Title
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Journal
Proceedings of the National Academy of Sciences of the United States of America, 103(5)

ISSN
1091-6490

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Publication Date
2006-01-23

Peer reviewed

Secondary sex ratios and male lifespan: Damaged or culled cohorts

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Communicated by Kirk R. Smith, University of California, Berkeley, CA, December 9, 2005 (received for review August 10, 2005)

Population stressors reportedly reduce the human secondary sex ratio (i.e., the odds of a newborn's being male) by, among other mechanisms, inducing the spontaneous abortion of males who would have been born live had mothers not been stressed. Controversy remains as to whether these abortions result from reduced maternal tolerance of males at the low end of a relatively constant distribution of survivability (i.e., the ''culled cohort'' explanation) or from shifts in the whole distribution of survivability such that more males fall below a relatively constant criterion of maternal tolerance for low survivability (i.e., the ''damaged cohort'' explanation). These alternatives make opposing predictions regarding the relationship between the secondary sex ratio and lifespan of male birth cohorts. We test the hypothesis that the secondary sex ratio among Swedish cohorts born in the years 1751 through 1912 predicts male cohort life expectancy at birth (i.e., realized lifespan). Our results support the culled cohort argument. We argue that these findings have implications for the basic literature concerned with temporal variation in the secondary sex ratio, for more applied work concerned with the fetal origins of adult health, and for pubic health surveillance.

fetal death | life expectancy | time series | population health

The human secondary sex ratio (i.e., the odds of a newborn's being male) reportedly declines when populations cope with shocks such as natural and human-made disasters (1–3), economic and political disruption (4–5), and terror attacks (6). Consistent with these findings, the sex ratio apparently varies inversely over time with the monthly incidence of treated anxiety among women (7). Explanations of this association include that gravid females subjected to stressful environments spontaneously abort weak male embryos and fetuses (8, 9). Empirical research supports this mechanism in that endocrine changes associated with the stress response in humans reportedly shorten gestation and affect males *in utero* more than females (10). The sex ratio of fetal deaths, moreover, reportedly increases when populations suffer environmental shocks (6, 11).

The literature offers two explanations of the association between maternal stress and the death of males *in utero*. The first posits that natural selection has conserved a mechanism by which gravid females in stressful environments improve their chances of grandchildren by affecting the gender of their children. According to Trivers and Willard (12), for example, aborting weak male embryos and fetuses increases the chances of grandchildren because, during times of environmental stress, weak sons produce fewer offspring than weak daughters. Aborting a weak male fetus presumably allows the mother to begin a new gestation that might yield either a daughter or a more robust son.

The above argument assumes that gravid females will spontaneously abort embryos and fetuses that, as illustrated in Fig. 1*A*, fall below some hypothetical criterion on a normal distribution of survivability. The stress response presumably shifts that criterion to the right, implying the abortion of embryos and fetuses that would have been carried to birth in less stressful times (Fig. 1*B*). Males predominate among these excess abortions because the distribution of males presumably lies to the left of that of females. This presumption arises from three facts. First, for reasons that remain unclear, death rates among males exceed those among females from birth through nearly the entire lifespan (13). Second, males outnumber females among fetal deaths (6, 11, 14, 15). Third, estimates of sex-specific death rates among fetuses report higher rates among males (16, 17).

The loss of male fetuses because of the ''right shift'' of the abortion criterion has two sequelae. First, the sex ratio of live births must fall because the sex ratio of abortuses rises. Second, males in birth cohorts with relatively low sex ratios should survive longer, on average, than those in other cohorts because the right shift culls weaker males *in utero*.

The second explanation of the association between environmental stress and the death of males *in utero* arises in response to the argument for maternal manipulation of the criterion for spontaneous abortion. Krackow (18), among others (19), characterizes the connection between offspring gender and likelihood of grandchildren, at least among higher vertebrates, as implausible. The statistical association between the sex ratio and ambient stressors more likely arises as a byproduct of the damage done to mothers and, in turn, embryos and fetuses by the stress response (20–22). Unlike the ''culled cohort'' argument, this ''damaged cohort'' mechanism does not assume maternal manipulation of the criterion for spontaneous abortion. That criterion remains constant, whereas the distribution of both males and females on survivability shifts (as illustrated in Fig. 1 *C* and *D*) to the left. This shift puts a greater fraction of the male distribution below the hypothetical abortion criterion because, as described above, the male distribution presumably lies to the left of that of females. The sex ratio of fetal deaths, therefore, should increase in times of environmental stress, requiring the secondary sex ratio of stressed cohorts to decline.

The damaged cohort argument has very different implications from the culled cohort theory for male fetuses who survive to birth. Their likelihood of further survival should be lower than males in birth cohorts with higher sex ratios. The culled and damaged cohort arguments, therefore, predict opposite associations between the secondary sex ratio of cohorts and cohort lifespan of males.

We contribute to the literature by testing the hypothesis that the secondary sex ratio among Swedish cohorts born in the years 1751 (earliest available data) through 1912 (most recent birth cohort with sufficient data to estimate true lifespan) predicts male cohort lifespan controlling for female cohort lifespan. An inverse association would support the culled cohort argument, whereas a positive association would support the damaged cohort argument.

Both the culled and damaged cohort theories imply that the association between the secondary sex ratio and lifespan may weaken over time with societal efforts to reduce the frequency and virulence of stressors with which populations must cope. Reduced doses of exogenous shock would reduce the culling of, or damage to, cohorts *in utero*. Changes in the sex ratio may,

Conflict of interest statement: No conflicts declared.

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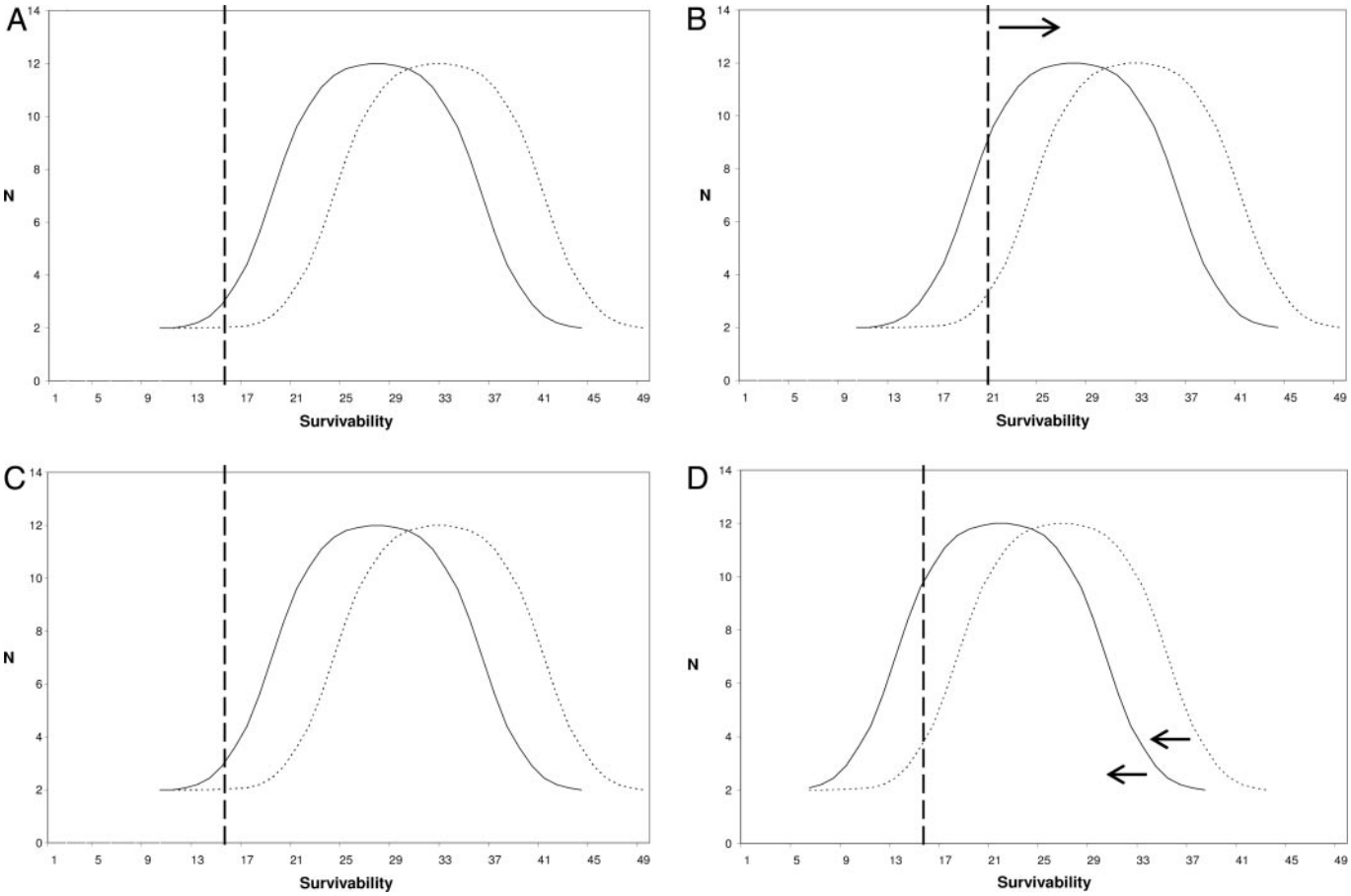

Fig. 1. Hypothetical representation of the survivability distribution of fetuses, by sex. The solid curve shows males, and the dotted curve shows females. Culled (*A* and *B*) and damaged (*C* and *D*) cohort models. (*A*) An average stress-level environment for the gravid female. The vertical dashed line represents the criterion below which a gravid female will spontaneously abort her fetus. (*B*) An elevated stress-level environment; the abortion criterion shifts right, whereas the fetal survivability distribution for males and females remains fixed. The marginal increase of fetal deaths among males exceeds that of females, resulting in a higher fetal death sex ratio and lower secondary sex ratio. (*C*) As in *A*, an average stress-level environment for the gravid female. (*D*) A higher stress environment; the abortion criterion remains fixed, whereas the fetal survivability distribution for males and females shifts left. The marginal increase of fetal deaths among males exceeds that of females, resulting in a higher fetal death sex ratio and lower secondary sex ratio.

therefore, be less indicative of culling or damage as time passes. The lifespan of the population may also increase through genetic mechanisms (23) as well as through reduced doses of exogenous shock. Our tests, therefore, adjust, as described below, for trends in both the sex ratio and lifespan. We also determine whether any association estimated over the entire test period results from early, rather than later, data.

Results

Figs. 2 and 3 show the secondary sex ratio and lifespan variables plotted over the test period. As implied by the conspicuous trends in Fig. 3, lifespan for both males and females required differencing (i.e., converting the series to annual changes) to render the series stationary in their mean.

As described in *Materials and Methods*, we began our analyses by building a base model in which we estimated annual changes in male cohort lifespan as a function of annual changes in female cohort lifespan and of autocorrelation in the residuals. The base model data in Table 1 show that annual changes in male and female cohort lifespan moved similarly over time. The coefficients in columns 2 and 3 indicate that male cohort lifespan exhibited autocorrelation in addition to that shared with female cohort lifespan. High or low values in male lifespan were typically followed in the next year, as well as 13 and 16 years later, by smaller but opposite outliers. Our analyses control for, but cannot explain, this male-specific autocorrelation. Any post hoc explanation of autocorrelation would be entirely speculative and akin to explaining the frequency of an outcome variable in the control group of a randomized experiment.

We then used Box–Jenkins routines (24) to decompose the secondary sex ratio into its statistically expected and unexpected components. This step yielded the following equation:

$$SR_t = 1.0491 + \frac{1}{(1 - 0.2158B - 0.2218B^3)}\, a_t. \qquad [1]$$

As expected, the sex ratio exhibited a mean >1 (i.e., 1.0491) over the test period. The first autoregressive parameter (i.e., −0.2158) suggests that movements above or below than mean, although diminished by ≈80%, carried into the following year. The second autoregressive parameter (i.e., −0.2218) implies that a value higher or lower than the mean in year *t* has an "echo" three years later. We used the residuals of this model as our independent variable because, as discussed in *Materials and Methods*, these measure the degree to which an observed value of the secondary sex ratio could not be expected from history.

The final model data in Table 1 show the results of estimating the equation formed by adding the residuals of Eq. **1** (i.e., the statistically unexpected values of the sex ratio) to the base model. The results support the culled cohort argument in that the

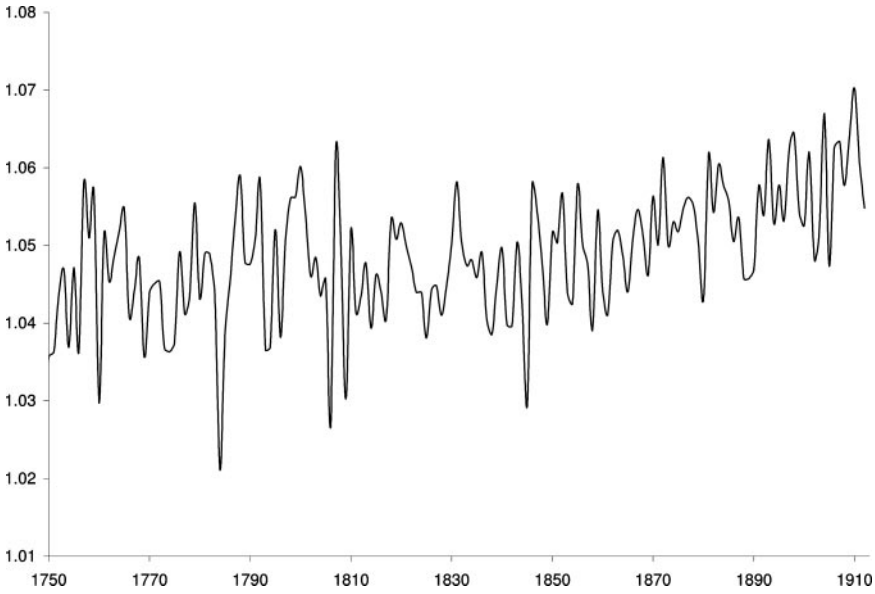

Fig. 2. Swedish secondary sex ratio for the 162 years beginning 1751.

coefficient for the sex ratio is significantly less than 0 ($P < 0.01$, two-tailed test).

The values of our independent variable, which gauges movement of the sex ratio around its expected value, ranged from −0.0276 to 0.0215. Applying the sex ratio coefficient (i.e., −11.2422) from Table 1 to these values suggests that the males in Sweden's "least culled" birth cohort (i.e., 1910) lived, on average, ≈3 (i.e., $11.2422 \times 12 \times 0.0215 = 2.9$) fewer months than expected from the lifespan of females in that cohort as well from historic trends unique to male cohort lifespan. Those in the most "most culled" cohort (i.e., 1784), on the other hand, lived ≈3.7 more months than was expected from history and from the lifespan of females in that cohort.

Our estimates may have been affected by outliers in the dependent variable. We therefore applied outlier detection and correction routines to our original analyses (25). The test found no outliers using the conventional tolerance for differences from expected values. We reduced the tolerance to the lowest level described in the literature (25) and detected five outlying values. Controlling these did not affect the outcome of our test in that the point estimate for the sex ratio variable changed very little and remained statistically different from 0 (from −11.2422 to −10.9770; SE = 0.0784).

As discussed in our Introduction, the association we discovered may have decreased over time as the dose of exogenous shock to populations fell. We tested this possibility by repeating our tests separately for the first and last 80 years of the period. The secondary sex ratio predicted male lifespan in both periods, but the point estimate was smaller in the later period (−15.5054; SE = 3.0926; −7.7548; SE = 3.7846).

Discussion

Our results support the culled cohort argument in that male cohort lifespan fell below values expected from both history and female lifespan among cohorts in which the secondary sex ratio increased above its expected value. Trends, cycles, or the tendency to remain elevated or depressed after high or low values could not have spuriously induced our results because we removed autocorrelation from both the dependent and independent variables. Nor could our findings have been spuriously induced by any unmeasured phenomenon that affects all fetuses because we specified female cohort lifespan as a covariate in our tests.

Fig. 3. Male and female cohort lifespan in Sweden for the 162 years beginning 1751.

Table 1. Coefficients (with SEs in parentheses) of the sex ratio and other variables predicting cohort lifespan of Swedish males for the years 1751–1912

Model	Cohort lifespan of females	Autoregressive parameters	Moving average parameters	Secondary sex ratio
Base model	0.9569** (0.0237)	$B^{13} = 0.1782$* (0.0822) $B^{16} = 0.2431$** (0.0841)	$B = 0.3280$** (0.0852)	
Final model	0.9674** (0.0199)	$B^{16} = 0.2124$** (0.0778)	$B = 0.2870$** (0.0828)	−11.2422** (2.3070)

*, $P < 0.05$; **, $P < 0.01$ (two-tailed test).

Intuitive questions raised by the above findings include whether they have implications for the literature reporting a positive association between early life illness and later morbidity (26, 27). Our results are consistent with such an association in that highly culled cohorts may have relatively low, whereas less culled cohorts may exhibit relatively high, death rates through much of the lifespan. Our results, however, conflict with the "fetal origins" inference (28), commonly drawn from the positive association between early and late life morbidity, that cohorts subjected to relatively high levels of stress *in utero* also experience relatively high levels of morbidity. Our findings suggest that, although circumstances *in utero* do affect the health of a birth cohort, we cannot assume that exogenous stressors reduce years of life for the cohort.

This study has several limitations, including that the results may not generalize beyond Sweden or to the contemporary experience there or elsewhere. Only replication can determine the external validity of these findings.

We cannot rule out the possibility that years in which the sex ratio declined below expected levels were also years in which relatively large fractions of births coincidentally occurred in months associated with longevity (29). Nor can we discriminate among the environmental insults (e.g., infectious or noninfectious toxins, wars, social disruptions, extreme weather, or food quantity or quality) that may have affected the sex ratio in the years we studied.

These limitations imply that our findings will be of more interest to demographers, human ecologists, and evolutionary biologists than to those interested in public health. We believe, however, that the work has implications for public health in that variation in the sex ratio may be a marker for changes in the fraction of the remainder of the population at risk of stress-related psychiatric and somatic illness. Gestation appears sensitive to ambient stressors that affect vulnerable populations. The close clinical observation we now give to pregnant women could provide us with sentinel data that might help professionals who plan and deliver a wide array of preventive and treatment programs for stressed populations to better anticipate the need for services. This possibility could be explored as part of the emerging effort to develop public health surveillance systems (30).

Materials and Methods

Data. We extracted our independent (i.e., Swedish secondary sex ratio for the years 1751–1912) and dependent (i.e., Swedish cohort life expectancy for males and females at birth) variables from the Human Mortality Database (www.mortality.org or www.humanmortality.de). We refer to cohort life expectancy at birth as cohort lifespan to avoid confusion with estimates, based on age-specific mortality rates, of life expectancy at birth among living cohorts. These data were available through 1912, the last year in which a sufficient proportion of a Swedish birth cohort, as defined in the Human Mortality Database Methods Protocol, was deceased to allow for lifespan estimation. Lifespan was not calculated for subsequent birth cohorts with many members still living.

We chose Swedish data for three reasons. First, Sweden has the longest series of life-table data available to researchers. Second, demographers have studied these data extensively and judge them of sufficient quality for testing hypotheses such as ours (www.mortality.org). Third, the literature includes reports of an association between environmental insults and the secondary sex ratio in Sweden (4, 7).

Design. Our test turns on whether male lifespan falls above or below its statistically expected value, controlling for female lifespan, in cohorts that exhibited secondary sex ratios higher or lower than their statistically expected value. Researchers typically assume that the statistically expected value of any variable is its mean. Cohort lifespan and sex ratios, however, exhibit trends and the tendency to remain elevated or depressed, or to oscillate, after high or low values. These patterns, referred to as "autocorrelation," complicate observational tests because the expected value of an autocorrelated series is not its mean.

Researchers dating at least to Fisher and his 1920 study of crop variation (31) have solved the autocorrelation problem by "decomposing" time series into temporally predictable and residual components. This approach removes patterns from the dependent variable before testing the effect of the independent variable and has the added benefit of avoiding spurious associations due to shared trends and cycles.

We implemented the Fisher approach to our test through the following six steps:

1. We regressed male cohort lifespan on female cohort lifespan. This step leaves male-specific changes that cannot be attributed to any phenomenon that induces autocorrelation or affects variability over time in both genders.
2. We used the methods devised by Dickey and Fuller (32) and Ljung and Box (33) to detect any male-specific autocorrelation in the residuals of the regression described in step 1. We then used the strategy developed by Box and Jenkins (24) to model any discovered autocorrelation. The strategy, autoregressive, integrated, moving average (i.e., ARIMA) modeling, allows any of a large family of possible models to be empirically fit to serial measurements. ARIMA models mathematically express various filters through which series without patterns can pass. Each filter imposes a unique pattern. The Box–Jenkins approach uses a model-building process by which the researcher infers the filter that imposed the observed pattern. The differences between the values predicted by the inferred model and the observed series are assumed to be the unpatterned values that were filtered.
3. We applied the routines described above to the secondary sex ratio in the same cohorts to separate the series into expected and unexpected components.
4. The unexpected component of the sex ratio series was added to the equation resulting from step 2. The test equation that emerges from step 4 is as follows:

$$\nabla^d Y_t = C + \omega_0 X_{1t} + \omega_1 X_{2t} + \frac{(1 - \theta_1 B - \theta_2 B^2 - \cdots - \theta_q B^q)}{(1 - \phi_1 B - \phi_2 B^2 - \cdots - \phi_p B^p)} a_t. \quad [2]$$

∇^d is the difference operator that indicates a series was differenced at order d (i.e., values at t subtracted from values at t-d) to remove secular trends or cycles detected by the Dickey–Fuller test. Y_t is lifespan for males in Sweden for the cohort born in year t. C is a constant. X_{1t} is the lifespan for females in Sweden for the cohort born in year t. X_{2t} is the statistically unexpected component of the secondary sex ratio for the cohort born in year t. ω_0 is the estimated parameter for the female lifespan variable. ω_1 is the estimated parameter for the secondary sex ratio variable. B^n is the "backshift operator" that yields the value of the lifespan variable at year n. θ is the moving average parameter. φ is the autoregressive parameter. B^p and B^q are backshift operators that yield the value of a at year t-p for autoregressive and t-q for moving average patterns, respectively. a_t is the error term for year t.

5. We estimated Eq. **2** and inspected the error terms to ensure that they exhibited no autocorrelation previously masked by variation shared with the predictor variables.
6. We measured the association between the error terms of the equation and X_1 and X_2 to ensure they were not related.

The analyses described in this article were supported by the Robert Wood Johnson Foundation.

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