Twinning in humans: maternal heterogeneity in reproduction and survival

Shannen L. Robson1,* and Ken R. Smith2,3

1Department of Anthropology, 2Department of Family and Consumer Studies, and 3Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA

While humans usually give birth to singletons, dizygotic twinning occurs at low rates in all populations worldwide. We evaluate two hypotheses that have differing expectations about the effects of bearing twins on maternal lifetime reproduction and survival. The maternal depletion hypothesis argues that mothers of twins will suffer negative outcomes owing to the higher physiological costs associated with bearing multiples. Alternatively, twinning, while costly, may indicate mothers with a greater capacity to bear that cost. Drawing from the vast natural fertility data in the Utah Population Database, we compared the reproductive and survival events of 4603 mothers who bore twins and 54,183 who had not. These mothers were born between 1807 and 1899, lived at least to the age of 50 years and married once to men who were alive when their wives were 50. Results from proportional hazards and regression analyses are consistent with the second hypothesis. Mothers of twins exhibit lower postmenopausal mortality, shorter average inter-birth intervals, later ages at last birth and higher lifetime fertility than their singleton-only bearing counterparts. From the largest historical sample of twinning mothers yet published, we conclude that bearing twins is more likely for those with a robust phenotype and is a useful index of maternal heterogeneity.

Keywords: twinning; heterogeneity; maternal depletion; reproduction; life history

1. INTRODUCTION

Though rare, twinning is not uncommon among humans, universally occurring at persistently low rates worldwide [1]. Rates of spontaneous twinning range from about 6 per thousand (‰) livebirths in Asia, 10–20‰ in Europe and the United States, to about 40‰ in Africa [2]. The overall twinning rate is primarily owing to differences in dizygotic twinning [2], the gestation of two separately fertilized ova. Monozygotic twinning, the split of one fertilized egg into two identical zygotes, is random and non-heritable, occurring at a fairly stable rate of 3.5–4.0‰ across populations sampled [3]. Dizygotic twinning results from polyovulation, which varies by population and clusters in families [4]. While dizygotic twinning may have a heritable component [2], many studies have shown that it is more environmentally facultative than genetic [5–9].

Twinning and increased litter size have high maternal and offspring mortality risks, reducing offspring quality and often cancelling out any fitness advantages of bearing multiples [10–12]. These mortality risks combined with the low rates of twinning in humans and other catarrhine primates [13,14] suggest that these primate species are all adapted to bear only one offspring per gestation [12]. Anderson [15] argues that twinning is not itself adaptive, but rather may be a by-product of ‘insurance ovulation’ designed to hedge the risks of early embryo loss and increase the survival of at least one viable zygote. It is well documented that many more twins are conceived than born, an event known as the ‘vanishing twin phenomenon’ [16]. This suggests that there is individual variation in both the frequency of polyovulation and the efficiency of embryo rejection [17]. As such, bearing twins may be a ‘cost-intensive error in an adaptive brood reduction system’ [10, p. 700]. The insurance ovulation hypothesis predicts that bearing twins exacts fitness costs that outweigh any fitness benefits gained from increased offspring quantity. Successful twin pregnancies are more costly than singletons and mothers of twins are expected to suffer maternal depletion effects [18].

Yet, evidence for a maternal depletion effect is equivocal [19]. Hurt et al. [20] found that in some selected cases, mortality actually declined with increasing births among 12 historical cohorts (populations unable to benefit from better healthcare available in modern societies), though results were inconsistent and not always significant.

In opposition to the maternal depletion hypothesis, mothers who are able to sustain the cost of twin pregnancies may gain a fitness advantage by doing so. Sear et al. [21] found that mothers in rural Gambia who had given birth to twins had higher overall fertility than mothers who bore only singletons. Twinning may be an indicator of higher maternal capacity and may identify those women whose enhanced phenotypic quality allows them to bear these elevated reproductive costs. Under this hypothesis, women who twin should outperform mothers of singletons on other life-history measures as well.

This heterogeneity hypothesis is consistent with observations that women with higher fertility rates and later ages at last birth (ALB) also have higher subsequent survival rates [22–24]. While these correlations appear to challenge the allocation trade-offs between somatic maintenance and reproduction predicted by most evolutionary models [25], the paradox of unmeasured heterogeneity obscures the trade-offs [26–28]. When subjects differ in their inherent quality, those with fewer resources are prone to fail at earlier ages while more robust individuals survive and thrive in measurable ways. Accordingly, twinning mothers should exhibit additional features of a robust

* Author for correspondence (robson@umnh.utah.edu).
phenotype, including shorter average inter-birth intervals, later ALB and longer reproductive spans resulting in higher parities, and longer postmenopausal lifespans.

To evaluate these alternative hypotheses, we measured correlations between twinning and maternal reproductive and life-history measures using a large sample of parous women from a vast historical database documenting a natural fertility population in Utah where fertility was high. We first compare survival past the age of 50 between twinning and singleton-only mothers. Then we compare several key reproductive traits: lifetime parity, average inter-birth interval, ALB and reproductive span length.

2. DEMOGRAPHIC DATA AND METHODS

We examined whether mothers of twins were more robust by comparing the reproductive and survival events of mothers who bore at least one set of twins with those women who did not in the Utah Population Database (UPDB). The UPDB is one of the world’s most comprehensive computerized genealogies collating the vital records of migrants to Utah and their Utah descendants for more than 1.6 million individuals born from the early 1800s to the mid-1970s (see http://www.huntsmancancer.org/groups/ppr/). Because these records include basic demographic information on parents and their children, fertility and mortality data are extensive with coverage up to the present [29]. Previous studies by Wyshak [4,30–35] investigated the inheritance, demographics and characteristics of human twinning using the UPDB. However, there are many limitations of these early studies that precede digitization, including a lack of non-twin control for comparison, very restrictive time periods (1850 and earlier) and data quality concerns (fallibility of hand sorting and linkage). A subsequent investigation on twinning in the UPDB by Carmelli et al. [36] describes the demographics and kinship survey of twins finding a variable twinning rate of 11.5–14.0‰ births between 1820 and 1910, with a steady decline in both fertility and twinning thereafter.

The large size of the UPDB allowed us to restrict our sample to parous women who were born between 1807 and 1899 and lived at least to the age of 50 years, thereby including only those women who experienced their entire reproductive span and complete fertility. To avoid confounding reproductive variables by widowhood, we limited the sample to those women who were married just once to men who were still alive when their wives were 50. We also excluded women in polygamous marriages, which constituted a small percent of the data. Even with these restrictions, we captured a sizable number of women who bore twins in a natural fertility population. The final restricted sample had records for 58,786 women, 4,603 of those were mothers of twins (7.84%) and 54,183 had singleton-only births. To examine social and cultural impacts of the demographic transition, we divided our sample into those women whose birth date was before or after 1870 to distinguish the natural fertility era from the early stages of fertility planning. We trimmed the pre-1870 birth cohort to those who were married after 1850. Those marrying prior to 1850 were generally a select set who often were married outside of Utah. Table 1 summarizes the descriptive statistics for all of the model variables for both cohorts.

We conducted several analyses to determine whether females in our sample who bore twins differed significantly.
3. RESULTS

(a) Postmenopausal survival

Table 2 reports the results of Cox proportional hazards regression comparing the postmenopausal survival of women who did or did not have a twin set during her reproductive career. We centred parity to control for the effects of collinearity introduced by the interaction term (twin-parity). Model results (table 2) show that when evaluated at average parity (pre-1870 cohort = 8.39, post-1870 cohort = 5.72), mothers of twins have a survival advantage over singleton-only bearing mothers (pre-1870) hazard rate ratio (HRR) = 0.924, p = 0.008, post-1870 HRR = 0.967, p = 0.1137. Although this effect is only significant for the pre-1870 birth cohort, there was a survival benefit of being a mother of twins that persisted until very high parities. The benefit of bearing twins did not diminish until a parity of 12, which is extreme for this population, when both sets of mothers then share the same survival.

(b) Parity

We examined whether total lifetime parity differed between twin and non-twin mothers using regression analyses. The overall average number of children per mother in the pre-1870 cohort was 8.39 and for the post-1870 cohort was 5.72 (table 1). Table 3(a) shows that mothers of twins in both birth cohorts had a significantly higher lifetime parity (pre-1870, p < 0.0001; post-1870, p < 0.0001), averaging 1.9 and 2.3 more children, respectively, than non-twinning mothers controlling for the effects of age at marriage and AFB, survival of husband after the mother reached age 50 and LDS religious affiliation. In table 3(b), we examined whether higher parity results from child replacement owing to higher offspring mortality of twins by controlling for child mortality before the age of 18. The parity advantage of twinning mothers dropped slightly to 1.24 in the pre-1870 cohort and 1.56 more children in the post-1870 than singleton-only mothers, but remained significantly greater than non-twinning mothers (both cohorts, p < 0.0001). While a twin set itself increases a mother’s parity by 1, the parities of twinning mothers in the UPDB exceed this advantage, showing that mothers of twins bear a higher number of singletons as well.

(c) Average inter-birth interval

Table 4 reports the results of a regression model showing that mothers of twins had shorter, albeit small, average inter-birth intervals than non-twinning mothers (pre-1870, p < 0.0001; post-1870, p = 0.0013), controlling for AFB and ALB, offspring mortality, survival of husband after the mother reached the age of 50 and LDS religious affiliation. The average inter-birth interval in the pre-1870 cohort was 2.62 years and for the post-1870 cohort was 3.24 years (table 1). As expected, the largest variable influencing the length of the average inter-birth interval is child mortality. The inter-birth intervals of twinning mothers were significantly shorter in the later era cohort even when average birth intervals were longer.

(d) Reproductive span and ALB

Tables 5(a) and 6(a) show that that mothers of twins had a significantly longer reproductive span (calculated as ALB minus AFB; pre-1870, p < 0.0001; post-1870, p < 0.0001) and later ages at last birth (pre-1870, p < 0.0001; post-1870, p = 0.0013).
post-1870, $p < 0.0001$) than non-twinning mothers, controlling for AFB, offspring mortality, survival of husband after the mother reached the age of 50 and LDS religious affiliation. Both dependent variables remain significant for the pre- and post-1870 birth cohorts after controlling for age at marriage (tables 5(b) and 6(b)).

4. DISCUSSION
Our results from analyses using a large, historical, natural fertility population show that twinning mothers ‘outperformed’ their singleton-only counterparts by living longer past menopause, having higher overall parity, shorter average inter-birth intervals, longer reproductive spans and later ALB than non-twinning mothers. We restricted our sample to parous women who had survived to the age of 50, already a robust subset of the UPDB, making the comparison groups more similar, and yet our results still found significant differences between twinning and non-twinning mothers. If twinning mothers had ‘underperformed’ on these measures, this would have supported the maternal depletion hypothesis that twinning is costly and detrimental to female health and fertility. We found that mothers of twins in the UPDB sample exhibit a robust phenotype on several reproductive and life-history measures compared with their singleton-only bearing counterparts, suggesting that bearing twins marks a more robust maternal phenotype.

Lack of support for negative long-term consequences of twin childbearing is consistent with the heterogeneity hypothesis, which predicts that some women in a population bear reproductive costs more readily than others.
Table 5. Linear regression results for the effects of bearing twins on total reproductive span. (The model in panel (a) controls for AFB while panel (b) includes marriage year. ALB, age at last birth; AFB, age at first birth; LDS, Latter-day Saints.)

<table>
<thead>
<tr>
<th>variable</th>
<th>dependent variable: reproductive interval (ALB–AFB)</th>
<th>mother’s birth year before 1870, n = 21 150</th>
<th>mother’s birth year 1870–1900, n = 37 636</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>lower CI</td>
<td>upper CI</td>
</tr>
<tr>
<td>(a)</td>
<td>p &gt; F ≤ 0.0001, r² = 0.4197</td>
<td>50.5754</td>
<td>30.0542</td>
</tr>
<tr>
<td>ever mother of twins</td>
<td>0.3038</td>
<td>0.0979</td>
<td>0.5097</td>
</tr>
<tr>
<td>AFB</td>
<td>-0.8417</td>
<td>-0.8578</td>
<td>-0.8034</td>
</tr>
<tr>
<td>children died before 18</td>
<td>0.0594</td>
<td>0.0546</td>
<td>0.0643</td>
</tr>
<tr>
<td>LDS religion</td>
<td>0.5533</td>
<td>0.4224</td>
<td>0.6843</td>
</tr>
<tr>
<td>(b)</td>
<td>p &gt; F ≤ 0.0001, r² = 0.1327</td>
<td>93.2099</td>
<td>81.1301</td>
</tr>
<tr>
<td>ever mother of twins</td>
<td>0.3118</td>
<td>0.0601</td>
<td>0.5636</td>
</tr>
<tr>
<td>marriage year</td>
<td>-0.0438</td>
<td>-0.0502</td>
<td>-0.0374</td>
</tr>
<tr>
<td>children died before 18</td>
<td>0.1073</td>
<td>0.10237</td>
<td>1.1226</td>
</tr>
<tr>
<td>LDS religion</td>
<td>1.3205</td>
<td>1.1615</td>
<td>1.4796</td>
</tr>
</tbody>
</table>

Table 6. Linear regression results for the effects of bearing twins on age at last birth. (The model results in panel (a) control for AFB while panel (b) controls for marriage year. ALB, age at last birth; AFB, age at first birth; LDS, Latter-day Saints.)

<table>
<thead>
<tr>
<th>variable</th>
<th>dependent variable: ALB</th>
<th>mother’s birth year before 1870, n = 21 150</th>
<th>mother’s birth year after 1870–1900, n = 37 636</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>lower CI</td>
<td>upper CI</td>
</tr>
<tr>
<td>(a)</td>
<td>p &gt; F ≤ 0.0001, r² = 0.1075</td>
<td>30.5965</td>
<td>30.0519</td>
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<tr>
<td>ever mother of twins</td>
<td>0.3893</td>
<td>0.1714</td>
<td>0.6072</td>
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<tr>
<td>AFB</td>
<td>0.1290</td>
<td>0.1124</td>
<td>0.1457</td>
</tr>
<tr>
<td>children died before 18</td>
<td>0.8653</td>
<td>0.8225</td>
<td>0.9081</td>
</tr>
<tr>
<td>husband lifespan</td>
<td>0.0621</td>
<td>0.0570</td>
<td>0.0671</td>
</tr>
<tr>
<td>LDS religion</td>
<td>0.6553</td>
<td>0.5180</td>
<td>0.7926</td>
</tr>
<tr>
<td>(b)</td>
<td>p &gt; F ≤ 0.0001, r² = 0.0984</td>
<td>53.7946</td>
<td>43.3852</td>
</tr>
<tr>
<td>ever mother of twins</td>
<td>0.3968</td>
<td>0.1778</td>
<td>0.6159</td>
</tr>
<tr>
<td>marriage year</td>
<td>-0.0108</td>
<td>-0.0163</td>
<td>-0.0052</td>
</tr>
<tr>
<td>children died before 18</td>
<td>0.7931</td>
<td>0.7503</td>
<td>0.8359</td>
</tr>
<tr>
<td>husband lifespan</td>
<td>0.0618</td>
<td>0.0567</td>
<td>0.0669</td>
</tr>
<tr>
<td>LDS religion</td>
<td>0.5356</td>
<td>0.3985</td>
<td>0.6727</td>
</tr>
</tbody>
</table>

[37]. More frail women have both longer inter-birth intervals and earlier ALB, resulting in lower fertility. The women who continue to bear offspring to older ages are a more robust subset who have higher fertilities and are more likely to successfully incur the cost of twins.

Several previous studies also have suggested that the ability to twin may reflect enhanced maternal phenotypic quality. Instead of twin deliveries, Helle et al. [38] used the expected productivity of a singleton delivery and found that ‘twin mothers would have had higher fitness than singleton mothers independently of twinning’...
did not increase lifetime reproduction in eighteenth and nineteenth century Finland owing to high maternal and offspring mortality. Gabler & Voland [10] report that that life expectancy of twinning mothers in the Krummhorn dataset of eighteenth to nineteenth century Germany was not statistically different from those only bearing singletons, therefore finding no maternal mortality costs as a result of twinning. They also report, as we do, that mothers of twins have shorter inter-birth intervals, longer reproductive spans, later ALB and a higher overall fecundity (though high parities in this population are not owing to twinning, but rather from a higher overall fertility rate of singletons). Skaaervo et al. [41] show that mothers of twins in 1700–1900 central Norway have higher fecundity, longer reproductive spans and later ALB.

Lummaa et al. [8] found no differences in inter-birth interval length between twinning and non-twinning mothers in historical data from northern Finland. Comparing two pre-industrial Finnish populations with differing food resource availability, Lummaa et al. [8,42] found that twins enhanced the reproductive success of mothers where food was abundant and reliable, but reduced lifetime fertility where crop failures and famines were more common. This suggests that twinning may be an opportunistic reproductive strategy, or its genetic frequency selected, during favourable environmental circumstances.

This pattern of reproductive robustness and enhanced survival among twinning mothers is also seen in a contemporary natural fertility population. Sear et al. [21] examined the reproductive histories of women in rural Gambia, Africa, and found that mothers of twins had shorter inter-birth intervals, higher age-specific fertility, more surviving offspring and higher anthropometric status during their teen years than mothers of singletons only. From these results, the authors suggest that ‘twin mothers may be of higher phenotypic quality than women who only give birth to singletons’ (p. 441).

Historical demographic data offer important value for testing evolutionary hypotheses in natural fertility populations that best approximate reproductive conditions during human evolutionary history [43,44]. The few studies that have investigated the reproductive and life-history effects of twinning in natural fertility populations have conducted analyses with very small sample sizes (largest \( \approx 250 \)) [10,12,21,38,41,42,45,46] often yielding equivocal results. Using the largest dataset of twin mothers yet published, at least 18 times larger than any previously analysed historical sample, we have shown that mothers of twins surpass their singleton-only bearing counterparts on several life-history and reproductive measures. Our results strongly support the hypothesis that twinning is an index of phenotypic quality associated with other dimensions of maternal heterogeneity.

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REFERENCES


20 Hurt, L. S., Ronismands, C. & Thomas, S. L. 2006 The effect of number of births on women’s mortality: systematic review of the evidence for women who have


