
Sex Ratios in Twin Families: Commentary on Fellman and Eriksson

William H. James

The Galton Laboratory, University College London, United Kingdom

Fellman and Eriksson (2008) wondered whether there is variation in the probability that a human birth will be male. Accordingly, they examined the sexes of sibs of index MM, MF, and FF twin pairs. For this purpose they used 19th century German data published by Geissler and Lommatsch. In these data, the sex ratio (proportion male at birth) of sibs of MM pairs was significantly high; while that of MF pairs was normal and that of FF pairs was significantly low (as contrasted with contemporaneous live birth sex ratios). Accordingly Fellman and Eriksson concluded that there is, indeed, variation across couples in the probability of producing a son. Here it will be noted that though there are external grounds supporting this conclusion, there is nevertheless some reason to suspect a form of systematic error in the data cited by these authors. (In Geissler's data, there is very substantial unexplained variation of sex ratio of the sibs preceding index twins by the sex and birth order of the twins). Both these points will be addressed here. In addition, evidence is adduced that (1) the sex ratio of MZ twins is low, and (2) the sex ratios of DZ twins and of their sibs are high. Lastly, appeals are made for (a) data that would test the reliability of the data of Geissler and Lommatsch on the point questioned above, and (b) data on the sex ratios of offspring of twins by the sex and zygosity of the twin parents.

The Variation of the Probability of a Boy Within and Across Sibships

Theoretical Background

Let p be the probability that a birth will be male. Then p is potentially subject to three forms of variation, namely Lexis, Markov, and Poisson variation. These are defined as follows:

Lexis Variation. Here p is constant within a given couple, but varies across couples.

Markov Variation. Here p varies within couples according to the sex (or sexes) of the preceding births.

Poisson Variation. Here p varies randomly from one pregnancy to the next within couples, regard-

less of the sexes of the existing sibs, and has the same mean for all couples.

To detect and estimate these forms of variation, one may analyse combinations or sequences of the sexes within sibships. However such analysis is made complicated by the fact that (some) couples use 'stopping rules' by which decisions to reproduce further are based on the sex(es) of the existing children. This falsifies the assumption of randomness that would simplify such analysis. There are two important forms of stopping rule, namely, type I, where couples wish for one or more children of one sex and cease reproducing when they have arrived, and type II, where couples wish for (given numbers of) children of both sexes, and cease reproducing when they have arrived. All these forms of variation and stopping rule may co-exist and interact, and (as far as I know) no statistical test has been devised for the independent presence of each. In the absence of such a paragon of tests, I shall try to outline the present understanding of these matters.

Markov Variation

I know no direct data suggesting the existence of Markov variation in p in mammals (including human beings), and there seems no biological reason to assume its existence. So such a possibility will be ignored in subsequent discussion here.

Lexis Variation

The standard deviation of the Lexis variation of p has been the subject of three closely similar estimates based on three different statistical procedures, namely .05 (Edwards, 1958), .045 (James, 1975a) and .051 (Pickles et al., 1982). It is not clear whether the agreement between these estimates is due to their accuracy or to a concordance of direction and magnitude across their sources of bias. I have suggested that they may be underestimates (James, 2000a), but whether the argument in the latter paper is valid, I leave to those more versed than I in probability theory.

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Address for correspondence: William H James, The Galton Laboratory, University College London, Wolfson House, 4 Stephenson Way, London NW 1 2 HE England. E-mail : whjames@waitrose.com

Poisson Variation

There are two grounds for supposing that if Lexis variation exists, then a roughly equal measure of Poisson variation also exists. These relate to (1) the correlation between the sexes within sibships and (2) the validity of Weinberg's Differential Rule. These will be treated in order.

(1) *The Correlations Between the Sexes Within Sibships.* In accordance with probability theory, the correlations between the sexes within sibships are increased by Lexis variation and decreased by Poisson variation of p . Two large studies (each relating to more than half a million births) concluded that these correlations are roughly zero (Jacobsen et al., 1999; Maconochie & Roman, 1997). One may infer that if there were Lexis variation across sibships, then there must also be roughly equal and counterbalancing Poisson variation within sibships.

(2) *Weinberg's Differential Rule.* Weinberg derived his rule from a premise that (as will be seen from considerations below) is almost certainly false. The derivation is as follows. Let p be the probability that a DZ twin zygote is male. If (as now seems false) all p were equal and independent, then the distribution of the combinations (MM, MF, and FF) of the sexes within DZ twin pairs should be binomial, namely as $p^2 : 2pq : q^2$, where $q = 1-p$. And since p is roughly .5, there should be almost exactly equal numbers of same-sexed and opposite-sexed DZ twin pairs. The practical importance of the rule is that if one has a sample of twin pairs of known sex combinations, one may thereby estimate the numbers of DZ and MZ pairs within the sample. Using external criteria, Fellman and Eriksson (2007) reported that (in spite of being apparently derived from a false premise) Weinberg's Differential Rule is nevertheless empirically correct to a close approximation. I inferred that if one makes the reasonable assumption that p is subject to Lexis variation across DZ twin births (comparable to that across singleton births), p must also be presumed to be subject to countervailing Poisson variation within DZ twin pairs (James, 2007). Thus DZ twinning data support the notion that human births exemplify simultaneous (and roughly equal) measures of Lexis and Poisson variation.

Empirical Data

Lexis Variation

I have cited a substantial quantity of direct evidence that the human sex ratio is subject to Lexis variation (James, 2006). For instance, in that paper I cited evidence that low offspring sex ratios are reportedly associated with paternal exposures to selected chemicals (e.g., dioxins, dibromochloropropane, fungicides, methylmercury, vinclozolin, borates, and alcohol); to selected pathological conditions (HLA B 15⁺ status, non-Hodgkin's lymphoma, and testicular cancer); and to selected occupations (diver, driver, pilot/astronaut). In James (2006) I also cited evidence that in women,

biased offspring sex ratios are associated with various obstetric conditions (dermatoses of pregnancy, extrauterine pregnancy, fatty liver of pregnancy, hyperemesis gravidarum, pre-eclampsia, and placenta accreta) and other pathological conditions (coeliac disease, cytomegalovirus seropositivity, hepatitis B status, and polycystic ovary syndrome). It may be acknowledged that this list may exemplify publication, and other, bias. However, some of these data have been extensively replicated (e.g., those relating to adverse obstetric conditions, hepatitis B status, cytomegalovirus status, and testicular cancer: and also those relating to paternal exposure to various forms of chemical). So, taken cumulatively, there is overwhelming empirical evidence for (an admittedly uncertain measure of) Lexis variation across human births.

Poisson Variation

A brief meta-analysis of ten independent studies concluded that p , the probability that a birth will be male, varies substantially and significantly with the time of insemination across the fruitful cycle (James, 2000b). Moreover, p also reportedly varies with the side of ovulation (James, 2001). Paternal sources of Poisson variation may also be suspected, but they will not be discussed here.

Thus there is good evidence that p , the probability of a human male birth, is subject to both Poisson variation within sibships, and Lexis variation across sibships. There is also evidence that the magnitudes of these variances are roughly equal. It is not clear whether existing estimates of them are to be trusted, or whether these estimates may be too low, as I suggested (James, 2000a). This problem may be solved (as I suggested in that paper) by examining the variances of the distributions of the sexes in artificially constructed random samples of human births. This is so because such variances may yield estimates of the *sum* of the Poisson and Lexis variances. If that were so, and if these variances are roughly equal, estimates are available for each (on the assumption that Markov variation does not exist). I would recommend anyone wishing to pursue this matter to read (at least the English summary of) the remarkable paper by Gini (1951).

The Sex Ratios of the Sibs of Twins

Schutzenberger (1950) reported that the sex ratio of the sibs of twins is high as contrasted with the relevant population live birth sex ratio. Turpin & Schutzenberger (1952) reported that the sex ratios of the sibs of 9125 MM, MF, and FF twin pairs were respectively, 0.536, 0.523, and 0.508. The differences between these sex ratios are significant: moreover, Milham (1980) confirmed that the sex ratio of the sibs of opposite-sexed twin pairs is also significantly high. Lastly, I offered evidence to suggest that the sex ratio of DZ twins (like that of their sibs) is also high (James, 1986).

Thus there is evidence to support Fellman & Eriksson's conclusion, namely that the sex ratios of the sibs of twins vary according to the sex combination of the index twin pair. However, as indicated above, one may wonder about the quality of the data cited by these authors. My concern (following that of Wedervang and Weinberg nearly a century ago as acknowledged by the authors) is as follows. In Geissler's data, the sexes of the singletons preceding index MM pairs that were ascertained following exactly one previous birth were 592 brothers and 391 sisters. The comparable data relating to FF pairs were 364 brothers and 566 sisters. These two sex ratios of .602 (SE = 0.016) and .391 (SE = 0.016) lie quite outside normal human experience (with the possible exceptions of serious prior parental exposure e.g. of the father to pesticides or of the mother to various pathological conditions). So it seems reasonable to wonder instead whether, in some cases, the sex of the preceding sib was recorded, in error, as that of the twins. Moreover, (and also suggesting a systematic error) the reported sib sex ratios progressively become more 'normal' as the number of previous older sibs increases (thus ex hypothesi 'diluting' the error).

Accordingly I suggest that those who have access to such data (e.g., in twin registries or vital statistics offices with record linkage facilities) should try to replicate these data of Geissler. If these data *were* successfully replicated, it would present twin researchers (and human reproductive biologists generally) with a highly interesting problem.

Potential Explanations for Sex Ratio Variation

Though not directly relevant to the points made above, explanations will be offered for the established variation in sex ratios cited above.

I have suggested that most of the variation in mammalian (including human) sex ratios at birth may be explained in terms of hormonal variation in parents around the time of conception (James, 1996, 2004).

However, this does not apply to the low sex ratio of MZ twins (James, 1975b). Judging from placental evidence, MZ twin sex ratios reportedly decline with the age of the zygote at the time of the MZ split (James, 1980). So it is possible that these sex ratios are related instead to anomalous X-inactivation (James, 1988).

Summary and Conclusions Relating to Sex Ratios in Twin Families

- 1 The sex ratio (proportion male) of MZ twins is low, and decreases with the age of the zygote at the time of the MZ split.
- 2 The sex ratio of DZ twins themselves is probably high (presumably as a consequence of their mothers' hormone levels around the time of conception).
- 3 The sex ratio of the sibs of twins is high, and varies with the sex combination of the index pair, being highest with MM pairs, and lowest with FF pairs.

- 4 Nothing is known specifically about the sex ratios of the sibs of twin pairs by the zygosity of those pairs.
- 5 So perhaps the variation of the sex ratios of the sibs of twins is mainly confined to the sibs of DZ pairs, and attributable also to variation in maternal hormone concentrations.
- 6 It would be interesting to see data on the sexes of offspring of twins by the twins' sex and zygosity. In particular, there is some evidence that women who are members of opposite-sexed (OS) twin pairs (like female rodents that lie adjacent to male litter-mates in utero) are androgenized as a consequence (van Anders et al., 2006; Voracek & Dressler, 2007). So, one may wonder whether women who are members of OS pairs produce a statistical excess of sons (in accordance with my hypothesis).

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