

Is fecundability associated with month of birth? An analysis of 19th and early 20th century family reconstitution data from The Netherlands

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The relationship between fecundability and month of birth was investigated in a cohort of 1526 women who married between 1802 and 1929, using only women whose first marriage occurred before the age of 35 years. On the basis of their time to pregnancy (TTP, calculated as time between wedding and first birth minus gestational length), women were categorized into two groups: fecunds (TTP up to 12 months or prenuptial conceptions, $n = 1348$) and subfecunds (TTP >18 months, $n = 118$). By use of logistic regression, cosinor functions with a period of 1 year or 6 months and variable shift and amplitude were fitted through the monthly odds of subfecunds versus fecunds. The best fitting curve was unimodal, with a zenith in September ($P = 0.13$ for H_0 : no differences). Exclusion of childless women ($n = 36$, minimum follow-up 5 years) from the subfecunds led to a similar curve ($P < 0.01$), while childless women, as compared with fecunds, showed a birth distribution that was best represented with a bimodal curve with zeniths in January and July ($P = 0.06$). This study provides evidence for the existence of differences in fecundability by month of birth. The cause of this relationship is unclear, but may lie in a melatonin-dependent circannual variability of the quality of the oocyte.

Key words: fecundability/month of birth

Introduction

Since the female reproductive system, like other organ systems, develops during the prenatal period, impairments of its extra-uterine functioning may be the result of influences before birth. Several kinds of prenatal exposure have been shown to affect female fecundity, among others, cigarette smoke (Baird and Wilcox, 1986), low doses of X-rays (Meyer and Tonascia, 1981), diethylstilbestrol (Herbst *et al.*, 1980; Senekjian *et al.*, 1988) and maternal famine (Lumey, 1992). Indirect evidence suggests that female fecundity may also be prenatally affected by seasonal factors. Various reproductive characteristics have

been reported to be associated with month of birth, such as early menarche and menstrual disorders (Jongbloet *et al.*, 1994), menstrual cycle length (Nakamura *et al.*, 1987), sex ratio of offspring (Nonaka *et al.*, 1987; Miura *et al.*, 1983), twinning (Miura *et al.*, 1984; Nonaka *et al.*, 1993), seasonality of birth of offspring (Nonaka *et al.*, 1990) and early or late menopause (Jongbloet *et al.*, 1994).

Fecundability, i.e. the risk of conception per month or menstrual cycle, has not yet been addressed as the primary outcome in studies of the relationship between month of birth and reproductive characteristics. Fecundability cannot be measured directly, but population distributions of time to pregnancy are usually considered to be the result of the operation of mixed couple fecundabilities. Therefore, time to pregnancy has been widely applied in studies of the determinants of differential fecundability (Fédération CECOS *et al.*, 1982; Baird and Wilcox, 1985; Baird *et al.*, 1986; Weinberg *et al.*, 1989; Bracken *et al.*, 1990; Joesoef *et al.*, 1990; Van Noord-Zaadstra *et al.*, 1991; Schaumburg and Boldsen, 1992; Alderete *et al.*, 1995; Stolwijk *et al.*, 1996).

In the present study, we investigated the relationship between fecundability (as estimated on the basis of time to pregnancy, TTP) and month of birth. For this purpose, we used family reconstitution data of a population in The Netherlands in the 19th and early 20th centuries. Time to pregnancy was measured in this population with virtually no contraception, by use of the interval between wedding and first birth.

Materials and methods

The technique of family reconstitution, developed 40 years ago by the French demographer Louis Henry, is a method that involves putting together data on birth, marriage, and death from civil and parish registries with respect to individual marriages. The 1622 family reconstitutions available for the present study were based on existing genealogies of 51 families inhabiting two adjoining polder regions in the heart of The Netherlands (Alblasserwaard and Vijfheerenlanden) between 1802 and 1929 (year of wedding). As far as possible, all genealogies had been checked for completeness and accuracy of information. If necessary, the original sources in the civil registration were reconsulted.

In the homogeneously Protestant (Calvinist) population inhabiting our study region, a relatively high rate of enforced marriages was seen, i.e. marriages contracted because of pregnancy. There may be several psychological, sociological and economic reasons for this phenomenon (Miedema, 1989), though probably no biological ones, in the sense that fecundity would be higher in this population. Yet, couples with enforced marriages probably were more fecund than others, not only because they were demonstrably able to conceive, but also because others may have had the same prenuptial sexual behaviour but without a pregnancy as a consequence.

Time from wedding to first pregnancy (TTP, in months) was calculated by subtracting a fixed gestational length from the interval between the wedding and first birth (in days) and dividing this by the mean length of one calendar month (30.4 days). Gestational length was estimated at 266 days in cases of a live birth (Zink, 1988) and 14 days shorter in cases of a stillbirth (Kline *et al.*, 1989). Thus, a TTP of 5 signifies that the first conception was calculated to have occurred within the fifth month after the wedding. A negative TTP means that the conception was considered to have occurred pre-nuptially.

On the basis of their TTP, couples were categorized into fecunds and subfecunds. As an aid in defining TTP limits for these categories, we modelled conception-free survival for couples with positive TTP by use of a function that describes a two-point mixture of exponentials (Heckman and Walker, 1990). This means that the distribution of TTP was assumed to be determined by the simultaneous operation of two groups with different (but constant) fecundability. With the help of this model, it was possible to calculate the specificity of the two categories with varying TTP limits. Couples with prenuptial conceptions were then added to the fecund category, for it may reasonably be argued that the irregular nature of premarital sexual intercourse strongly selected the most fecund for conception.

Follow-up was defined as the shortest time interval between the wedding date and one of four events: (i) death of wife (minus 266 days), (ii) death of husband, (iii) end of marriage due to reasons other than death of spouse and (iv) woman reached 45th birthday. We excluded couples with a follow-up of <5 years who did not conceive before the end of follow-up. In addition, second and later marriages (of the wife) were excluded, and so were women who married after age 35 years, to limit the number of marriages that were childless because of early menopause.

Our main analysis was directed at determining whether the risks of subfecundity connected with each month of birth followed a seasonal pattern. Our choice of a detection method for a seasonal pattern was directed by the assumption that any potential environmental determinants would follow smoothed, sinoid variations across the year, as is the case with daylight and temperature. The χ^2 -test is not an appropriate method for detecting such patterns, because it may react to any departure from a straight line, and, as it takes no account of the ordering of the monthly rates, may not be sensitive for small, but meaningful, smoothed variations (Edwards, 1961). Instead, we modelled the observed annual risk pattern, as expressed by the odds of subfecundity versus fecundity, by a cosinor function in logistic regression (which allowed us to control simultaneously for cofactors). This method is an adaptation for logistic regression of a method proposed by Edwards (1961) and modified by others (Cave and Freedman, 1975; Walter and Elwood, 1975; Roger, 1977; Jones *et al.*, 1988; Reijneveld, 1990). A brief technical description of the method is given in the Appendix. Two types of cosinor functions were fitted, one with a period of 1 year (unimodal) and one with a period of 0.5 year (bimodal); the latter may be relevant if change in the occurrence of a seasonal factor, e.g. hours of daylight, is the risk determinant. Next, we assessed the degree to which the two cosinor functions, calculated by logistic regression, gave a good description of the data, and the function with the better fit was eventually presented.

Results

In total, 1622 family reconstitutions were available, of which 1526 remained after exclusion of non-first marriages ($n = 39$), weddings after age 35 years ($n = 51$) and childless couples with a follow-up of <5 years ($n = 13$). The distribution of TTP in this group, and within the subgroup of couples who

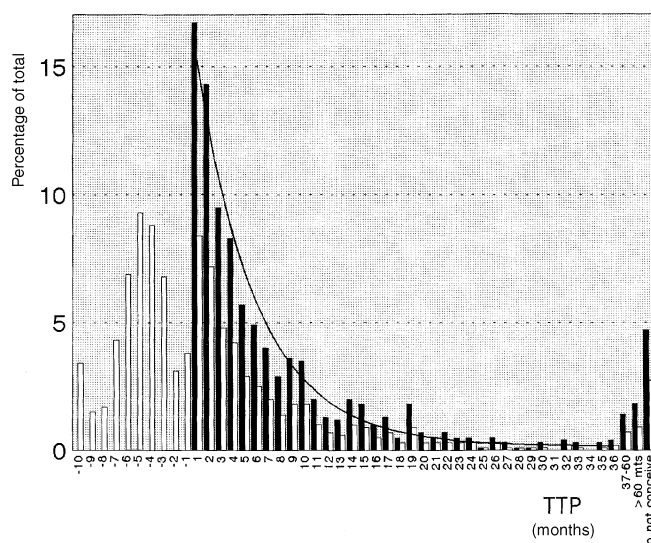


Figure 1. Distribution of times to pregnancy (TTP) for total study population (white bars, $n = 1526$) and for couples with postnuptial conceptions (including childless; black bars, $n = 773$), and predicted distribution of TTP on the basis of the function $S(t) = 0.825(e^{-0.200t}) + 0.175(e^{-0.019t})$ (solid line).

conceived postnuptially, is depicted in Figure 1. Couples with prenuptial births were assigned a TTP of -10 . The first peak of the graph roughly represents conceptions that led to enforced marriages. The 5-month time gap between conception and marriage was the result of at least three delaying factors: the time from conception to the woman's perception that she was pregnant (at least 1 month), additional time before the social environment was informed about this, and a time period (at least 2 weeks) from legal engagement to marriage. The second peak can be ascribed to nuptial conceptions. In all, 758 (49.7%) of the couples had conceived prenuptially. Of the remainder, 50% conceived within 5 months after marriage, and 36 (4.7%) remained conceptionless during follow-up. Mean follow-up was 17.8 years in all couples and 18.2 years in couples with non-negative TTP.

The conception-free survival calculable from the TTP distribution of those who did not conceive before marriage was modelled by the function:

$$P [TTP > t] = 0.825e^{-0.200t} + 0.175e^{-0.019t}$$

in which t = number of months passed since the wedding. The fit of this model was adequate as measured by a χ^2 goodness-of-fit test ($P = 0.09$) (Heckman and Walker, 1990). According to this model, 82.5% of the couples had a fecundability of 20.0%, while 17.5% of them had a fecundability of 1.9%. On the basis of the model, we calculated the TTP distribution for couples not conceiving before marriage (see solid line in Figure 1). It was calculable with the model that, of the couples conceiving within the first year of marriage, ~95% derived from the group with a fecundability of 20.0%, while among those not having conceived within 1.5 years, ~85% were from the group with a fecundability of 1.9%. These limits were maintained as upper and lower limits for 'fecunds' and 'subfecunds' respectively, with fecunds including

Table I. Distribution of co-variables in fecunds and subfecunds

	Fecunds (<i>n</i> = 1348) (TTP ≤12 months)		Subfecunds (<i>n</i> = 118) (TTP >18 months)	
	<i>n</i>	%	<i>n</i>	%
Age at wedding (years)				
15–20	247	18.3	10	8.5
21–25	741	55.0	59	50.0
26–30	284	21.1	36	30.5
31–35	76	5.6	13	11.0
Year of birth				
1781–1825	306	22.7	27	22.9
1826–1850	346	25.7	28	23.7
1851–1875	371	27.5	32	27.1
1876–1906	325	24.1	31	26.3
Year of wedding				
1802–1825	90	6.7	4	3.4
1826–1850	226	16.8	23	19.5
1851–1875	353	26.2	28	23.7
1876–1900	362	26.9	32	27.1
1901–1929	317	23.5	31	26.3
Husband's occupation				
Physical separation	303	22.5	17	14.4
Other	1044	77.5	101	85.6
Unknown	1		29	

TTP = time to pregnancy.

couples who conceived prenatally. The resulting numbers in the two groups were 1348 for fecunds and 118 for subfecunds.

Table I shows the distribution of covariables in fecunds and subfecunds. Women from fecund couples were generally married at a younger age, mainly due to the high proportion of women with prenuptial conceptions (23.1% of whom were under 21 years of age at marriage). They were born and married in somewhat earlier years. Strikingly, husbands from fecund couples more often had occupations at marriage associated with a potentially reduced coital frequency due to physical separation of the spouses (fishermen, commercial travellers and casual labourers). (In 30 couples, the husband's occupation was unknown, 29 of which were in the group of childless couples; it is unclear why this clustering occurred.)

Figure 2 shows the relative month of birth distribution of subfecunds, with, as a reference, the month of birth distribution of fecunds and subfecunds together. The best fitting curve (deviance 5.80 with *df* = 9, *P* = 0.76) was unimodal with a zenith in September. The curve is somewhat extracted towards the upper end as a result of antilog conversion. The *P* value for the (null) hypothesis that fecunds and subfecunds do not have a different month of birth distribution was 0.13. To examine whether the shape of the best fitting curve was dependent on the month of birth distribution of the prenuptially conceiving women, a similar analysis was performed while leaving this group out. This did not lead to a different shift or amplitude.

In modern Western populations, 2.4–5.9% of couples remain involuntarily childless (Greenhall and Vessey, 1990). In our historical sample, 2.4% (36/1526) of all couples were childless—more exactly, without a conception leading to childbirth—during follow-up. The cause of the relative lowness of this figure may lie in the genealogical origin of the data:

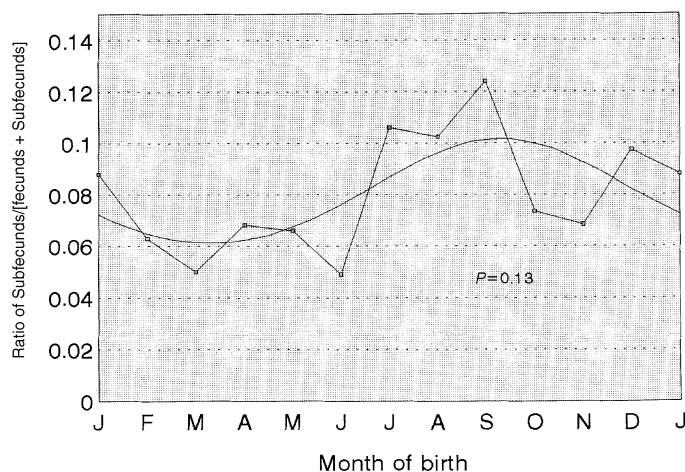


Figure 2. Relative month-of-birth distribution and best fitting curves for subfecunds/(subfecunds + fecunds). Subfecunds, *n* = 118; fecunds, *n* = 1348.

childless couples have a lower chance of being traced by later relatives. Our fecundability estimation model, although allowing differential fecundability, does not account for complete sterility (in the present model, the conception-free survival $\rightarrow 0$ when $t \rightarrow \infty$). Since the aetiology of unresolved primary infertility may be different from that of less severe subfertility, two analyses similar to the above were performed, one excluding childless couples and one including only childless couples in the subfecund category. The results are shown in Figure 3a and b. After exclusion of childless couples, the best fitting curve (deviance 3.46, *df* = 9, *P* = 0.94) was unimodal, with a zenith in September, and had a *P* value of 0.002. For childless couples versus fecunds, the best fitting curve (deviance 8.55, *df* = 9, *P* = 0.48) was bimodal with zeniths in January and July, and had a *P* value of 0.06. All aforementioned models, including the unselected ones, are shown in Table II. Numbers of fecunds and subfecunds, with the latter broken up into the two subgroups, as well as χ^2 values, can be found in Table III. The comparatively high χ^2 -associated *P* values exemplify the low sensitivity of the χ^2 -test for smoothed seasonal patterns.

We evaluated age at wedding, year of wedding and occupation-related risk of physical separation as potential confounders by adding them separately and simultaneously, and classified, as shown in Table I, to the regression models. Year of wedding was considered a potential confounder in view of the emerging practice, in the more recent marriage cohorts, of family planning by reduction of the coital rate. None of the results, however, were confounded by these cofactors.

Discussion

The results of this study indicate that fecundability is associated with month of birth. The relationship, however, is not straightforward; both childless women and women with long TTP differ from those with short TTP as to month of birth, but they do so in a different way. The latter are born more often in the second half of the year, while the former are born more often in two periods, June–August and December–February.

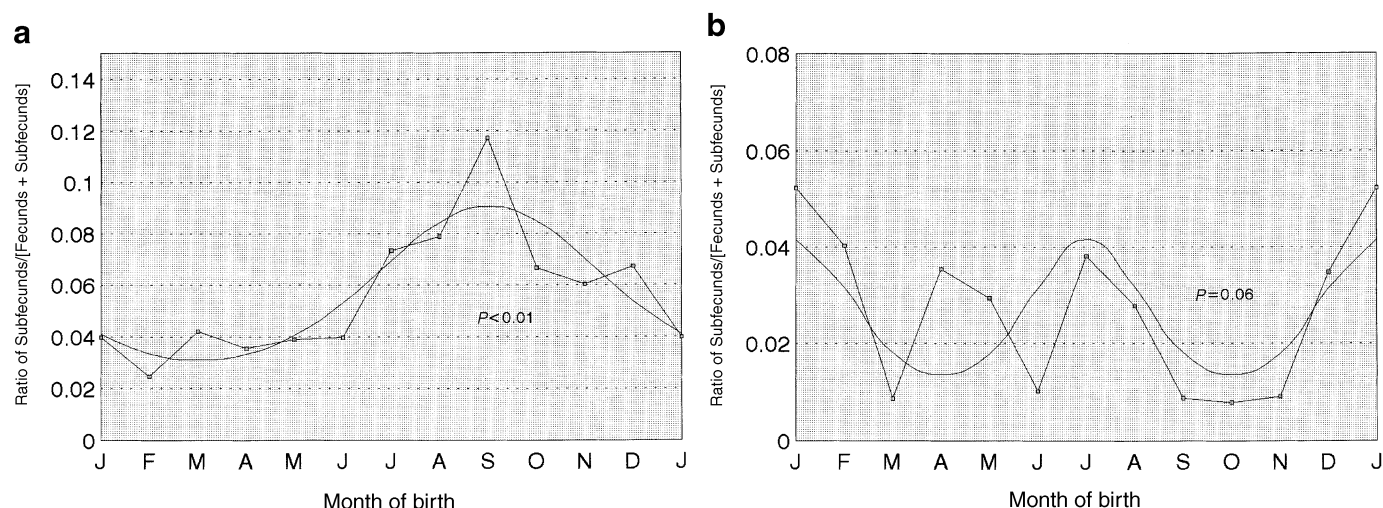


Figure 3. (a) Relative month-of-birth distribution and best fitting curves for subfecunds/(subfecunds + fecunds), with childless couples excluded. Subfecunds, $n = 82$; fecunds, $n = 1348$. (b) Relative month-of-birth distribution and best fitting curves for subfecunds/(subfecunds + fecunds), with only childless couples in the subfecund group. Subfecunds, $n = 36$; fecunds, $n = 1348$.

Table II. -2 Log likelihoods, degrees of freedom, P values, and values of β_1 and β_2 and their SE with different comparisons (I, fecunds; II, all subfecunds; III, late conceivers; IV, childless) and different models

Comparison	Model ^a	-2 Log likelihood	df	P value	β_1 (SE)	β_2 (SE)
I/II	1 year versus uniform	4.04	2	0.13	-0.27 (0.14)	-0.03 (0.14)
	0.5 year versus uniform	1.37	2	0.50	0.15 (0.14)	0.05 (0.13)
I/III	1 year versus uniform	12.08	2	0.002	-0.55 (0.17)	-0.14 (0.17)
	0.5 year versus uniform	1.05	2	0.59	0.09 (0.16)	-0.14 (0.16)
I/IV	1 year versus uniform	2.84	2	0.24	0.34 (0.25)	0.22 (0.25)
	0.5 year versus uniform	5.59	2	0.06	0.29 (0.25)	0.49 (0.25)

^aFor a description of the method used for modelling, see the Appendix.

Table III. Numbers of fecunds and subfecunds per month of birth, with subfecunds as a whole and split up into late conceivers and childless. The χ^2 and P values (11 df) for subfecunds, late conceivers and childless as compared with fecunds were 9.94 ($P = 0.53$), 16.49 ($P = 0.12$), and 13.14 ($P = 0.29$) respectively

	Month of birth											
	J	F	M	A	M	J	J	A	S	O	N	D
Fecunds	145	119	114	109	99	97	101	105	113	126	109	111
All subfecunds	14	8	6	8	7	5	12	12	16	10	8	12
Late conceivers	6	3	5	4	4	4	8	9	15	9	7	8
Childless	8	5	1	4	3	1	4	3	1	1	1	4
Total	159	127	120	117	106	102	113	117	129	136	117	123

In their study of the relationship between season of birth and seasonality of birth of offspring, Nonaka *et al.* (1990) observed that women born between August and October had the lowest proportion of immediate conceptions after marriage, and those born between May and July the highest. Our results only partially confirm these observations. It should be noted that their population was restricted to women who gave birth within 2 years after marriage.

How may the observations of the present study be explained? Two causal hypotheses have been proposed regarding differences in female reproductive characteristics by month of birth. Miura (1987) stipulated the existence of virus-like seasonal agents causing seasonal abortion of some embryos and, at the

same time, immunity in others. Those having survived infection would be immune to the factors in the future and produce no birth seasonality in their offspring, while those not having had any contact with the agents would remain susceptible and produce birth seasonality. Differences in time to pregnancy by month of birth would be an indirect effect of the differential sensitivity to such factors (Nonaka *et al.*, 1990). We have pointed out earlier (Smits *et al.*, 1995) that this theory is difficult to reconcile with contemporary embryology, which states that up to several months after birth, humans are incompetent at forming specific immunity. Furthermore, the stipulated immunological factors have yet to be identified.

Jongbloet (1993) explained differences of reproductive traits

by month of birth by 'seasonal preovulatory overripeness of the oocyte' (SPrOO hypothesis). Preovulatory overripeness of the oocyte is the effect of a disturbed hormonal regulation of the preovulatory phase of the menstrual cycle. Although preovulatory overripeness has been observed in a direct way only in laboratory animals (Fugo and Butcher, 1966, 1971; Butcher and Fugo, 1967; Butcher *et al.*, 1969, 1974; Mikamo, 1968; Freeman *et al.*, 1970; Mikamo and Hamaguchi, 1975; Bomsel-Helmreich, 1976; Peluso and Butcher, 1974a,b; Peluso *et al.*, 1980), there is indirect evidence that it also plays a significant role in human reproductive failure (Hertig, 1967; Spira *et al.*, 1985; Troya *et al.*, 1985). In amphibians, pre- and postovulatory overripeness of the oocyte has been shown to lead to malformations of the gonads in the conceptus, ranging from symmetrical or asymmetrical underdevelopment to apparently normal ovaries with, however, reduced numbers of fertile gonocytes (Witschi, 1952; Mikamo, 1968).

One of the assumptions of the SPrOO hypothesis is that the risk of hormonal disturbances varies across the year. This assumption is supported by the observation that, in Northern countries, ovarian steroidogenic activity is suppressed while luteal phase gonadotrophin secretion is high during the dark half of the year; during spring, oestradiol production increases under the influence of rising concentrations of follicular phase follicle stimulating hormone (Kauppila *et al.*, 1987). A mediating factor may be melatonin, a hormone secreted by the pineal gland that reflects differences in exposure to daylight, with high levels at low exposure and vice versa, and which in seasonal breeders modulates gonadal function (Aleandri *et al.*, 1996). Follicular fluid concentrations of melatonin, which are higher than serum concentrations (Rönnerberg *et al.*, 1990), and of oestradiol exhibit opposite seasonal rhythms both in subarctic (Kauppila *et al.*, 1987) and more temperate zones (Yie *et al.*, 1995). Melatonin may also have a role in the timing of the midcycle luteinizing hormone surge (Brzezinski *et al.*, 1987). A small seasonal variation in menstrual cycle length was observed by Sundararaj *et al.* (1978), with summer cycles being shortest. Photoperiod and temperature are considered the two most important determinants of cyclicality of reproduction (Roenneberg and Aschoff, 1990), although seasonal marriage patterns, holidays, temporary migration and economic variables may also make small contributions (Lam and Miron, 1991). Owing to artificial lighting and heating, the influence of photoperiod and temperature on reproduction may have diminished in Western populations (Roenneberg and Aschoff, 1990). Our research population, however, may have experienced more natural patterns of light and temperature.

A challenging question is what causes childless women to show month-of-birth deviations different from those of the other subfecunds. One explanation could be that these two groups have different types of reproductive impairment, with each type associated with particular risk months. It is, however, difficult to determine which type of impairments predominated among childless couples in our sample. Reduced fertility is generally attributable to either ovulatory problems, anatomical obstructions of the reproductive tract, cervical mucus defects, or low sperm quality. In historical populations, in which valid treatment of infertility was virtually absent, all four conditions

may have led to childlessness. A relationship with the wife's month of birth, however, is not expected for impairments that are mostly due to pathology during extrauterine life, as is the case with tubal obstruction, nor is it expected for low sperm quality. As ovulatory disorders may arise from defects at different levels of the hypothalamic-pituitary-ovarian axis, they may be the month-of-birth related impairment in both the childless and the late conceiving women.

This study has some limitations. First, the reconstitution of families from the 19th or early 20th century involves consulting multiple sources throughout the country. Despite the fact that several thousands of checks, additions and corrections were carried out on the available genealogical material, it cannot be ruled out that some inaccuracies occurred in the data. It is unlikely, however, that their occurrence is associated with both month of birth and TTP, so that the effect may be a bias towards the null hypothesis. Because our data derive from genealogies, some of the subjects are genetically and socially connected. For instance, the mothers of 382 women were in this file, and 189 women had at least one sister who was in this file. Exclusion of these groups did not, however, yield essentially different results.

Second, the use of the interval between wedding and first birth for the calculation of time to pregnancy involves several assumptions which do not fully hold in this study. The assumption that the wedding date is the starting point for unprotected intercourse obviously does not hold for couples with prenuptial conceptions, nor probably for a portion of the postnuptially conceiving and childless couples. Moreover, calculation of TTP by subtracting a fixed gestational length from the date of birth assumes that gestational length is identical for all births within a specific category (still- or live births), which is a simplifying assumption. Finally, the assumption that the first birth reflects the first pregnancy, and that the absence of birth reflects absence of pregnancy, is not true, as at least 15% of all recognized pregnancies end in an abortion. However, the fact that these assumptions do not fully hold has probably only led to bias towards the null hypothesis (in this case, a decrease of the amplitude) as a result of non-differential misclassification of the outcome. Bias away from the null hypothesis can only occur if the reproductive features involved in the above assumptions are linked to month of birth, which has not yet been established in the literature.

Third, we are aware of the fact that couple fecundability is not only dependent on female but also male fecundity and on coital frequency. In this study we have controlled for a proxy of coital frequency (husband's occupation in connection with temporal physical separation of the spouses), but this may not have accounted for all its variation; we had no possibility of controlling for variation in male fecundity. Differences in coital frequency and male fecundity were presumably not associated with the female's month of birth, and therefore responsible for non-differential misclassification and, hence, a bias towards the null hypothesis.

In conclusion, this study provides evidence for the existence of differences in fecundability by month of birth. If these differences prove to be consistent in future studies, it may

eventually lead to new insights into the early causes of subfecundity.

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Appendix

Technical description of the method of using a cosinor function for the modelling of differences in fecundability by month of birth

The log odds of subfecundity was modelled as:

$$\ln \left(\frac{p}{1-p} \right) = \beta_0 + \beta_1 \sin(x) + \beta_2 \cos(x) + \beta_{C_1} C_1 + \dots + \beta_{C_N} C_N \quad (1)$$

in which P is the risk of subfecundity, β_0 is the intercept, C indicates a cofactor, and x is defined as given below:

$$x = \frac{\pi}{t_n} + \frac{2\pi(t_i - 1)}{t_n} \quad (2)$$

in which t_n = period in months (6 or 12 in this study) and t_i = i th month (for January, $t_i = 1$, for February, $t_i = 2$, etc.).

Hence, the model-based risk of subfecundity is:

$$p = \frac{e^{(\beta_0 + \beta_1 \sin(x) + \beta_2 \cos(x) + \beta_{C_1} C_1 + \dots + \beta_{C_N} C_N)}}{1 + e^{(\beta_0 + \beta_1 \sin(x) + \beta_2 \cos(x) + \beta_{C_1} C_1 + \dots + \beta_{C_N} C_N)}} \quad (3)$$

By use of standard geometric rules, the phrase $\beta_1 \sin(x) + \beta_2 \cos(x)$ in equation 1 can be rewritten as:

$$\alpha \cos(x - \theta) \quad (4)$$

which specifies a cosinor function with α = amplitude (>0) and θ = shift (in radials).

Readers interested in a numerical example should contact L.J.Smits.