

Selection *in utero* & the Black survival advantage

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NH Black / NH white differences in infant death



Preterm birth (<37 wks GA) increases risk of infant death, developmental delays, and low educ attainment

In US, NH Black mothers have 1.6 fold increased risk of delivering preterm (vs. NHW)

NH Black infants die before age 1 yr at 2x rate of NH white infants

But . . . a pediatric paradox (1989-2015 data, US)

Fig 1a. Risk of neonatal mortality, gestational ages 24–29 weeks

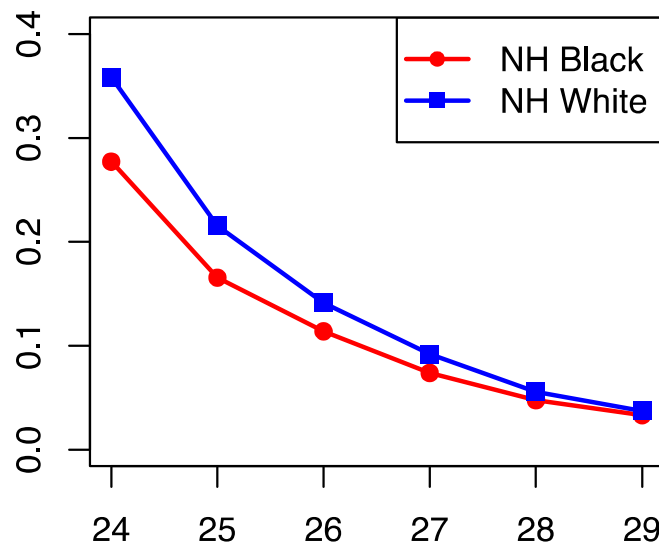
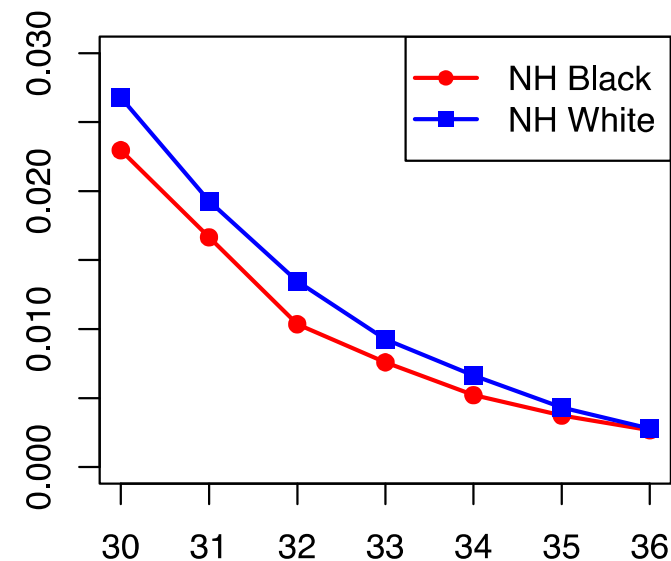


Fig 1b. Risk of neonatal mortality, gestational ages 30–36 weeks



- At each GA, risk of neonatal death is lower for NH Black births
- Largest risk difference in periviable period (<26 wks GA)

1 assumed cause of paradox

- * Greater *selection in utero* (left-truncation) against frail NH Black fetuses
- * Many very PTB have more in common with fetal deaths than with term infants
- * Fetal death >20 wks for NHB is 2x that of NHW; greater risk of earlier loss too
- * socio-economic and other stressors among NHB persons may lead to more spontaneous loss that, absent the stressors, would have led to vPTB
- * few empirical tests of left-truncation argument

Male twins and twin sex ratios

Male twins rank among the frailest of all live births

- typically born preterm
- historically, lower survival (infancy and beyond) vs. singletons and female twins

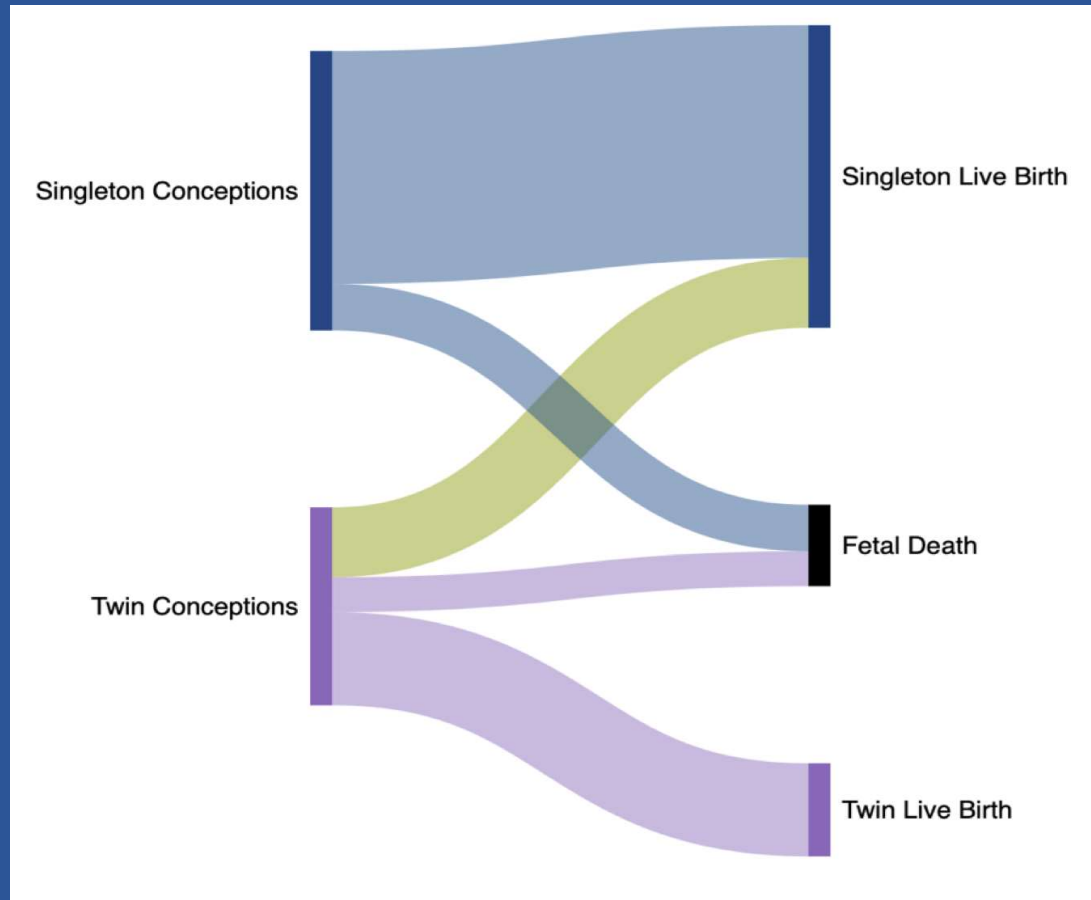
Twin sex ratios (m:f) fall after population shocks

- COVID-19 (spring 2020) in both Sweden and US
- Oslo massacre

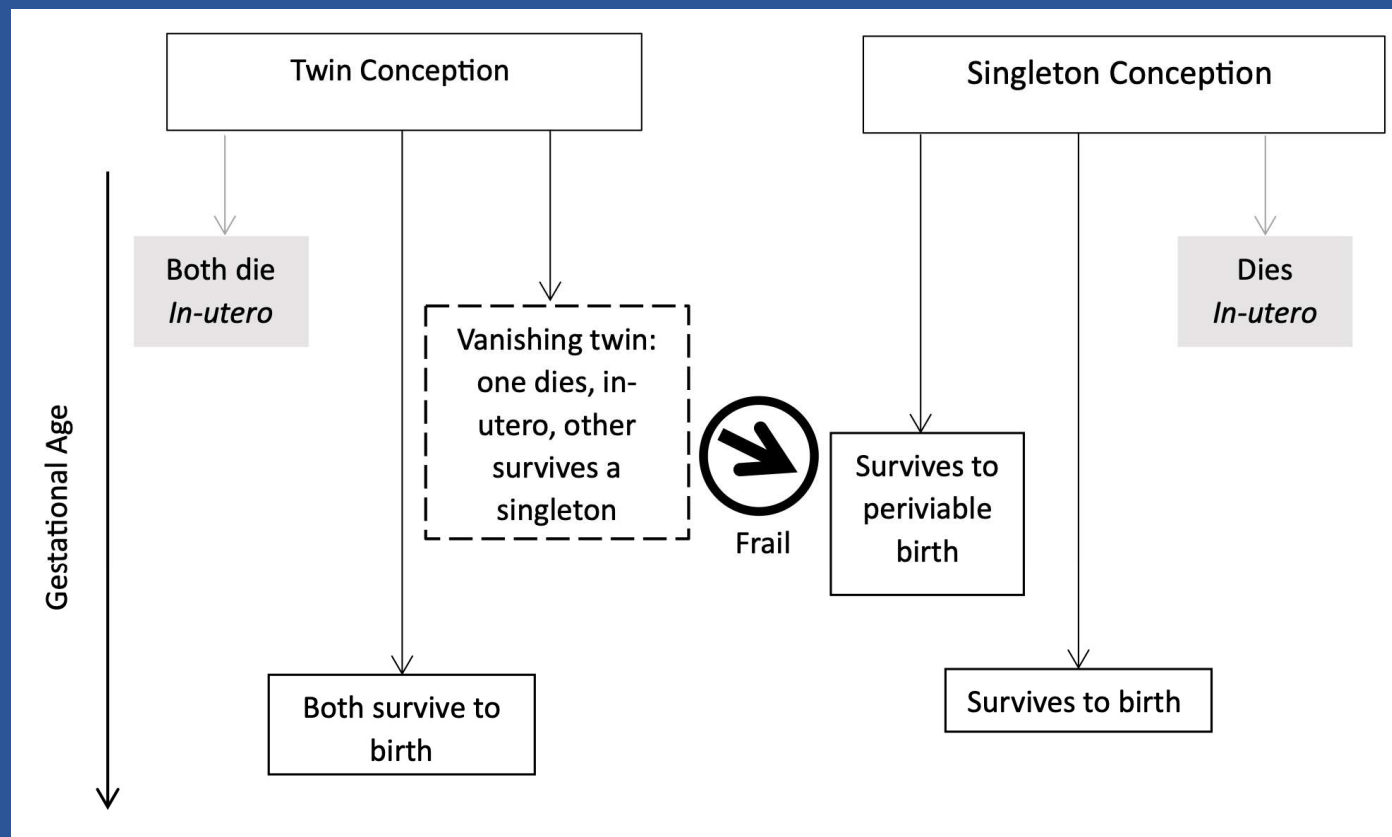
“Vanishing twin” – up to 35% of twin fetuses convert to singletons before live birth

- smaller (slower-growing) fetus dies *in utero*
- survivors of vanishing twins are lighter than “true singletons” of same GA
- we cannot observe vanishing twins directly

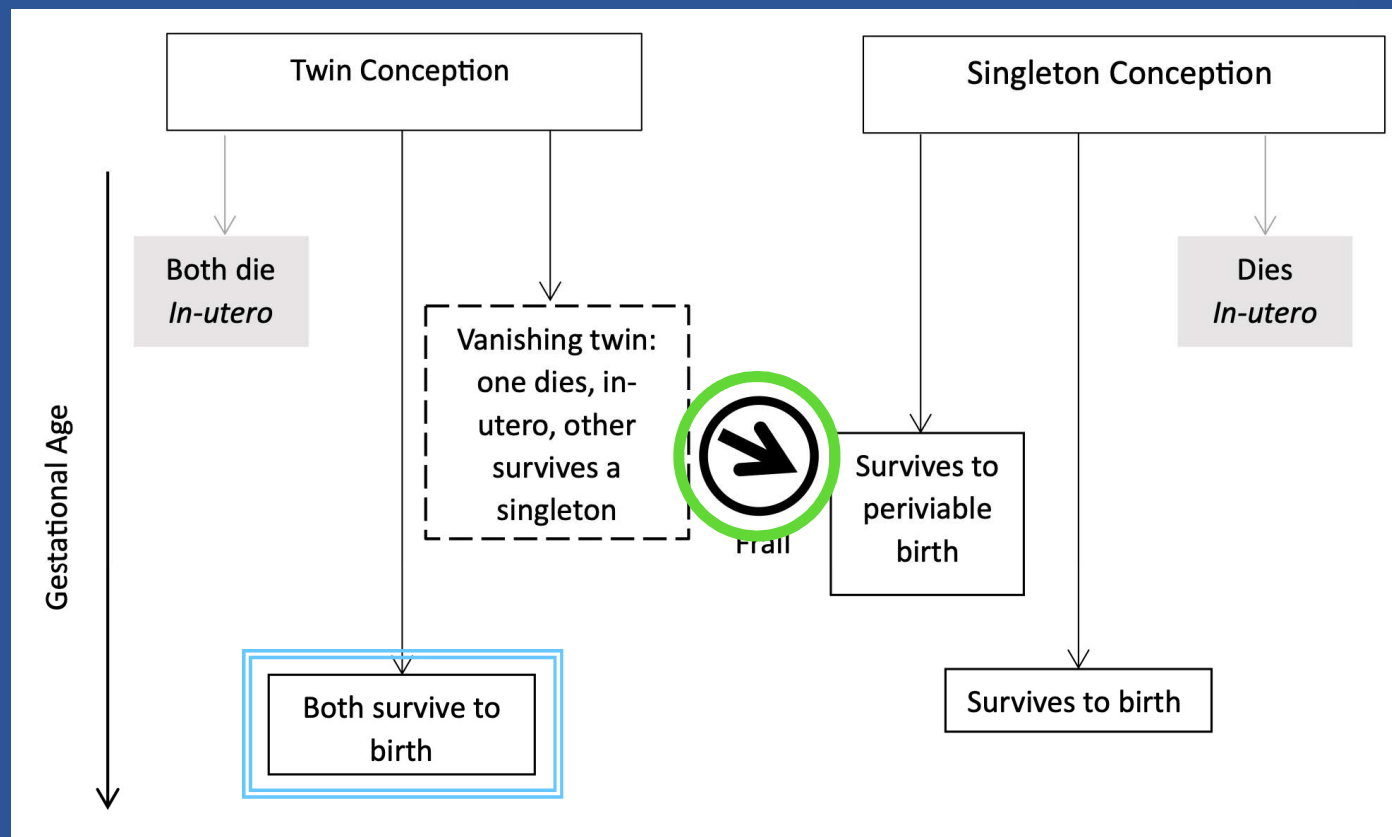
Vanishing Twin Syndrome (VTS) → **Green**



Could vanishing twins affect male periviable singleton survival?



Use **twin ratio** among ePTB to gauge strength of male VTS



If twin sex ratio among ePTB is high . . .

- * Fewer than expected male twins would “convert,” via vanishing twin, to a frail male periviable birth
 - the males “stay” as twins until live birth (and don’t become light singletons)
- * Observed male periviable singletons in that same conception cohort would therefore show reduced risk of infant death
- * We test the hypothesis that singleton periviable risk of infant death among NHB males varies inversely with ePTB twin ratio in that same conception cohort

Data

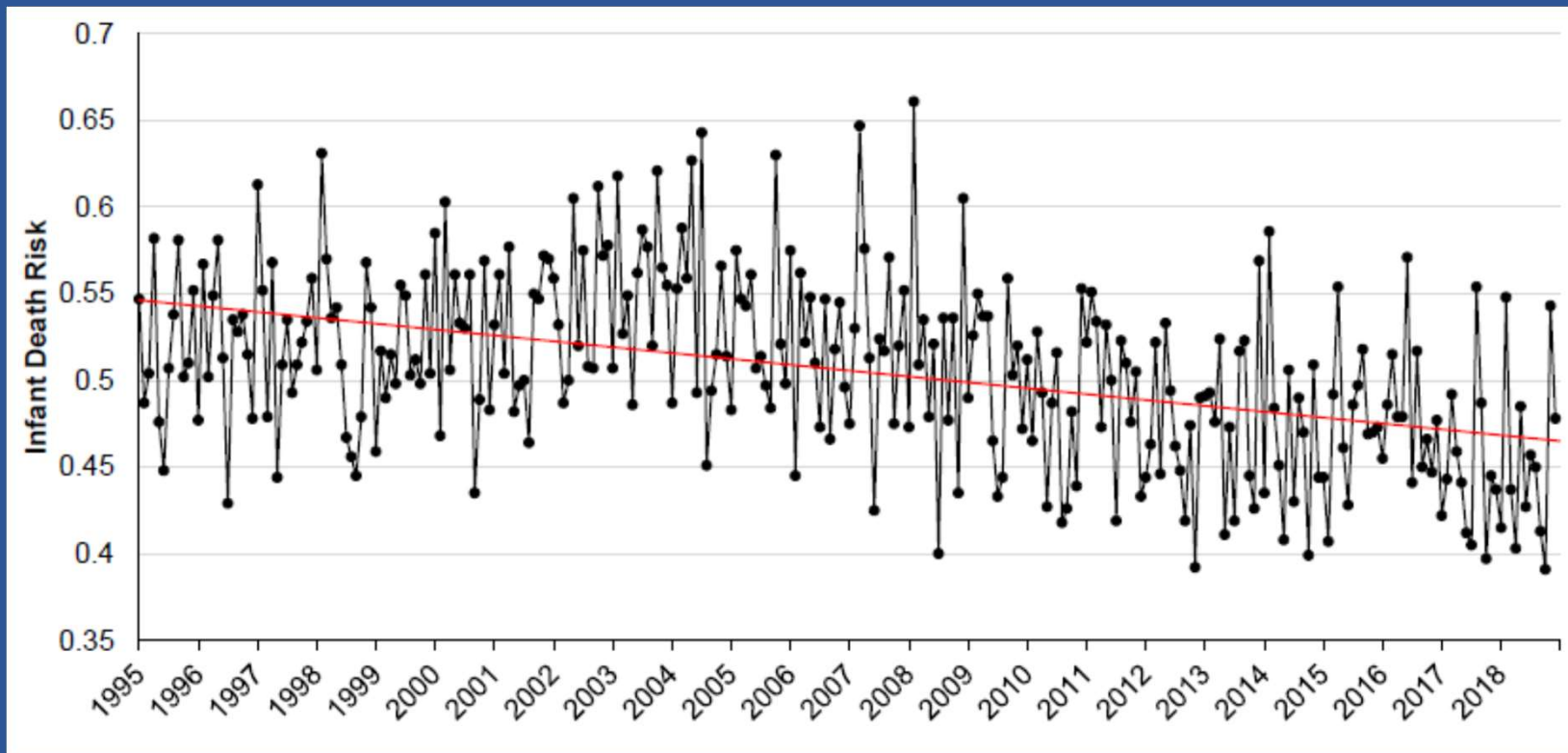
US Natality File, 1995 to 2019; over 10 million preterm births
used combined GA estimate (OB and LMP)

Information on

- race/ethnicity (NHB and NHW)
- sex
- singleton / twin

Organized all data by estimated conception month (to align with cohort structure)

NHB periviable male singletons, risk of infant death



monthly mean # of births=215;
288 months;

mean risk of death = 0.506
>62,000 births over test period

Augmented time-series methods (ARIMA)

Remove shared autocorrelation from 2 other conception cohort series

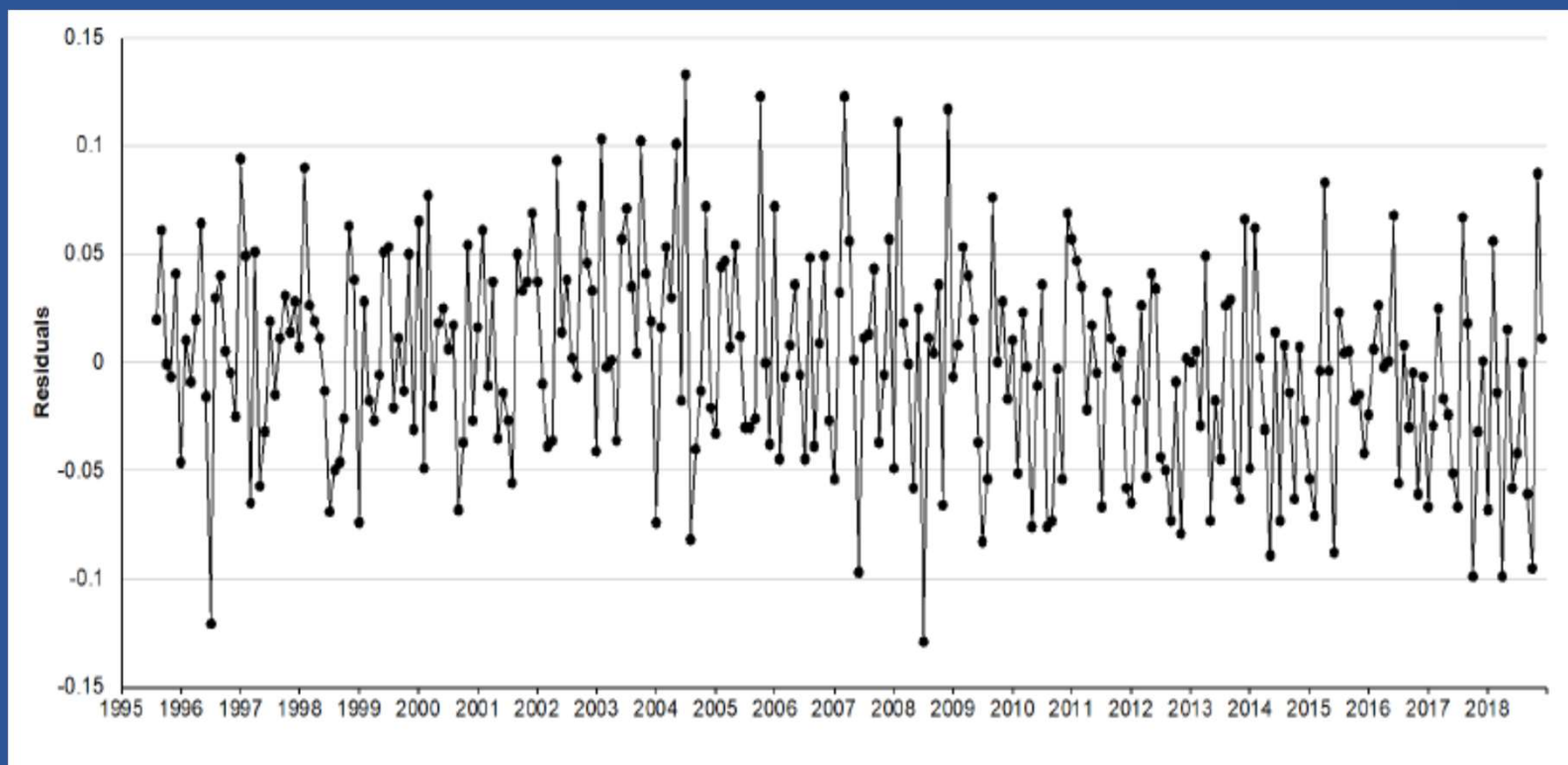
- NHB periviable singleton **females**
- **NHW** periviable singleton males
- analogous to a triple difference model; can interpret as a “paradox” coef.

Then, use ARIMA methods to remove any remaining patterns unique to dependent variable series

Once series is “white noise”, then add the NHB twin sex ratios (by conception cohort) as the key independent variable

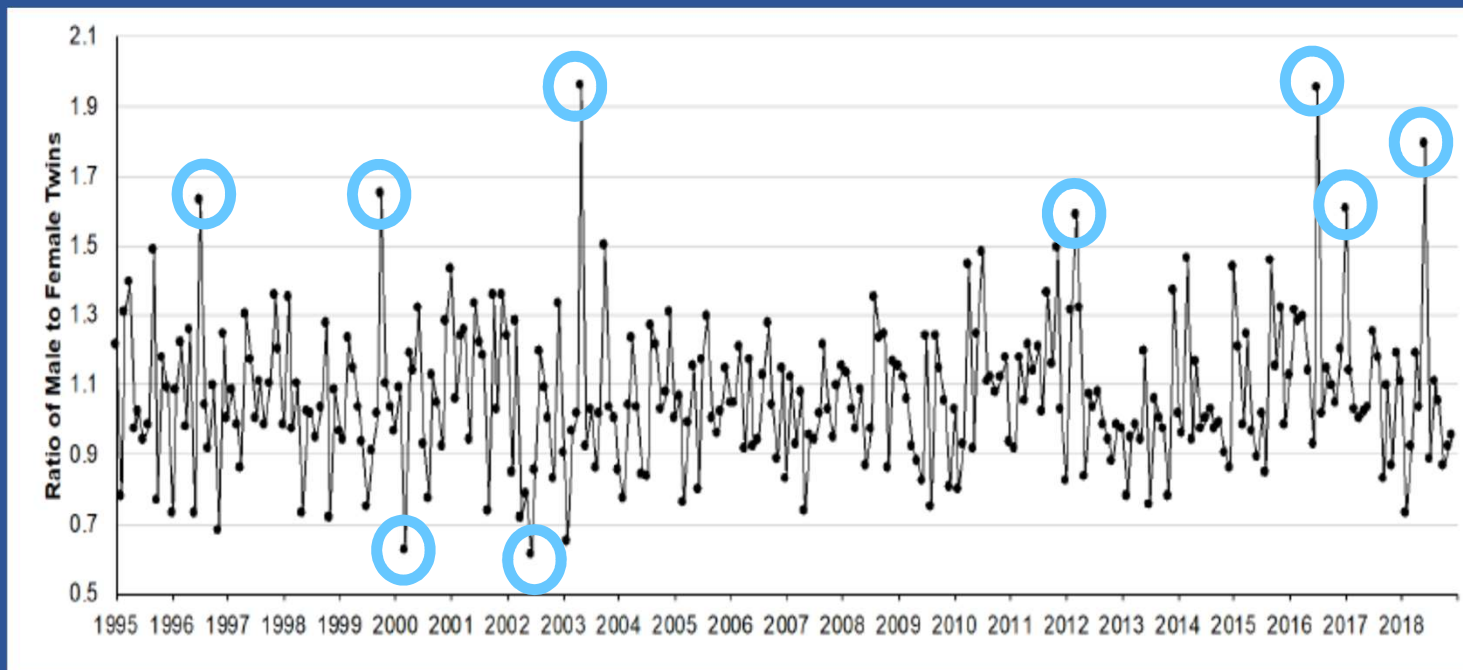
- given stochastic variability of twin sex ratio series, use outliers (high and low)

“White noise” NHB periviable male singletons, risk of infant death



Mean=0; all values are serially independent of one another

NHB Twin Ratio for <28 weeks



Mean=1.06;

range: 0.61 to 1.95;

~130 per month

○ = outlier

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ARIMA results: Risk of infant death among NHB singleton periviable males

	Extremes Test coef (95% CI)
NH Black Twin sex ratio ^a	-0.066 (-.115, -.017)
<u>Infant Death Risks among</u>	
NH white periviable male singletons	.181 (.060, .301)
NH Black periviable female singletons	.190 (.073, .306)
<u>Autoregressive parameters</u>	
B^2	.165 (.048, .282)
B^5	.192 (.075, .308)
Constant	.322 (.250, .395)

4.2 per 100 fewer infant deaths among NH Black periviable singleton males when male twin frequency in that conception cohort is very high (i.e., vanishing male twin rate is presumably low).

8.3% reduction in risk during high twin ratio outlier months

Inference

When vanishing twins are “missing” from periviable singleton group, NHB male risk of infant death falls

Provides empirical support for left-truncation as a contributor to survival advantage among NHB males in periviable period

Interpretation

- Our test focuses on specific conception cohorts; it does not attempt to explain racial differences in mean infant survival
- Whereas focus on periviable period is justified, the search for quality measures of selection *in utero* continues...
- I welcome collaborators—especially when thinking about the extent to which stillbirth (fetal death) data could be used to approximate variation across place/time in selection

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Thank you

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Lab Website



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Sex ratio as one measure of left-truncation

Fetal deaths remain woefully under-reported in vital statistics

Scholars have attempted to infer left-truncation from characteristics of live births

Sex ratio (M:F) of live births falls following population stressors



Sex ratio / male infant survival

Males born to most “selected” cohorts show relatively

- greater infant survival
- fewer birth defects
- less childhood cancers
- improved child development (i.e., test scores)

(esp. for very low sex ratio cohorts)

<https://doi.org/10.1016/j.socscimed.2012.10.012>

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<https://doi.org/10.1158/1055-9965.EPI-21-0053>

<https://doi.org/10.1073/pnas.051056710>



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Research objectives using US Data, 1995 - 2018

Does strength of selection against males explain a portion of pediatric paradox?
- deep dive into **twin sex ratios** & survival among singleton periviable male births

Questions?

