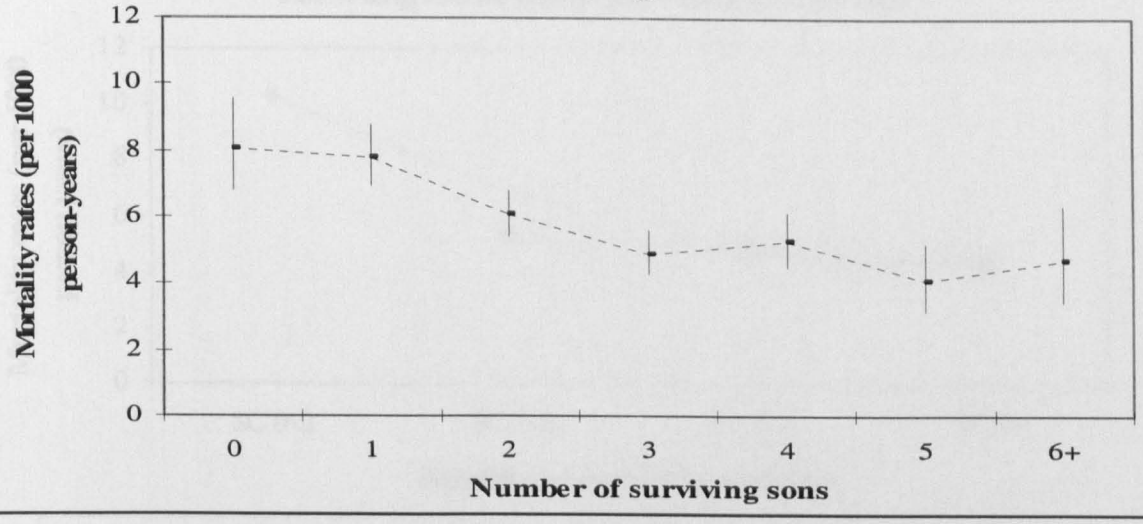


Table A6.9: Mortality In Women Who Have Completed Their Reproduction By Surviving Sons

Variable	Number of deaths	Person-years of follow-up	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	1939	202322.20	**9.58**	-	-	-	-
Surviving sons?							
No	136	16866.34	**8.06**	**1.00**	-	**1.00**	-
Yes	1009	176125.35	**5.73**	**0.71**	0.59-0.85	**0.72**	0.60-0.86
Unknown	794	9330.51	**85.10**	**10.55**	8.80-12.66	**18.98**	15.65-23.01
LR statistic = 2658.12, p < 0.001							
Surviving sons:							
0	136	16866.34	**8.06**	**1.65**	1.33-2.04	**1.64**	1.32-2.04
1	262	33603.63	**7.80**	**1.59**	1.33-1.91	**1.56**	1.30-1.87
2	276	45611.90	**6.05**	**1.23**	1.03-1.48	**1.23**	1.02-1.47
3	209	42643.17	**4.90**	**1.00**	-	**1.00**	-
4	160	30428.60	**5.26**	***1.07***	*0.87-1.32*	***1.08***	*0.88-1.33*
5	62	15259.27	**4.06**	***0.83***	*0.62-1.10*	***0.84***	*0.64-1.12*
6+	40	8578.78	**4.66**	***0.95***	*0.68-1.33*	***0.97***	*0.69-1.36*
Unknown	794	9330.51	**85.10**	**17.36**	14.91-20.22	**31.25**	26.45-36.92
LR statistic = 2693.25, p < 0.001							
Surviving sons:							
0-2	674	96081.87	**7.02**	**1.44**	1.27-1.62	**1.41**	1.25-1.59
3-5	431	88331.04	**4.88**	**1.00**	-	**1.00**	-
6+	40	8578.78	**4.66**	**0.96**	*0.69-1.32*	**0.97**	*0.70-1.34*
Unknown	794	9330.51	**85.10**	**17.44**	15.51-19.61	**31.03**	27.09-35.54
LR statistic = 1894.26, p < 0.001							
Percentage of children borne who were male:							
0-24.9%	162	24806.47	**6.53**	***1.11***	*0.93-1.33*	***1.16***	*0.97-1.39*
25.0-49.9%	325	56670.06	**5.74**	***0.98***	*0.85-1.12*	***0.99***	*0.86-1.13*
50.0-74.9%	508	86384.16	**5.88**	**1.00**	-	**1.00**	-
75.0-100%	150	25131.00	**5.97**	***1.01***	*0.85-1.22*	***1.02***	*0.85-1.22*
Unknown	794	9330.51	**85.10**	**14.47**	12.95-16.18	**25.88**	22.75-29.44
LR statistic = 1866.14, p < 0.001							
Percentage of children surviving who were male:							
0-24.9%	204	29477.83	**6.92**	**1.20**	1.01-1.41	**1.22** ***0.98***	1.03-1.44
25.0-49.9%	280	50109.84	**5.59**	***0.97***	*0.83-1.12*	**1.00**	*0.84-1.14*
50.0-74.9%	454	78528.42	**5.78**	**1.00**	-	***1.02***	-
75.0-100%	207	34875.60	**5.94**	***1.03***	*0.87-1.21*	**26.28**	*0.87-1.21*
Unknown	794	9330.51	**85.10**	**14.72**	13.12-16.51		23.01-30.01
LR statistic = 1869.34, p < 0.001							

Figure A6.5: Crude female mortality rates by number of surviving children in surviving son groups

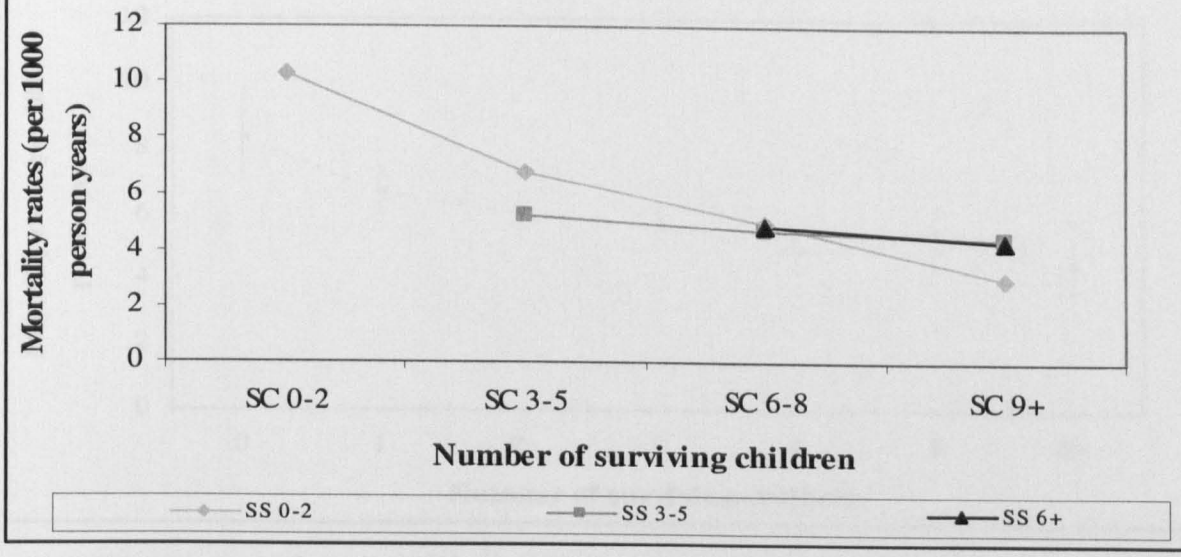


Table A6.10: Crude Rate Ratios for Surviving Children and Surviving Sons			
	Number of surviving sons		
Surviving children	0-2	3-5	6+
0-2	1.96 (1.59-2.41)	-	-
3-5	1.28 (1.07-1.54)	**1.00 (reference)**	-
6-8	*0.93 (0.73-1.19)*	*0.89 (0.73-1.09)*	*0.93 (0.61-1.43)*
9+	*0.56 (0.18-1.75)*	*0.85 (0.57-1.26)*	*0.82 (0.49-1.37)*
Unknown	-	-	16.14 (13.64-19.10)
Adjusted Rate Ratios for Surviving Children and Surviving Sons *			
	Number of surviving sons		
Surviving children	0-2	3-5	6+
0-2	1.89 (1.53-2.33)	-	-
3-5	1.29 (1.07-1.55)	**1.00 (reference)**	-
6-8	*0.96 (0.75-1.22)*	*0.91 (0.75-1.11)*	*0.96 (0.63-1.48)*
9+	*0.58 (0.18-1.82)*	*0.85 (0.57-1.27)*	*0.84 (0.50-1.40)*
Unknown	-	-	29.46 (24.59-35.30)

* LR test statistic = 1931.20, $p < 0.001$

Figure A6.6: Crude female mortality rates (+95% CI) by number of surviving children

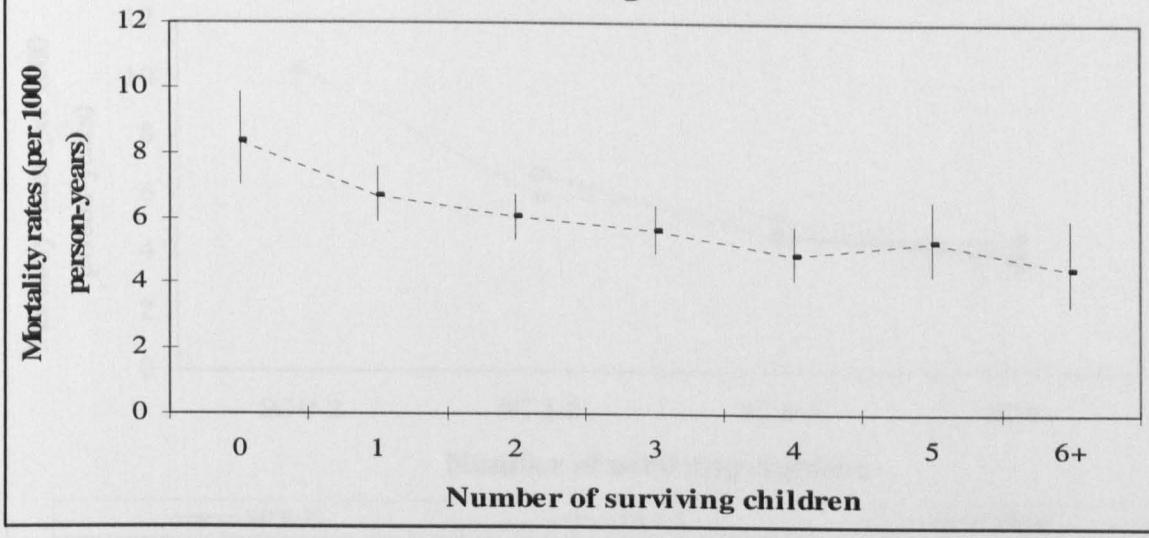


Table A6.11: Mortality In Women Who Have Completed Their Reproduction By Surviving Daughters

Variable	Number of deaths	Person-years of follow-up	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	1939	202322.20	**9.58**	-	-	-	-
Surviving daughters?							
No	134	16167.20	**8.29**	**1.00**	-	**1.00**	-
Yes	1011	176824.49	**5.72**	**0.69**	0.58-0.83	**0.73**	0.61-0.88
Unknown	794	9330.51	**85.10**	**10.27**	8.55-12.33	**19.30**	15.90-23.43
	LR statistic = 2656.66, $p < 0.001$						
Surviving daughters:							
0	134	16167.20	**8.29**	**1.48**	1.20-1.84	**1.39**	1.12-1.72
1	239	35747.49	**6.69**	**1.20**	1.00-1.43	***1.15***	*0.96-1.38*
2	282	40804.73	**6.02**	***1.08***	*0.90-1.28*	***1.04***	*0.88-1.24*
3	228	46867.83	**5.59**	**1.00**	-	**1.00**	-
4	135	27671.80	**4.88**	***0.87***	*0.71-1.08*	***0.88***	*0.71-1.09*
5	80	15213.37	**5.26**	***0.94***	*0.73-1.21*	***0.93***	*0.72-1.20*
6+	47	10519.27	**4.47**	***0.80***	*0.58-1.09*	***0.81***	*0.59-1.11*
Unknown	794	9330.51	**85.10**	**15.23**	13.14-17.65	**26.76**	22.75-31.47
	LR statistic = 2430.28, $p < 0.001$						
Surviving daughters:							
0-2	655	92719.42	**6.63**	**1.25**	1.11-1.41	**1.20**	1.06-1.35
3-5	443	89753.00	**5.29**	**1.00**	-	**1.00**	-
6+	47	10519.27	**4.47**	***0.84***	*0.62-1.14*	***0.85***	*0.63-1.15*
Unknown	794	9330.51	**85.10**	**16.08**	14.31-18.06	**28.11**	24.56-32.17
	LR statistic = 2658.02, $p < 0.001$						
% of children surviving who were female:							
0-24.9%	195	29016.29	**6.72**	**1.22**	1.03-1.44	**1.20**	1.01-1.42
25.0-49.9%	315	56995.07	**5.53**	***1.00***	*0.86-1.16*	***1.01***	*0.87-1.17*
50.0-74.9%	403	72933.14	**5.53**	**1.00**	-	**1.00**	-
75.0-100%	232	34047.19	**6.81**	**1.23**	1.05-1.45	**1.27**	1.08-1.49
Unknown	794	9330.51	**85.10**	**15.40**	13.66-17.36	**27.53**	24.00-31.56
	LR statistic = 2971.39, $p < 0.001$						

Figure A6.7: Crude female mortality rates for number of surviving children in surviving daughters groups

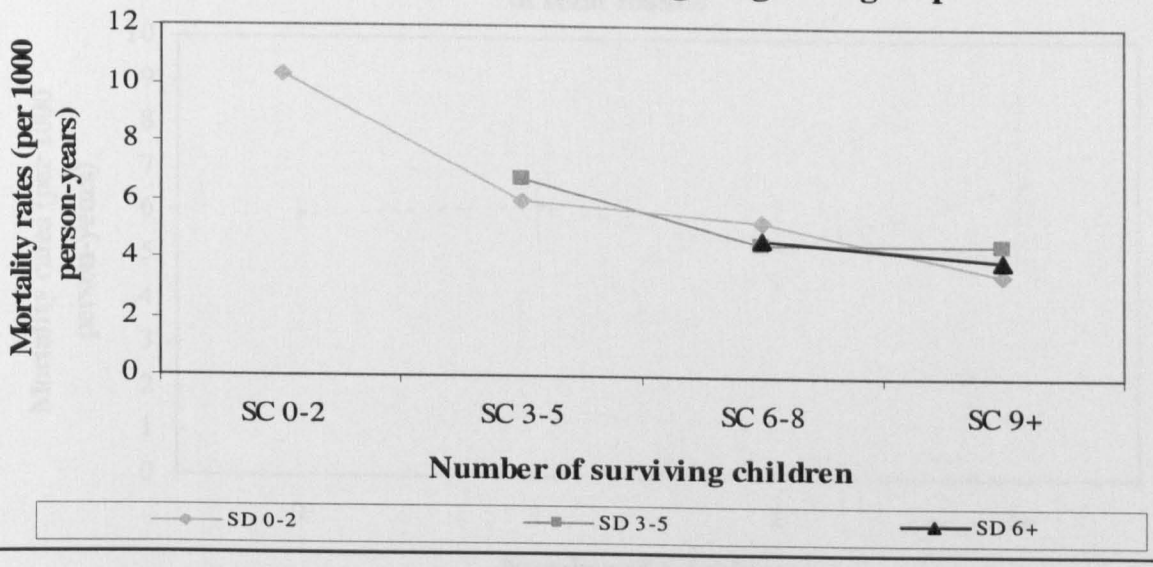


Table A6.12:
Crude Rate Ratios for Surviving Children and Surviving Daughters

	Number of surviving daughters		
Surviving children	0-2	3-5	6+
0-2	1.53 (1.25-1.86)	-	-
3-5	*0.88 (0.73-1.05)*	**1.00 (reference)**	-
6-8	0.78 (0.62-0.99)	0.67 (0.55-0.82)	0.69 (0.48-0.99)
9+	*0.51 (0.16-1.61)*	0.67 (0.46-0.97)	*0.59 (0.34-1.04)*
Unknown	-	-	12.58 (10.75-14.73)

Adjusted Rate Ratios for Surviving Children and Surviving Daughters

	Number of surviving daughters		
Surviving children	0-2	3-5	6+
0-2	1.42 (1.16-1.73)	-	-
3-5	*0.84 (0.70-1.00)*	**1.00 (reference)**	-
6-8	0.77 (0.62-0.97)	0.66 (0.55-0.81)	*0.69 (0.48-1.00)*
9+	*0.54 (0.17-1.68)*	0.64 (0.44-0.93)	*0.59 (0.34-1.03)*
Unknown	-	-	22.09 (18.61-26.21)

Figure A6.8: Crude female mortality rates (+95% CI) by number of fetal losses

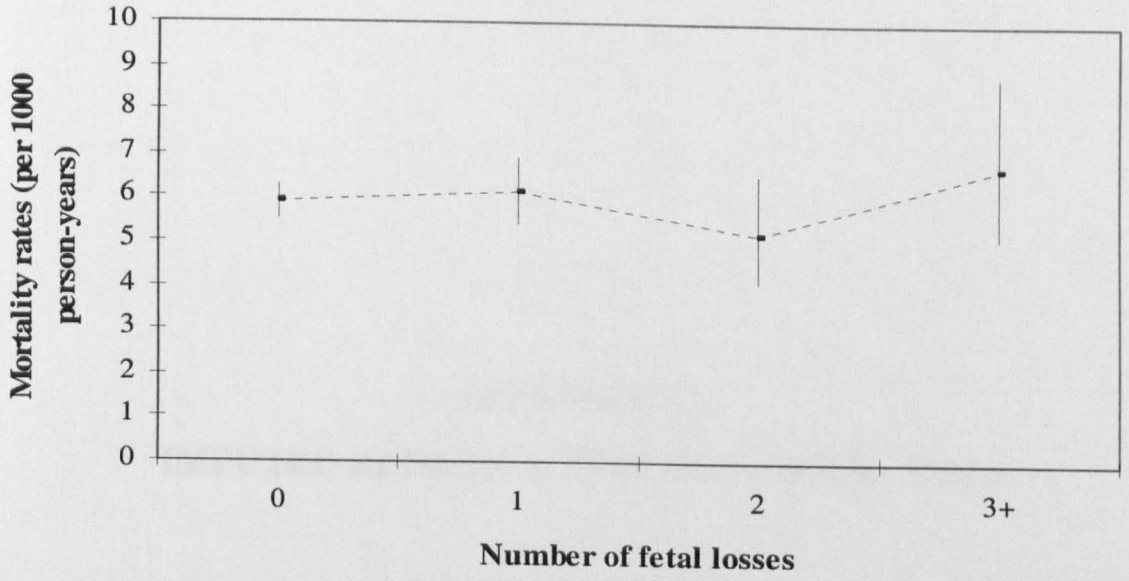


Table A6.13: Mortality In Women Who Have Completed Their Reproduction By Fetal Losses

Variable	Number of deaths	Person-years of follow-up	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	1939	202322.20	**9.58**	-	-	-	-
Fetal loss?:							
No	780	132154.03	**5.90**	**1.00**	-	**1.00**	-
Yes	365	60837.66	**6.00**	***1.02***	*0.90-1.15*	***1.07***	*0.95-1.21*
Unknown	794	9330.51	**85.10**	**14.42**	13.06-15.92	**26.03**	23.14-29.28
LR statistic = 1849.37, p < 0.001							
Fetal losses:							
0	780	132154.03	**5.90**	**1.00**	-	**1.00**	-
1	245	39926.57	**6.14**	***1.04***	*0.90-1.20*	***1.10***	*0.95-1.27*
2	68	13146.77	**5.17**	***0.88***	*0.68-1.12*	***0.92***	*0.72-1.18*
3+	52	7764.32	**6.70**	***1.13***	*0.86-1.50*	***1.20***	*0.91-1.60*
Unknown	794	9330.51	**85.10**	**14.42**	13.06-15.92	**26.03**	23.15-29.28
LR statistic = 1948.56, p < 0.001							
Fetal losses:							
No fetal losses	753	129782.43	**5.80**	**1.00**	-	**1.00**	-
Nulligravid	27	2371.60	**11.39**	**1.96**	1.34-2.88	**1.96**	1.33-2.88
1-2 fetal losses	313	53073.34	**5.90**	***1.02***	*0.89-1.16*	***1.07***	*0.94-1.22*
3+ fetal losses	52	7764.32	**6.70**	***1.15***	*0.87-1.53*	***1.22***	*0.92-1.62*
Unknown	794	9330.51	**85.10**	**14.67**	13.28-16.20	**26.50**	23.54-29.83
LR statistic = 2018.21, p < 0.001							
Percentage fetal losses:							
No fetal losses	753	129782.43	**5.80**	**1.00**	-	**1.00**	-
Nulligravid	27	2371.60	**11.39**	**1.96**	1.37-2.88	**1.96**	1.33-2.89
< 25% pregnancies lost	282	47445.39	**5.94**	***1.02***	*0.89-1.17*	***1.08***	*0.94-1.24*
> 25% pregnancies lost	83	13392.27	**6.20**	***1.07***	*0.85-1.34*	***1.13***	*0.90-1.42*
Unknown	794	9330.51	**85.10**	**14.67**	13.28-16.20	**26.50**	23.55-29.83
LR statistic = 2034.52, p < 0.001							

APPENDIX 7.1:
IMPUTED REPRODUCTIVE HISTORIES - MALE

Table A7.1: Number of live sons – original male data set and imputed data

Original Data Set				First Imputed Data Set					Second Imputed Data Set				
Living sons	Number	Percentage	Cumulative percentage	Living sons	Number	%	Number imputed	%	Living sons	Number	%	Number imputed	%
0	966	6.93	6.93	0	1049	7.09	83	9.64	0	1047	7.07	81	9.41
1	2055	14.74	21.67	1	2179	14.72	124	14.40	1	2182	14.74	127	14.75
2	3296	23.64	45.31	2	3502	23.66	206	23.93	2	3488	23.56	192	22.30
3	3302	23.68	68.99	3	3489	23.57	187	21.72	3	3499	23.64	197	22.88
4	2380	17.07	86.06	4	2538	17.15	158	18.35	4	2528	17.08	148	17.19
5	1239	8.89	94.95	5	1321	8.92	82	9.52	5	1319	8.91	80	9.29
6	501	3.59	98.54	6	516	3.49	15	1.74	6	530	3.58	29	3.37
7	158	1.13	99.68	7	162	1.09	4	0.46	7	165	1.11	7	0.81
8	34	0.24	99.92	8	36	0.24	2	0.23	8	34	0.23	0	0.00
9	9	0.06	99.99	9	9	0.06	0	0.00	9	9	0.06	0	0.00
10	0	0.00	99.99	10	0	0.00	0	0.00	10	1	0.01	0	0.00
11	1	0.01	99.99	11	1	0.01	0	0.00	11	0	0.00	0	0.00
12	1	0.01	100.00	12	1	0.01	0	0.00	12	1	0.01	0	0.00
Total	13942[1]	100.00		Total	14803[2]	100.00	861	100.00	Total	14803	100.00	861	100.00
Mean (Standard Deviation) = 2.77 (1.59) Median = 3				Mean (Standard Deviation) = 2.77 (1.59) Median = 3					Mean (Standard Deviation) = 2.77 (1.59) Median = 3				

Third Imputed Data Set					Fourth Imputed Data Set					Fifth Imputed Data Set				
Living sons	Number	%	Number imputed	%	Living sons	Number	%	Number imputed	%	Living sons	Number	%	Number imputed	%
0	1043	7.05	77	8.94	0	1044	7.05	78	9.06	0	1051	7.10	85	9.87
1	2183	14.75	128	14.87	1	2171	14.67	116	13.47	1	2168	14.65	113	13.12
2	3489	23.57	193	22.42	2	3500	23.64	204	23.69	2	3500	23.64	204	23.69
3	3500	23.64	198	23.00	3	3489	23.57	187	21.72	3	3492	23.59	190	22.07
4	2540	17.16	160	18.58	4	2539	17.15	159	18.47	4	2553	17.25	173	20.09
5	1320	8.92	81	9.41	5	1327	8.96	88	10.22	5	1308	8.84	69	8.01
6	519	3.51	18	2.09	6	524	3.54	23	2.67	6	522	3.53	21	2.44
7	163	1.10	5	0.58	7	162	1.09	4	0.46	7	164	1.11	6	0.70
8	35	0.24	1	0.12	8	36	0.24	2	0.23	8	34	0.23	0	0.00
9	9	0.06	0	0.00	9	9	0.06	0	0.00	9	9	0.06	0	0.00
10	0	0.00	0	0.00	10	0	0.00	0	0.00	10	0	0.00	0	0.00
11	1	0.01	0	0.00	11	1	0.01	0	0.00	11	1	0.01	0	0.00
12	1	0.01	0	0.00	12	1	0.01	0	0.00	12	1	0.01	0	0.00
Total	14803	100.00	861	100.00	Total	14803	100.00	861	100.00	Total	14803	100.00	861	100.00
Mean (Standard Deviation) = 2.77 (1.59) Median = 3					Mean (Standard Deviation) = 2.78 (1.59) Median = 3					Mean (Standard Deviation) = 2.77 (1.59) Median = 3				

1. Missing values not included

2. Imputed values included

Table A7.2: Number of dead sons – original male data set and imputed data

Original Data Set				First Imputed Data Set					Second Imputed Data Set				
Dead sons	Number	Percentage	Cumulative percentage	Dead sons	Number	%	Number imputed	%	Dead sons	Number	%	Number imputed	%
0	6702	48.07	48.07	0	6957	47.00	255	29.62	0	6964	47.04	262	30.43
1	4259	30.55	78.62	1	4580	30.94	321	37.28	1	4549	30.73	290	33.68
2	1901	13.64	92.25	2	2102	14.20	201	23.34	2	2133	14.41	232	26.95
3	724	5.19	97.45	3	800	5.40	76	8.83	3	792	5.35	68	7.90
4	248	1.78	99.23	4	255	1.72	7	0.81	4	257	1.74	9	1.05
5	77	0.55	99.78	5	78	0.53	1	0.12	5	77	0.52	0	0.00
6	23	0.16	99.94	6	23	0.16	0	0.00	6	23	0.16	0	0.00
7	5	0.04	99.98	7	5	0.03	0	0.00	7	5	0.03	0	0.00
8	3	0.02	100.00	8	3	0.02	0	0.00	8	3	0.02	0	0.00
Total	13942[1]	100.00		Total	14803[2]	100.00	861	100.00	Total	14803	100.00	861	100.00
Mean (Standard Deviation) = 0.85 (1.06) Median = 1				Mean (Standard Deviation) = 0.86 (1.05) Median = 1					Mean (Standard Deviation) = 0.86 (1.05) Median = 1				

Third Imputed Data Set					Fourth Imputed Data Set					Fifth Imputed Data Set				
Dead sons	Number	%	Number imputed	%	Dead sons	Number	%	Number imputed	%	Dead sons	Number	%	Number imputed	%
0	6957	47.00	255	29.62	0	6970	47.09	268	31.13	0	6951	46.96	249	28.92
1	4568	30.86	309	35.89	1	4558	30.79	299	34.73	1	4563	30.82	304	35.31
2	2125	14.36	224	26.02	2	2127	14.37	226	26.25	2	2127	14.37	226	26.25
3	787	5.32	63	7.32	3	783	5.29	59	6.85	3	796	5.38	72	8.36
4	258	1.74	10	1.16	4	256	1.73	8	0.93	4	257	1.74	9	1.05
5	77	0.52	0	0.00	5	78	0.53	1	0.12	5	78	0.53	1	0.12
6	23	0.16	0	0.00	6	23	0.16	0	0.00	6	23	0.16	0	0.00
7	5	0.03	0	0.00	7	5	0.03	0	0.00	7	5	0.03	0	0.00
8	3	0.02	0	0.00	8	3	0.02	0	0.00	8	3	0.02	0	0.00
Total	14803	100.00	861	100.00	Total	14803	100.00	861	100.00	Total	14803	100.00	861	100.00
Mean (Standard Deviation) = 0.86 (1.05) Median = 1					Mean (Standard Deviation) = 0.86 (1.05) Median = 1					Mean (Standard Deviation) = 0.87 (1.05) Median = 1				

1. Missing values not included

2. Imputed values included

Table A7.3: Number of living daughters – original male data set and imputed data

Original Data Set

Living daughters	Number	Percentage	Cumulative percentage
0	**888**	6.37	6.37
1	**2424**	17.39	23.76
2	**3397**	24.37	48.12
3	**3080**	22.09	70.21
4	**2183**	15.66	85.87
5	**1183**	8.49	94.36
6	**502**	3.60	97.96
7	**186**	1.33	99.29
8	**78**	0.56	99.85
9	**18**	0.13	99.98
10	**2**	0.01	99.99
11	**0**	0.00	99.99
12	**1**	0.01	100.00
Total	13942[1]	100.00	

Mean (Standard Deviation) = 2.74 (1.64)
Median = 3

First Imputed Data Set

Living dau	Number	%	Number imputed	%
0	**962**	6.50	**74**	8.59
1	**2540**	17.16	**116**	13.47
2	**3614**	24.41	**217**	25.20
3	**3264**	22.05	**184**	21.37
4	**2343**	15.83	**160**	18.58
5	**1256**	8.48	**73**	8.48
6	**530**	3.58	**28**	3.25
7	**192**	1.30	**6**	0.70
8	**81**	0.55	**3**	0.35
9	**18**	0.12	**0**	0.00
10	**2**	0.01	**0**	0.00
11	**0**	0.00	**0**	0.00
12	**1**	0.01	**0**	0.00
Total	14803[2]	100.00	861	100.00

Mean (Standard Deviation) = 2.74 (1.63)
Median = 3

Second Imputed Data Set

Living dau	Number	%	Number imputed	%
0	**971**	6.56	**83**	9.64
1	**2541**	17.17	**117**	13.59
2	**3581**	24.19	**184**	21.37
3	**3279**	22.15	**199**	23.11
4	**2338**	15.79	**155**	18.00
5	**1269**	8.57	**86**	9.99
6	**534**	3.61	**32**	3.72
7	**190**	1.28	**4**	0.46
8	**79**	0.53	**1**	0.12
9	**18**	0.12	**0**	0.00
10	**2**	0.01	**0**	0.00
11	**0**	0.00	**0**	0.00
12	**1**	0.01	**0**	0.00
Total	14803	100.00	861	100.00

Mean (Standard Deviation) = 2.74 (1.63)
Median = 3

Third Imputed Data Set

Living dau	Number	%	Number imputed	%
0	**964**	6.51	**76**	8.83
1	**2561**	17.30	**137**	15.91
2	**3581**	24.19	**184**	21.37
3	**3284**	22.18	**204**	23.69
4	**2328**	15.73	**145**	16.84
5	**1253**	8.46	**70**	8.13
6	**539**	3.64	**37**	4.30
7	**194**	1.31	**8**	0.93
8	**78**	0.53	**0**	0.00
9	**18**	0.12	**0**	0.00
10	**2**	0.01	**0**	0.00
11	**0**	0.00	**0**	0.00
12	**1**	0.01	**0**	0.00
Total	14803	100.00	861	100.00

Mean (Standard Deviation) = 2.74 (1.64)
Median = 3

Fourth Imputed Data Set

Living dau	Number	%	Number imputed	%
0	**979**	6.61	**91**	10.57
1	**2537**	17.14	**113**	13.12
2	**3594**	24.28	**197**	22.88
3	**3268**	22.08	**188**	21.84
4	**2336**	15.78	**153**	17.77
5	**1264**	8.54	**81**	9.41
6	**526**	3.55	**24**	2.79
7	**196**	1.32	**10**	1.16
8	**81**	0.55	**3**	0.35
9	**18**	0.12	**0**	0.00
10	**3**	0.02	**1**	0.12
11	**0**	0.00	**0**	0.00
12	**1**	0.01	**0**	0.00
Total	14803	100.00	861	100.00

Mean (Standard Deviation) = 2.74 (1.64)
Median = 3

Fifth Imputed Data Set

Living dau	Number	%	Number imputed	%
0	**970**	6.55	**82**	9.52
1	**2533**	17.11	**109**	12.66
2	**3582**	24.20	**185**	21.49
3	**3290**	22.23	**210**	24.39
4	**2350**	15.88	**167**	19.40
5	**1252**	8.46	**69**	8.01
6	**530**	3.58	**28**	3.25
7	**196**	1.32	**10**	1.16
8	**79**	0.53	**1**	0.12
9	**18**	0.12	**0**	0.00
10	**2**	0.01	**0**	0.00
11	**0**	0.00	**0**	0.00
12	**1**	0.01	**0**	0.00
Total	14803	100.00	861	100.00

Mean (Standard Deviation) = 2.74 (1.63)
Median = 3

1. Missing values not included

2. Imputed values included

Table A7.4: Number of dead daughters – original data set and imputed data

Original Data Set			
Dead daughters	Number	Percentage	Cumulative percentage
0	6061	43.47	43.47
1	4462	32.00	75.48
2	2129	15.27	90.75
3	843	6.05	96.79
4	309	2.22	99.01
5	92	0.66	99.67
6	28	0.20	99.87
7	13	0.09	99.96
8	4	0.03	99.99
9	1	0.01	100.00
Total	13942[1]	100.00	
Mean (Standard Deviation) = 0.95 (1.11) Median = 1			

First Imputed Data Set				
Dead dau	Number	%	Number imputed	%
0	6291	42.50	230	26.71
1	4749	32.08	287	33.33
2	2369	16.00	240	27.87
3	931	6.29	88	10.22
4	322	2.18	13	1.51
5	94	0.64	2	0.23
6	29	0.20	1	0.12
7	13	0.09	0	0.00
8	4	0.03	0	0.00
9	1	0.01	0	0.00
Total	14803[2]	100.00	861	100.00
Mean (Standard Deviation) = 0.97 (1.11) Median = 1				

Second Imputed Data Set				
Dead dau	Number	%	Number imputed	%
0	6264	42.32	203	23.58
1	4783	32.31	321	37.28
2	2354	15.90	225	26.13
3	937	6.33	94	10.92
4	324	2.19	15	1.74
5	95	0.64	3	0.35
6	28	0.19	0	0.00
7	13	0.09	0	0.00
8	4	0.03	0	0.00
9	1	0.01	0	0.00
Total	14803	100.00	861	100.00
Mean (Standard Deviation) = 0.97 (1.11) Median = 1				

Third Imputed Data Set				
Dead dau	Number	%	Number imputed	%
0	6299	42.55	238	27.64
1	4748	32.07	286	33.22
2	2367	15.99	238	27.64
3	924	6.24	81	9.41
4	325	2.20	16	1.86
5	94	0.64	2	0.23
6	28	0.19	0	0.00
7	13	0.09	0	0.00
8	4	0.03	0	0.00
9	1	0.01	0	0.00
Total	14803	100.00	861	100.00
Mean (Standard Deviation) = 0.97 (1.11) Median = 1				

Fourth Imputed Data Set				
Dead dau	Number	%	Number imputed	%
0	6276	42.40	215	24.97
1	4768	32.21	306	35.54
2	2367	15.99	238	27.64
3	928	6.27	85	9.87
4	323	2.18	14	1.63
5	95	0.64	3	0.35
6	28	0.19	0	0.00
7	13	0.09	0	0.00
8	4	0.03	0	0.00
9	1	0.01	0	0.00
Total	14803	100.00	861	100.00
Mean (Standard Deviation) = 0.97 (1.11) Median = 1				

Fifth Imputed Data Set				
Dead dau	Number	%	Number imputed	%
0	6283	42.44	222	25.78
1	4758	32.14	296	34.38
2	2368	16.00	239	27.76
3	935	6.32	92	10.69
4	319	2.15	10	1.16
5	94	0.64	2	0.23
6	28	0.19	0	0.00
7	13	0.09	0	0.00
8	4	0.03	0	0.00
9	1	0.01	0	0.00
Total	14803	100.00	861	100.00
Mean (Standard Deviation) = 0.97 (1.11) Median = 1				

1. Missing values not included

2. Imputed values included

Table A7.5: Number of fetal losses – original data set and imputed data

Original Data Set

Fetal losses	Number	Percentage	Cumulative percentage
0	8971	64.35	64.35
1	3214	23.05	87.40
2	1091	7.83	95.22
3	407	2.92	98.14
4	148	1.06	99.20
5	55	0.39	99.60
6	25	0.18	99.78
7	17	0.12	99.90
8	8	0.06	99.96
9	4	0.03	99.99
10	1	0.01	99.99
11	0	0.00	99.99
12	1	0.01	100.00
Total	13942[1]	100.00	

Mean (Standard Deviation) = 0.56 (0.98)
Median = 0

First Imputed Data Set

Fetal losses	Number	%	Number imputed	%
0	9397	63.48	426	49.48
1	3519	23.77	305	35.42
2	1202	8.12	111	12.89
3	426	2.88	19	2.21
4	148	1.00	0	0.00
5	55	0.37	0	0.00
6	25	0.17	0	0.00
7	17	0.11	0	0.00
8	8	0.05	0	0.00
9	4	0.03	0	0.00
10	1	0.01	0	0.00
11	0	0.00	0	0.00
12	1	0.01	0	0.00
Total	14803[2]	100.00	861	100.00

Mean (Standard Deviation) = 0.57 (0.97)
Median = 0

Second Imputed Data Set

Fetal losses	Number	%	Number imputed	%
0	9402	63.51	431	50.06
1	3505	23.68	291	33.80
2	1207	8.15	116	13.47
3	429	2.90	22	2.56
4	149	1.01	1	0.12
5	55	0.37	0	0.00
6	25	0.17	0	0.00
7	17	0.11	0	0.00
8	8	0.05	0	0.00
9	4	0.03	0	0.00
10	1	0.01	0	0.00
11	0	0.00	0	0.00
12	1	0.01	0	0.00
Total	14803	100.00	861	100.00

Mean (Standard Deviation) = 0.57 (0.97)
Median = 0

Third Imputed Data Set

Fetal losses	Number	%	Number imputed	%
0	9397	63.48	426	49.48
1	3515	23.75	301	34.96
2	1206	8.15	115	13.36
3	423	2.86	16	1.86
4	151	1.02	3	0.35
5	55	0.37	0	0.00
6	25	0.17	0	0.00
7	17	0.11	0	0.00
8	8	0.05	0	0.00
9	4	0.03	0	0.00
10	1	0.01	0	0.00
11	0	0.00	0	0.00
12	1	0.01	0	0.00
Total	14803	100.00	861	100.00

Mean (Standard Deviation) = 0.57 (0.97)
Median = 0

Fourth Imputed Data Set

Fetal losses	Number	%	Number imputed	%
0	9403	63.52	432	50.17
1	3489	23.57	275	31.94
2	1235	8.34	144	16.72
3	417	2.82	10	1.16
4	148	1.00	0	0.00
5	55	0.37	0	0.00
6	25	0.17	0	0.00
7	17	0.11	0	0.00
8	8	0.05	0	0.00
9	4	0.03	0	0.00
10	1	0.01	0	0.00
11	0	0.00	0	0.00
12	1	0.01	0	0.00
Total	14803	100.00	861	100.00

Mean (Standard Deviation) = 0.57 (0.97)
Median = 0

Fifth Imputed Data Set

Fetal losses	Number	%	Number imputed	%
0	9385	63.40	414	48.08
1	3525	23.81	311	36.12
2	1214	8.20	123	14.29
3	418	2.82	11	1.28
4	150	1.01	2	0.23
5	55	0.37	0	0.00
6	25	0.17	0	0.00
7	17	0.11	0	0.00
8	8	0.05	0	0.00
9	4	0.03	0	0.00
10	1	0.01	0	0.00
11	0	0.00	0	0.00
12	1	0.01	0	0.00
Total	14803	100.00	861	100.00

Mean (Standard Deviation) = 0.57 (0.97)
Median = 0

1. Missing values not included

2. Imputed values included

APPENDIX 7.2:

THE EFFECTS OF REPRODUCTION ON MORTALITY – RESULTS FROM THE ORIGINAL MALE DATA SET

Figure A7.1: Crude male mortality rates (+95% CI) by wife's parity

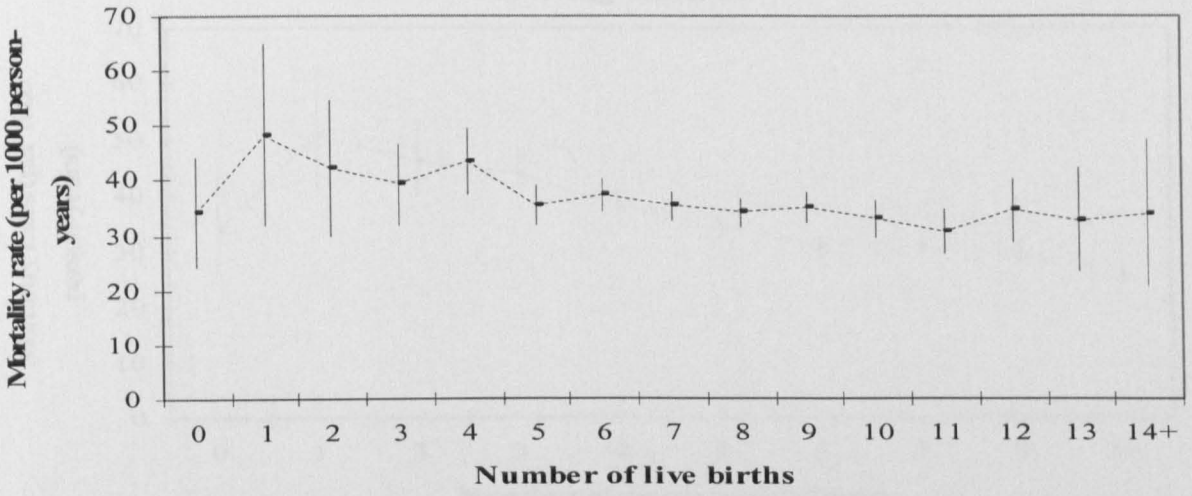


Table A7.6: Mortality In Men Who Have Completed Their Reproduction By Wife's Parity

Variable	Number of deaths	Person-years of follow-up	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	4394	12450.00	**35.29**	-	-	-	-
Parity:							
Parous	3918	116551.09	**33.62**	**1.00**	-	**1.00**	-
Nulliparous	45	1326.92	**33.94**	***1.01***	*0.75-1.35*	***0.90***	*0.67-1.20*
Unknown	431	6621.99	**65.09**	**1.94**	1.75-2.14	**1.42**	1.26-1.60
LR statistic = 871.17, p < 0.001							
Number of live births:							
0	45	1326.92	**33.94**	***1.01***	*0.75-1.36*	***0.88***	*0.65-1.19*
1	33	707.10	**46.67**	***1.39***	*0.98-1.97*	***1.35***	*0.95-1.92*
2	42	1046.33	**40.14**	***1.19***	*0.87-1.63*	***1.14***	*0.84-1.56*
3	101	2737.00	**36.90**	***1.10***	*0.89-1.35*	***0.96***	*0.78-1.19*
4	202	4858.01	**41.58**	**1.23**	1.05-1.45	**1.27**	1.08-1.48
5	343	10275.43	**33.38**	***0.99***	*0.87-1.13*	***1.03***	*0.90-1.17*
6	580	16210.81	**35.78**	***1.06***	*0.95-1.19*	***1.07***	*0.95-1.19*
7	654	19409.17	**33.70**	**1.00**	-	**1.00**	-
8	665	20343.35	**32.69**	***0.97***	*0.87-1.08*	***0.95***	*0.86-1.06*
9	561	16676.50	**33.64**	***1.00***	*0.89-1.12*	***0.98***	*0.88-1.10*
10	366	11758.21	**31.13**	***0.92***	*0.81-1.05*	**0.87**	0.76-0.99
11	195	6877.24	**28.35**	**0.84**	0.72-0.99	**0.81**	0.69-0.96
12	106	3328.47	**31.85**	***0.95***	*0.77-1.16*	***0.83***	*0.68-1.02*
13	47	1588.52	**29.59**	***0.88***	*0.65-1.18*	***0.80***	*0.60-1.08*
14+	23	734.95	**31.29**	***0.93***	*0.61-1.41*	***0.90***	*0.59-1.36*
Unknown	431	6621.99	**65.09**	**1.93**	1.71-2.18	**1.39**	1.21-1.60
LR statistic = 902.81, p < 0.001							
Number of live births:							
0-2	120	3080.35	**38.97**	***1.15***	*0.96-1.38*	***1.07***	*0.89-1.29*
3-5	646	17870.44	**36.15**	***1.07***	*0.97-1.17*	***1.08***	*0.98-1.18*
6-8	1899	55963.33	**33.93**	**1.00**	-	**1.00**	-
9+	1298	40963.89	**31.69**	***0.94***	*0.87-1.00*	**0.90**	0.84-0.96
Unknown	431	6621.99	**65.09**	**1.91**	1.73-2.13	**1.39**	1.22-1.57
LR statistic = 834.36, p < 0.001							

Figure A7.2: Crude male mortality rates (+95% CI) by number of surviving children

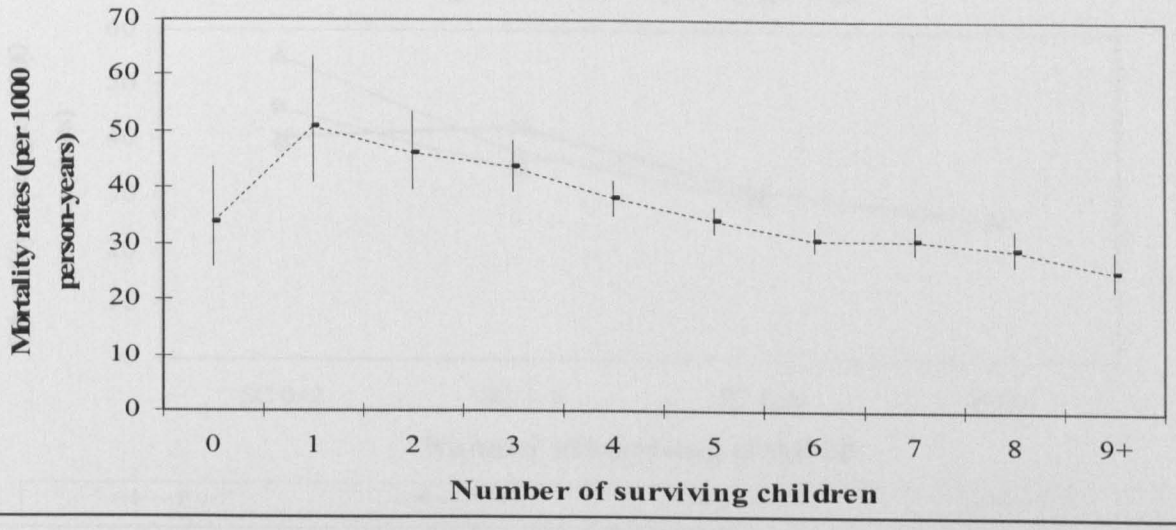


Table A7.7: Mortality In Men Who Have Completed Their Reproduction By Surviving Children

Variable	Number of deaths	Person-years of follow-up	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	4394	12450.00	**35.29**	-	-	-	-
Any surviving children?:							
No	57	1689.13	**33.77**	**1.00**	-	**1.00**	-
Yes	3906	116188.88	**33.62**	***1.00***	*0.77-1.29*	***1.13***	*0.87-1.48*
Unknown	431	6621.99	**65.09**	**1.93**	1.46-2.54	**1.61**	1.21-2.14
LR statistic = 782.99, p < 0.001							
Number of surviving children on entry:							
0	57	1689.13	**33.77**	***0.99***	*0.75-1.29*	***0.85***	*0.65-1.12*
1	79	1556.15	**50.77**	**1.48**	1.18-1.87	**1.33**	1.05-1.68
2	168	3653.24	**45.99**	**1.34**	1.14-1.59	***1.11***	*0.93-1.31*
3	376	8630.96	**43.56**	**1.27**	1.13-1.44	**1.19**	1.05-1.34
4	624	16398.66	**38.05**	**1.11**	1.00-1.24	***1.07***	*0.96-1.19*
5	773	22580.44	**34.23**	**1.00**	-	**1.00**	-
6	733	23795.30	**30.80**	***0.90***	*0.81-1.00*	***0.90***	*0.81-1.00*
7	599	19452.61	**30.79**	***0.90***	*0.81-1.00*	***0.91***	*0.82-1.01*
8	336	11519.37	**29.17**	**0.85**	0.75-0.97	**0.87**	0.76-0.99
9+	218	8602.15	**25.34**	**0.74**	0.64-0.86	**0.73**	0.63-0.85
Unknown	431	6621.99	**65.09**	**1.90**	1.69-2.14	**1.39**	1.21-1.59
LR statistic = 862.34, p < 0.001							
Number of surviving children on entry:							
0-2	304	6897.2	**44.08**	**1.18**	1.05-1.34	***1.03***	*0.91-1.17*
3-5	1773	47609.9	**37.24**	**1.00**	-	**1.00**	-
6-8	1668	54766.9	**30.46**	**0.82**	0.77-0.87	**0.85**	0.79-0.91
9+	218	8602.2	**25.34**	**0.68**	0.59-0.78	**0.69**	0.60-0.80
Unknown	431	6621.99	**65.09**	**1.75**	1.57-1.94	**1.30**	1.15-1.48
LR statistic = 822.98, p < 0.001							
Percentage of children surviving:							
0-24.9%	90	2229.83	**40.37**	**1.31**	1.06-1.62	***1.07***	*0.87-1.33*
25.0-49.9%	327	7010.74	**46.65**	**1.51**	1.35-1.70	**1.26**	1.12-1.41
50.0-74.9%	1427	39898.89	**35.77**	**1.16**	1.08-1.24	***1.06***	*0.99-1.13*
75.0-100%	2119	68738.55	**30.83**	**1.00**	-	**1.00**	-
Unknown	431	6621.99	**65.09**	**2.11**	1.90-2.34	**1.49**	1.31-1.69
LR statistic = 795.37, p < 0.001							

Figure A7.3: Crude male mortality rates by number of sruviving children, in parity groups

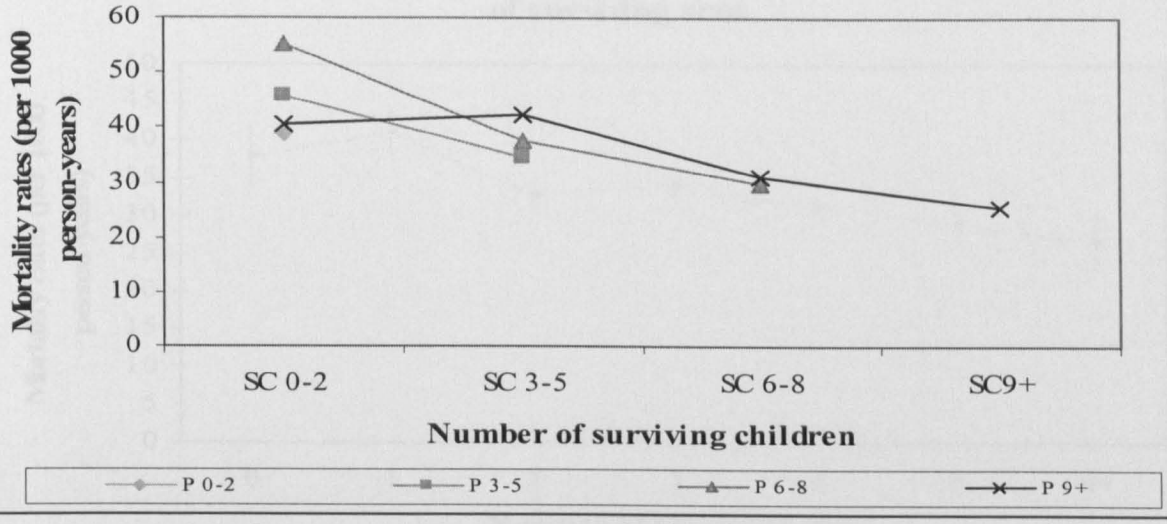


Table A7.8: Crude Rate Ratios for Parity and Surviving Children				
	Number of surviving children on entry			
Parity	0-2	3-5	6-8	9+
0-2	*1.04 (0.86-1.25)*	-	-	-
3-5	1.22 (1.01-1.48)	*0.92 (0.83-1.02)*	-	-
6-8	1.47 (1.13-1.92)	**1.00 (reference)**	0.80 (0.73-0.87)	-
9+	*1.08 (0.56-2.09)*	*1.12 (0.98-1.28)*	0.82 (0.75-0.91)	0.67 (0.58-0.78)
Unknown	-	-	-	1.73 (1.55-1.94)
Adjusted Rate Ratios for Parity and Surviving Children				
	Number of surviving children on entry			
Parity	0-2	3-5	6-8	9+
0-2	*1.00 (0.83-1.22)*	-	-	-
3-5	*1.03 (0.85-1.24)*	*1.01 (0.91-1.12)*	-	-
6-8	*1.16 (0.89-1.52)*	**1.00 (reference)**	0.87 (0.80-0.96)	-
9+	*1.06 (0.55-2.04)*	*1.04 (0.91-1.19)*	0.83 (0.76-0.92)	0.70 (0.60-0.81)
Unknown	-	-	-	1.32 (1.15-1.50)

Figure A7.4: Crude male mortality rates (+95% CI) by number of surviving sons

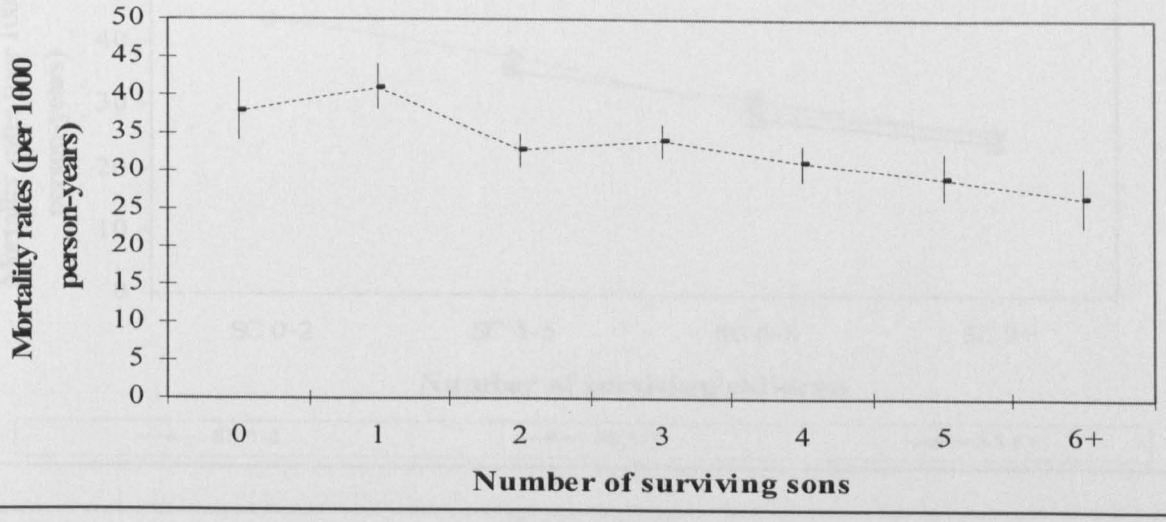


Table A7.9: Mortality In Men Who Have Completed Their Reproduction By Surviving Sons

Variable	Number of deaths	Person-years of follow-up	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	4394	12450.00	**35.29**	-	-	-	-
Any surviving sons?:							
No	326	8615.1	**37.84**	**1.00**	-	**1.00**	-
Yes	3637	109261	**33.29**	**0.88**	0.79-0.99	***0.94***	*0.84-1.05*
Unknown	431	6621.99	**65.09**	**1.72**	1.49-1.99	**1.34**	1.15-1.58
LR statistic = 745.74, p < 0.001							
Surviving sons:							
0	326	8615.13	**37.84**	***1.11***	*0.98-1.26*	***1.01***	*0.89-1.15*
1	694	16938.83	**40.97**	**1.20**	1.09-1.33	**1.13**	1.02-1.24
2	869	26575.47	**32.70**	***0.96***	*0.87-1.05*	***0.92***	*0.84-1.01*
3	918	26921.96	**34.10**	**1.00**	-	**1.00**	-
4	656	21090.36	**31.10**	***0.92***	*0.83-1.01*	**0.89**	0.81-0.99
5	323	11056.87	**29.21**	**0.86**	0.75-0.97	**0.85**	0.75-0.96
6+	177	6677.51	**26.51**	**0.77**	0.66-0.91	**0.78**	0.67-0.92
Unknown	431	6621.99	**65.09**	**1.91**	1.70-2.14	**1.37**	1.20-1.56
LR statistic = 804.29, p < 0.001							
Surviving sons:							
0-2	1889	52129.4	**36.24**	**1.13**	1.06-1.20	**1.08**	1.01-1.15
3-5	1897	59069.2	**32.12**	**1.00**	-	**1.00**	-
6+	177	6677.5	**26.51**	**0.85**	0.71-0.96	**0.84**	0.72-0.98
Unknown	431	6621.99	**65.09**	**2.03**	1.83-2.25	**1.46**	1.29-1.66
LR statistic = 746.32, p < 0.001							
Percentage of children who were male:							
0-24.9%	521	14676	**35.50**	***1.05***	*0.95-1.16*	***1.05***	*0.95-1.15*
25.0-49.9%	1155	35813.1	**32.25**	***0.95***	*0.89-1.03*	***0.97***	*0.90-1.04*
50.0-74.9%	1795	53061.2	**33.83**	**1.00**	-	**1.00**	-
75.0-100%	492	14325.8	**34.34**	***1.02***	*0.92-1.12*	***1.03***	*0.93-1.14*
Unknown	431	6621.99	**65.09**	**1.92**	1.73-2.14	**1.42**	1.25-1.61
LR statistic = 759.10, p < 0.001							
Percentage of children surviving who were male:							
0-24.9%	591	16845.4	**35.08**	***1.06***	*0.96-1.16*	***1.04***	*0.95-1.15*
25.0-49.9%	1066	32060.5	**33.25**	***1.00***	*0.93-1.08*	***1.02***	*0.95-1.10*
50.0-74.9%	1617	48754.6	**33.17**	**1.00**	-	**1.00**	-
75.0-100%	689	20215.6	**34.08**	***1.03***	*0.94-1.12*	***1.03***	*0.94-1.13*
Unknown	431	6621.99	**65.09**	**1.96**	1.76-2.18	**1.45**	1.28-1.64
LR statistic = 701.22, p < 0.001							

Figure A 7.5: Crude male mortality rates by number of surviving children, in surviving son groups

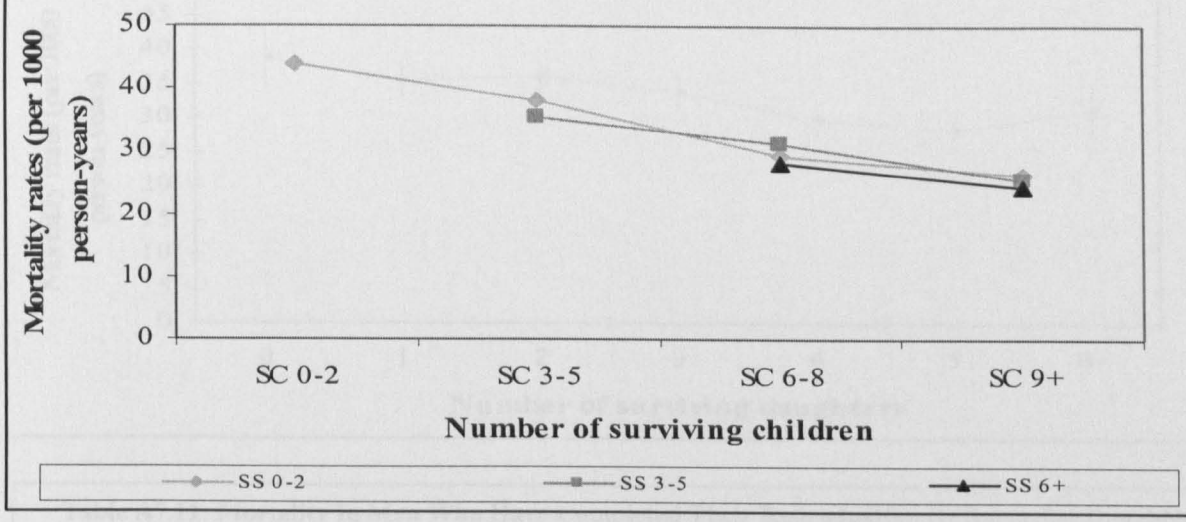


Table A7.10: Crude Rate Ratios for Surviving Children and Surviving Sons			
	Number of surviving sons		
Surviving children	0-2	3-5	6+
0-2	1.24 (1.08-1.42)	-	-
3-5	*1.08 (0.98-1.19)*	**1.00 (reference)**	-
6-8	0.82 (0.73-0.93)	0.88 (0.80-0.97)	0.79 (0.64-0.97)
9+	*0.74 (0.47-1.15)*	0.72 (0.60-0.88)	0.69 (0.54-0.88)
Unknown	-	-	1.83 (1.62-2.07)
Adjusted Rate Ratios for Surviving Children and Surviving Sons			
	Number of surviving sons		
Surviving children	0-2	3-5	6+
0-2	*1.07 (0.93-1.22)*	-	-
3-5	*1.05 (0.96-1.16)*	**1.00 (reference)**	-
6-8	0.83 (0.74-0.94)	0.90 (0.82-0.99)	0.81 (0.66-0.99)
9+	*0.69 (0.44-1.08)*	0.72 (0.59-0.87)	0.72 (0.56-0.91)
Unknown	-	-	1.35 (1.17-1.55)

Figure A7.6: Crude male mortality rates (+95% CI) by number of surviving daughters

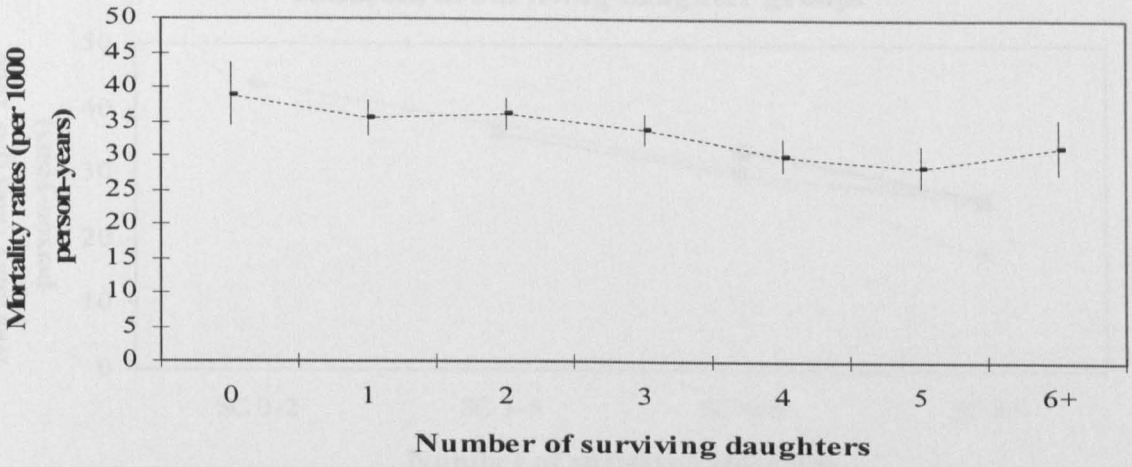


Table A7.11: Mortality In Men Who Have Completed Their Reproduction By Surviving Daughters

Variable	Number of deaths	Person-years of follow-up	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	4394	12450.00	**35.29**	-	-	-	-
Surviving daughters?:							
No	277	7160.97	**38.69**	**1.00**	-	**1.00**	-
Yes	3686	110717.04	**33.29**	**0.86**	0.76-0.97	***0.95***	*0.84-1.07*
Unknown	431	6621.99	**65.09**	**1.68**	1.45-1.96	**1.35**	1.15-1.60
LR statistic = 717.12, p < 0.001							
Surviving daughters:							
0	277	7160.97	**38.69**	**1.14**	1.00-1.31	***1.02***	*0.90-1.17*
1	684	19326.58	**35.39**	***1.05***	*0.95-1.16*	***1.01***	*0.92-1.12*
2	1001	27802.62	**36.00**	***1.06***	*0.97-1.16*	***1.03***	*0.94-1.13*
3	886	26165.83	**33.85**	**1.00**	-	**1.00**	-
4	571	19016.44	**30.02**	**0.89**	0.80-0.99	**0.89**	0.80-0.99
5	307	10815.48	**28.39**	**0.84**	0.74-0.95	**0.83**	0.73-0.95
6+	237	7590.09	**31.30**	***0.92***	*0.80-1.07*	***0.93***	*0.80-1.07*
Unknown	431	6621.99	**65.09**	**1.92**	1.71-2.16	**1.39**	1.21-1.59
LR statistic = 776.88, p < 0.001							
Surviving daughters:							
0-2	1962	54290.17	**36.14**	**1.15**	1.08-1.22	**1.10**	1.03-1.17
3-5	1764	55997.75	**31.49**	**1.00**	-	**1.00**	-
6+	237	7590.09	**31.30**	***0.99***	*0.87-1.14*	***0.99***	*0.87-1.14*
Unknown	431	6621.99	**65.09**	**2.07**	1.86-2.30	**1.49**	1.31-1.69
LR statistic = 701.37, p < 0.001							
% of children surviving who were female:							
0-24.9%	550	15995.26	**34.39**	***1.03***	*0.94-1.14*	**1.01**	0.91-1.11
25.0-49.9%	1187	36874.34	**32.19**	***0.97***	*0.90-1.04*	**0.97**	0.90-1.05
50.0-74.9%	1495	44869.55	**33.32**	**1.00**	-	**1.00**	-
75.0-100%	731	20138.86	**36.3**	**1.09**	1.00-1.19	**1.07**	0.98-1.17
Unknown	431	6621.99	**65.09**	**1.95**	1.75-2.17	**1.43**	1.26-1.62
LR statistic = 698.73, p < 0.001							

Figure A 7.7: Crude male mortality rates by number of surviving children, in surviving daughter groups

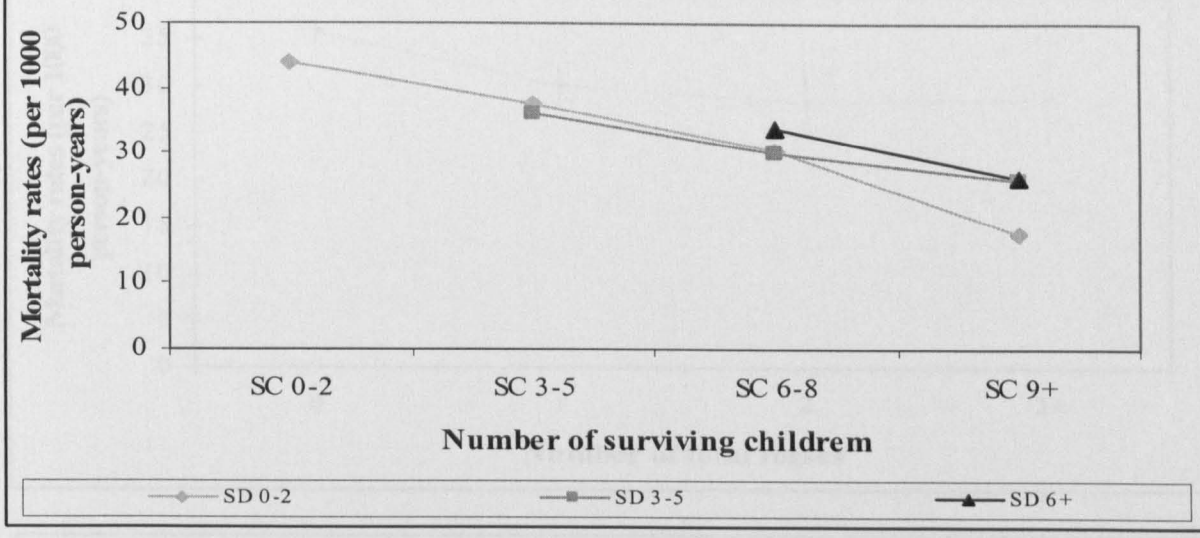


Table A7.12: Crude Rate Ratios for Surviving Children and Surviving Daughters			
Number of surviving daughters			
Surviving children	0-2	3-5	6+
0-2	1.22 (1.06-1.40)	-	-
3-5	*1.04 (0.95-1.15)*	**1.00 (reference)**	-
6-8	0.84 (0.74-0.94)	0.83 (0.75-0.92)	*0.93 (0.79-1.10)*
9+	0.49 (0.28-0.87)	0.71 (0.59-0.86)	0.73 (0.56-0.94)
Unknown	-	-	1.80 (1.59-2.03)
Adjusted Rate Ratios for Surviving Children and Surviving Daughters			
Number of surviving daughters			
Surviving children	0-2	3-5	6+
0-2	*1.05 (0.92-1.21)*	-	-
3-5	*1.03 (0.93-1.14)*	**1.00 (reference)**	-
6-8	0.84 (0.75-0.95)	0.86 (0.78-0.95)	*0.95 (0.80-1.13)*
9+	*0.58 (0.33-1.02)*	0.70 (0.58-0.85)	0.74 (0.57-0.95)
Unknown	-	-	1.33 (1.16-1.53)

Figure A7.8: Crude male mortality rates (+95% CI) by number of fetal losses experienced by wife

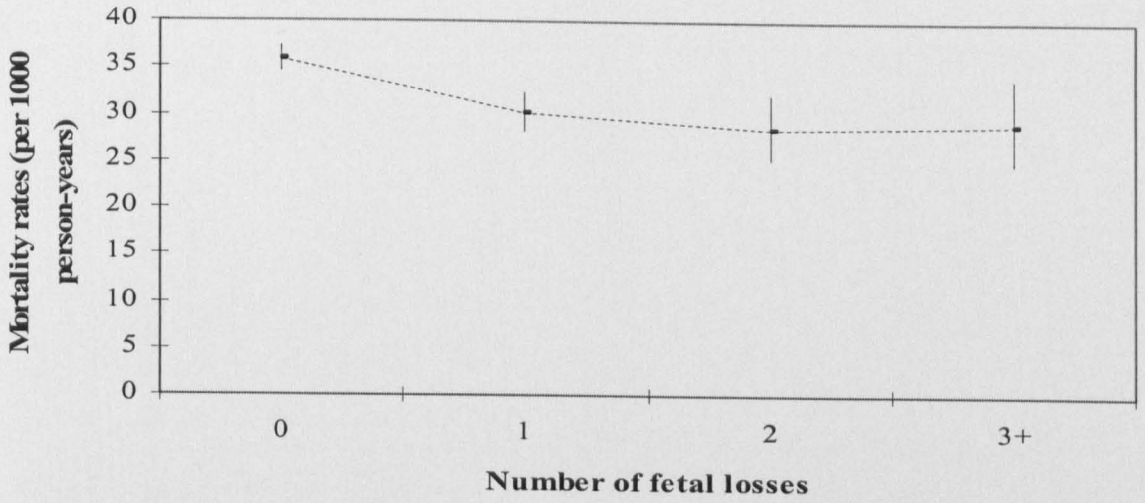


Table A7.13: Mortality In Men Who Have Completed Their Reproduction By Wife's Fetal Losses

Variable	Number of deaths	Person-years of follow-up	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	4394	12450.00	**35.29**	-	-	-	-
Fetal loss?:							
No	2730	76202.67	**35.83**	**1.00**	-	**1.00**	-
Yes	1233	41675.34	**29.59**	**0.83**	0.77-0.88	**0.87**	0.81-0.93
Unknown	431	6621.99	**65.09**	**1.82**	1.64-2.01	**1.36**	1.20-1.54
LR statistic = 809.74, $p < 0.001$							
Fetal losses:							
0	2730	76202.67	**35.83**	**1.00**	-	**1.00**	-
1	819	27190.25	**30.12**	**0.84**	0.78-0.91	**0.88**	0.82-0.95
2	253	8919.82	**28.37**	**0.79**	0.70-0.90	**0.84**	0.74-0.95
3+ fetal losses	161	5565.27	**28.93**	**0.81**	0.69-0.95	**0.85**	0.72-0.99
Unknown	431	6621.99	**65.09**	**1.82**	1.64-2.01	**1.36**	1.20-1.54
LR statistic = 898.54, $p < 0.001$							
Fetal losses:							
No fetal losses	2693	75062.77	**35.88**	**1.00**	-	**1.00**	-
Nulligravid	37	1139.90	**32.46**	***0.90***	*0.65-1.25*	***0.82***	*0.59-1.13*
1-2 fetal losses	1072	36110.07	**29.69**	**0.83**	0.77-0.89	**0.87**	0.81-0.93
3+ fetal losses	161	5565.27	**28.93**	**0.81**	0.69-0.95	**0.84**	0.72-0.99
Unknown	431	6621.99	**65.09**	**1.81**	1.64-2.01	**1.36**	1.20-1.53
LR statistic = 857.29, $p < 0.001$							
Percentage of pregnancies lost:							
No fetal losses	2693	75062.77	**35.88**	**1.00**	-	**1.00**	-
Nulligravid	37	1139.90	**32.46**	***0.90***	*0.65-1.25*	***0.82***	*0.59-1.13*
Up to 25% lost	975	33230.36	**29.34**	**0.82**	0.76-0.88	**0.86**	0.80-0.92
Over 25% lost	258	8444.98	**30.55**	**0.85**	0.75-0.97	***0.89***	*0.78-1.01*
Unknown	431	6621.99	**65.09**	**1.81**	1.64-2.01	**1.36**	1.20-1.53
LR statistic = 867.94, $p < 0.001$							

APPENDIX 7.3:
THE EFFECTS OF REPRODUCTION ON MORTALITY – MALE RESULTS USING DATA FROM THE FEMALE IMPUTATIONS

Figure A7.9: Crude male mortality rates (+95% CI) by wife's parity

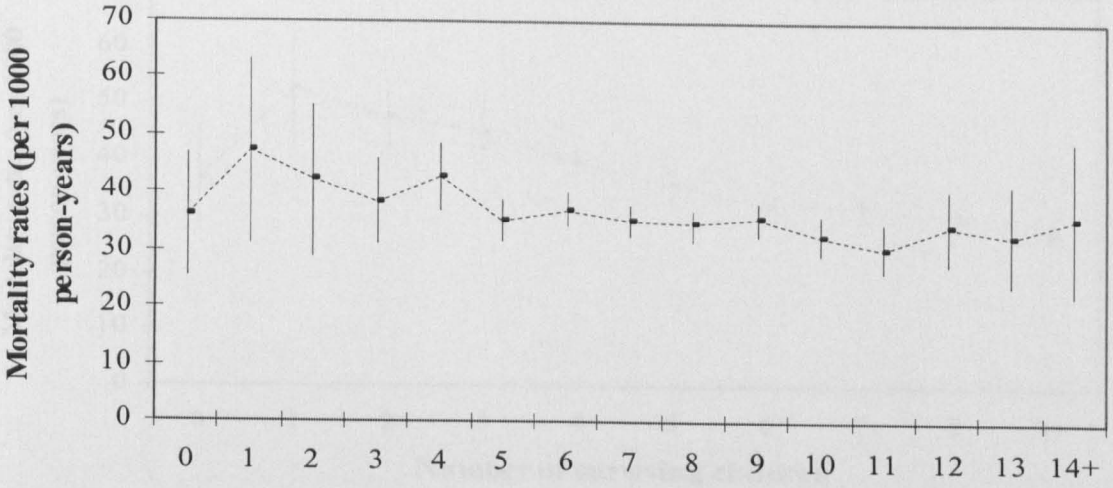


Table A7.14: Mortality In Men Who Have Completed Their Reproduction By Wife's Parity

Variable	Average number deaths	Average person years	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	4394.00	12450.00	**35.29**	-	-	-	-
Parity:							
Parous	4349.63	123272.06	**35.29**	**1.00**	-	**1.00**	-
Nulliparous	44.37	1227.94	**36.19**	***1.03***	*0.72-1.33*	***0.92***	*0.65-1.20*
LR statistic = 0.30, p = 0.870							
Number of live births:							
0	44.37	1227.94	**36.19**	***1.03***	*0.71-1.34*	***0.90***	*0.63-1.18*
1	35.00	740.64	**47.27**	***1.34***	*0.86-1.82*	***1.32***	*0.84-1.79*
2	47.03	1114.57	**42.18**	***1.20***	*0.82-1.58*	***1.14***	*0.78-1.50*
3	111.78	2916.76	**38.39**	***1.09***	*0.86-1.31*	***0.95***	*0.76-1.15*
4	227.57	5310.88	**42.86**	**1.22**	1.02-1.41	**1.21**	1.00-1.42
5	383.70	10932.64	**35.09**	***1.00***	*0.87-1.13*	***1.02***	*0.89-1.15*
6	635.45	17102.31	**37.15**	***1.05***	*0.93-1.17*	***1.06***	*0.94-1.18*
7	716.49	20321.17	**35.25**	**1.00**	-	**1.00**	-
8	730.21	21305.80	**34.72**	***0.97***	*0.87-1.08*	***0.96***	*0.85-1.06*
9	620.77	17515.99	**35.45**	***1.01***	*0.89-1.12*	***0.99***	*0.87-1.11*
10	405.67	12426.44	**32.64**	***0.93***	*0.80-1.05*	**0.87**	0.76-0.98
11	226.87	7431.04	**30.52**	***0.87***	*0.72-1.01*	**0.83**	0.69-0.96
12	123.32	3608.71	**34.19**	***0.97***	*0.78-1.16*	***0.85***	*0.67-1.03*
13	55.77	1702.34	**32.77**	***0.93***	*0.67-1.19*	***0.84***	*0.60-1.07*
14+	30.00	842.77	**35.56**	***1.01***	*0.61-1.40*	***0.94***	*0.58-1.31*
LR statistic = 37.03, p = 0.222							
Number of live births:							
0-2	126.40	3083.15	**41.04**	***1.16***	*0.94-1.37*	***1.08***	*0.88-1.28*
3-5	723.05	19160.28	**37.75**	***1.06***	*0.97-1.16*	***1.06***	*0.97-1.16*
6-8	2082.15	58729.28	**35.45**	**1.00**	-	**1.00**	-
9+	1462.40	43527.29	**33.60**	***0.95***	*0.88-1.02*	**0.91**	0.84-0.97
LR statistic = 15.37, p = 0.094							

Figure A7.10: Crude male mortality rates (+95% CI) by number of surviving children

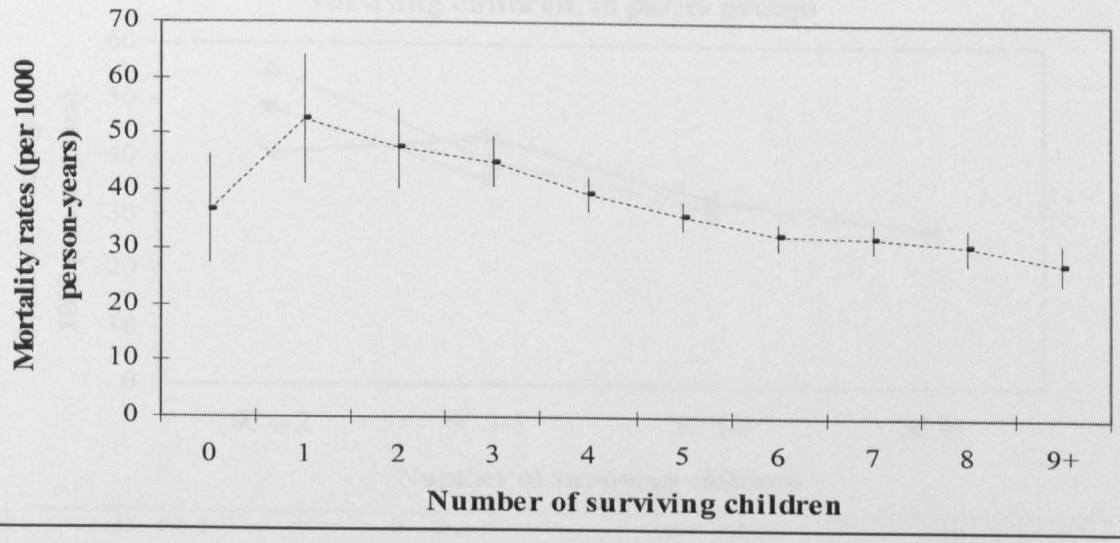


Table A7.15: Mortality In Men Who Have Completed Their Reproduction By Surviving Children

Variable	Average number deaths	Average person years	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	4394	12450.00	**35.29**	-	-	-	-
Any surviving children?:							
No	59.67	1623.74	**36.74**	**1.00**	-	**1.00**	-
Yes	4334.33	122876.26	**35.27**	***0.96***	*0.71-1.21*	***1.10***	*0.81-1.39*
LR statistic = 0.57, p = 0.760							
Number of surviving children on entry:							
0	59.67	1623.74	**36.74**	***1.03***	*0.75-1.30*	***0.88***	*0.64-1.12*
1	91.00	1731.21	**52.58**	**1.47**	1.13-1.81	***1.29***	*0.96-1.62*
2	194.41	4082.17	**47.62**	**1.33**	1.11-1.55	***1.08***	*0.90-1.27*
3	426.37	9440.36	**45.21**	**1.27**	1.11-1.42	**1.16**	1.02-1.31
4	693.25	17442.84	**39.72**	***1.11***	*0.99-1.23*	***1.06***	*0.94-1.18*
5	851.30	23803.38	**35.74**	**1.00**	-	**1.00**	-
6	805.00	24829.32	**32.41**	***0.91***	*0.82-1.00*	***0.91***	*0.82-1.00*
7	652.22	20350.26	**32.05**	**0.90**	0.80-0.99	***0.91***	*0.81-1.00*
8	371.09	12093.44	**30.68**	**0.86**	0.75-0.97	**0.88**	0.76-0.99
9+	249.69	9103.28	**27.53**	**0.77**	0.65-0.89	**0.76**	0.64-0.88
LR statistic = 52.14, p = 0.002							
Number of surviving children on entry:							
0-2	345	7435.74	**46.40**	**1.19**	1.05-1.34	***1.03***	*0.90-1.16*
3-5	1971	50702.74	**38.88**	**1.00**	-	**1.00**	-
6-8	1828.4	57256.34	**31.93**	**0.82**	0.77-0.87	**0.86**	0.80-0.91
9+	249.6	9103.28	**27.42**	**0.71**	0.61-0.80	**0.72**	0.62-0.82
LR statistic = 42.51, p < 0.001							
Percentage of children surviving:							
0-24.9%	96.53	2210.46	**43.70**	**1.37**	1.08-1.65	***1.09***	*0.86-1.32*
25.0-49.9%	368.67	7601.38	**48.50**	**1.52**	1.34-1.70	**1.24**	1.08-1.39
50.0-74.9%	1644.80	43302.64	**37.99**	**1.19**	1.11-1.27	***1.06***	*0.98-1.14*
75.0-100%	2284.00	71385.52	**32.00**	**1.00**	-	**1.00**	-
LR statistic = 14.99, p = 0.027							

Figure A7.11: Crude male mortality rates by number of surviving children, in parity groups

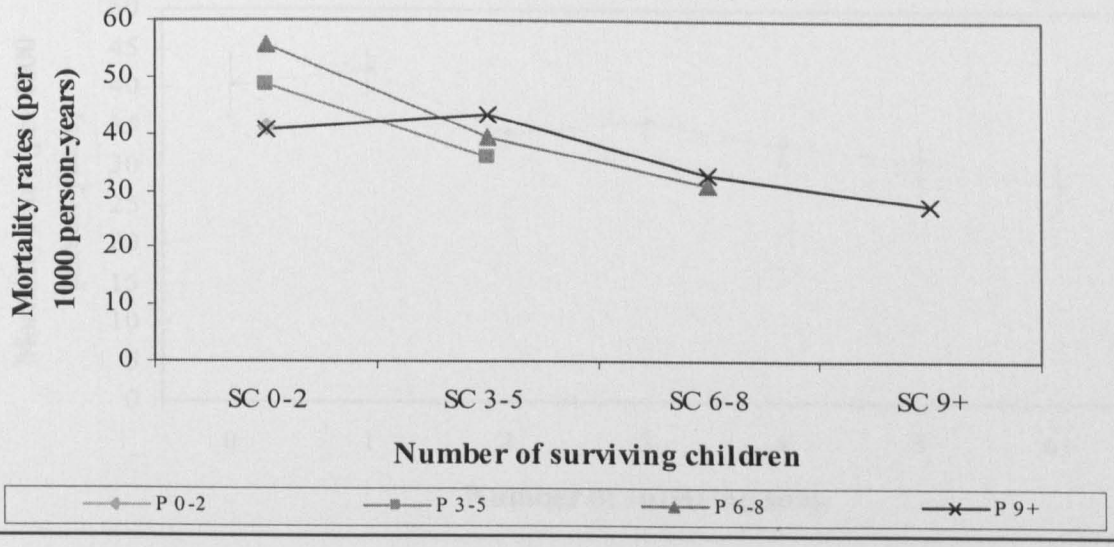


Table A7.16: Crude Rate Ratios for Parity and Surviving Children				
	Number of surviving children on entry			
Parity	0-2	3-5	6-8	9+
0-2	*1.04 (0.84-1.23)*	-	-	-
3-5	1.24 (1.01-1.47)	*0.90 (0.81-1.00)*	-	-
6-8	1.40 (1.04-1.77)	**1.00 (reference)**	0.78 (0.71-0.85)	-
9+	*1.03 (0.35-1.70)*	*1.10 (0.95-1.25)*	0.83 (0.76-0.91)	0.69 (0.59-0.80)
Adjusted Rate Ratios for Parity and Surviving Children *				
	Number of surviving children on entry			
Parity	0-2	3-5	6-8	9+
0-2	*1.02 (0.82-1.21)*	-	-	-
3-5	*1.02 (0.83-1.22)*	*0.99 (0.89-1.10)*	-	-
6-8	*1.10 (0.79-1.41)*	**1.00 (reference)**	0.87 (0.80-0.95)	-
9+	*1.02 (0.35-1.69)*	*1.03 (0.90-1.17)*	0.84 (0.77-0.92)	0.73 (0.62-0.83)

* LR statistic = 44.16, $p < 0.001$

Figure A7.12: Crude male mortality rate (+95% CI) by number of surviving sons

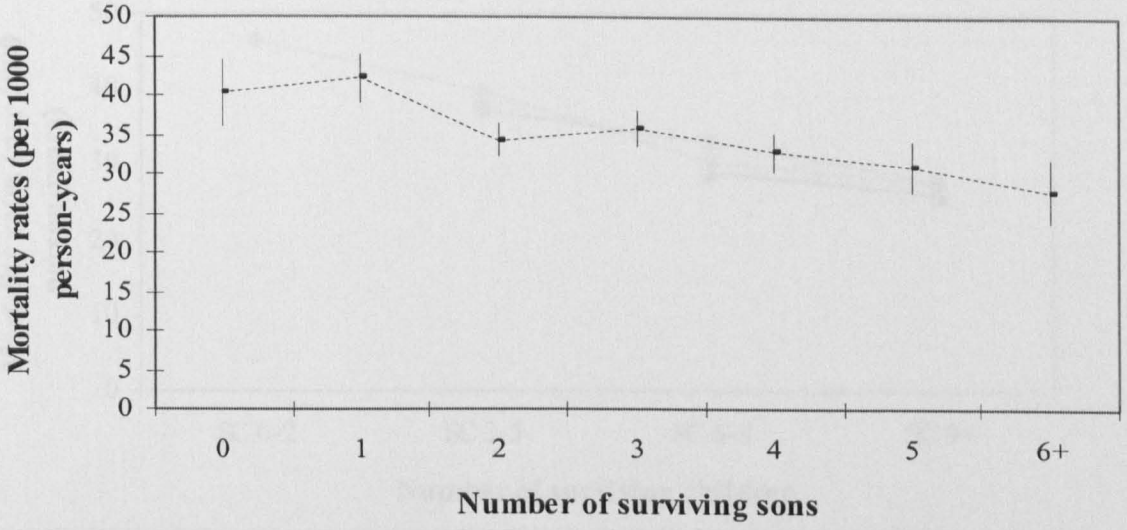


Table A7.17: Mortality In Men Who Have Completed Their Reproduction By Surviving Sons

Variable	Average number deaths	Average person years	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	4394	12450.00	**35.29**	-	-	-	-
Any surviving sons?:							
No	367.16	9089.89	**40.40**	**1.00**	-	**1.00**	-
Yes	4026.84	115410.11	**34.89**	**0.86**	0.77-0.96	***0.94***	*0.83-1.05*
LR statistic = 1.50, p = 0.889							
Surviving sons:							
0	367.16	9089.89	**40.40**	***1.13***	*0.99-1.27*	***1.02***	*0.88-1.15*
1	762.43	18059.74	**42.22**	**1.18**	1.06-1.29	**1.10**	1.00-1.21
2	964.81	28143.97	**34.28**	***0.96***	*0.87-1.04*	***0.92***	*0.84-1.00*
3	1021.27	28494.85	**35.84**	**1.00**	-	**1.00**	-
4	727.55	22200.43	**32.77**	***0.91***	*0.82-1.01*	**0.90**	0.81-0.99
5	359.62	11625.12	**30.93**	**0.86**	0.76-0.97	**0.86**	0.75-0.98
6+	191.16	6886.00	**27.77**	**0.77**	0.65-0.90	**0.79**	0.66-0.91
LR statistic = 38.99, p < 0.001							
Surviving sons:							
0-2	2094.40	55293.60	**37.88**	**1.12**	1.05-1.19	**1.06**	1.00-1.13
3-5	2108.44	62320.40	**33.83**	**1.00**	-	**1.00**	-
6+	191.16	6886.00	**27.77**	**0.82**	0.69-0.95	**0.84**	0.71-0.97
LR statistic = 12.33, p < 0.001							
Percentage of children who were male:							
0-24.9%	558.27	15081.72	**37.02**	***1.05***	*0.95-1.15*	***1.05***	*0.94-1.15*
25.0-49.9%	1311.57	38326.75	**34.22**	***0.97***	*0.90-1.04*	***0.98***	*0.90-1.05*
50.0-74.9%	1985.16	56120.99	**35.37**	**1.00**	-	**1.00**	-
75.0-100%	539.00	14970.54	**36.01**	***1.02***	*0.92-1.12*	***1.03***	*0.93-1.13*
LR statistic = 2.67, p = 0.338							
Percentage of children surviving who were male:							
0-24.9%	657.73	17678.86	**37.21**	***1.07***	*0.97-1.17*	***1.05***	*0.95-1.14*
25.0-49.9%	1182.55	34022.44	**34.76**	***1.00***	*0.93-1.08*	***1.02***	*0.94-1.09*
50.0-74.9%	1788.53	51470.78	**34.74**	**1.00**	-	**1.00**	-
75.0-100%	765.19	21327.92	**35.88**	***1.03***	*0.94-1.12*	***1.03***	*0.95-1.12*
LR statistic = 1.38, p = 0.702							

Figure A7.13: Crude male mortality rates by number of surviving children, in surviving son groups

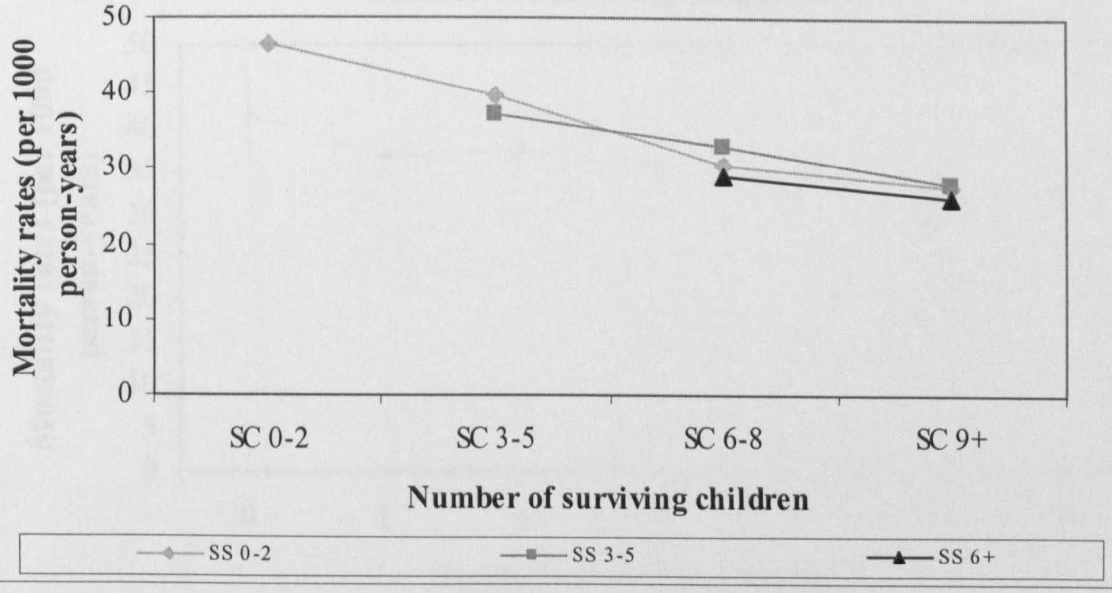


Table A7.18: Crude Rate Ratios for Surviving Children and Surviving Sons			
	Number of surviving sons		
Surviving children	0-2	3-5	6+
0-2	1.24 (1.07-1.41)	-	-
3-5	*1.07 (0.97-1.17)*	**1.00 (reference)**	-
6-8	0.82 (0.72-0.91)	0.88 (0.80-0.96)	0.77 (0.62-0.93)
9+	*0.74 (0.39-1.08)*	0.75 (0.61-0.89)	0.70 (0.54-0.87)
Adjusted Rate Ratios for Surviving Children and Surviving Sons *			
	Number of surviving sons		
Surviving children	0-2	3-5	6+
0-2	*1.06 (0.91-1.21)*	-	-
3-5	*1.04 (0.94-1.14)*	**1.00 (reference)**	-
6-8	0.83 (0.74-0.93)	0.91 (0.82-0.99)	0.81 (0.64-0.98)
9+	*0.71 (0.38-1.04)*	0.75 (0.61-0.90)	0.73 (0.56-0.91)

* LR statistic = 47.26, p = 0.011

Figure A7.14: Crude male mortality rates (+95% CI) by number of surviving daughters

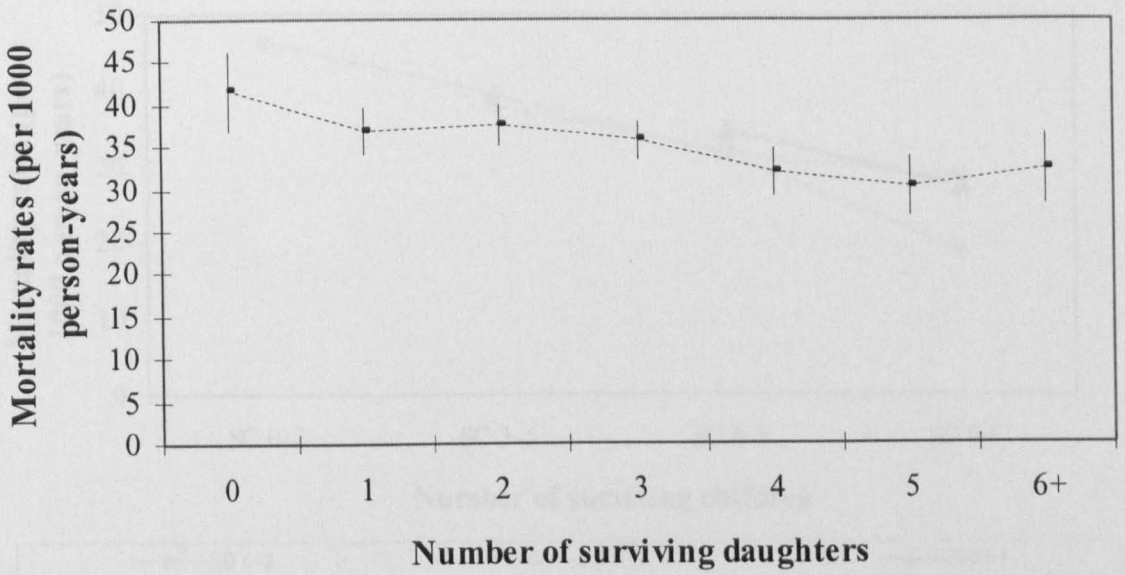


Table A7.19: Mortality In Men Who Have Completed Their Reproduction By Surviving Daughters

Variable	Average number deaths	Average person years	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	4394	12450.00	**35.29**	-	-	-	-
Any surviving daughters?:							
No	318.46	7651.76	**41.56**	**1.00**	-	***1.00***	-
Yes	4075.54	116846.34	**34.88**	**0.84**	0.74-0.94	***0.93***	*0.83-1.04*
LR statistic = 1.38, p = 0.883							
Surviving daughters:							
0	318.46	7651.76	**41.56**	**1.17**	1.02-1.32	***1.04***	*0.91-1.18*
1	746.53	20298.99	**36.79**	***1.03***	*0.93-1.13*	***1.00***	*0.91-1.10*
2	1098.00	29341.44	**37.42**	***1.05***	*0.96-1.14*	***1.03***	*0.94-1.12*
3	991.17	27835.10	**35.63**	**1.00**	-	**1.00**	-
4	645.35	20160.66	**32.00**	**0.90**	0.80-0.99	***0.91***	*0.82-1.01*
5	343.63	11416.43	**30.10**	**0.84**	0.73-0.96	**0.84**	0.73-0.95
6+	250.86	7795.62	**32.17**	***0.90***	*0.78-1.03*	***0.92***	*0.79-1.05*
LR statistic = 20.07, p = 0.062							
Surviving daughters:							
0-2	2162.99	57292.19	**37.75**	**1.13**	1.06-1.20	**1.09**	1.02-1.16
3-5	1980.15	59412.19	**33.33**	**1.00**	-	**1.00**	-
6+	250.86	7795.62	**32.17**	***0.97***	*0.83-1.10*	***0.98***	*0.85-1.12*
LR statistic = 8.35, p = 0.084							
% of children surviving who were female:							
0-24.9%	610.38	16764.63	**36.41**	***1.04***	*0.94-1.14*	***1.02***	*0.92-1.12*
25.0-49.9%	1308.18	38739.89	**33.77**	***0.97***	*0.90-1.04*	***0.97***	*0.90-1.04*
50.0-74.9%	1662.55	47681.34	**34.87**	**1.00**	-	**1.00**	-
75.0-100%	812.89	21314.14	**38.14**	**1.09**	1.00-1.19	***1.07***	*0.98-1.16*
LR statistic = 4.68, p = 0.593							

Figure A7.15: Crude male mortality rates by number of surviving children, in surviving daughter groups

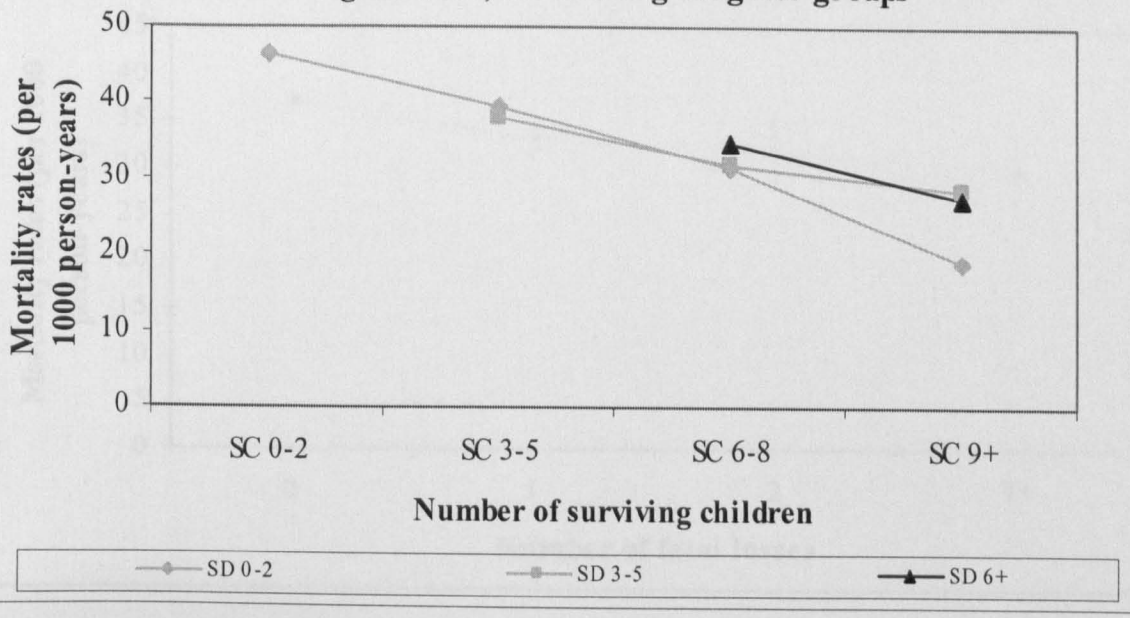


Table A7.20: Crude Rate Ratios for Surviving Children and Surviving Daughters			
	Number of surviving daughters		
Surviving children	0-2	3-5	6+
0-2	1.22 (1.06-1.39)	-	-
3-5	*1.04 (0.93-1.14)*	**1.00 (reference)**	-
6-8	0.83 (0.73-0.93)	0.84 (0.76-0.92)	*0.91 (0.76-1.06)*
9+	0.50 (0.22-0.78)	0.75 (0.62-0.88)	0.72 (0.53-0.92)
Adjusted Rate Ratios for Surviving Children and Surviving Daughters*			
	Number of surviving daughters		
Surviving children	0-2	3-5	6+
0-2	*1.05 (0.91-1.19)*	-	-
3-5	*1.03 (0.93-1.13)*	**1.00 (reference)**	-
6-8	0.85 (0.75-0.95)	0.87 (0.79-0.96)	*0.95 (0.79-1.11)*
9+	0.59 (0.27-0.91)	0.75 (0.62-0.88)	0.75 (0.55-0.95)

* LR statistic = 45.48, p = 0.034

Figure A 7.16: Crude male mortality (+95% CI) by number of fetal losses experienced by wife

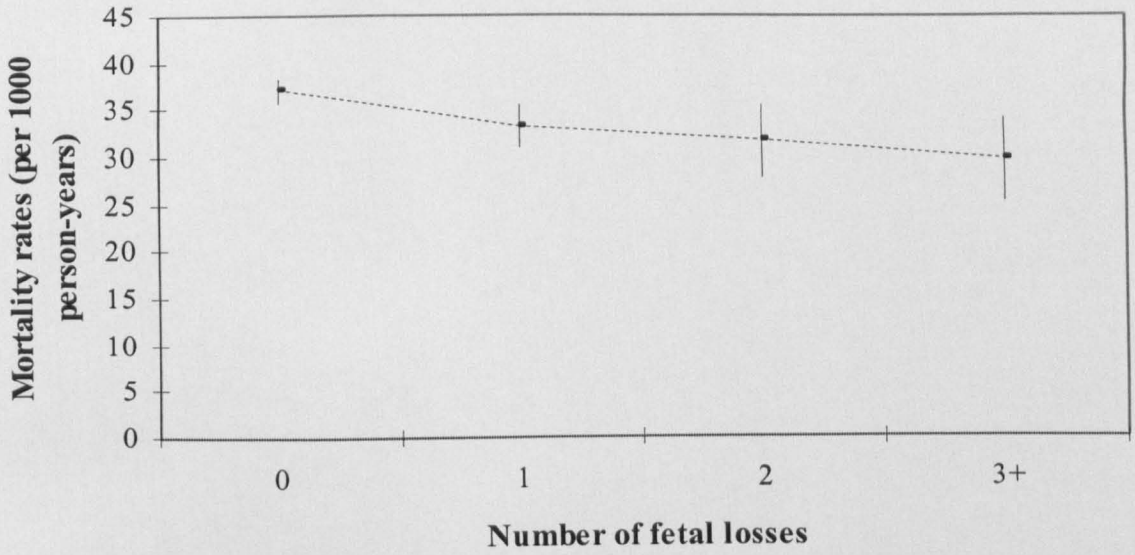


Table A7.21: Mortality In Men Who Have Completed Their Reproduction By Wife's Fetal Losses

Variable	Average number deaths	Average person years	Mortality rate (per 1000 pyrs)	Crude Rate Ratio	95% CI	Adj. Rate Ratio	95% CI
Total	4394	12450.00	**35.29**	-	-	-	-
Fetal loss?:							
No	2938.16	79487.37	**36.96**	**1.00**	-	**1.00**	-
Yes	1455.84	45012.63	**32.34**	**0.87**	0.82-0.93	**0.90**	0.85-0.96
LR statistic = 9.85, $p < 0.001$							
Fetal losses:							
0	2938.16	79487.37	**36.96**	**1.00**	-	**1.00**	-
1	976.71	29486.72	**33.12**	**0.90**	0.83-0.96	***0.92***	*0.85-1.00*
2	311.80	9868.81	**31.59**	**0.85**	0.75-0.96	**0.88**	0.77-0.99
3+ fetal losses	167.33	5657.10	**29.59**	**0.80**	0.67-0.93	**0.85**	0.72-0.99
LR statistic = 12.73, $p < 0.001$							
Fetal losses:							
No fetal losses	2901.96	78438.39	**37.00**	**1.00**	-	**1.00**	-
Nulligravid	36.20	1048.98	**34.51**	***0.93***	*0.63-1.24*	***0.85***	*0.57-1.13*
1-2 fetal losses	1288.51	39355.53	**32.74**	**0.88**	0.82-0.95	**0.91**	0.85-0.97
3+ fetal losses	167.33	5657.10	**29.59**	**0.80**	0.67-0.93	**0.85**	0.72-0.99
LR statistic = 11.49, $p < 0.001$							
Percentage of pregnancies lost:							
No fetal losses	2901.96	78438.39	**37.00**	**1.00**	-	**1.00**	-
Nulligravid	36.20	1048.98	**34.51**	***0.93***	*0.63-1.24*	***0.85***	*0.57-1.13*
Up to 25% lost	1167.31	36091.64	**32.34**	**0.87**	0.81-0.94	**0.90**	0.84-0.96
Over 25% lost	288.53	8920.99	**32.35**	**0.87**	0.76-0.98	***0.91***	*0.79-1.03*
LR statistic = 10.97, $p = 0.072$							