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Response to W. Kramer: The human sex odds at birth after the atmospheric atomic bomb tests, after Chernobyl, and in the vicinity of nuclear facilities: comment (doi:10.1007/s11356-011-0644-8)

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Abstract

Introduction This paper is in response to criticism of our article “The human sex odds at birth after the atmospheric atomic bomb tests, after Chernobyl, and in the vicinity of nuclear facilities” published in Environ Sci Pollut Res 18 (5):697–707, 2011.

Methods Our findings and methods concerning the disturbed human sex odds at birth have been criticized in this journal for being artifacts of data mining, that the concept of statistical significance was misunderstood, and that confounding factors have not been accounted for. Here, we show that this criticism has no basis. We applied well-established statistical methods to large official data sets, and confounding is less important at the level of secular sex odds trends in aggregated annual figures from countries or continents.

Results and conclusions Moreover, our results are strengthened by recent findings concerning increased infant death sex odds in Germany and increased Down syndrome prevalence at birth across Europe after Chernobyl. Prompted by our studies, an official investigation in Lower Saxony, Germany, by the “Niedersächsisches Landesgesundheitsamt (NLGA)” confirmed our observation of severely escalated sex odds within 40 km distance from the nuclear storage site in Gorleben, Germany.

Keywords Binomial distribution · Radiation-induced genetic effects · Sex ratio · Statistical inference

1 Distributional assumptions and statistical independence

Two important methodological concepts underlying the thinking about the human secondary sex odds are: independence of statistical events and the assumption of a binomial distribution based on statistical independence. The famous discovery by John Arbuthnot in 1710 “*An argument for Divine Providence, taken from the constant regularity observed in the births of both sexes*” is an early application of probability theory in statistics and includes a formal hypothesis test of significance. Based on the striking similarity between the gender outcome in human births and the outcome of independently tossing a fair or slightly biased coin, Arbuthnot observed and documented for the first time ever that in the long run, significantly more boys than girls are born. His elucidating reasoning begins with the words: “Let there be a Die of Two sides, *M(ale)* and *F(emale)*, which denote Cross and Pile”. This is the classical form of a distributional assumption. A further important concept underlying valid statistical inference is independence. In successively tossing a coin, it is obvious that the outcome (heads or tails, or cross or pile) of a present trial is not influenced by the outcomes of past trials. In child birth statistics, this may be violated to a minor extent when there is more than one child born to the same parents. However, in long secular time series of births, this restriction is negligible. At the population level, statistical independence applies to the birth sex odds.

Table 1 and Fig. 1 contain a basic example illustrating the methodology we applied. We might want to test the null hypothesis of equal male proportions in the two periods 1980–1986 and 1987–1992 in the 39 European countries studied in our paper (Scherb and Voigt 2011). Applying a two-sided 2×2 table test based on the Wald Chi-square

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Table 1 Births by gender from 1980 to 1992 in 39 European countries (Scherb and Voigt 2011), sex odds (SO), and sex odds ratio (SOR), see Fig. 1; \ln natural logarithm, SE standard error, p value Wald Chi-square

Period	Live births			SO	SOR	$\ln(SOR)$ SE	p value
	Total	M	F				
1980–1986	69,557,207	35,719,497	33,837,710	1.0556	1.0015	0.001547	0.000018
1987–1992	55,339,391	28,439,653	26,899,738	1.0572		0.000360	
Total	124,896,598	64,159,150	60,737,448				

statistic yields, a sex odds ratio (SOR)=1.0015 with 95% confidence interval 95% CI (1.0008, 1.0023), and a significant p value 0.000018. Krämer (2011) criticizes “that it is quite inappropriate, from a statistical point of view, to fit linear trends to short time series of the type considered here”. This objection is incorrect because the above 2×2 table method fits, so to speak, a linear trend (represented by the sex odds ratio) to only two data points, i.e., one point before and one point after Chernobyl (April 26, 1986).

While Arbuthnot intuitively assumed the occurrence of boys among births to be binomially distributed, it is also possible to derive this formally. In human populations, one child will be born to potential parents in every 100 persons per year, as a rule and in the order of magnitude. Therefore, we

may assume two Poisson distributions for the occurrence of boys and girls separately in appropriate populations. In mathematical statistics, it is well known that the conditional distribution for comparing two Poisson distributions is a binomial whose odds equals the ratio of the Poisson parameters involved, which in this case is the human birth sex odds (Przyborowski and Wilenski 1940; Lehmann 1966). The step from two Poisson distributions for gender specific births to one binomial distribution for male births within female and male births together demonstrates that the total number of births is a random variable too. This may, therefore, help to overcome the occasional misunderstanding that birth statistics would be free of random error because they are largely free of recording error.

As an empirical fortification of the binomial assumption, we emphasize that in our sex odds analyses, we generally found only minor heterogeneity as measured by the deviance divided by the degrees of freedom of the logistic model. For example, the combined US and European regression model in our paper is based on 61 observations (33 European+28 US continent \times years) and seven parameters (two intercepts, four trends, and one jump); Fig. 2 in Scherb and Voigt (2011). This model has a deviance of 56.92 according to $61 - 7 = 54$ degrees of freedom, which yields a heterogeneity parameter of 1.054, i.e., only 5.4% nonsignificant ($p=0.3671$) overdispersion. This is an impressive empirical compliance with the binomial assumption in a large dataset of 392.9 million births.

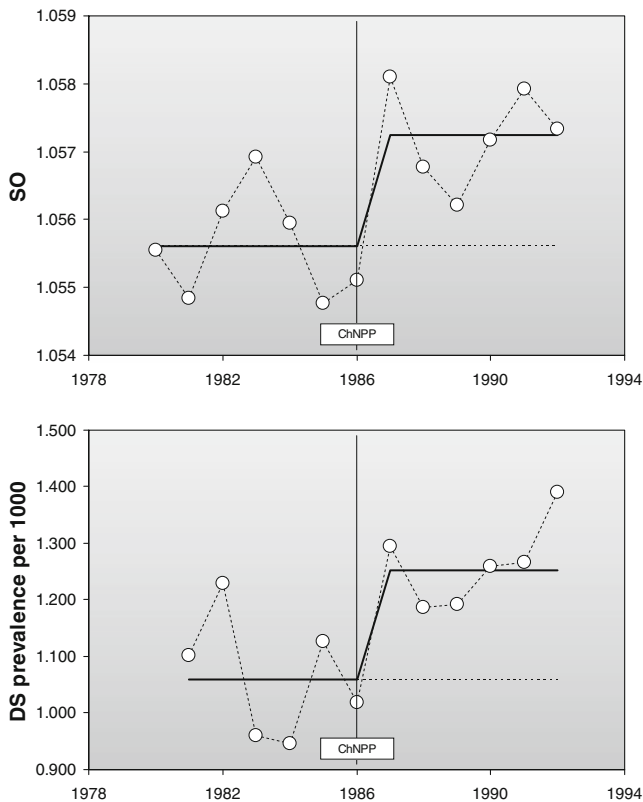


Fig. 1 Upper diagram Live birth sex odds (SO) in 39 European countries (Scherb and Voigt 2011), see Table 1. Lower diagram Down syndrome (DS) prevalence in Europe (Sperling et al. 2012), see Table 2; ChNPP Chernobyl Nuclear Power Plant

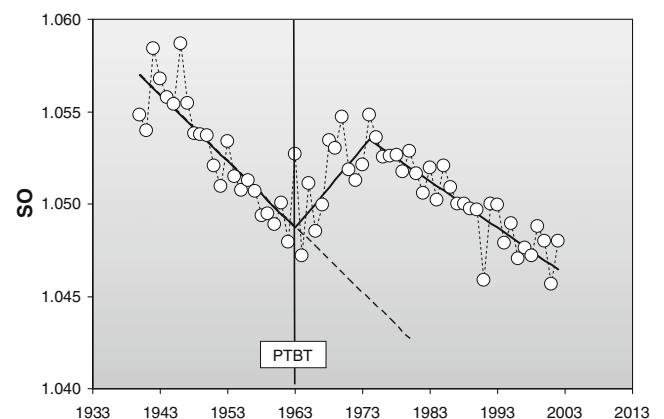


Fig. 2 Live birth sex odds (SO) data for the USA in 1940–2002 and significant change-point model: F test p value $< E - 6$; $R^2=0.76$; PTBT (Partial Test Ban Treaty 1963)

2 Autoregressive processes

Krämer (2011) suggests AR(1) processes with $r=0.90$ for the analysis of sex odds data. This is an artificial and unrealistic assumption because it means that the value of the sex odds in a given year (t) is determined by as much as 90% of the value of the sex odds in the preceding year ($t-1$) plus a certain non-informative random component ε_t : $SO_t = \text{constant} + 0.90 \times SO_{t-1} + \varepsilon_t$. The data patterns that may be generated by AR(1) processes are highly variable because of the internal dynamics generated by the built in memory or feedback. Therefore, AR or ARMA processes have essentially nothing in common with real-world sex odds data. High autocorrelation, also in more general AR(n) or ARMA (p, q) processes, is in clear contrast to the independence leading to the binomial in coin tossing or in human births because a deterministic portion of the past carries over to the present. Also, the variance structure of an autoregressive process is rather complicated because it confounds the variability of the deterministic parts with the variability of the error components, whereas the variance structure under the binomial assumption is simple and adequate for coping with the requisite inferential issues: the variance is determined by the binomial parameter p and the population size n : $\text{variance} = n \times p \times (1-p)$. A trend in the binomial parameter may be modeled applying logistic regression. In conclusion, the assumption of autocorrelation for sex odds data is inappropriate.

3 USA and Europe

Figure 1 by Krämer (2011) shows the full US trend from 1940 to 2002 (Mathews and Hamilton 2005). Krämer criticizes us for the omission of data points in Fig. 1 of our paper (Scherb and Voigt 2011). Our reason for cutting off left and right data points from the US trend (1940–2002) was to get it congruent with the shorter European trend (1950–1990) from Martuzzi et al. (2001). Completing the US dataset again, does not change our argument because the left and right extensions fit rather well to the left and right sides of our truncated US trend, respectively. In Fig. 2, we display the fully available US trend together with an appropriate highly significant change-point model (F test, p value $< E-6$). It is symptomatic for the comment by Krämer (2011) that he criticizes us for omitting data points where he himself omits the whole continent of Europe in his Fig. 1. It was a new and important observation (Scherb and Voigt 2011) that the USA and Europe had essentially parallel sex odds trends from 1950 to 1986 and that this parallelism disappeared immediately after Chernobyl from 1987 on.

Krämer sees an inconsistency in our interpretation of the different timing of the effects after Chernobyl in Europe

(1987—immediate) and after the atmospheric atomic bomb tests in the USA and Europe (1963—delayed). He argues that the different timing would detract from the common cause ionizing fallout. However, in report no. 3 of the Federal Radiation Council (FRC 1962) it is explained: "Furthermore, the tests are planned to avoid local fallout or to confine it to locations where it will have minimal effects. Hence, in weapons testing, the problem is largely confined to delayed fallout which decays greatly in the upper atmosphere and is dispersed at low concentrations over the earth's surface." After Chernobyl, short-lived radionuclides reached the European populations within days or weeks in significant amounts before their decay. From this point of view, the immediate effect after Chernobyl in Europe and the delayed effects after the atmospheric atomic bomb tests in the USA and in Europe are plausible.

4 Confounding

Krämer (2011) states "there is an impressive list of factors, which indeed are known to affect the sex odds at birth". This point of view is not supported by current research in this field. In a comprehensive review on possible environmental and occupational determinants of the sex odds covering approximately 100 publications, Terrell et al. (2011) concluded: "Limitations in study design and methodological issues make it difficult to draw firm conclusions from the existing sex ratio literature". From the statistical power perspective (Scherb and Voigt 2009), the paper by Terrell et al. (2011) offers interesting insights. The vast majority of the 100 studies discussed have no more than 1,000 exposed cases, and only four investigations are based on numbers of births between 10,000 and 40,000. With such small numbers, it is virtually impossible to generate firm knowledge on sex odds determinants. Even for acknowledged mutagens, the situation is not clear: "There is no compelling or consistent evidence that well established reproductive hazards such as tobacco smoke, ionizing radiation or inorganic lead have any impact on the sex ratio of offspring" (Bonde and Wilcox 2007). We may well assume that one of the main reasons for this knowledge gap is the lack of sufficiently large and informative study populations. In fact, there are only few firmly known determinants of the human secondary sex odds, among them race. And even if a factor is a proven one, e.g. seasonality, its influence is rather small in general (Lerchl 1998) and irrelevant for annual data. It has often been claimed that the sex odds would decrease with maternal age, but closer inspection does not support this assertion. In a recent paper investigating 2.2 million births in Norway (1967–2006), Rueness et al. (2012) state "Overall, there was no association of maternal age with the human sex ratio". James (2008) has offered the hypothesis that human

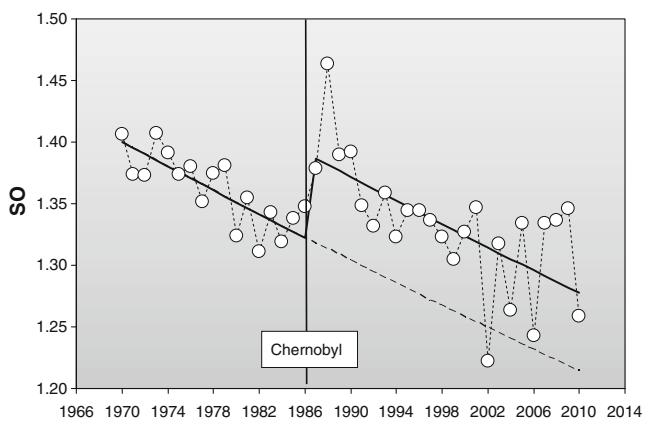


Fig. 3 Sex odds (SO) of infant death (<1 year) in Germany from 1970 to 2010 (DESTATIS 2011), jump sex odds ratio (SOR) in 1987: 1.052, 95% CI (1.018, 1.088), *p* value=0.0028

sex odds are causally related to the hormone levels of parents at conception. However, this hypothesis also remains to be established in large enough populations.

Therefore, criticizing our approach for missing confounders is not justified as long it is not precisely stated what kind of confounders are meant and what proven effects of those confounders are relevant to the trend analyses of annual and aggregated data. Moreover, Krämer’s line of reasoning is inconsistent concerning the confounder issue, because if sex odds data were highly autocorrelated AR(1), there would be no room left for confounding factors.

5 Significance and evidence

Krämer’s comment (2011) contains some other not clearly specified pieces of criticism, which we will not comment on in detail here. One interesting example, however, is Krämer’s unsupported claim of decreased childhood leukemia in the vicinity of nuclear power plants. Recently, it has been shown that in France also, childhood leukemia has doubled around nuclear power plants (Sermage-Faure et al. 2012). This supports the corresponding observation in Germany (Spix et al. 2008). Furthermore, several statements concerning statistical inference deserve consideration. It is well known that statistical inference in general and statistical tests in particular may be abused. An important example is

the bad habit of taking a nonsignificant result as evidence of the null hypothesis, without considering the statistical power. Therefore, at least as a partial remedy, it has been recommended not only to report significances or *p* values but also effect estimates and confidence limits (Van Eimeren et al. 1987). This is why we routinely report the effect estimate, the 95% confidence limits, and the *p* value jointly. The confidence interval has the advantage of indicating which parameters or effects are compatible with the observation given the variability of the data. Krämer’s idea “error of the third kind” is of no help because it is merely a terminological fuzzy fusion of the concepts “statistical test” and “interpretation of test outcome” carefully to be distinguished.

Krämer misreads our interpretation “The atmospheric atomic bomb test fallout affected the human sex odds at birth overall, and the Chernobyl fallout had a similar impact in Europe and parts of Asia.” as being the result of “a statistical test of significance”. We base our conclusions not only on statistical tests but also on the accumulated evidence in the scientific literature on detrimental genetic effects after Chernobyl across Europe: increased stillbirth, perinatal mortality, infant death, birth defects like cleft lip and palates (Scherb and Weigelt 2004; Zieglowski and Hemprich 1999), and Down syndrome (Sperling et al. 2012). For more references, see also Scherb and Voigt (2011).

6 Further evidence

Figure 3 presents the German infant death sex odds trend from 1970 to 2010 (DESTATIS 2011) subject to a significant (*p*=0.0028) jump in 1987, immediately after Chernobyl. Moreover, in a recent paper (Sperling et al. 2012), we show that the time trend in the occurrence of Down syndrome is essentially parallel to the sex odds trend in Europe: in both datasets, we see long-term increases after Chernobyl from 1987 onward (Fig. 1, Tables 1 and 2).

During our recent research, we detected increased sex odds near nuclear facilities in Germany and Switzerland, especially around the nuclear storage site TBL Gorleben (Transportbehälterlager: nuclear waste shipping casks storage) in Lower Saxony, Germany (Kusmierz et al. 2010; Scherb and Voigt 2011). The continuous discussion about the nuclear waste

Table 2 Down syndrome (DS) in seven European countries or regions before and after Chernobyl (Sperling et al. 2012), see Fig. 1; *ln* natural logarithm, *SE* standard error, *p* value Wald Chi-square

Period	Live births			Odds	OR	ln(SOR) SE	<i>p</i> value
	Total	no DS	DS				
1981–1986	2,516,747	2,514,081	2,666	0.0011	1.1829	0.1679	<E–10
1987–1992	2,798,653	2,795,146	3,507	0.0013		0.0257	
Total	5,315,400	5,309,227	6,173				

Table 3 Births by gender within 40 km from the nuclear storage site Gorleben (TBL) before and after the TBL went in operation in April 1995 (NLGA 2011), sex odds (SO) and sex odds ratio (SOR), see

Period	Live births			SO	SOR	ln(SOR) SE	p value
	Total	M	F				
1981–1995	13,861	6,939	6,922	1.0025	1.0838	0.0805	0.000180
1996–2010	23,135	12,047	11,088	1.0865		0.0215	
Total	36,996	18,986	18,010				

shipping casks storage in Gorleben increased our interest in taking a closer look at this location. We performed data analyses and we issued several fact sheets, which can be found at the webpage of the first author (Scherb et al. 2011). The main outcome of our studies is shown in Table 3. Applying a Wald Chi-square two-sided 2×2 table test yields a rather high SOR 1.0838 with 95% CI (1.0391, 1.1305), and a significant p value of 0.000180. The corresponding SOR distance law around the TBL Gorleben is shown in Fig. 4. The elevated sex odds around Gorleben might be due to an increased scattered neutron dose that tripled as far as 2 km away from the TBL in the village of Gorleben after the TBL went in operation in April 1995 (GNS 2008). Figure 5 shows essentially parallel trends of the neutron dose in the village of Gorleben and the birth sex odds within the 40 km zone of the TBL nuclear storage site. It is possible that the biologically or genetically effective neutron dose is severely underestimated by established radiation protection standards (Heimers 2001). Also, the significant Rayleigh curve in Fig. 4 might be the epidemiological reflection of a far-reaching direct or indirect scattered neutron “skyshine” effect (Lagutina et al. 1989).

The enduring concern of the people around Gorleben, as well as our research results triggered an official study by the

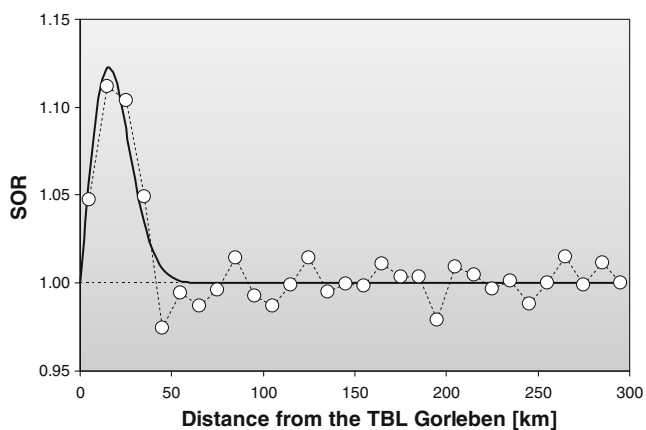


Fig. 4 Spatial trend of the sex odds ratio (SOR) of aggregated live birth data for 10 km distance rings, after vs. before the first Castor went to Gorleben in April 1995 and significant Rayleigh function model, F test, p value=0.0091; TBL Transportbehälterlager: nuclear waste shipping casks storage

Fig. 5; ln natural logarithm, SE standard error, p value Wald Chi-square, TBL Transportbehälterlager: nuclear waste shipping casks storage

“Niedersächsisches Landesgesundheitsamt” (NLGA 2011), which, on the one hand, confirmed our finding for Lower Saxony and, on the other hand, corroborated it by fresh data from the remaining municipalities within 35 km belonging to Mecklenburg-West Pomerania, Saxony-Anhalt, and Brandenburg, see also Scherb et al. (2011).

7 Conclusion

Elevated infant death sex odds and Down syndrome prevalence at birth after Chernobyl in Europe, as well as escalated

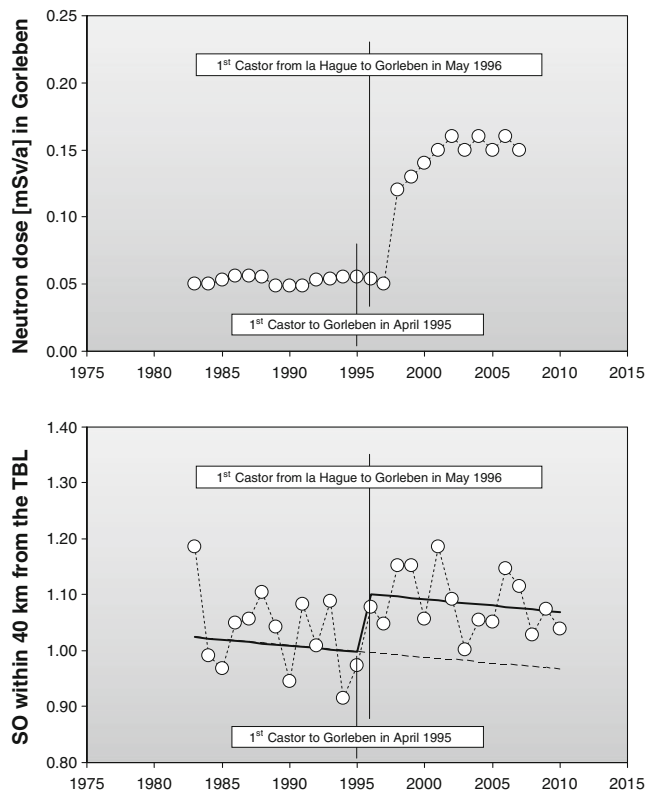


Fig. 5 Upper diagram: Neutron dose 2 km distant from the TBL in the village of Gorleben (GNS 2008). Lower diagram: sex odds (SO) trend within 40 km from the TBL Gorleben, see Table 3; TBL Transportbehälterlager: nuclear waste shipping casks storage

sex odds in the 40 km zone of Gorleben, after the first Castor was transported to the TBL Gorleben, add evidence to our paper debated by Krämer (2011). Krämer neither takes note of proven detrimental genetic effects after Chernobyl nor does he acknowledge important prerequisites in the methodology of sex odds studies: statistical independence and appropriate distributional assumptions. While Arbuthnot looked for a teleological argument or a proof of God's existence by using the binomial distribution, Krämer tries to strengthen the belief in nuclear safety by ignoring the binomial distribution. This is significant scientific regression—300 years after Arbuthnot.

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