Dizygotic twinning and fecundity – is there an association between a family history of twinning and birth intervals in contemporary Sweden?

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Introduction

There is plenty of evidence suggesting a heritable component to human fertility, but the extent of this has been hard to examine. Some researchers have for theoretical reasons suggested that the heritability of human fertility should be low, as it as a key life history trait should have low heritable variation (cf. Fisher, 1930), but this has been contested (Okasha, 2008). In this study we will focus on the potential link between female fecundity and twinning. Researchers have documented that twinning is heritable (Davenport, 1920; Hoekstra et al., 2008a; Parisi et al., 1983). It appears that only dizygotic twinning has a major heritable genetic component while monozygotic twinning appears to be largely random. Researchers have long speculated on a link between overall fecundity, and the propensity for twinning (Hoekstra et al., 2008b; James, 2007; Pison & Couvert, 2004; Tong & Short, 1998) but there is little direct evidence of this association. In this study we examine if there is an association between a history of parental twinning and fecundity for women in contemporary Sweden. Alter and Pison (2008) suggested and examined this relationship between a history of twinning and fecundity, using data from pre-industrial Belgium and found some support for such an effect. Basso et al. (2004) similarly examined this relationship by studying the subsequent birth intervals of mothers who had given birth to twins themselves. They found that time to pregnancy was significantly lower for mothers who gave birth to twins, and that this effect was bigger for the mothers of dizygotic twins than the mothers of monozygotic twins.

We use Swedish population register data to study if fecundity is higher for siblings whose parents had a twin birth, excluding twins themselves, using data for the entire Swedish population, using a number of robustness checks not previously used in the study of this relationship. As we have access to the complete population, complete reproductive histories, two generations, and all twin births in Sweden, we also have considerable statistical power to examine this relationship.

Biodemography of dizygotic twinning

Dizygotic twinning has been shown to be related to the release of viable ova (egg cells). A dizygotic conception is the result of a multiple ovulation event, in which two separate (and genetically different) ova are released during the same menstrual cycle. The frequency of multiple ovulation is most likely determined by two hormones, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) (Martin et al., 1991). These hormones regulate follicle growth and large quantities of FSH increases the chance of multiple follicle growth, and, by extension, multiple ovulation.

The frequency of dizygotic twinning increases rapidly with age (Hoekstra et al., 2008b). This increase in dizygotic twinning is most likely the result of an increase in multiple ovulation by age (Beemsterboer et al., 2006), with the purpose of increasing the probability of a viable ovum implanting itself in the womb . From an evolutionary perceptive, the increase in twinning by age can be seen as a tradeoff between the probability of twinning (typically with very poor outcomes for both children and mother historically) and a chance to offset decreasing fecundity by age. Thus, increasing levels of multiple ovulation would both increase the probability of a viable ovum at the expense of an increased chance of a twinning with, on average, adverse consequences. Earlier in life the higher probability of twinning as well as higher reproductive value of the mother would decrease the benefits of multiple ovulations. The strong heritable component of dizygotic twinning (Hoekstra et al., 2008b; Parisi et al., 1983) simultaneously suggest that there is both a heritable component to human twinning, as well as

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genetic variation for twinning in the population. If there is an association between fecundity and twinning this variation could be related to a historical tradeoff between these factors.

Unlike dizygotic twinning, monozygotic twinning appears to be largely unrelated to both hereditary and environmental factors (Scott, 2002). The reason for this is that the physiological trigger of monozygotic twinning (the division of one embryo into two separate but genetically identical embryos) is very different, and is currently poorly understood (Scott, 2002). The theoretical mechanism suggested in this study would only apply to dizygotic and not monozygotic twinning.

Proposed Mechanism

The goal of the study is to find evidence for a link between overall fecundity, operationalized as birth intervals, and twinning. The logic of our proposed mechanism is that the propensity of woman to have multiple ovulations has a genetic basis, and is associated both with increased overall female fecundity and frequency of twinning. Thus, women whose parents had twins would themselves, due to shared genes, be more fecund than other women. We base this hypothesis on the widely documented fact that dizygotic twinning has a major genetic component. It also appears likely that the heritability of twinning is related to the frequency with which the mother experiences multiple ovulation events (Martin et al., 1991), and the development of more than one viable ovum. We therefore suggest that women differ in their propensities for multiple ovulation events, this difference has a genetic basis, and that this will affect both overall fecundity and the rate of twinning. Basso et al.'s (2004) finding of a shorter time to pregnancy for mothers who gave birth to twins and Alter & Pison's (2008) findings both suggest the existence of such a mechanism.

Research Design

We want to test this mechanism by examining if a history of twinning is associated with birth intervals for young women in contemporary Sweden. As contraceptive usage is almost universal in Sweden, fertility is largely a matter of individual agency. Thus fertility is governed by many other factors besides female fecundity. To avoid this problem we only focus on the transition to 2^{nd} birth, which is almost universal and also characterized by short (average) birth intervals. The government also offers a powerful incentive through parental leave policy for short birth intervals, which we will discuss later. We also run models on transition to 3^{rd} birth, as these birth intervals are also typically short. We avoid running models on becoming a parent, as well as later births, as the role of physiological fecundity for the timing of these transitions is likely to be quite low in contemporary Sweden. We can examine everyone whose parents had a twin birth, but we avoid including index individuals who themselves are twins. In other words, we include individuals who have twins as siblings. Twins have a different fertility pattern from the rest of the population (Tollebrant, 2001), and are thus inappropriate for our analysis.

Robustness checks

Many other factors besides the fecundity of the mother undoubtedly affect the transition to 2^{nd} and 3^{rd} birth in Sweden, but it appears very plausible that if there is a substantive difference in fecundity between mothers with and without a family history of twinning we will observe significantly different birth hazards between these groups. To further strengthen our primary results we fortunately have access to a number of robustness checks.

To test of our finding we can use four robustness checks. The first one is testing the hypothesis outlined above both before and after a parental leave reform in Sweden. The Swedish government offers a powerful incentive for short birth intervals through a parental leave policy from the social insurance agency. Mothers, who have a birth within 24 months, and later 30 months (we use the latter reform as the latter reform was associated with a more substantive change in behavior), received more generous parental leave. Parental leave is generously calculated at 80% of the salary at the time of birth (up to almost 50,000 USD/year). If the birth interval between two births is smaller than 30 months the parents can calculate their parental leave for the second birth from their income before the 1^{st} birth and not the time before the 2^{nd} birth (where the income in most cases is much lower). Thus, for working women there is typically a great financial incentive to have a shorter

birth interval than 30 months. The introduction of the new parental leave policy had a major affect on transition to 2nd birth in Sweden (Andersson, Hoem & Duvander 2006). As women had a greater incentive for short birth spacing after the reform, the role of fecundity should have increased as physiological differences between women with an interest in short birth intervals should be more important if the women wanted closely spaced births. Thus, the effect of our marker for twinning related fecundity should be larger after the reform.

Our second robustness check is that our theory would predict that dizygotic and not monozygotic twinning is associated with fecundity. We cannot directly observe zygozity in the administrative registers but we can partly and indirectly infer it from whether the mother has twins of the opposite or the same sex. Around 70% of all twin births were dizygotic during the time period under analysis. Thus, for same sex twins a little more than half of all twins should be dizygotic, and half monozygotic. All opposite sex twins are dizygotic. Thus, if the mother has opposite sex twins, she should on average be twice as likely to have had a dizygotic birth, and thus potentially have a high fecundity phenotype.

The third robustness check is that we can look at birth intervals for both men and women. While twinning is largely random there are some known factors which are associated with dizygotic twinning such as childbearing at later ages. These factors could plausibly also be (weakly) associated with the timing of the 2nd birth through, for example, socioeconomic pathways. If there are these socioeconomic biases they are likely to affect both men and women similarly. On the other hand, our proposed mechanism, genes expressing themselves as a high fecundity phenotype, would only affect women. Both sons and daughters would inherit the genes associated with dizygotic twinning but only daughters would display the higher fertility. Thus, if we find very similar effects of twinning on birth intervals for men and women there could be an endogeneity problem between twinning and timing of second birth unrelated to our proposed mechanism, while the observation of an effect for women but not for men would strengthen the support for our hypothesis.

Finally, in-vitro-fertilization (IVF), and infertility therapy, such as the use of follicle-stimulating hormone, is known to be correlated with dizygotic twinning (Fauser et al., 2005), and more controversially monozygotic twinning (Aston et al., 2008). After the introduction of IVF doctors often inserted a large number of fertilized eggs to increase the chance of a successful pregnancy. As IVF is costly it could also be associated with endogeneity problems. Infertility treatments use hormones to stimulate follicle growth and could therefore also be associated with both twinning and overall fecundity. At the time that the parental generation gave birth to the index generation none of these treatments were available.

Data

The data material for the study is a collection of Swedish administrative register data. The population is all Swedish born men and women in Sweden living in Sweden between 1968 and 2007. People are followed from their 1st birth until their 2nd and 3rd birth. Individuals are right censored at age 45, the year 2007, death or first outmigration. Information on birth histories of parents are collected from the Swedish multigenerational register. By means of a unique personal identification number, siblings can be connected to their mother, and twin status can be inferred from if two siblings were born by the same mother in the same month and year. A condition for a successful linkage and inclusion in the study is that the mother of the index generation, and all siblings (including twins) were alive in 1960. For mothers in the 1960s and the 1970s this means that some the degrees of twinning in their cohorts might be slightly underestimated. Index person who themselves had twin births are excluded from the analysis as their fertility behavior might deviate from the rest of the population. In total we analyze transition to 2nd birth for over 3 million men and women.

Methods

We use event history analysis (piece-wise exponential hazard models) to measure timing to 2nd and 3rd births for our index generation. In addition to a history of twinning, our main explanatory covariate, we also control for period and age. We run two main sets of models. Our first models examines time to 2nd birth until any right censoring, while our second model only

looks at birth hazards within 30 months of the 1st birth. We check for pre/post the previous mentioned parental leave policy with a time varying dummy. We additionally run separate models for men and women.

Results

Our first results on transition to 2nd birth are presented in Table 1 below. We only show results for the main covariate of interest, familial history of twinning, decomposed by sex composition of the sibling. Our results are of small to moderate strength and are consistent with our proposed mechanism. Women, who have twin siblings, but are not twins themselves, have higher transition rates to 2nd birth than women whose mothers did not give birth to twins. We suggested that results would be stronger for opposite sex twins (100% dizygotic) than same sex twins (50-60% dizygotic), which is supported by our data, roughly in proportion to the share of dizygotic twins among same/opposite sex twins. All results for women are statistically significant (at a 95 % confidence level). For triplets we find shorter birth intervals, though the results are not statistically significant. We also conducted robustness checks for men where we find non-significant positive effects for a maternal twin birth on own birth hazard to 2nd birth. We proposed no effect of familial twinning on men, which is supported in the data, though the small non-significant effect might suggest a minor bias towards that siblings with twin-siblings have slightly larger transition rates, due to social circumstances shared by men and women.

Table 1: Piecewise exponential proportional hazard models on transition to 2nd birth for women in Sweden from 1968-2007, covariates on if the women's mother gave birth to twins, women who are not themselves twins

	Women				**Men**		
Without controls for maternal age							
	relative risks	95 % C. I.			relative risks	95 % C. I.	
No twin birth	1 (ref.)			No twin birth	1 (ref.)		
Same sex twin birth	1.022	1.005	1.041	Same sex twin birth	1.013	0.992	1.034
Opposite sex twin birth	1.033	1.010	1.057	Opposite sex twin birth	1.016	0.988	1.044
Triplet	1.029	0.857	1.235	Triplet	0.974	0.790	1.202
With controls for maternal age							
No twin birth	1 (ref.)			No twin birth	1 (ref.)		
Same sex twin birth	1.024	1.007	1.042	Same sex twin birth	1.017	0.996	1.038
Opposite sex twin birth	1.035	1.011	1.059	Opposite sex twin birth	1.019	0.991	1.047
Triplet	1.035	0.862	1.242	Triplet	0.979	0.793	1.208

Additional control variables: Duration since 1st birth (baseline time), period (time-varying), age of mother (time-varying)

Conclusions

Our models offer preliminary evidence on a clear population level link between propensity for dizygotic twinning and overall fecundity. This mechanism has been suspected among reproductive biologists, but direct evidence has been limited. Our results both give new evidence for such a link, and also offer support for that the magnitude of such a finding that has population level consequences. In further analyses, we intend to run all of the robustness checks mentioned in the abstract to further strengthen our conclusions. We want to expand the analysis to include 3rd birth as well. We also aim to analyze only the birth hazard for the first 30 months, when we presume that the effect of fecundity would be more pronounced. We will also study the potential effect of the Swedish parental leave reform as it could be associated with an increasing role of fecundity for the transition to 2nd birth.

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