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Selection *in utero* against male twins in the US early in the COVID-19 pandemic

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Abstract

Objectives: We aim to contribute to the literature reporting tests of selection *in utero*. The theory of reproductive suppression predicts that natural selection would conserve mechanisms, referred to collectively as selection *in utero*, that spontaneously abort fetuses unlikely to thrive as infants in the prevailing environment. Tests of this prediction include reports that women give birth to fewer than expected male twins, historically among the frailest of infants, during stressful times. The onset of the COVID-19 pandemic in the United States (US) in Spring 2020 demonstrably stressed the population. We test the hypothesis that conception cohorts in gestation at the onset of the pandemic in the US yielded fewer than expected live male twin births.

Methods: We retrieved de-identified data on the universe of live births in the US from the National Center for Health Statistics birth certificate records. We applied Box-Jenkins time-series methods to the twin secondary sex ratio computed for 77 monthly conception cohorts spanning August 2013 to December 2019 to detect outlying cohorts in gestation at the onset of the pandemic.

Author's Contributions
Tim A. Bruckner: Conceptualization, formal analysis, methodology, writing- original draft preparation, writing- review & editing. **Brenda Bustos**: Visualization, writing- original draft preparation, writing- review & editing. **Claire Margerison:** writing- original draft preparation, writing- review & editing. **Alison Gemmill:** writing- original draft preparation, writing- review & editing. **Joan Casey:** writing- original draft preparation, writing- review & editing. **Ralph Catalano:** formal analysis, writing- original draft preparation, writing- review & editing.

Ethical Statement
Data are de-identified and informed consent is not needed.

Conflict of Interest
The authors declare no conflict of interest.

Results: The twin secondary sex ratio fell below expected values in three conception cohorts (i.e., July, September, and October 2019, all $p<.05$) exposed *in utero* to the onset of the pandemic.

Conclusions: Our results add to prior findings consistent with selection *in utero*. The role of selection *in utero* in shaping the characteristics of live births cohorts, especially during the COVID-19 pandemic, warrants further scrutiny.

INTRODUCTION

The theory of reproductive suppression posits that natural selection has conserved mutations that enable women to avoid or end gestation when the environment threatens the salutary development of infants (Beehner & Lu, 2013). These conserved mutations include selection *in utero*, a mechanism that allows women to estimate, without cognition, the likelihood that a fetus, if born, will thrive in the prevailing environment (Bruckner & Catalano, 2018). Low estimates of thriving presumably induce spontaneous abortion before the woman makes additional somatic investment in a pregnancy that would otherwise yield a less reproductively fit offspring (Baird, 2009).

Selection *in utero* predicts, and empirical research finds (Baird, 2009; Hardy, Hardy, Jacobs, Lewallen, & Hassold, 2016), that genetic and chromosomal abnormalities that impede salutary development regardless of the environment disproportionately appear among fetuses spontaneously aborted early in gestation. The theory further predicts, and research supports, that fetuses spontaneously aborted later in gestation will include many without such abnormalities, but which have other characteristics that reduce, if born live, the chances of reaching reproductive age (Byrne & Warburton, 1987; Cnattingius, Haglund, & Kramer, 1998). These characteristics include male sex and birthweight (Catalano, Saxton, Bruckner, Goldman, & Anderson, 2009; Wells, 2000).

Male infants have, for every society and virtually every year for which we have dependable vital statistics, died more frequently than any other age by sex group before the end of reproductive life (Human Mortality Database, 2022). Male twins, typically the smallest of male infants, die more frequently than male singletons (Murray, MacKay, Stock, Pell, & Norman, 2020; Wenstrom & Gall, 1988). As a result, gestations of male twins born into challenging environments have historically produced fewer grandchildren than have gestations of female twins and of all singletons (Gabler & Voland, 1994; Lummaa, Jokela, & Haukioja, 2001). This relatively low fitness suggests that natural selection would conserve any mutations encoding a set of mechanistic pathways (e.g., hormonal cascades, metabolic changes) that spontaneously abort male twins when the environment stresses women of reproductive age (Bruckner & Catalano, 2018; Bruckner, Catalano, & Ahern, 2010; Catalano, Bruckner, Anderson, & Gould, 2005). This selection *in utero* does not require loss of both twins. In fact, improved early surveillance of gestations has led to the inference that at least a third of twin pregnancies convert to singletons before delivery (Landy, 1998).

Reports of selection *in utero* against male twins during stressful times appear in the epidemiologic literature (Catalano et al., 2012; Karasek et al., 2015). Research from Norway suggests that the onset of the COVID-19 pandemic may have triggered selection *in utero* (Catalano et al., 2021). Using time-series analyses, researchers detected fewer than expected male twins two months after the enactment of "shelter-in-place" policies. While suggestive, the Norwegian test used cohorts arrayed by month of birth rather than by month of conception. This aggregation combines live births of different gestational ages at birth (i.e., from 22 weeks to 42 weeks) and, therefore, from five different monthly conception cohorts. This approach makes it difficult to identify gestational weeks at which exposure to the onset of the pandemic increased selection *in utero*. Increasingly, scholars examining the effect of acute stressors on gestation have arrayed cohorts by estimated month of conception to identify sensitive periods in pregnancy (Brown, 2020; Bruckner, Lebreton, Perrone, Mortensen, & Blondel, 2019; Margerison et al., 2022). In addition, the external validity of the Norwegian study remains unknown because no replications appear in the literature.

We extend prior work to examine whether, in the United States (US), conception cohorts in gestation in Spring 2020 yielded fewer than expected male twin births. The US provides a useful setting for replication for two reasons. First, the US recorded an average of 5,180 male twins and 155,688 male births per month over the last five years, which minimizes the risk that variability due to a low volume of male twin births induces spurious findings. Second, surveillance epidemiology in the US detected fewer preterm births than expected from history among the 6 monthly cohorts conceived in the US from July through December 2019 (Catalano et al., 2021; Gemmill et al., 2022; Harvey et al., 2021) and in gestation during the "shelter-in-place" phase of the COVID-19 pandemic. This circumstance raises the possibility that if selection *in utero* contributed to "missing" preterm births during COVID-19, then at least 1 of those conception cohorts should also exhibit fewer than expected male twin births.

METHODS

Data

We used de-identified data from the National Center for Health Statistics (NCHS) birth certificate records. The NCHS natality files contain month and year of birth and gestational age in weeks (multiplied by 7 to obtain gestational age in days), which we used to define conception cohorts. Because we lacked exact birth dates, we assigned all births a random day of birth from the set of possible days of birth in that month (e.g., January = 31, February = 28 except in 2016 where February = 29). We then subtracted gestational age in days from the assigned birth date to estimate month of conception.

Previous research finds reduced risk of preterm birth in the US among conception cohorts, dating from July 2019 through December 2019, who were exposed *in utero* to COVID-19 related societal restrictions in Spring 2020 (Margerison et al., 2022). We therefore focused our test examining selection *in utero* against male twins on cohorts conceived through December 2019. The NCHS yielded 77 monthly conception cohorts starting August 2013 and ending December 2019. Our analytic sample included births to US residents ages 15 to 49 years (over 23 million). We excluded records missing length of gestation or birth weight and with implausible combinations of birth weight and gestational age (n=344,263). In addition, we excluded records from the "unrevised" (1989) version of the US Standard Certificate of Live Birth (instead of the "revised" 2003 version) (n=209,624).

For each monthly conception cohort nationwide, we computed the twin sex ratio (i.e., odds that a twin would be male) by dividing the count of male twins by the count of female twins. Use of this metric controls for fluctuations over time in the size of conception cohorts that equally affect the count of male and female twins.

Statistical analysis—Testing our argument requires comparing observed twin sex ratios to "counterfactuals" or values expected had sheltering in place not affected the processes that yield male twin births. The intuitive approach to devising these counterfactuals assumes that the twin sex ratio appears normally and independently distributed over time. If true, the counterfactual ratios for cohorts conceived from July through December 2019 (i.e., those exposed *in utero* to sheltering in place and reported to yield fewer than expected preterm births) would equal the mean of ratios among cohorts conceived earlier. The researcher could define "unexpected" values as those falling outside a detection interval set *a priori*.

Although the logic of the above approach seems straightforward, it cannot apply to twin sex ratios measured over time because they violate the assumption of independent distribution. As described below, we found that the 71 monthly ratios before July 2019 exhibited seasonality and the tendency to remain elevated or depressed after high or low values. The counterfactual for each of these ratios is, therefore, not their mean but the value expected from this "autocorrelation." Subtracting these counterfactuals from the observed values leaves residuals that meet the assumptions of independent distribution with an expected value (i.e., mean) of 0. If sheltering in place did not affect the mechanisms that yield twin sex ratios, subtracting the same autocorrelative pattern from the July through December 2019 ratios should leave residuals that fall within the 95% detection interval (i.e., 1.96 X the standard deviation) of the pre-July residuals.

Based on the above logic, we devised our counterfactuals with Box-Jenkins (Box & Jenkins, 1976) methods widely used in engineering and in the natural as well social sciences (McDowall, McCleary, & Bartos, 2019) to detect and model autocorrelation in serial measurements. These models "fit" autocorrelation and leave monthly residuals that meet the assumption of normal and independent distribution with an expected value of zero.

Our analyses proceeded through the following steps. First, we used Box-Jenkins methods to identify and model autocorrelation in the twin sex ratio yielded by the 71 cohorts conceived from August 2013 through June 2019. The residuals of this model meet the assumption of normal and independent distribution with an expected value of zero. Second, we defined the 95% detection interval of the residual series as the product of 1.96 and the residual series' standard deviation. Third, we applied the model, with parameter values fixed to those estimated in Step 1, to cohorts conceived from July through December 2019 (i.e., those found in earlier research to have yielded fewer than expected preterm births in the US). Fourth, we combined the residuals of from Steps 1 and 3 and graphed them as well as the 95% detection interval. Fifth, we inferred that the selection *in utero* argument survived our test if more than one cohort conceived from July through December 2019 had a twin sex ratio which fell below the detection interval.

A decline in the twin sex ratio could arise from either a fall in the numerator (i.e., odds of a male twin) or a rise in the denominator (i.e., odds of a female twin). If we discovered any support for a decline in the twin sex ratio among the COVID-19 exposed conception cohorts, we assessed whether this decline arose from changes in the numerator or the denominator. To do so, we used male- and female-specific twin ratios (i.e., the odds of a twin birth among males only and, separately, among females only) among the affected conception cohorts and re-estimated our equations, using these dependent variables, through the time-series steps described above. We then scored a binary variable as 1 for the months in which any conception cohorts showed, in our main test, lower than expected twin sex ratios and 0 otherwise. We added this binary variable to the models for the male and female twin ratios and estimated each.

RESULTS

Twin sex ratios, shown as points in Figure 1, over the 77 test cohorts ranged from 0.877 to 1.155 with a mean of 1.011. Box and Jenkins methods produced the following model for autocorrelation in the 71 cohorts conceived from August 2013 through June 2019.

$$\Delta_{12}Z_t = (1 - 0.344B)\left(1 - 0.651B^{12}\right)a_t$$

Z_t is the twin sex ratio for the cohort conceived in month t. Δ_{12} is the “difference operator” that indicates Z has been transformed such that Z_t has been subtracted from Z_{12} to model seasonality. The estimated coefficients −0.344B (Standard Error 0.123) and $-0.651B^{12}$ (Standard Error 0.106) are moving average parameters that imply high or low value twin sex ratios persist, although diminished, for a month and “echo,” as in seasonality, a year later.

Figure 1 also shows, as a line, the best fitting counterfactual values derived from applying the above model, with parameters fixed to those estimated for the first 71 cohorts, to the 77 cohorts. Figure 2 shows the differences between the counterfactual and observed values, and the 95% detection interval, for the 6 test cohorts. As shown, the cohorts conceived in July, September, and October yielded fewer than expected male twins (all $p<.05$). We infer that the argument for selection *in utero* survived our test and remains a plausible explanation of the fewer than expected preterm births among cohorts in gestation during the “shelter-in-place” phase of the COVID-19 pandemic. In addition, whereas two other adjacent cohorts exposed *in utero* (i.e., August and November 2019) did not show lower twin sex ratios that were statistically detectable, they similarly moved in the direction of lower twin ratios.

Variation over time in the twin sex ratio can reflect changes in the numerator or denominator of the ratio. As described in the Methods, we scored a binary variable score 1 for the months in which conception cohorts showed, in our main test, lower than expected twins sex ratios (i.e., July, September, and October 2019) and 0 otherwise. The binary-variable coefficient for males (i.e., −0.0008, Standard Error 0.0004; see Table 1) falls below the 95% detection interval whereas that for females (i.e., 0.0004, Standard Error 0.0005) fell within the interval.

To give the reader a sense of the magnitude of the discovered findings, we estimated the number of "missing" male twins in the 3 affected conception cohorts. Subtracting the observed number of male twins from their counterfactuals yielded 348 fewer male twins across the three cohorts. This value implies ~2.4% fewer male twins born than expected among the three conception cohorts affected *in utero* by COVID-19 events in Spring 2020.

DISCUSSION

Whereas much literature finds changes in live birth outcomes following the initial phase of COVID-19, less work examines the possibility that the stressful nature of the early pandemic induced selection *in utero*. We used conception cohorts and focused on male twin gestations, a subgroup which much theory and empirical work identifies as a sensitive gauge of selection *in utero*. Results using the universe of births in the US indicate fewer than expected male twin births among three monthly conception cohorts *in utero* at the time of COVID-19 "shelter-in-place" policies in March 2020. We hope these findings will encourage further research into the extent to which selection *in utero* accounts for unexpected patterns of perinatal outcomes in months immediately after the onset of the COVID-19 pandemic.

The magnitude of our results (in terms of percentage reduction of male twins during COVID-19 shelter-in-place policies) appears smaller than that reported for Norway, where odds of male twin births decreased by 27% (Catalano et al., 2021). We, however, caution against direct comparisons for two reasons. First, our US study examined conception, rather than birth, cohorts. Second, we focused on cohorts conceived before January 2020 because earlier research reports these exhibited characteristics (e.g., fewer than expected preterm births) consistent with selection *in utero*. By contrast, the largest declines in male twinning in Norway occurred among birth cohorts likely conceived *after* December 2019. We expect that the large observed reductions in fertility, as well as reduced availability of assisted reproductive technology in March 2020 (Vermeulen et al., 2020), could similarly reduce male twinning in the US among cohorts conceived in 2020.

Strengths of the study involve the conception cohort approach, use of the universe of twin births in the US, and application of rigorous time-series methods to rule out confounding by factors that affect male and female twin births equally. Well-developed theory of selection *in utero*, combined with a narrow time window specified *a priori* in which the onset of the pandemic likely affected male twin gestations, further enhances internal validity. In addition, although twin births appear more frequent among pregnancies conceived using assisted reproductive technologies (ART) (Maalouf, Mincheva, Campbell, & Hardy, 2014; Supramaniam et al., 2019), our findings cannot arise from COVID-induced disruptions in ART service provision that occurred in March and April of 2020, since the affected cohorts we identified were conceived in July, September, and October of 2019. Likewise, changes in fertility behaviors caused by the pandemic cannot drive our findings because the affected cohorts were conceived prior to the pandemic.

Limitations include the lack of direct measures of selection *in utero* such as fetal loss and/or spontaneous pregnancy losses before the 2nd trimester. Our study relies solely on the live birth data and the gestational age of delivery of live births. Very few countries (e.g., Denmark), however, routinely collect data describing early pregnancy loss at the population level and these data were not available to us. We also do not have information on the zygosity of twins, which precludes examination of whether selection against male twins occurred more for monozygotic than dizygotic twin gestations. We are currently pursuing the feasibility of both analyses using Scandinavian data.

The US data include only month and year of birth thereby requiring us to randomly assign parturition to days of the birth month. Although this strategy may lead to error in estimation of conception date, we know of no reason to infer that such errors biased counts of twin male births toward pre-pandemic conception cohorts. Finally, our analyses assess the US in aggregate. Different regions of the US may have responded differently to COVID-19 pandemic exposure or experienced stressors at different time points (e.g., New York City faced the brunt of the pandemic early on) (Van Dorn, Cooney, & Sabin, 2020). Future studies may wish to assess regional impacts of the COVID-19 pandemic on male twin births.

Our results add to the empirical research consistent with the argument that reproductive suppression in humans includes selection *in utero*. They also suggest that selection *in utero* may account for some as yet unknown, but worth estimating, fraction of the unusual characteristics (e.g., low frequency of preterm births) of infants born during the early months of the COVID-19 pandemic. Further attempts to quantify selection *in utero* during the pandemic would benefit from arraying putatively frail sets of gestations by conception, rather than by birth, cohorts.

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Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

Baird D (2009). The gestational timing of pregnancy loss: Adaptive strategy? American Journal of Human Biology. Retrieved from 10.1002/ajhb.20935

Beehner JC, & Lu A (2013). Reproductive suppression in female primates: A review. Evolutionary Anthropology, 22(5), 226–238. 10.1002/evan.21369 [PubMed: 24166923]

Box GE, & Jenkins GM (1976). Time series analysis: Forecasting and control San Francisco. Calif: Holden-Day

Brown R (2020). The intergenerational impact of terror: Did the 9/11 tragedy impact the initial human capital of the next generation? Demography, 57(4), 1459–1481. 10.1007/s13524-020-00876-6 [PubMed: 32514847]

Bruckner TA, & Catalano R (2018). Selection in utero and population health: Theory and typology of research. SSM - Population Health, 5, 101–113. 10.1016/j.ssmph.2018.05.010 [PubMed: 29928686]

Bruckner TA, Catalano R, & Ahern J (2010). Male fetal loss in the U.S. following the terrorist attacks of September 11, 2001. BMC Public Health, 10, 273. 10.1186/1471-2458-10-273 [PubMed: 20500812]

Bruckner TA, Lebreton É, Perrone N, Mortensen LH, & Blondel B (2019). Preterm birth and selection in utero among males following the November 2015 Paris attacks. International Journal of Epidemiology, 48(5), 1614–1622. 10.1093/ije/dyz089 [PubMed: 31231759]

Byrne J, & Warburton D (1987). Male excess among anatomically normal fetuses in spontaneous abortions. American Journal of Medical Genetics, 26(3), 605–611. 10.1002/ajmg.1320260315 [PubMed: 3565477]

Catalano RA, Saxton K, Bruckner T, Goldman S, & Anderson E (2009). A sex-specific test of selection in utero. Journal of Theoretical Biology, 257(3), 475–479. 10.1016/j.jtbi.2008.12.008 [PubMed: 19146859]

Catalano R, Goodman J, Margerison-Zilko CE, Saxton KB, Anderson E, & Epstein M (2012). Selection against small males in utero: A test of the Wells hypothesis. Human Reproduction (Oxford, England), 27(4), 1202–1208. 10.1093/humrep/der480 [PubMed: 22298840]

Catalano R, Bruckner T, Anderson E, & Gould JB (2005). Fetal death sex ratios: A test of the economic stress hypothesis. International Journal of Epidemiology, 34(4), 944–948. 10.1093/ije/dyi081 [PubMed: 15833788]

Catalano R, Bruckner T, Casey JA, Gemmill A, Margerison C, & Hartig T (2021). Twinning during the pandemic: Evidence of selection in utero. Evolution, Medicine, and Public Health, 9(1), 374–382. 10.1093/emph/eoab033 [PubMed: 34858596]

Cnattingius S, Haglund B, & Kramer MS (1998). Differences in late fetal death rates in association with determinants of small for gestational age fetuses: Population based cohort study. BMJ (Clinical Research Ed.), 316(7143), 1483–1487. 10.1136/bmj.316.7143.1483

Dorn A.van , Cooney RE, & Sabin ML. (2020). COVID-19 exacerbating inequalities in the US. The Lancet, 395(10232), 1243–1244. 10.1016/S0140-6736(20)30893-X

Gabler S, & Voland E (1994). Fitness of twinning. Human Biology, 66(4), 699–713. [PubMed: 8088755]

Gemmill A, Casey JA, Catalano R, Karasek D, Margerison CE, & Bruckner T (2022). Changes in preterm birth and caesarean deliveries in the United States during the SARS-CoV-2 pandemic. Paediatric and Perinatal Epidemiology, 36(4), 485–489. 10.1111/ppe.12811 [PubMed: 34515360]

Hardy K, Hardy PJ, Jacobs PA, Lewallen K, & Hassold TJ (2016). Temporal changes in chromosome abnormalities in human spontaneous abortions: Results of 40 years of analysis. American Journal of Medical Genetics Part A, 170(10), 2671–2680. 10.1002/ajmg.a.37795 [PubMed: 27287007]

Harvey EM, McNeer E, McDonald MF, Shapiro-Mendoza CK, Dupont WD, Barfield W, & Patrick SW (2021). Association of preterm birth rate with COVID-19 statewide stay-at-home orders in Tennessee. JAMA Pediatrics, 175(6), 635–637. 10.1001/jamapediatrics.2020.6512 [PubMed: 33720307]

Karasek D, Goodman J, Gemmill A, Falconi A, Hartig T, Magganas A, & Catalano R (2015). Twins less frequent than expected among male births in risk averse populations. Twin Research and Human Genetics, 18(3), 314–320. 10.1017/thg.2015.22 [PubMed: 25917386]

Landy H (1998). The vanishing twin: A review. Human Reproduction Update, 4(2), 177–183. 10.1093/humupd/4.2.177 [PubMed: 9683354]

Lummaa V, Jokela J, & Haukioja E (2001). Gender difference in benefits of twinning in pre-industrial humans: Boys did not pay. Journal of Animal Ecology, 70(5), 739–746. 10.1046/j.0021-8790.2001.00537.x

Maalouf WE, Mincheva MN, Campbell BK, & Hardy ICW (2014). Effects of assisted reproductive technologies on human sex ratio at birth. Fertility and Sterility, 101(5), 1321–1325. 10.1016/j.fertnstert.2014.01.041 [PubMed: 24602756]

Margerison C, Bruckner T, MacCallum-Bridges C, Catalano R, Casey J, & Gemmill A (2022). Exposure to the early COVID-19 pandemic and early, moderate, and overall preterm births in the US: a conception cohort approach. Paediatric and Perinatal Epidemiology.

McDowall D, McCleary R, & Bartos BJ (2019). Interrupted Time Series Analysis. Oxford University Press.

Murray S, MacKay D, Stock S, Pell J, & Norman J (2020). Association of gestational age at birth with risk of perinatal mortality and special educational need among twins. JAMA Pediatrics, 174(5), 437–445. 10.1001/jamapediatrics.2019.6317 [PubMed: 32150231]

Supramaniam PR, Mittal M, Ohuma EO, Lim LN, McVeigh E, Granne I, & Becker CM (2019). Secondary sex ratio in assisted reproduction: An analysis of 1 376 454 treatment cycles performed in the UK. Human Reproduction Open, 2019(4), hoz020. 10.1093/hropen/hoz020 [PubMed: 31598568]

Vermeulen N, Ata B, Gianaroli L, Lundin K, Mocanu E, Rautakallio-Hokkanen S, … Veiga A (2020). A picture of medically assisted reproduction activities during the COVID-19 pandemic in Europe. Human Reproduction Open, 2020(3), hoaa035. 10.1093/hropen/hoaa035 [PubMed: 32821857]

Wells JCK (2000). Natural selection and sex differences in morbidity and mortality in early life. Journal of Theoretical Biology, 202(1), 65–76. 10.1006/jtbi.1999.1044 [PubMed: 10623500]

Wenstrom KD, & Gall SA (1988). Incidence, morbidity and mortality, and diagnosis of twin gestations. Clinics in Perinatology, 15(1), 1–11. 10.1016/s0095-5108(18)30721-8

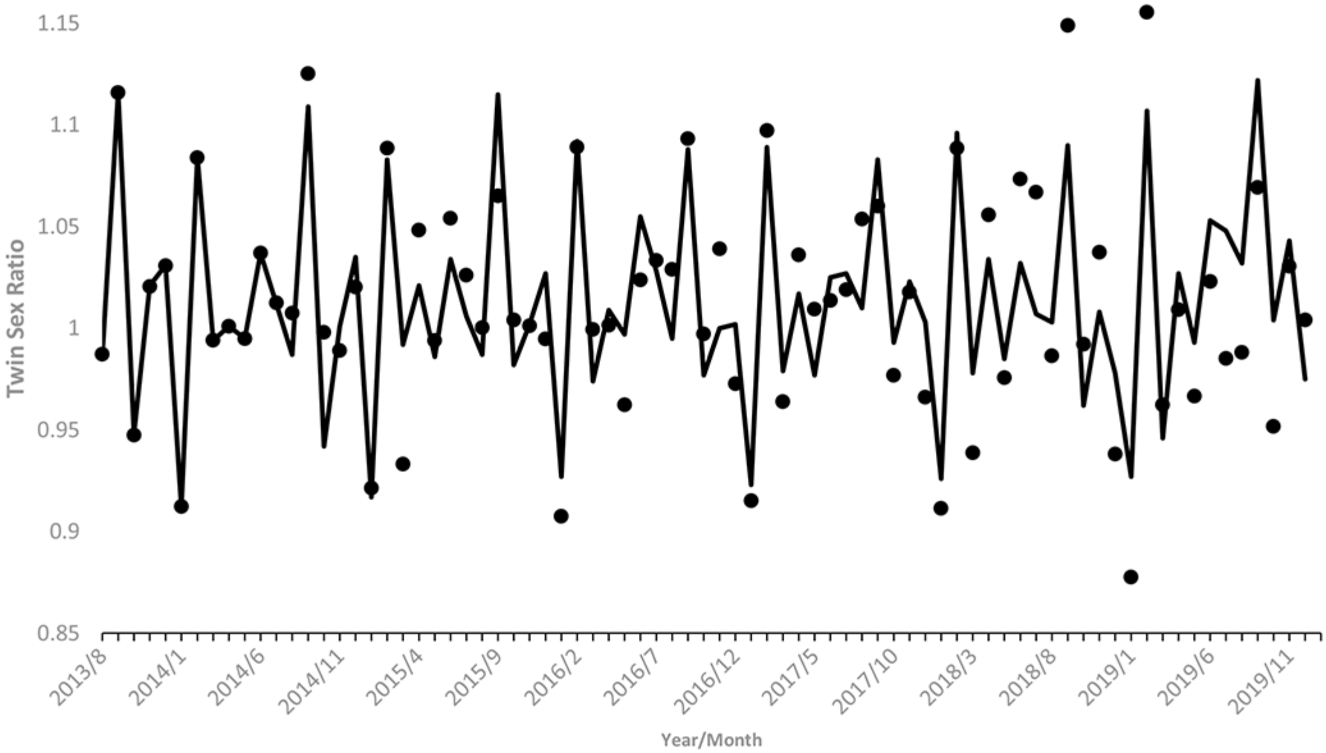

Figure 1.

The US twin sex ratio (odds that a twin would be male versus female) over 77 monthly conception cohorts from August 2013 to December 2019. The points represent the observed twin sex ratio. The line represents the best fitting counterfactual using the model.

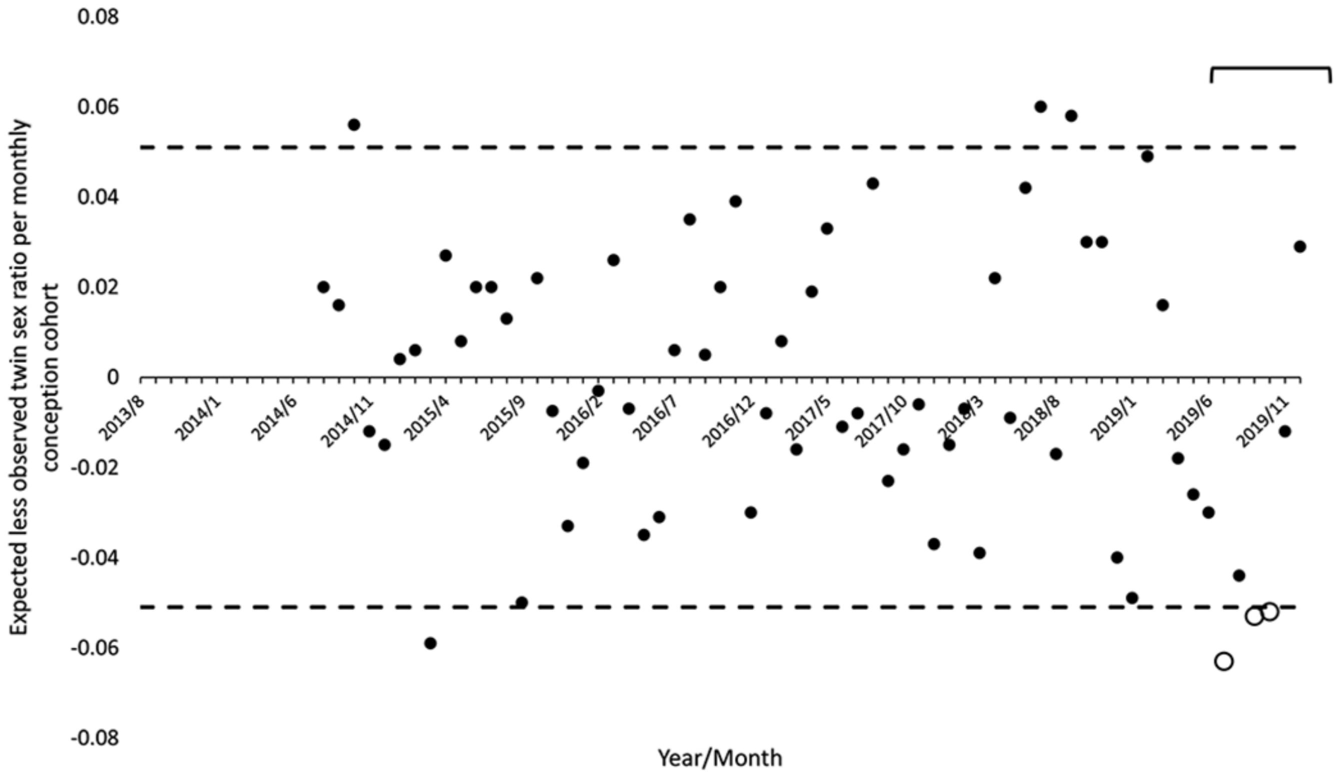

Figure 2.
The expected less observed twin sex ratio for 77 US monthly conception cohorts from August 2013 to December 2019. The dashed line represents the 95% detection interval. The six conception cohorts exposed *in utero* to initial COVID-19 societal restrictions in March 2020 are shown in brackets. Additionally, the three conception cohorts with fewer than expected male twins are shown as open circles.

Table 1

Time-series results predicting monthly values of male twin births in the US for conception cohorts from August 2013 to December 2019 as a function of sex-specific twin ratios, autocorrelation, and the discovered outlier in male twin ratios among COVID-19 exposed conception cohorts.

Parameter	Coef.	SE
Constant	−.003***	.00005
Outlier-detected indicator during COVID-19	−.0008*	.0004
Moving Average at lag 5 months	−.28*	.11
Moving Average at lag 12 months	.92***	.08

* p<.05;

** p < .01;

*** p<.001