Does the lack of heritability of human sex ratios require a rethink of sex ratio theory? No : a Comment on Zietsch et al. 2020

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9   **sex ratio theory? No: a response to Zietsch *et al*. 2020**

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32   Zietsch et al. (2020) estimated the heritability of the sex ratio at birth in humans by
33   measuring the association between the sex ratios produced by over 14 million Swedish sibling
34   pairs. The heritability estimate was 0.00058, with a 95% confidence interval of -0.00076 - 0.00196.
35   They concluded that the sex ratio differences observed among the families of siblings are not due to
36   genetic differences in the tendency to produce one sex more than the other. Zietsch et al. also
37   concluded that this result renders (p.1) "Fisher's principle untenable … [as a framework] for
38   understanding human offspring sex ratio". Here, we discuss why the latter conclusion is incorrect.

39   Düsing (1884) created the theoretical framework from which our understanding of sex ratio
40   evolution derives. This framework was then elaborated in important ways by, among others, Fisher
41   (1930), Shaw and Mohler (1953), Shaw (1955, 1958), Kolman (1960), MacArthur (1965),
42   Hamilton (1967), Leigh (1970), Charlesworth (1977, 1994), Kahn et al. (2015) and Argasinski and
43   Broom (2020). Overviews of the current state of theory and its empirical application can be found
44   in Charnov (1982), Bull and Charnov (1988), Karlin and Lessard (1986), Wrensch and Ebbert
45   (1993), Hardy (2002) and West (2009). A key result of this theory is that there can be an "equal
46   investment" equilibrium resulting from the action of natural selection in a randomly-mating
47   population. It occurs when the cumulative resource invested in female offspring and the cumulative
48   resource invested in male offspring are equal at the end of parental investment. If the ratio of
49   resource investments is 1 and females and males have identical mortality rates, the equilibrium
50   occurs when there are equal proportions of females and males in the mating pool of adults. This is
51   often referred to as the 1:1 sex ratio equilibrium. If the cumulative resource investments are not
52   equal, the evolutionary equilibrium is an unequal numerical sex ratio, with the more costly sex
53   being in the minority.

54   What is the evolutionary process that can result in the evolution of the equal investment
55   equilibrium? Consider the case when females and males are equally costly to produce and have
56   identical mortality rates. If equal proportions of females and males are not present in the mating
57   pool, parents that produce more of the rarer sex will leave more descendants. If the tendency to
58   produce the rarer sex is inherited, these descendants will also produce more offspring of the rarer
59   sex. This decreases the sex ratio bias in the mating pool formed by these offspring, which means
60   that the advantage of producing the rarer sex decreases. This dynamic attains an evolutionary
61   equilbrium only when both sexes have equal proportions in the mating pool. This equilibrium is
62   consistent with the absence or presence of genetic variation influencing the sex ratio (see below).

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63 Empirical investigations confirm that this process of "frequency-dependent" natural selection can

64 result in the attainment of this evolutionary equilibrium (e.g., Conover and Van Voorhees 1990;

65 Basolo 1994). Additional theory describes the conditions under which the equilibrium sex ratio

66 produced by the population is predicted to be produced by each individual or mated pair (see

67 Orzack and Hines 2005 and references therein). Zietsch et al. denote as "Fisher's principle" the

68 process by which individuals producing the rarer sex have an evolutionary advantage, which

69 thereby increases the frequency of the sex they produce: we refer to it as the "Düsing-Fisher

70 principle".

71   For the Düsing-Fisher principle to cause the sex ratio to evolve, offspring sex ratio must be

72 inherited from parents to offspring, at least in part, and there must be inherited variation among

73 individuals or couples in regard to the offspring sex ratio they produce (the latter condition is that

74 the trait be "heritable", see Falconer and Mackay 1996 for the distinction between this condition

75 and the condition that a trait be inherited). However, contrary to the claims of Zietsch et al. (2020),

76 the Düsing-Fisher principle makes no inference that the sex ratio be heritable *at the evolutionary*

77 *equilibrium*. For example, a 1:1 sex ratio equilibrium is consistent with, say, each individual having

78 a genotype that causes them to produce the same 1:1 sex ratio (not heritable) or with half of them

79 having a genotype that causes them to produce all daughters and half of them having a genotype

80 that causes them to produce all sons ("maximally" heritable; cf., Patterson 1928). No implication

81 about the realized importance of the Düsing-Fisher principle as an evolutionary explanation for the

82 human sex ratio can be drawn from the fact that the sex ratio is not heritable in the Swedish sample.

83 The evolutionary equilibrium arising from the Düsing-Fisher principle is like those arising in many

84 other evolutionary contexts: the attainment of the equilibrium erases the evidence of the causal

85 process that led to its evolution (e.g., Hartl et al. 1985). Therefore, Zietsch et al.'s results do not

86 render the Düsing-Fisher principle inherently untenable as a framework for understanding the

87 evolution of the human offspring sex ratio. In this context, we note that Zietsch et al. appear to

88 assume that the absence of genetic variation for the sex ratio at birth implies that there is no genetic

89 variation for the human sex ratio at any age, especially the later age at which the evolutionary

90 equilibrium attained by the Düsing-Fisher principle might be attained. There is no reason that this

91 assumption must be true, especially given the age-specificity of the expression of many traits (e.g.,

92 Leips et al. 2006).

93   Zietsch et al. conclude (p. 6) that their results are consistent with "the simple explanation
94   that variation in offspring sex ratio in humans is due to unbiased Mendelian segregation of sex
95   chromosomes during spermatogenesis and unbiased fertilization". This is correct, although it does
96   not have precedence over the Düsing-Fisher principle as an evolutionary explanation. In human
97   spermatogenesis, meiosis results in the production of statistically-equal proportions of gametes
98   containing an X chromosome and of those containing a Y chromosome and equal numbers of
99   females and males appear to be conceived (see results and discussion in Orzack et al. 2015). These
100   outcomes could be the result of natural selection for "honest meiosis" (Leigh 1977) and thereby not
101   arise from natural selection on the sex ratio in a direct sense. However, both processes of natural
102   selection could operate or have operated simultaneously. It is also possible that the XY process of
103   sex determination is an outcome of natural selection for a 1:1 sex ratio. Even if natural selection on
104   the sex ratio was the sole evolutionary influence on the human sex ratio in the past, it is arguable
105   that the extent to which the Düsing-Fisher principle, or other adaptive sex ratio processes, can
106   operate currently is greatly limited by the presence of chromosomal sex determination (Williams
107   1979). We note in this context that investigators seeking an adaptive explanation for the human sex
108   ratio sometimes implicitly assume that it has evolved via natural selection within *Homo sapiens*.
109   There is no compelling reason to think that this is true and there is evidence to indicate that it is not.
110   For example, estimates of the sex ratio at birth vary among primates, but many are statistically
111   similar to the male-bias observed in many human populations or to a 1:1 sex ratio at birth
112   (Sugiyama 2004; White 2009; Bronikowski et al. 2016). Similarly, post-birth age-specific mortality
113   rates are lower for females than for males in several primate species, just as in humans
114   (Bronikowski et al. 2011). Evolutionary explanations for the sex ratios observed among primate
115   species remain controversial (e.g., Schino 2004; Silk et al. 2005). Whatever the conclusion about
116   the adaptive significance of sex ratios in other primates, it is essential to assess the influence of
117   evolutionary history when attempting to understand the evolution of human sex ratios. Even if one
118   assumes that the Düsing-Fisher principle is the evolutionary explanation for the human sex ratio,
119   this does not identify when this process of natural selection occurred. It could, for example, have
120   occurred when mammals evolved in the Mesozoic, when primates evolved in the Paleocene, or
121   more recently when apes evolved in the Oligocene. If so, the sex ratio of *Homo sapiens* would be at
122   least in part a result of past evolution, instead of being entirely a result of current evolution in
123   human populations, and indeed this potential influence of past evolution is mentioned by Zietsch et
124   al. (p. 7). Consideration of the influence of such "phylogenetic inertia" (Felsenstein 1985; Hansen

125 and Orzack 2005) is rare among analyses that attempt to compare the predictions of sex allocation
126 theory to data from humans and other vertebrates and can render their conclusions ambiguous.

127   Finally, we comment more broadly on what is and is not known about the evolution of the
128 human sex ratio. The sex ratio at birth in most populations is slightly, but significantly, biased
129 towards males (Garenne 2002, 2008; Mathews and Hamilton 2005; Chao et al. 2019; Zietsch et al.
130 2020) and thereafter is statistically equal for only a small portion of a cohort's existence. Neither
131 fact can be interpreted as evidence for or against the Düsing-Fisher principle, and sex allocation
132 theory more generally, given the absence of evidence about the empirical validity of the
133 assumptions underlying the equal investment equilibrium. For example, there is extensive evidence
134 for non-random mating within and between human populations but its influence on the evolutionary
135 success of individuals or couples producing different sex ratios remains unclear. In addition, the age
136 at which resource investment by parents ends is poorly known at best for humans and many other
137 species. To this extent, the age(s) at which the observed sex ratio should be compared with the sex
138 ratio predicted by the Düsing-Fisher principle are unknown.

139

140 **Conclusion**

141   Attaining a full understanding of the evolutionary basis for human sex ratio biology is
142 challenging at best and is likely unattainable. Important reasons for this are the subtle sex ratio
143 effects predicted for humans by sex ratio theory, cultural practices, such as son preference (e.g.,
144 Malpani et al. 2002) and sex-balancing of families (e.g., Pennings 1996) that can obscure the
145 influence of natural selection, plus ethical constraints on experimentation (Lazarus 2002; Mace and
146 Jordan 2005; West and Burton-Chellew 2013; Hardy and Maalouf 2017; Gellatly 2020)

147   The substantial evidence provided by Zietsch et al. (2020) leaves little doubt that differences
148 among siblings in regard to the sex ratio at birth of offspring they produce are not due to inherited
149 differences. However, this absence of inherited variation is not evidence against the claim that
150 Düsing-Fisher frequency-dependent selection has influenced the human sex ratio. Nonetheless, if
151 and when this process of natural selection has influenced the human sex ratio remains unresolved.

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159 **Authors' contributions statement**

160 The order of authorship was determined randomly, with equal contributions.

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162 **Ethics statement**

163 The authors know of no ethical concerns associated with this commentary.

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165 **Data accessibility statement**

166 There are no data associated with this commentary.

167

168 **Competing interests statement**

169 The authors declare no completing interests.

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