Research supported by the European Research Council Grant Number 324055

Do short birth intervals have long-term implications for parental health?

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Introduction

Short inter-pregnancy intervals are known to be adversely associated with perinatal outcomes and child survival in low-income countries (Cleland et al 2012) and the World Health Organization recommends an interval of at least 24 months from a live birth to the start of the next pregnancy (WHO 2006). Studies from a number of richer countries have also found associations between short (and very long) birth intervals and adverse birth outcomes (Auger et al 2008; de Weger et al 2011; Hogue et al 2011; Nabukera et al 2008; Zhu 2005). Inter-pregnancy or inter-birth intervals have additionally been associated with maternal outcomes in both poor and richer societies, again with some indication of a U shaped association (Cardwell et al 2012; Conde-Agudelo et al 2007; Razzaque et al 2005). However, results are less clear cut than for infant outcomes and have been disputed (Dewey and Cohen 2007; Ronsmans and Campbell 1998; Wendt et al 2012).

Reasons underlying these associations are hypothesised to include important pathways through maternal depletion and nutritional status and whether there is sufficient time to lose weight gained during pregnancy and return to the normal pre-pregnancy metabolic state (King 2003). Consistent with this, one study of Dutch mothers found evidence of modification of effects by folic acid use (van Eijsden et al 2008) and a recent prospective United States study found that risks of maternal obesity increased substantially with each inter-pregnancy interval of <12 months (Davis et al 2013).

In addition to specific physiological mechanisms, short birth intervals may lead to other forms of stress for both children and parents arising from the difficulties involved in meeting the needs of two or more young children close in age. Mothers of twins, for example, suffer from higher rates of post

natal depression than mothers of singletons (Choi et al 2009; Savitz et al 2011; Ross et al 2011) and there is some evidence that multiple births are associated with higher risks of subsequent divorce (Jena, Goldman and Joyce 2011). Similar, if less marked, effects might apply to parents of closely spaced singleton children.

Nearly all studies of associations between birth or inter-pregnancy intervals and parental health have considered only short term effects on mothers. However, given what is known about the importance of accumulated life course effects on health in mid and later life, short intervals might also be expected to have longer term implications. Support for this hypothesis comes from two recent studies from the UK which have reported associations between experience of one or more short birth intervals and higher mortality risks for mothers at ages over 50 (Grundy and Tomassini 2005) and between short birth intervals and faster acquisition of health limitations among mothers and fathers in late mid-life (Read, Grundy and Wolf 2011).

In this study we add to the small literature on possible long-term health implications of short (and very long) birth intervals using register data for complete Norwegian cohorts born 1935-1968. We consider both women and men as this may provide insights into the extent to which any associations reflect long term physiological consequences for women or broader biosocial effects relevant to both mothers and fathers. We analyze associations between birth interval lengths and mortality at ages over 40 and also use linked data on purchase (encashment) of prescribed medications to investigate associations between birth interval length and morbidity.

Methods

The study is based on data from the Norwegian Central Population Register which was established drawing on the 1960 Census and has been continuously updated. All Norwegian residents are included in the register and are assigned a personal identification number used in all dealings with official agencies. Other registers using the same identification number include an Educational Database and, since 2004, the Norwegian Prescription Database (NorPD; Furu et al. 2010). This includes records of all purchases of prescription medicine (defined by Anatomical Therapeutic Code (ATC) codes) by all Norwegian residents, except for those in health care institutions.

We include all men and women born between 1935 and 1968. For these cohorts almost complete maternity and paternity histories can be assembled as parents' identification numbers have been recorded at registration of births since 1965 and children born earlier can be linked to their parents using information collected in the 1970 Census. We analyze mortality at ages 40 and over, when women have very largely completed their childbearing, for the period 1980-2008 and purchase of prescription medicine during the period 2004-2008. Because everyone included in the analysis was born in 1935 or later and the last possible year of observation is 2008, the oldest age considered is 73. As the variable of interest is birth interval length, those with only one child are excluded. We also

excluded the small proportion of parents (5%) who had had five or more children in order to simplify the analysis.

There is no agreement about how to construct health indicators from medication data. In this analysis, we used the total number of different medicines purchased (defined as the first 4 ATC digits being different) and the total number of diseases using Kuo et al.'s (2011) identification (based on ATC codes) of 32 diseases treated by drugs uniquely prescribed to treat these diseases.

Inter-birth intervals

In the main mortality analysis, birth interval length (in months) was grouped into seven categories denoting at one end of the distribution multiple births and at the other intervals of 90 or more months. We undertook separate analyses of associations between mortality and the length of the first and the length of the last birth interval, but focus mainly on the former as over half of the study population had had only two births. For data protection reasons only year, not month, of births was available for the analysis of medication purchase and for this analysis we therefore categorized birth interval lengths in years, ranging from less than 1 (including multiple births) to seven or more.

Co-*variates*

In all analyses we included current age and period (in five year groups) as these are strongly associated with health and mortality risk and also, in combination, capture period and cohort variations in the fertility patterns of those included in the study. Current educational level and marital status are included in all models as these are associated with health and with the corresponding earlier characteristics which are likely to have also influenced fertility patterns. In a separate step, we additionally include controls for age at first birth and the total number of children born. Previous studies have shown that both are associated with mortality risks in late mid and early old age and they are also likely to be associated with birth interval lengths (for example, women who start childbearing at older ages may seek to compress subsequent birth intervals), or may be jointly determined with the birth interval (i.e. there are common determinants of all these elements of reproductive trajectories). The length of the birth interval also has *implications* for completed fertility, so by including the latter variable we leave out that part of the (potentially) causal effect of birth intervals. Re-partnering after partnership disruption may be associated with particularly long birth intervals and partnership disruption is known to be associated with later health. In a final step, we therefore included change of co-parent over the birth interval as an additional indicator of family situation. This variable was defined as 1 (yes) if the personal identification numbers of the two relevant parents were different or if one or both was missing. All variables refer to the situation at the beginning of each one-year observation period (see description of method below), or are by definition constant.

Statistical analysis

Mortality analysis:

Discrete time hazard models were estimated for the period 1980-2008 following standard procedures (Allison 1984). A series of one-year observations was created, starting in January the year the person turned 40 or, for those born 1935-39, from the beginning of 1980. The last observation was the year of death, the year of emigration or 2008, whichever came first. After further excluding observations relating to temporary absences abroad, sex-specific logistic models were estimated from all observations using the Proc Logistic procedure in the SAS software suite. In the period considered, fewer than 2% of men and 1% of women died before age 40 so those included in the study constitute the vast majority of their respective birth cohorts (Statistics Norway 2013).

Analysis of prescription drug purchase:

We estimated OLS models of drug purchases, and number of diseases inferred from these purchases, during the period 2004-2008 for women and men who were 40-69 in 2004 (i.e. born 1935-1964) and alive and in the country in 2004 and at the end of 2008. This data design resembles that used in the mortality analysis, and further comparability was achieved by estimating supplementary mortality models for the years 2004-2008 with a similar definition of birth intervals.

Results

Mortality analysis

Table 1 shows the number of deaths and the distribution of exposure time across categories of length of interval between the first and second birth and other variables used in the analysis. 1% of those who had had two or more children had a twin or multiple birth first, and a further 10% had a first inter-birth interval shorter than 18 months. 18% had intervals longer than 5 years and about half had intervals of 18-29 or 30-41 months.

Table 2 shows estimates from three models of variation in mortality associated with the length of the first or last inter-birth interval. Model 1 includes age, period, education, and marital status; Model 2 additionally includes age at first birth and parity; and Model 3 also the indicator of change in co-parent between the first and second, or penultimate and last birth.

Short birth intervals and mortality

Relative to those with intervals of 30-41 months between births (a range including the WHO recommended interval), results from Model 3 show that for mothers twin first maternities were associated with an excess mortality risk of 15%; among mothers whose last maternity was multiple

the excess was 21%. There was no such elevated mortality among fathers of twins, though the point estimates go in the same direction. Other first and last birth intervals of less than 18 months were associated with higher mortality risks of 12-13% among women and 16-17% among men; mortality of mothers and fathers with a last interval of 18-29 months, and that of fathers with a first interval of this length, were also slightly raised in comparison with the reference group. Results from Model 2 (not including change of co-parent) and Model 1 (not including other fertility history variables) were very similar to those from the fully adjusted model except that the association between a twin birth and female mortality was slightly stronger in models including other fertility variables (Models 2 and 3) than in Model 1.

Very long birth intervals and mortality

In the case of associations between very long intervals and mortality risks, results from different models showed different patterns of association. In Model 1 and to a lesser extent Model 2, the association between first inter-birth intervals of 90+ months and mortality risk was positive but a high proportion of these parents (47% of men and 43% of women) had experienced a change a co-parent and when this variable was included (Model 3) the direction of the association changed and became negative. Similarly first inter-birth intervals of 60-89 months were positively associated with mortality in Model 1 (and Model 2 for mothers) but not significantly raised in Model 3. Very long (90+ months) last birth intervals were negatively associated with mortality in Model 3 (and for women, in Model 2), but showed no significant association with mortality risk in Model 1.

Associations between other co-variates and mortality risks were all in the expected direction. Mortality risks increased with age and decreased with period of observation and years of education. Consistent with other research on the Norwegian population, (Grundy and Kravdal 2008, 2010) they were raised for non-married groups, particularly the divorced, and reduced with older age at first birth and higher parity (within the range 2-4). As already implied, they were significantly raised among those who had their second child with a different co-parent from the first child (OR for women 1.33 (1.27-1.39); for men 1.24 (1.19-1.29)).

Purchase of prescription medicine, and number of associated diseases, 2004-8

Table 3 shows results of analyses of associations between first inter-birth interval length and annual number of different prescription drug purchases 2004-8 and number of inferred diseases. For comparison purposes, results from mortality analyses conducted as before but relating only to deaths 2004-08 and including classification of birth intervals in years, rather than months, are also shown. Results are from models equivalent to Model 3 in the mortality analysis and include all the same co-variates (except period of observation). Results show a positive association between short first inter-

birth intervals and both drug purchase and inferred number of diseases. A very long birth interval is associated with fewer purchases of medicine, and, for women, fewer diseases.

The excess mortality among those having two children in the same or two successive years is of roughly the same magnitude for men, but rather lower for women, as the excess mortality among those with a first interval shorter than 18 months previously shown in Table 2. However, results did not show the same low mortality for those with long birth intervals as found in the fully adjusted model in the main analysis. Supplementary analyses, not shown, indicate that these differences are more the result of the restriction to 2004-2008 than the use of intervals grouped in years rather than months.

Discussion

Most previous studies of the implications of birth interval lengths for parental health have focused on short term implications for maternal health with little attention to possible long-term health consequences for both mothers and fathers of having closely spaced children. Our results suggest long term adverse effects of inter birth intervals of less than 18 months for both women and men, and for women additionally adverse effects of multiple births. The analysis of purchases of prescription medicine accords with the mortality analysis, in that it suggests an association between short birth intervals and later health. These results are consistent with two previous studies (Grundy and Tomassini 2005; Read et al 2011) conducted using data from UK populations which also reported positive associations between short birth intervals and women's mortality, and between short birth intervals and later life health impairment among women and men. Neither of these studies was large enough to allow separate analysis of possible effects of twin births. Our results on associations between twin maternities and later mortality are less consistent with previous studies. Tomassini et al (2006) for example, found no significant raised mortality after age 45 among mothers of twins in England & Wales or mothers and fathers of twins in Denmark. However, it was not possible in that analysis to control for socio-economic status or other potential confounders.

Previous research on possible health consequences of very long birth intervals has been inconclusive although it has been suggested that very long intervals may lead to physiological regression among mothers such that the 'priming' effect of previous births is lost and risks of pregnancy and delivery revert to those associated with primigravidae women (Conde-Agudelo et al 2012). We have been unable to identify any previous studies which have examined possible long-term consequences of very long birth intervals with which to compare our results. These showed that, taking account of whether or not there had been a change of co-parent (linked to high mortality), very long intervals were generally associated with lower mortality and prescription drug use; however if this variable was not included, associations between very long birth intervals and mortality went in the other direction.

Overall the rather similar effects we observe for mothers and fathers in our analysis– except in the case of parents of twins- suggest that biosocial mechanisms may underlie linkages between birth interval lengths and mortality and health in mid and later life. Plausibly these might include the results of accumulated stress arising from the demands of having closely spaced births and raising children close in age. Our analyses were undertaken using high quality data from a complete population and therefore there is little risk of bias from non-response or attrition as might be in the case in survey based studies. However there are some limitations of this study. The data on prescription drug use is only available for a four year period and inferences about morbidity based on drug use maybe flawed. Additionally the analysis excludes those in medical institutions, although in the age groups we consider here this proportion is very small. More importantly, we lacked the kind of detailed information collected across the lifecourse that would enable elucidation of possible pathways from birth intervals of particular lengths to later life health outcomes taking account of a wider range of factors that may confound reported associations.

The question we addressed in this paper has been neglected in the literature, even though it is potentially a very important public health issue, probably more so in poorer countries than in Norway, and the effects we found in our mortality analysis were large. . Further work using more detailed data sets for other populations is warranted.

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Table 1. Number of deaths and distribution (%) of exposure time in different categories, men and women born 1935-1968 and aged 40-73 in 1980-2008 who had had 2-4 children

		Men		Women	
		Deaths	% of exposure time	Deaths	% of exposure time
Period	1980-84	1378	5.7	757	5.5
	1985-89	3180	10.6	1871	10.4
	1990-94	5151	15.5	3207	15.3
	1995-99	8212	20.2	5363	20.2
	2000-04	12018	24.8	8321	25.0
	2005-08	13348	23.2	9213	23.6
Age group	40-44	4006	27.5	2717	28.0
	45-49	6186	24.8	4084	24.5
	50-54	7564	19.5	5060	19.2
	55-59	8498	14.2	5802	14.1
	60-64	8583	8.9	5529	8.9
	65-69	6310	4.2	4087	4.3
	70-73	2140	1.0	1453	1.1
Education (Years)	10	15227	23.7	12483	29.5
	11-13	20083	46.8	12256	46.9
	14-17	5838	20.3	3617	21.0
	18+	2139	9.2	376	2.6
Marital status	Never-married	882	2.6	447	2.6
	Married	29304	81.4	18587	76.5
	Widowed	1383	1.2	3036	4.5
	Separated/divorced	11718	14.8	6662	16.4
Number of children	2	22112	53.9	14736	53.1
	3	15093	34.7	10015	35.1
	4	6082	11.4	3981	11.8
Age at first birth	<20	1485	2.5	5187	13.6
	20-22	9035	16.5	9932	30.8
	23-25	13225	28.3	7205	26.8
	26-28	9910	25.0	3838	16.4
	29-31	5381	14.9	1616	7.6
	32-34	2455	7.4	661	3.1
	35-37	1027	3.4	222	1.2
	38+	769	2.1	71	0.4
Interval between 1st	0 (twin)	385	1.0	266	1.0
	1-17	6069	10.0	3717	10.3

and 2nd birth (months)	18-29	11436	25.8	7480	26.0
	30-41	9602	24.6	6444	24.2
	42-59	8052	20.5	5492	20.5
	60-89	4766	11.3	3423	11.5
	90+	2977	6.7	1910	6.4
Change of co-parent	No	40132	93.8	26160	93.0
	Yes	3155	6.2	2572	7.0

Table 2. Odds Ratios and 95% confidence intervals from discrete-time survival models of associations between length of first or last inter-birth interval and mortality 1980-2008, men and women born 1935 -1968 and aged 40-73 with 2-4 children.

		MEN			**WOMEN**		
		Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Interval	0 (multiple)	1.01 (0.97-1.12)	1.05 (0.94-1.16)	1.05 (0.95-1.16)	1.11 (0.98-1.25)	1.14** (1.01-1.29)	1.15** (1.01-1.30)
between 1st	0>18	1.18*** (1.14-1.22)	1.17 ***(1.13-1.21)	1.17*** (1.13-1.21)	1.10***(1.06-1.15)	1.12*** (1.07-1.16)	1.13*** (1.08-1.17)
and 2nd	18-29	1.04*** (1.02-1.07)	1.05*** (1.02-1.08)	1.05*** (1.02-1.08)	1.01 (0.97-1.04)	1.02 (0.98-1.05)	1.02 (0.99-1.06)
birth	30-41	1	1	1	1	1	1
(months)	42-59	1.01 (0.98-1.04)	0.99 (0.96-1.02)	0.99 (0.96-1.02)	1.00 (0.96-1.03)	0.98 (0.94-1.02)	0.97 (0.94-1.01)
	60-89	1.06*** (1.02-1.09)	1.03 (0.99-1.02)	1.01 (0.97-1.00)	1.08*** (1.03-1.12)	1.05** (1.00-1.09)	1.01 (0.97-1.06)
	90+	1.11*** (1.06-1.15)	1.06** (1.01-1.10)	0.96 (0.92-1.01)	1.11*** (1.05-1.16)	1.05 (1.00-1.11)	0.95 (0.90-1.00)
Interval	0 (multiple)	1.02 (0.94-1.10)	1.04 (0.97-1.13)	1.05 (0.97-1.13)	1.14*** (1.04-1.25)	1.20*** 1.10-1.32)	1.21***(1.10-1.32)
between	0>18	1.18*** (1.13-1.22)	1.16*** (1.11-1.21)	1.16 *** (1.11-1.20)	1.13*** (1.07-1.18)	1.12*** (1.07-1.18)	1.12***(1.07-1.17)
penultimate	18-29	1.08*** (1.05-1.12)	1.08*** (1.05-1.11)	1.08*** (1.05-1.12)	1.06*** (1.02-1.10)	1.06*** (1.02-1.10)	1.06***(1.02-1.10)
and last	30-41	1	1	1	1	1	1
birth	42-59	1.00 (0.97-1.03)	0.99 (0.97-1.02)	0.99 (0.96-1.02)	0.99 (0.95-1.02)	0.98 (0.95-1.02)	0.98(0.94-1.02)
(months)	60-89c	1.01 (0.98-1.04)	1.00 (0.96-1.03)	0.98 (0.95-1.02)	0.99 (0.98-1.04)	0.99 (0.95-1.03)	0.97 (94-1.01)
	90+	1.02 (0.99-1.06)	0.99 (0.96-1.02)	0.92*** (0.88-0.95)	0.98 (0.94-1.02)	0.96 (0.97-1.01)	0.89*** (0.85-0.93)

** p<0.05; *** p<0.01

Model 1: age; period; educational level; marital status. Model 2: + age at first birth; parity. Model 3 :+ change in co-parent since last birth.

Table 3. Associations between the length of the first birth interval (in years) and mortality 2004-8 (ORS 95% CIs from discrete time hazards models) or indicators of use of prescription medicine (coefficients and standard errors from OLS regression models) 2004-8, men and women born 1935 -1968 and with 2-4 children

	Birth interval (years)	**% in category[a]**	**OR (95% CI) of mortality**	**Number of different medicines purchased**	**Total number of diseases**
Men	0-1	10.8	1.14*** (1.08-1.21)	0.300*** (0.029)	0.141*** (0.011)
	2	24.5	1.05*** (1.00-1.10)	0.073 (0.023)	0.045*** (0.009)
	3	24.7	1	0	0
	4	15.8	0.95 (0.90-1.01)	-0.011 (0.026)	0.017 (0.010)
	5-6	13.6	1.00 (0.95-1.06)	-0.012 (0.027)	0.018 (0.010)
	7+	10.5	1.01 (0.95-1.08)	-0.026 (0.033)	0.001 (0.013)
Women	0-1	11.1	1.07*** (1.00-1.14)	0.129*** (0.034)	0.092*** (0.011)
	2	24.6	1.03 (0.97-1.09)	-0.004 (0.027)	0.020*** (0.009)
	3	24.3	1	0	0
	4	15.8	0.95 (0.89-1.01)	0.032 (0.030)	0.013 (0.010)
	5-6	13.8	1.02 (0.95-1.11)	0.050 (0.032)	0.027*** (0.010)
	7+	10.4	0.97 (0.90-1.04)	-0.121*** (0.037	-0.021 (0.012)

Notes: The following variables measured in the beginning of 2004 were also included: age, education, marital status, number of children, age at first birth, and whether there has been a change of co-parent.

[a] in the drug analysis

** p<0.05; *** p<0.01