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The effect of number of births on women's mortality: Systematic review of the evidence for women who have completed their childbearing

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Mortality in women who have completed their childbearing may increase with the number of births experienced because of maternal depletion or a trade-off between reproduction and mortality. We report a systematic review of the evidence on this association. We searched Medline, Embase, Popline, and the Science Citation Index for published and unpublished studies up to September 2003, and the book catalogues of relevant London libraries. Where necessary we also contacted authors for additional information. Mortality declined with increasing numbers of births in twelve historical cohorts, but in eight contemporary cohorts the highest mortality was seen in the nulliparous and in women with more than four births. All effects seen were small and there were few statistically significant results. Studies examining the relationship in other ways (such as by linear trends or by mean number of births by age at death) found inconsistent associations. We discuss methodological, social, and biological factors that may have affected these associations.

Keywords: reproductive history; childbearing; parity; women; survival; mortality

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A woman's risk of dying increases during pregnancy and the immediate postpartum, but the precise length of the postpartum risk period is not well known. Although women are thought to remain vulnerable up to 1 year after birth (WHO 1992), empirical evidence is inconsistent. One study in Nepal suggests that women are at increased risk of mortality for up to 90 days postpartum (Pradhan et al. 2002), but an analysis in Bangladesh suggests that risks remain elevated for up to 2 years (Menken et al. 2003). Pregnancy may also affect diseasespecific mortality in the long term. For example, mortality from cancers of the breast, endometrium, and ovaries is lower in women who have had many children, whereas mortality from conditions such as cardiovascular disease or cervical cancer may increase with an increasing number of births (Pike 1987; Kelsey et al. 1993; Ness et al. 1994).

It has also been suggested that all-cause mortality might increase with the number of births in the long term because of accumulated physiological demands associated with repeated pregnancies, particularly with numerous closely spaced pregnancies (Jelliffe and Jelliffe 1978; Winikoff 1978, 1983; Winkvist et al. 1992). This possible detrimental effect has been used as part of the justification for family planning programmes. Nevertheless, evidence for the existence of a maternal depletion effect is inconsistent (Menken et al. 2003).

Demographers have recently embarked on a new line of research in the field—the determinants of post-reproductive ageing from the standpoint of evolutionary theories (Smith et al. 2002). These theories propose a trade-off between childbearing and survival in the long term, and suggest that somatic maintenance is reduced with an increasing number of births because physical resources used during childbearing cannot be used for later repair (Kirkwood and Rose 1991). Controlled laboratory experiments have shown reduced life spans in fruit flies with higher fertility, but the existence of any such effect in humans has not been established (Partridge 2001).

We thought it would be useful at this stage to survey the numerous studies that have examined the association between number of births and all-cause mortality among women who have completed their childbearing. We decided to undertake a systematic review of the literature on this association as a means of summarizing the results and identifying areas that require further investigation.

Materials and methods

We searched Medline, Embase, and Popline for published and (in the case of Popline) unpublished studies up to September 2003 in any language, using a comprehensive search strategy designed to identify all possible relevant studies. A search on reproductive history, including both exploded thesaurus and free-text terms (reproduction, reproducti*, 'reproductive history', childbearing, parity, gravidity, livebirth*, 'live births', motherhood, 'family size', and parental), was combined with a search for articles with exploded thesaurus and free-text terms for mortality (mortality, longevity, survival, death, ageing, and aging). We also searched the databases for review articles and editorials on the determinants of mortality in women to identify further studies that included reproductive history. Reference lists from all relevant articles were checked. Additional searches were carried out in the Science Citation Index (Expanded), and the book catalogues of the London School of Hygiene and Tropical Medicine, the London School of Economics, and the British Library. Authors were contacted for additional information where necessary and possible. The full search strategy is available on request.

We included studies examining the association between number of births (whether live or still) and all-cause mortality in women who had completed their childbearing. Studies were included if they reported numerical data on relative risks of mortality by number of births or provided data that allowed their calculation, including mean age at death, mortality rates, or relative risks of mortality (for example, rate ratios, standardized mortality ratios, and odds ratios). We also included studies that looked at linear trends in relative risks of mortality, and studies that examined mean number of births by age at death or life expectancy by number of births.

We excluded studies that only compared mortality in childless women with mortality in parous women, both because nulliparous women are likely to be different from parous women in many ways that affect mortality and because our objective was to examine the pattern of the association between each individual number of births and mortality. Secondly, studies were included only if they restricted the study population to women aged ≥ 40 years or provided stratified estimates for this age group. We excluded data on younger women because they might not have completed their childbearing, and because their mortality might have been directly linked to pregnancy. Mortality during and shortly after pregnancy is known to be associated with parity, with mortality highest during the first pregnancy and at higher pregnancy orders (AbouZahr and Royston 1991), and we were concerned that these parity-specific patterns in mortality in younger women might mask a longer-term effect of reproduction on survival. We defined women who had completed their childbearing as women aged 40 and over, since age-specific fertility is very low after this age (Macfarlane and Mugford 2000). Thirdly, we excluded duplicated results. Where results from a single study population were reported in more than one publication, we chose either the largest study, or the one adjusting for most potential confounders, or the one that allowed examination of the risk of mortality by individual number of births. Different study populations within one investigation were treated as separate cohorts.

Information was extracted by one reviewer using a standardized form, and checked by a second. The information abstracted included the study population, study design, number of women and deaths in the sample, the woman's age at entry, the definition of reproductive exposure, and the relative risk of mortality by number of births or, if these were not presented, data as reported by the authors. We also extracted data on methods that may have influenced the study results, such as how exposure and outcome were ascertained, and which variables were adjusted for in the analysis. Where adjusted estimates were presented, the measures of association extracted were those that were most fully adjusted for confounders. When analyses were stratified by factors such as age, we extracted data for each stratum.

The association between number of births and mortality in historical or natural-fertility populations may differ from the association found in populations of women with access to modern contraceptive methods. Few of the studies provided data on contraceptive use in their cohorts, and we assumed the pattern of contraceptive use in their populations from the periods over which the cohorts were followed. Studies using historical data (that is, sixteenth to early twentieth century) were considered to represent natural-fertility populations, while contemporary studies conducted in the late twentieth century were assumed to include contracepting populations. For this reason, study results were summarized separately for historical and contemporary populations.

Because the studies spanned time periods with different fertility patterns, the choice of a unique baseline group for calculating relative risks was not straightforward. We reasoned that nulliparous women and women with only one birth were different from other parous women in most populations, and thus were not an appropriate reference group. We therefore opted to extract relative risks using women with two births as the baseline category. If studies used a different reference category, the risk of mortality was recalculated relative to women with two births.

Data on the mean age at death by number of children were converted into relative risks of mortality by number of children, assuming that such data represented a full cohort with no loss to follow-up. Under this assumption, the mean number of years lived after a given age represents the average person-years at risk in the cohort after that age. Person-years data were therefore obtained by multiplying the number of deaths in each birth category by the mean number of years lived after the age of 45, which allowed for the calculation of mortality rates and crude rate ratios with 95-per-cent confidence intervals (CIs).

In order to gain further insight into the pattern of the relationships, pooled estimates of the relative risk of mortality by the number of births relative to women with two births were obtained by conducting a series of meta-analyses of data from a sub-set of studies. Studies were included in the meta-analyses if they reported relative risks and 95-per-cent CIs with two births as the reference category, or presented data that allowed for the calculation of these relative risks with the appropriate CIs. Analyses were carried out in Stata Version 7 (Stata Corporation 2001) using a random-effects model because we assumed that there would be a different underlying effect in each study owing to differences between populations. This model uses the inverse variance method to weight individual study estimates, modifying the weights by incorporating additional between-study variance, and using the Q test to assess heterogeneity between studies (Sharp and Sterne 1997). A sensitivity analysis was also conducted to assess the impact of one study that was much larger than the others on the results of the meta-analysis.

The screening procedure and its outcome

A total of 39,638 abstracts were identified in the databases and screened. The vast majority of these papers did not contain any information that was relevant for this review and were discarded. Of the 379 papers retrieved for further evaluation, the following 24 appeared to satisfy the inclusion criteria: Arvay and Takacs 1966; Philippe and Yelle 1976; Beral 1985; Bideau 1986; Lapidus and Bengtsson 1986; Green et al. 1988; Lund et al. 1990; Moser et al. 1990; Hibbard and Pope 1991; Le Bourg et al. 1993; Kvale et al. 1994; Weatherall et al. 1994; Friedlander 1996; Westendorp and Kirkwood 1998; Cooper et al. 2000; Doblhammer 2000; Korpelainen 2000; Lycett et al. 2000; Manor et al. 2000; Helle et al. 2002; Muller et al. 2002; Smith et al. 2002; Doblhammer and Oeppen 2003; Menken et al. 2003. A further 14 publications were identified by searching bibliographies and follow-up of reports cited by others: Beeton et al. 1900; Powys 1905; Bell 1918; Freeman 1935; Dorn and McDowell 1939; Henry 1956; Gautier and Henry 1958; Ganiage 1963; Lachiver 1969; Charbonneau 1970, 1975; Kitagawa and Hauser 1973; Fox and Goldblatt 1982; Voland and Engel 1989. A re-analysis of previously published data was obtained from the authors of one study (Kumle and Lund 2000), and one study was conducted by the authors of this review (Hurt et al. 2004). On detailed examination, nine of these 40 studies turned out not to match the inclusion criteria. One compared only nulliparous and parous women (Beral 1985) and five included women who were of reproductive age (Lapidus and Bengtsson 1986; Green et al. 1988; Moser et al. 1990; Hibbard and Pope 1991; Weatherall et al. 1994). Three were of populations analysed more fully elsewhere. We included Muller et al. 2002 rather than Le Bourg et al. 1993, because the former presented results as hazard ratios, while the latter presented them in the form of a principal components analysis, which did not give an estimate of the size of the association. Kumle and Lund 2000 was a re-analysis of Lund et al. 1990, with longer follow-up and more adjustment for potential confounders. We included data from the former though the conclusions of both papers were the same. Finally, the population in Menken et al. 2003 was a complete sub-set of that included in Hurt et al. 2004. Since the results from both studies were comparable, we included the largest (Hurt et al. 2004).

The selection process left 31 eligible publications: Beeton et al. 1900; Powys 1905; Bell 1918; Freeman

1935; Dorn and McDowell 1939; Henry 1956; Gautier and Henry 1958; Ganiage 1963; Arvay and Takacs 1966; Lachiver 1969; Charbonneau 1970, 1975; Kitagawa and Hauser 1973; Philippe and Yelle 1976; Fox and Goldblatt 1982; Bideau 1986; Voland and Engel 1989; Kvale et al. 1994; Friedlander 1996; Westendorp and Kirkwood 1998; Cooper et al. 2000; Doblhammer 2000; Korpelainen 2000; Kumle and Lund 2000; Lycett et al. 2000; Manor et al. 2000; Helle et al. 2002; Muller et al. 2002; Smith et al. 2002; Doblhammer and Oeppen 2003; Hurt et al. 2004. Together these studies yielded a total of 33 cohorts, because three papers reported results for two separate populations (Beeton et al. 1900; Bideau 1986; Doblhammer 2000), and we included the results of every population except one (a British cohort that had been analysed more fully in another paper-Doblhammer 2000, analysed in Fox and Goldblatt 1982).

Tables 1-3 show, for each study, study population, data source, follow-up period, sample size, exposure definition, and variables for which adjustments had been made. Studies in historical or natural-fertility populations that presented relative risks or data which allowed their calculation are shown in Table 1. Where possible, relative risk of mortality against a baseline of two births with a 95-per-cent CI are shown. Table 2 includes all studies in contemporary populations which presented relative mortality risks. It was not possible to recalculate the relative risks with appropriate CIs using a consistent baseline group for these studies because the necessary data were not given in the papers. Table 3 shows studies reporting linear trends, mean number of births by age at death, or life expectancy by number of births.

Study populations and sample sizes varied substantially, ranging from small highly selected subgroups (such as aristocrats) to full population cohorts using census data. A total of 20 cohorts had used historical data, with mortality and reproductive history determined from parish records or genealogical sources. Of the other cohorts, seven were based on census data, five used prospective cohort data, and one used data from a demographic surveillance system. Reproductive exposure was defined as live births for ten cohorts, as births (without further specification) for 22, and as fullterm deliveries for one. Most studies restricted their analyses to ever-married women, but adjustment for other potential confounders was variable. There was little control for confounding in studies using historical data (Table 1), whereas most of the later studies adjusted for age and some measure of socioeconomic status (Table 2). Adjustment for other potential confounders, such as contraceptive use, was rare. Three studies stratified their data by age of women on entry into the cohorts, presenting separate results for two sub-cohorts (Kitagawa and Hauser 1973; Friedlander 1996; Manor et al. 2000), and two stratified by age and year of marriage with 17 sub-cohorts in one (Freeman 1935) and 29 in the other (Dorn and McDowell 1939).

Results

Relative risk of mortality by number of births

The data available for 13 historical or naturalfertility cohorts allowed mortality rates and relative risks with 95-per-cent CIs to be calculated, and it was possible to use women with two births as the baseline group in all but one of these (Table 1). Eleven cohorts were reconstructed using data from the sixteenth to eighteenth centuries (Beeton et al. 1900; Henry 1956; Gautier and Henry 1958; Ganiage 1963; Lachiver 1969; Charbonneau 1970, 1975; Philippe and Yelle 1976; Bideau 1986), and two were based on more recent census populations, one from the Australian census (Powys 1905) and one from a demographic surveillance system in rural Bangladesh (Hurt et al. 2004). All included women were at least 45 years of age at entry into the cohort. All except one study (Hurt et al. 2004) restricted the sample used to married women but did not adjust for other potential confounders.

There is no consistent pattern in the relative-risk estimates of mortality by number of births compared to two births, and most 95-per-cent CIs for individual estimates are wide. One study shows a clear decrease in mortality with number of births (Beeton et al. 1900) and another shows a decrease after two births (Hurt et al. 2004). Relative mortality risks are consistently below the null value of one for women with more than two births in five further cohorts (Beeton et al. 1900; Ganiage 1963; Charbonneau 1975; Bideau 1986), and consistently above one in one cohort (Gautier and Henry 1958). There is no pattern at all in the remaining four cohorts: relative mortality rates are all around the null value in one cohort (Powys 1905); they show no discernible patterns in two (Lachiver 1969; Charbonneau 1970); and mortality is lower in all parous women compared with the nulliparous in the final cohort, although these results are difficult to interpret because of the wide parity groupings used (Philippe and Yelle 1976).

1st Author	· · ·	1	Women (deaths)	Age ²	Exposure		d RRs (+95-per-cent CI) of mortality by number of births, relative to women with two births ³										
(country)	population	period	(deaths)			for	0 births	1 birth	3 births	4 births	5 births	6 births	7 births	8 births	9 births	10+ births	
Beeton 1900	Quakers	NR	NR	50	Births	Nothing	1.30	0.94	0.81	0.82	0.73	0.71	0.75	0.68	0.71	0.62	
(USA)			(1,275)				(0.70-2.39)	(0.58-1.54)	(0.56 - 1.17)	(0.56 - 1.20)	(0.51-1.05)	(0.49-1.03)	(0.52-1.09)	(0.48 - 0.98)	(0.49 - 1.02)	(0.45-0.86)	
Beeton 1900	Quakers	NR	NR	50	Births	Nothing	0.87	0.93	0.94	0.94	1.01	0.90	0.84	0.96	0.88	0.93	
(England)			(1,560)				(0.47-1.60)	(0.65-1.33)	(0.67 - 1.33)	(0.68 - 1.31)	(0.74 - 1.37)	(0.65-1.25)	(0.62 - 1.17)	(0.69 - 1.34)	(0.63 - 1.24)	(0.69 - 1.24)	
Powys 1905	Population of	1898-1902	NR	45	Births	Marital	1.04	1.05	1.03	1.00	0.98	0.99	1.02	1.00	1.01	1.03	
(Australia)	New South Wales		(10,519)			status	(0.94 - 1.14)	(0.93-1.18)	(0.92-1.15)	(0.90 - 1.12)	(0.88 - 1.09)	(0.89-1.10)	(0.92 - 1.13)	(0.90 - 1.11)	(0.91 - 1.12)	(0.94 - 1.13)	
Henry 1956	Bourgeoisie	16th-20th	NR	45	Births	Marital	0.91	0.95	0.94	0.90	0.98	1.09	0.70	1.03	2.03	1.06	
(Switzerland)	-	с.	(310)			status	(0.56 - 1.47)	(0.55 - 1.66)	(0.60 - 1.48)	(0.57 - 1.41)	(0.60 - 1.61)	(0.61-1.92)	(0.39 - 1.26)	(0.56-1.87)	(1.09 - 3.75)	(0.64 - 1.75)	
Gautier 1958	Population of	17th-18th	NR	45	Births	Marital	1.30	1.05	1.01	1.94	1.05	1.11	1.56	1.20	1.40	1.01	
(France)	one parish	с.	(63)			status	(0.37-4.59)	(0.26 - 4.21)	(0.36 - 2.85)	(0.48 - 7.75)	(0.35-3.13)	(0.37-3.30)	(0.52 - 4.64)	(0.39 - 3.72)	(0.47-4.17)	(0.29 - 3.59)	
Ganiage 1963	Population of	18th c.	NR	45	Births	Marital	0.77	1.14	0.67	0.93	0.66	0.86	0.84	0.84	1.00	0.74	
(France)	three villages		(107)			status	(0.15-3.82)	(0.32 - 4.05)	(0.20 - 2.19)	(0.36 - 2.38)	(0.23-1.89)	(0.33 - 2.23)	(0.32-2.16)	(0.33-2.17)	(0.32-3.10)	(0.29 - 1.89)	
Lachiver 1969	Population of	17th-18th	NR	45	Births	Marital	1.14	1.02	1.02	1.09	1.00	1.12	1.02	1.00	1.02	1.00	
(France)	three parishes	с.	(406)			status	(0.72-1.79)	(0.55 - 1.89)	(0.61 - 1.72)	(0.67 - 1.77)	(0.62 - 1.61)	(0.71 - 1.78)	(0.61 - 1.70)	(0.61-1.63)	(0.60 - 1.71)	(0.66 - 1.53)	
Charbonneau	Population of	17th-18th	NR	45	Births	Marital	1.05	1.76	1.11	1.58	1.01	0.89	1.18	1.39	1.28	1.06	
1970 (France)	two villages	с.	(176)			status	(0.48 - 2.31)	(0.58 - 5.34)	(0.49 - 2.49)	(0.78 - 3.17)	(0.54-1.89)	(0.42-1.86)	(0.55 - 2.51)	(0.69-2.80)	(0.59 - 2.76)	(0.56 - 2.00)	
Charbonneau	All Canadians	17th-18th	NR	45	Births	Marital	0.30	0.32	0.31	0.27	0.27	0.41	0.34	0.34	0.38	0.31	
1975 (Canada)	before 1700 who	с.	(146)			status	(0.03-2.68)	(0.03-3.52)	(0.03-2.98)	(0.03-2.28)	(0.02-3.01)	(0.05-3.37)	(0.04-2.65)	(0.04–2.56)	(0.05-2.84)	(0.04-2.26)	
Philippe 1976	left descendants Population of	Unclear.	873	47	Births	Marital	1.00		0.78^{5}			0.83			0.94^{6}		
(Canada)	Isle-aux-Coudres	before 1800	(119)	••	Dirtito	status	1.00		(0.32 - 1.84)			(0.30-2.12)			(0.53 - 1.80)	1	
Bideau 1986	Population of	1670-1799	NR	45	Births	Marital	0.52	0.61	0.43	0.58	0.83	0.55	0.61	0.60	0.55	0.53	
(France)	Mogneneins village		(174)	45	Dirtito	status	(0.13 - 2.07)	(0.16 - 2.31)	(0.12 - 1.60)	(0.17 - 1.98)	(0.24 - 2.84)	(0.16 - 1.91)	(0.19 - 2.02)	(0.18 - 2.05)	(0.16 - 1.86)	(0.16 - 1.71)	
Bideau 1986	Population of	1740 - 89	NR	45	Births	Marital	1.00	1.02	0.92	0.81	0.86	0.74	0.90	0.98	0.85	0.89	
(France)	Thoissey village	1740-07	(133)	-15	Direns	status	(0.36 - 2.81)	(0.31 - 3.34)	(0.34 - 2.44)	(0.26 - 2.50)	(0.32 - 2.33)	(0.27 - 2.09)	(0.34 - 2.40)	(0.38 - 2.51)	(0.29 - 2.45)	(0.38 - 2.11)	
Hurt 2004	Population of	1982 - 98	20,383	45	Live	status	(0.30-2.81)	0.81	0.83	0.86	0.88	0.74	0.76	0.69	0.75	(0.38 - 2.11) 0.74	
(Bangladesh)	Matlab district	1702 70	(1,939)	ъ	births ⁴		(0.38-1.12)	(0.41 - 1.21)	(0.49–1.17)	(0.57-1.15)	(0.56–1.19)	(0.46-1.03)	(0.64–1.23)	(0.55-1.09)	(0.59–1.16)	(0.54-1.05)	

Table 1 Relative risk of mortality by number of births (with 95-per-cent confidence intervals) among women reported in studies of historical populations¹

¹Baseline of two births used wherever possible. ²Minimum age of women at entry into the study. ³Recalculated from data presented in the papers, except for Hurt et al. 2004. ⁴Adjusted for age, time period, marital status, religion, education, area of residence.

⁵Group: 1–5 births.

⁶Group: 7–11 births.

NR = not reported.

1st Author	Study	Follow-up	Women (deaths)	Age ²	Exposure	Adju	isted	for ³			Effect measure	Relative ef	fect (95-per-c	ent CI or p-	value) of num	ber of births	on mortality	ý	
(country)	population	period	(deaths)			A	В	С	D	Е	measure	0 births	1 birth	2 births	3 births	4 births	5 births	6 births	7+ births
Kitagawa 1973	All Americans	May-Aug	NR	45	Live births	Yes	Yes	Yes	No	Yes	SMR	107	104	94	89	96	105		114
(USA, i)	in 1960 census ⁴	1960	(8,825)									(102–112)	(99–109)	(90–98)	(84–94)	(89–103)	(98–112)		(106–123)
Kitagawa 1973	All Americans	May-Aug	NR	65	Live births	Yes	Yes	Yes	No	Yes	SMR	102	95	103	98	101	95		106
(USA, ii)	in 1960 census	1960	(27,358)									(99-105)	(92–98)	(100–106)	(95–101)	(97–105)	(92–98)		(103–109)
Fox 1982	1 per cent of 1970	1971–75	NR	50	Live births	Yes	Yes	Yes	No	No	SMR	97	91	111	89	102	110	(5+)	
(UK)	census population		(627)		in marriage							(77–120)	(77–107)	(96-126)	(71–109)	(74–137)	(79–148)		
Kvale 1994	Attendees at a breast	1961 - 81	NR	50	Full term	Yes	No	Yes	No	Yes	SMR	100	99	94	99	100	107	(5+)	
(Norway)	cancer screening programme		(11,445)		deliveries							(96–104)	(94–104)	(90-98)	(94–104)	(95-106)	(103–112)		
Cooper 2000	Minnesota students	1991	826	63	Live births	Yes	No	No	No	Yes	OR	1.00	0.82		0.81		0.83	(5+)	
(USA)	1934-39		(108)										(0.49 - 1.39)		(0.49 - 1.34)		(0.41 - 1.69)		
Doblhammer	All Austrians in	1981	1,254,153	50	Live births	Yes	Yes	Yes	No	No	OR	1.15	1.01	1.00	1.02	1.06	1.10	(5+)	
2000 (Austria)	1981 census		(35,234)									(<0.01)	(>0.05)		(>0.05)	(<0.05)	(<0.01)		
Kumle 2000	All Norwegians in	1970 - 89	516,906	40	Births in	Yes	Yes	Yes	No	No	RR	_	1.00	0.94	0.92	0.95		1.03	(6+)
(Norway)	1970 census		(149,044)		present marriage									(0.92-0.95)	(0.90-0.94)	(0.93-0.97)		(1.01-1.06)	
Manor 2000	20 per cent of 1983	1983 - 92	61,807	45	Live births	Yes	Yes	Yes	No	Yes	OR	1.00	0.88	0.70	0.73	0.73		0.76	(6+)
(Israel, i)	census population ⁴		(6,181)										(<0.01)	(<0.01)	(<0.01)	(<0.01)		(<0.01)	
Manor 2000	20 per cent of 1983	1983-92	17,816	70	Live births	Yes	Yes	Yes	No	Yes	OR	1.00	0.92	0.83	0.84	0.86		0.77	(6+)
(Israel, ii)	census population		(8,178)										(>0.05)	(<0.01)	(<0.01)	(<0.05)		(<0.01)	
Smith 2002	Individuals in the	1934-92	NR	60	Live births	Yes	Yes	Yes	Yes	Yes	HR	_		0.86^{5}			0.95^{6}		1.00^{7}
(USA)	Utah population genealogical database		(13,987)											(<0.01)			(<0.05)		

Table 2	Relative risk of mortality b	by number of births (w	with 95-per-cent	confidence intervals)	among women re	ported in studies of contem	porary populations ¹

¹No uniform baseline group could be identified. ²Minimum age of women at entry into the study.

 3 A = age; B = marital status; C = socio-economic status (e.g., education, occupation, religion, race, area of residence); D = time period (e.g., birth cohort, date of marriage); E = other (e.g., BMI, smoking, HRT).

⁴Results presented separately for younger and older women within the cohort.

⁵Group: 1–3 births.

⁶Group: 4–6 births.

⁷Baseline group = 7-11 births, also gives HR for 12-14 and 15+.

NR = not reported; SMR = standardized mortality ratio; OR = odds ratio; RR = rate ratio; HR = hazard ratio.

Table 3 The association between number of births and mortality among women, using measures other than relative risk, in historical and contemporary populations

1st Author	Study	Follow-up	Women	Age ¹	Exposure	Adjusted for ²					Results
(country)	population	period	(deaths)			Α	В	С	D	Е	
Freeman 1935 (USA)	Genealogies	NR-1909	NR (2,614)	45	Live births	Yes	Yes	No	Yes	No	No significant trend, but 1 mortality per birth in 14 of 17 cohorts
Helle 2002 (Scandinavia)	Sámi women	1640-1870	NR (375)	50	Births	Yes	Yes	No	No	No	No significant linear trend (p 0.56)
Muller 2002 (Canada)	Canadians	17th-18th c.	NR (1,635)	50	Births	No	Yes	No	No	No	Significant linear trend of \downarrow mortality per child born (RR 0.986, p 0.04)
Doblhammer 2003 (UK)	Genealogies	1641-1850	NR (1,854)	50	Births	Yes	Yes	Yes	Yes	Yes	No linear trend if women with 0 or 1 births included in models (p 0.24); \uparrow Mortality per birth if on women with 2+ births included (RR 1.038, p 0.04)

Evidence of a linear trend in mortality with number of births? (Historical populations)

Evidence of a linear trend in mortality with number of births? (Contemporary populations)

Friedlander 1996	Ongoing cohort ³ 1972–90	1,138 (150)	43	Live births	Yes	No	Yes	Yes	Yes	No significant linear trend (p 0.96)
(USA, i) Friedlander 1996 (USA, ii)	Ongoing cohort 1972–90	385 (162)	68	Live births	Yes	No	Yes	Yes	Yes	Significant linear trend of \uparrow mortality per birth (RR 1.15, p 0.01)

Mean number of children (95-per-cent CI) by age at death (Mostly historical populations)

1st Author	Study population	Follow-up period	Women	Age ¹	Exposure	Adju	sted f	or ²			Results	Results								
(country)			(deaths)	-	-	A	В	С	D	Е	40-	45-	50-	55-	60-	65 -	70-	75-	80-	4
Bell 1918 (USA)	Descendants of	NR	NR (541)	40	Births	No	Yes	No	No	No	6.2				6.6				7.2	
· · · ·	William Hyde										(40 - 60)	years)			(60-79	years)			(80 + years)	
Dorn 1939 (Australia)	All Australians	1909 - 28	NR (195,000)	45	Births	No	Yes	No	No	Yes	-	_	-	6.80	6.75	6.9	6.98	6.97	7.03	6.99
Westendorp 1998	Aristocrats	NR	NR (1,472)	41	Births	No	Yes	Yes	No	No	2.01		2.40		2.36		2.64		2.08	1.80
(Britain)											(1.30-3.	.11)	(1.56-	3.71)	(1.53-	3.63)	(1.71-	-4.07)	(1.12 - 3.24)	(1.12 - 2.90)
Korpelainen 2000	Farmers and	1700-at least	NR (527)	50	Births	No	Yes	No	No	No	-		5.40						4.34	
(ten countries ⁵)	aristocrats	1979											(50-79	9 years)					(80 + years)	
Lycett 2000	Population of	1720 - 1870	NR (1,276)	40	Births	No	Yes	Yes	No	No	4.94		4.87		4.98		5.06		4.82	
(Germany)	13 parishes										(4.59-5.	.29)	(4.52-	5.22)	(4.69-	5.27)	(4.79-	-5.33)	(4.45 - 5.19)	

Life expectancy from current age by number of births (All historical populations)

1st Author (country)	Study population	Follow-up period	Women (deaths)	Age ¹	Exposure	Adjı A	isted f B	for ² C	D	E	Results 0	1	2	3	4-5	6+
Arvay 1996 (Hungary) Voland 1989 (Germany)	All Hungarians ⁶ Women from seven parishes	1959–60 NR	NR (1,330,362) NR (811)	50 47	Births Live births, pregnancies				No No	No No	32.31 Data only preser	32.63 nted graphically, but	32.75 no clear pattern obse	32.93 ervable	33.05	33.42

¹Minimum age of women at entry into the study. ²A = age; B = marital status; C = socio-economic status (e.g., education, occupation, religion, race, area of residence); D = time period (e.g., birth cohort, date of marriage); E = other. ³Results presented separately for young and older women within the cohort.

 $^{4}85-90$ for Dorn, 90+ for Westendorp.

⁵Britain, France, Spain, Germany, the Netherlands, Austria, Russia, Denmark, Sweden, and Finland.

⁶Women currently aged 50–54.

NR = not reported.

Eight cohorts from contemporary populations also provided data on relative mortality risks (Kitagawa and Hauser 1973; Fox and Goldblatt 1982; Kvale et al. 1994; Cooper et al. 2000; Doblhammer 2000; Kumle and Lund 2000; Manor et al. 2000; Smith et al. 2002; Table 2). For these cohorts, data presented in the papers were not sufficient to allow calculation of 95-per-cent CIs relative to a consistent baseline group. All were based on census or cohort data from contemporary populations in the developed world. These studies had larger sample sizes than the studies using historical data and there was more adjustment for potential confounders. The original relative risks reported by the authors (using a variety of reference categories) are summarized in Table 2. This table includes two sub-cohorts from two papers in which women were stratified according to their age on entry into the study (Kitagawa and Hauser 1973; Manor et al. 2000). Figure 1 shows the recalculated point estimates for risk of mortality relative to women with two births in eight cohorts or age-stratified sub-cohorts. Two studies (Cooper et al. 2000; Smith et al. 2002) are not shown in the figure because they grouped women with two births with other parities.

Overall, relative differences in mortality in these studies are slight (usually less than 20 per cent). The most common pattern in the association between mortality and number of births is that of a u-shaped or reverse j-shaped curve. The mortality of women with no births or one birth shows wide variation but is higher than that of women with two births in six cohorts (Kitagawa and Hauser 1973; Kvale et al. 1994; Doblhammer 2000; Kumle and Lund 2000; Manor et al. 2000). This difference is statistically significant in four of the analyses (Kitagawa and Hauser 1973; Doblhammer 2000; Manor et al. 2000). Six analyses from five populations also show increased mortality in women with the highest number of births (Kitagawa and Hauser 1973; Kvale et al. 1994; Doblhammer 2000; Kumle and Lund 2000; Manor et al. 2000), with only the older sub-cohort in the Kitagawa and Hauser study showing no evidence of a trend in increasing risk. Four of these analyses show statistically significant differences between women with the highest number of births and those with two births (Kitagawa and Hauser 1973; Kvale et al. 1994; Doblhammer 2000; Kumle and Lund 2000). Of the remaining analyses, the study by Fox and Goldblatt (1982) shows an erratic pattern, and there is a slight reduction in risk amongst women with the highest number of births in the older sub-cohort of the study by Manor et al. (2000). In the studies not shown on the graph, one shows little change in risk

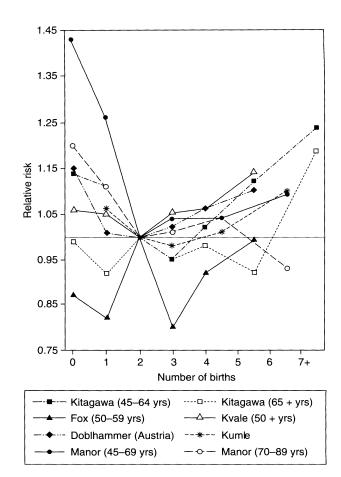


Figure 1 Relative risk of mortality by number of births among women reported in studies of contemporary populations

Notes: The vertical axis has been extended to distinguish between the results of different studies. Groups: Kumle, Manor 4-5; Cooper 5+; Kitagawa 5-6; Kumle, Manor 6+. Studies not included in meta-analysis because relative risks and 95-per-cent CIs using women with two births as the baseline group could not be calculated *Source*: See Table 2.

with increasing number of births (Cooper et al. 2000). The other shows increasing mortality with an increasing number of births, although these patterns are based on wide groupings of the number of births (Smith et al. 2002).

Linear trends in the relationship between mortality and number of births

The results of five studies that looked for linear trends in mortality with each additional birth are summarized in Table 3. The findings are inconsistent. In historical populations, one study shows lower mortality with increasing number of births in 14 of 17 cohorts (stratified by age at and year of marriage) but the differences are small and not statistically significant (Freeman 1935); one finds no significant linear trend (p = 0.56, Helle et al. 2002), and one finds a significant reduction in mortality per birth (Muller et al. 2002, RR per birth 0.986, p for linear trend =0.04). The last study finds a nonsignificant increase in mortality with number of births when all women in a genealogy are included in the models (RR per birth 1.02, p for linear trend =0.24), which becomes significant once analyses are restricted to women with two or more births, although the magnitude of increased risk remains small (RR 1.04, p for linear trend =0.04, Doblhammer and Oeppen 2003). A study of linear trends in a contemporary population (Friedlander 1996) finds no association in women born in the period 1905–29 (p for linear trend = 0.96) but a significant increase in mortality per child in women born in the period 1880-1904 (RR per birth 1.15, p for linear trend = 0.01).

Mean number of children by age at death

Four historical studies and one study using early census data examined the mean number of births by age at death. Mean number of births increases with mean age at death in one cohort (Bell 1918), decreases in one cohort (Korpelainen 2000), increases until age 80 then decreases in one cohort (Westendorp and Kirkwood 1998), and shows no pattern in two cohorts (Dorn and McDowell 1939; Lycett et al. 2000). In the two studies that presented CIs, there are no statistically significant differences (Westendorp and Kirkwood 1998; Lycett et al. 2000, Table 3). Dorn and McDowell (1939) stratified their analyses by age and date of marriage, giving 29 cohorts. The results from the largest are presented in Table 3. In this study, mean number of births increases with age at death in 21 cohorts, but no statistical analyses of these patterns are reported.

Life expectancy by number of births

Two studies in historical populations examined life expectancy from current age by number of births. Arvay and Takacs (1966) find small increases in life expectancy from age 50 with increasing number of births. It is not possible to calculate CIs for these estimates, but their analyses are based on over a million women. Voland and Engel (1989) present the results of their study only graphically. The figures show no association between life expectancy and number of births from age 47, and no statistical tests are presented.

Meta-analysis of the association between number of births and mortality

The pooling of estimates was possible for twelve of the studies in historical populations for which we could obtain relative risks and 95-per-cent CIs compared to the same baseline group of two births. Figure 2(a) shows the pooled relative-risk estimates from these twelve cohorts with the 95-per-cent CI and the p-value for heterogeneity for each estimate. Overall, mortality declines with increasing numbers

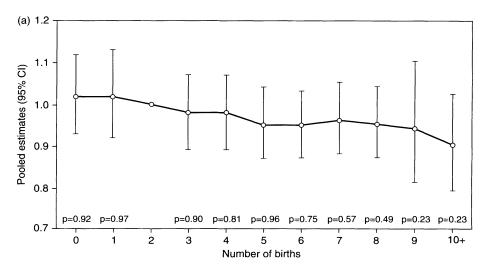


Figure 2(a) Pooled estimates of relative risk of mortality by number of births among women relative to risk for women with two births, in historical populations (with 95-per-cent CIs and p-value for test for heterogeneity) Source: See Table 1.

of births, but no estimate reaches statistical significance. The relative risk of mortality is highest in women with no births (pooled RR 1.02, 95-per-cent CI: 0.93, 1.12), and lowest in women with ten or more births (pooled RR 0.90, 95-per-cent CI: 0.79, 1.02). There is no significant statistical heterogeneity between the studies, and similar results are obtained from the fixed-effects meta-analysis (details not shown).

These summary estimates are dominated by the findings of one large study in a contemporary population (Powys 1905), which shows no association between number of births and mortality. As part of a sensitivity analysis, this study was excluded, and the nature of the association then changes (Figure 2(b)). Mortality is significantly lower among women with no births than among those with two births (pooled RR 0.83, 95-per-cent CI: 0.71, 0.96) and, after two births, declines relatively steadily with increasing number of births, with several statistically significant estimates. For example, mortality in women with ten or more births was 17 per cent lower than in women with two births (pooled RR 0.83, 95-per-cent CI: 0.71, 0.96).

Discussion

The review of individual studies does not reveal consistent associations between mortality and number of births among women who have completed their childbearing. The magnitude of effects in each study is small, and the nature of the association appears to vary by time period or population included. In most contemporary populations, there is either no effect or an increase in mortality at the extremes of the family-size range. In contrast, in the meta-analysis based on data from historical populations and one less developed population, there is some evidence that high fertility confers a survival benefit, although this effect too is small and inconsistent. Studies examining the association in other ways are also inconsistent, and there are no obvious differences between studies in historical and contemporary populations. It is important to note however that linear trends have to be viewed with particular caution since they may hide a u-shaped or j-shaped pattern.

Below, we consider how differences in method between studies, as well as biological and social differences between historical and contemporary populations, may explain some of the inconsistencies we have found (summarized in Table 4).

Limitations of the methods used may explain some of the differences found between historical and contemporary studies. Firstly, given the small differences in mortality risk by number of births and the small numbers at the extremes of family size in individual studies, inconsistencies may be due to random error. In principle meta-analysis could play an important role in establishing a real effect in these studies. However, pooling results was only possible in a sub-sample of studies in which the appropriate relative-risk estimates along with their 95-per-cent CIs were presented, all of which were studies in historical populations. The remaining studies (most of them in contemporary populations) could not be included because they used different

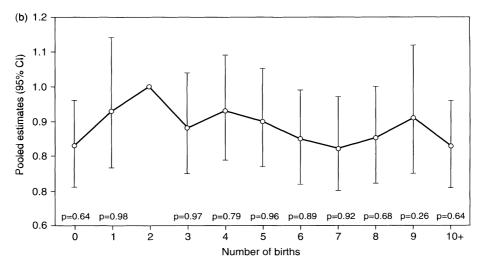


Figure 2(b) Pooled estimates of relative risk of mortality by number of births among women relative to risk for women with two births, in historical populations excluding the study by Powys (1905) (with 95-per-cent CIs and p-value for test for heterogeneity)

Source: See Table 1, excluding the results of Powys 1905.

Historical populations Contemporary populations which control their fertility Methodological factors Random error Random error reduced by pooled results Substantial uncertainty remains because no pooled analysis was possible Residual confounding Underestimated reduction in mortality Effects overestimated, but probably with number of births, but probably has has little impact because most studies little impact because of homogeneous adjusted for important confounders populations Loss to follow-up Unknown Unknown Non-differential misclassification Underestimated reduction in mortality Little impact because misclassification with number of births of exposure less likely Underlying mechanisms Maternal depletion Leads to increased mortality with Less impact because women are number of births, because of poor well-nourished and fertility is low nutrition and high fertility Effects of other reproductive factors Uncertain effects: requires further study Uncertain effects: requires further study Healthy-pregnant-woman effect Leads to reduced mortality with number Leads to reduced mortality with of births; major impact because of number of births; less impact because natural fertility of controlled fertility Social consequences of having children Leads to reduced mortality with number Leads to mixed effects on mortality, of births, because of support in old age because of financial strain but also better care from children Underlying diseases Infectious disease leading cause of death Cardiovascular disease (CVD) leading in women: unknown association between cause of death in women: increasing births and infectious disease mortality CVD mortality with increasing births Selection of women with no live births Increased mortality (illness, social Mixed protective and harmful effects or low parity or both exclusion), but frequently missed from data collection

Table 4 Methodological, social, and biological factors that may explain inconsistencies between historical and contemporary populations in the association between number of births and long-term mortality

groupings of the number of births or because they did not present the data required to recalculate CIs; the results of these studies remain subject to substantial uncertainty.

Secondly, insufficient adjustment for confounding could explain inconsistencies because fertility and mortality share common determinants. Failure to adjust for age, time period, and socio-economic status could result in an overestimation of any positive association between number of births and mortality and an underestimation of protective associations, as poorer women and those of earlier birth cohorts tended to have higher fertility and higher mortality (Chesnais 1992; dos Santos Silva and Beral 1997). Most analyses from contemporary populations took account of these confounders, but the older studies made less use of stratified or multivariate analyses. However, confounding may also be less important in the historical data since study populations were small and relatively homogeneous, and fertility did not decline until the midnineteenth century (Chesnais 1992). In addition, in a

cohort of women who have completed their childbearing, age and parity are unlikely to be associated and age is therefore unlikely to confound the association between parity and mortality. Nevertheless, there may have been some residual confounding in historical populations leading to an underestimation of the effects in these studies.

Thirdly, loss to follow-up may have been a problem, particularly in studies of historical populations that did not rely on census data. Parish records are known to under-report deaths (Bacci and Reher 1993; Bonneuil 1993), because migration from the parish of birth was common (Bideau and Brunet 1993), and because early records were based on burials not deaths (Bacci and Reher 1993). Such losses introduce bias if the association between number of births and mortality is systematically different among those included and those lost. There is no evidence in the literature of systematic errors in registration of deaths in relation to the number of births, but loss to follow-up may have affected study results.

Fourthly, there may be misclassification of the number of births. Literate women in contemporary populations generally report the number of live births accurately (Harlow and Linet 1989; Collaborative Group 2002), but reproductive histories are difficult to determine precisely from illiterate women or from historical data (Chidambaram et al. 1992; Bacci and Reher 1993). Children who died before they were baptized may not be included in parish records (Hollingsworth 1976; Bacci and Reher 1993), and genealogies are known to underreport the number of female children (Freeman 1935; Gavrilov and Gavrilova 1999). A small number of studies (none of which were included in the metaanalysis) also included women from age 40 upwards, and some of these women may have had additional births during the study period. Each underestimation in the total number of births is likely to be nondifferential, particularly as data on births were often collected several years before the data on mortality. Random misclassification may therefore have led to an underestimation of the effects, particularly in the historical studies included in the meta-analysis. This does not, however, explain the apparently different direction in effects between historical and contemporary populations.

Limitations of the methods used do not therefore fully account for the discrepancies between studies, particularly the differences between historical and contemporary populations. We therefore also considered whether the nature of the association between mortality and number of births might vary between populations. Here, we put forward four mechanisms that may mediate the association under study, and examine why historical and contemporary populations may show distinct patterns.

Firstly, it has been suggested that long-term mortality increases with number of births because women become depleted with repeated pregnancies or have no physical resources remaining for the repair of the body (Jelliffe and Jelliffe 1978; Winikoff 1978, 1983; Kirkwood and Rose 1991; Winkvist et al. 1992). The apparent absence of negative longterm effects in historical populations and one less developed population is therefore surprising, because these women were less well nourished and arguably more susceptible to the physical stresses experienced during and after childbearing. However, it has been suggested that maternal depletion is also related to spacing between pregnancies and to length and intensity of breastfeeding, so that merely counting the number of births may not adequately reflect a woman's exposure to the burden of reproduction (Friedlander 1996). Breastfeeding has

positive consequences for the mother, protecting her against haemorrhage immediately after birth (Dermer 1998), and against breast cancer in the longer term (Collaborative Group 2002), but it is also nutritionally demanding (Jelliffe and Jelliffe 1978; Gigante et al. 2001). Its net effect on mortality in the long term is not known. Other reproductive factors may also be important. For example, six studies show that mortality after age 45 was lower in women whose first birth was late (Fox and Goldblatt 1982; Westendorp and Kirkwood 1998; Doblhammer 2000; Korpelainen 2000; Kumle and Lund 2000; Smith et al. 2002). In addition, three studies demonstrate reduced mortality in women whose last births were late (Voland and Engel 1989; Perls et al. 1997; Doblhammer 2000), although another shows increased long-term mortality in older mothers (Cooper et al. 2000). Therefore, the number of births on its own may not be the best measure of the reproductive burden, and differences in additional reproductive factors between historical and contemporary populations may explain some of the variation in the effect of number of births on mortality.

Secondly, it has been suggested that women who are healthy or strong have higher fertility than those who are ill or weak (Beeton et al. 1900; Freeman 1935; Khlat and Ronsmans 2000; Ronsmans et al. 2001). If such a 'healthy pregnant woman effect' coexists with a negative effect of numerous births on mortality, the absence of an association between number of births and mortality is not surprising (Mace 2000). The impact of such a selection effect probably depends on the extent of fertility control available to women, and on current levels of maternal mortality. In historical populations, differences in fertility will usually be due to differences in the health or strength of women. One study using historical data attempted to adjust for differences in health, and found a trend of increasing mortality with increasing number of births after this adjustment (Doblhammer and Oeppen 2003). The protective effects seen in our meta-analysis may therefore suggest that a 'healthy pregnant woman effect' is predominant in these mainly historical data. In contemporary populations, many more of the women studied will have used contraception, although none of the studies give estimates of this. Contracepting women probably have more contact with health services than other women, may be more health conscious, and may also exercise a greater control over other aspects of their life (although this is difficult to quantify). Therefore, the selection of healthy pregnant women may be less likely in these

studies because populations of low fertility include fitter women who have chosen to limit their fertility, and evolutionary theories of trade-offs between childbearing and mortality may not apply to such populations. In addition, when maternal mortality is high, those most vulnerable to the risks of repeated pregnancies may die before they reach the age of 45. For example, in rural Bangladesh, whilst mortality among women of reproductive age has been shown to remain elevated for several years after giving birth, there is no significant association between parity and mortality in women aged 55 and above (Menken et al. 2003).

Thirdly, having a large family may confer a survival benefit on women in historical or less affluent populations. Having many children was the norm in historical populations and has been so in less developed populations such as Bangladesh (Sirageldin et al. 1975; Chesnais 1992). Children were needed for support in old age (Aziz and Mosley 1994; Rahman 1998), and mortality in such situations has been shown to fall with an increasing number of surviving children (Tucker et al. 1999; Hurt et al. 2004). In contemporary populations with low fertility, large families may be a burden rather than a benefit owing to the stress of caring for them (D'Elio et al. 1997), increased financial strain, and deterioration in the quality of the parents' relationship (Ross et al. 1990). These effects may partially explain the small increases in mortality among contemporary women with a high number of births. However, studies examining the effects of women's multiple roles have found little evidence of 'role strain' among modern mothers (Kotler and Wingard 1989; Macran 1993; Martikainen 1995; Waldron et al. 1998), and inconsistencies between contemporary studies in the association between mortality and many births may arise because children also bring positive benefits to contemporary parents. For example, the likelihood of receiving care from children increases with number of children (Spitze and Logan 1990), and total hours of care received increase with total number of living children (Wolf 1994). In populations where these social effects are important, the benefits of surviving children or children living at home may therefore mask a negative physiological effect of bearing children, and further studies are needed to examine how such variables interact.

Fourthly, the number of births is known to be associated with the risks of developing specific diseases, and the underlying burden of disease in different populations may affect the relationship between fertility and mortality. Systematically exam-

ining the large literature on the association between number of births and mortality from specific causes was beyond the scope of this review. However, studies relating number of births to infectious diseases such as pneumonia and tuberculosis have generally been inconclusive (Lim et al. 2001; Ormerod 2001), and we do not know how number of births may have been related to disease-specific mortality patterns in populations where infectious diseases were the main cause of death. Mortality from cardiovascular diseases, on the other hand, increases with increasing births (Pike 1987; Ness et al. 1994). Cardiovascular deaths now account for more deaths of women in England and Wales than breast, endometrial, and ovarian cancers combined (Griffiths and Brock 2003). Thus, the increases in mortality with increasing numbers of births in later studies may reflect levels of cardiovascular disease within these populations.

Women with very few or no births are a distinct group in both historical and contemporary populations. In the former, they included women who were too ill to conceive or who were ostracized owing to their inability to have children (Poston and Kramer 1983; Poston et al. 1983). It is therefore surprising that the meta-analysis indicates that they have lower mortality than women with two children. Women with no births are frequently missed from datacollection systems because childless women are not asked to give their reproductive histories or are not thought important enough to include in historical records. However, this would lead to a systematic bias only if deaths were less likely or more likely to be recorded in this group than among other women (Freeman 1935; Hurt et al. 2004). It is also possible that the illnesses associated with low fertility also lead to early death, so that many women of low fertility died before the age of 40 and are therefore excluded from these analyses. In contemporary populations, the childless include individuals who have never married or whose marriage has broken down (Kiernan 1989), which may explain why some have higher mortality. On the other hand, they are better educated (Kiernan 1989; dos Santos Silva and Beral 1997), more financially secure (Rempel 1985), and may feel more in control of their lives than do women with children (Rubinstein 1987), and these factors may explain why childless women do not consistently have higher mortality in the contemporary populations. Finally, fertility treatments have also become more readily available, although most of the cohorts included in this review had completed their childbearing before the widespread introduction of these treatments. The treatments increase the

parity of women who would otherwise be nulliparous or of low parity, and their impact will need to be considered in future studies of this association.

Conclusion

This review does not reveal a consistent pattern in the association between mortality and number of births among women who have completed their childbearing. The degree to which conventional observational epidemiology can assess the effects of number of births is limited by substantial obstacles-selection bias, measurement imprecision, confounding, and the small size of the excess risks. However, improvements can be made. For example, two recent studies have attempted to determine whether biological or social factors predominate in any given population by comparing associations among women with those among men (Smith et al. 2002; Hurt et al. 2004), because men are not subject to the physiological stresses of childbearing but may experience socio-economic benefits from their children (Kravdal 1995). Both studies found no effects of number of births among men, but further comparisons which allow for the examination of the mechanisms involved are needed. Another approach is to assess the separate contribution of various reproductive factors on long-term mortality, and examine whether they interact. In addition, future studies need to examine further how health status affects fertility or to incorporate into the analyses measures of health status during the fertile years in order to quantify the impact of the selection of healthy pregnant women on results.

The results of this review do not contradict the parity-specific relationships with mortality during pregnancy. However, they do suggest that there may be no negative long-term effects of parity on mortality. They also suggest that the effect of number of births may differ between populations, both because of prevailing fertility patterns and because of the way in which these interact with selection factors in the populations under study.

Notes

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