Sex Odds an Important Indicator for Changes in Environmental Health

Kristina Voigt [1], Hagen Scherb[1], Ralf Kusmierz[2]

Abstract

The aim of our research is to investigate sex odds trends in the vicinity of nuclear facilities and chemical plants in Germany. We collected human sex odds data from the nineteen fiftieth till 2010. To assess time trends in the occurrence of boys among all live births, and to investigate whether there have been significant changes in the trend functions after distinct chemical or radiological events, we applied ordinary linear logistic regression. We give two examples, one for the trend in the human sex odds around the nuclear storage site TBL Gorleben and the second one around the chemical plant Hoechst-Griessheim after an accident in 1993. Both events (storage of nuclear casks as well as accidental release of chemicals) had a strong influence on the human sex odds at birth.

1. Introduction

Epidemiological effects of environmental pollution can be modelled in many different ways. An important indicator is the human sex ratio at birth. Sex ratio is the ratio of males to females in a population. The primary sex ratio is the ratio at the time of conception, secondary sex ratio is the ratio at time of birth, and tertiary sex ratio is the ratio of mature organisms. According to Neel and Schull [1991], the sex odds is unique among the genetic indicators. Its uniqueness arises from the fact that maternal exposure would be expected to produce an effect different from paternal exposure. For methodological reasons, we prefer "sex odds" over "sex ratio" to not confuse it with the statistical term ratio (see also statistical methods). We put the focus on the changes in the human sex odds at birth (secondary sex ratio) in our studies. The aim of our research is to investigate sex odds trends in the vicinity of nuclear facilities and chemical plants in Germany. This kind of study is called ecological study. An ecological study is an epidemiological study in which the unit of analysis is a population rather than an individual. In these cases, there is no information available about the individual members of the populations compared. Many epidemiologists consider an ecological study as inferior to non-ecological designs such as cohort and case-control studies because it is susceptible to the ecological fallacy. However, ecological studies are very useful because they can be carried out easily, quickly and inexpensively using data that are generally already available. Another advantage of ecological studies is the fact that large datasets can be analyzed, whereas non-ecological studies are extremely limited in their sample sizes due to high cost and feasibility. Moreover, analytical studies also are subject to many biases in general, and may, therefore, be even invalidated by uncontrolled confounding.

The ratio of male to female offspring at birth may be a simple and non-invasive way to monitor the reproductive health of a population. Except in societies where selective abortion skews the sex ratio (SR),

[1] Helmholtz Zentrum Muenchen, German Research Center for Environmental Health,
Institute of Biomathematics and Biometry, Ingolstaedter Landstr.1, 85764 Neuherberg, Germany, kvoigt@helmholtz-muenchen.de

2 Bremen, kusmierz@t-online.de

approximately 105 boys are born for every 100 girls. The authors concluded from a large retrospective cohort study that the sex ratio at birth is remarkably constant [Ein-Mor et al., 2010].

2. Evaluation Method for Human Sex Odds at Birth

2.1 Geo-spatial background and requirements

Kusmierz et al. [2012] gave an overview on the data sources for modeling epidemiological effects of environmental pollution. They explained the special situation and challenges in collecting, handling and analyzing the human sex odds data in Germany. The geographic coordinates given in the Gauss–Krüger coordinate system are used. The Gauss–Krüger coordinate system is a special transverse Mercator map projection used in Germany, Austria and Finland rather than the UTM-system but similar to this. The central meridians of the Gauss–Krüger zones are only 3° apart, as opposed to 6° in UTM. A transverse Mercator map projection approximates the reference ellipsoid by a cylinder sector, which perimeter smoothes the central meridian of the mapped zone some depth below the reference surface, so the elliptical cylinder intersects the ellipsoid. The transverse Mercator map projection provides a nearly conformal mapping of earth's surface in smaller regions, so distances can simply be computed by using the Euclidean distance from the numerical differences of the coordinate components with very small errors.

Before and after the German reunification, the lowest administrative levels (NUTS- 3-regions) split into districts, which are either cities or management associations from municipalities. The smallest statistical units information is published for, the community, may be rather different in size, e.g., the large metropolises Berlin, Frankfurt, Munich, are single municipalities, and the smallest municipalities have fewer than 10 residents. The data provided by the statistical offices for the states can sometimes be downloaded from the Internet. For other states, fees must be paid for the data. The states of Schleswig-Holstein and Hamburg, and of Brandenburg and Berlin each have a joint National Institute of Statistics, respectively. From 2008, birth data can be downloaded free of charge via the Internet from the "regional database" at the German Federal Statistical Office DESTATIS for all communities under the URL https://www.regionalstatistik.de.

2.2 German Municipalities 1957 to 2010

Kusmierz et al. [2010] compiled official gender specific annual live births statistics for all municipalities in Germany. To calculate the distances of the municipalities from nuclear facilities, we determined uniform coordinates for the geographic positions of those municipalities including the geographic positions of 28 pertinent nuclear facilities including all nuclear power plants in Germany and Switzerland. We now use the same data background for the evaluation of the sex odds in the vicinity of chemical sites in Germany.

2.3 Statistical Methods: Ordinary Linear Logistic Regression

To assess time trends in the occurrence of boys among all live births, and to investigate whether there have been changes in the trend functions after distinct events, we applied ordinary linear logistic regression. This involves considering the male proportion among all male (m) and female (f) births: $p_m = m/(m+f)$. Important and useful parameters in this context are the sex odds: $SO = p_m/(1- p_m) = m/f$, and the sex odds ratio (SOR), which is the ratio of two interesting sex odds if those two sex odds have to be compared, e.g. in exposed versus non-exposed populations. We used dummy coding for single points in time and for time periods as well. For example, the dummy variable for the time window from 1994 on is de-

fined as d94(t) = 0 for t < 1994 and d94(t) = 1 for t ≥ 1994. The simple and parsimonious logistic model for a trend and a jump in 1994 has the following form (LB = live births):

$$Boys_t \sim Binomial(LB_t, \pi_t)$$
$$\log \text{ odds}(\pi_t) = intercept + \alpha * t + \beta * d_{1994}(t)$$

To allow for changing sex odds trend slopes (broken sticks) after chemical or radiological events, we used dummy coding of time windows and interactions of those time windows with time. The data in this study were processed with Microsoft Excel 2003. For statistical analyses, we used R 2.11.1, MATHEMATICA 8.2, and mostly SAS 9.2 (SAS Institute Inc: SAS/STAT User's Guide, Version 9.2. Cary NC: SAS Institute Inc; 2003).

3. Evaluating Nuclear Facilities and Chemical Plants in Germany

3.1 Nuclear Facilities

A study performed by the authors [Kusmierz et al., 2010] and [Scherb and Voigt, 2011] revealed an increase in sex odds in the vicinity of running nuclear facilities, especially around the nuclear storage site TBL Gorleben (Transportbehälterlager: nuclear waste shipping casks storage) in Lower Saxony, Germany. In Germany a continuous discussion about the nuclear waste shipping casks storage in Gorleben increased our interest in taking a closer look at this location. We published a spatial sex odds distance law according to a Rayleigh function, and a temporal trend function including a simple jump (change-point analysis) [Scherb and Voigt, 2012].
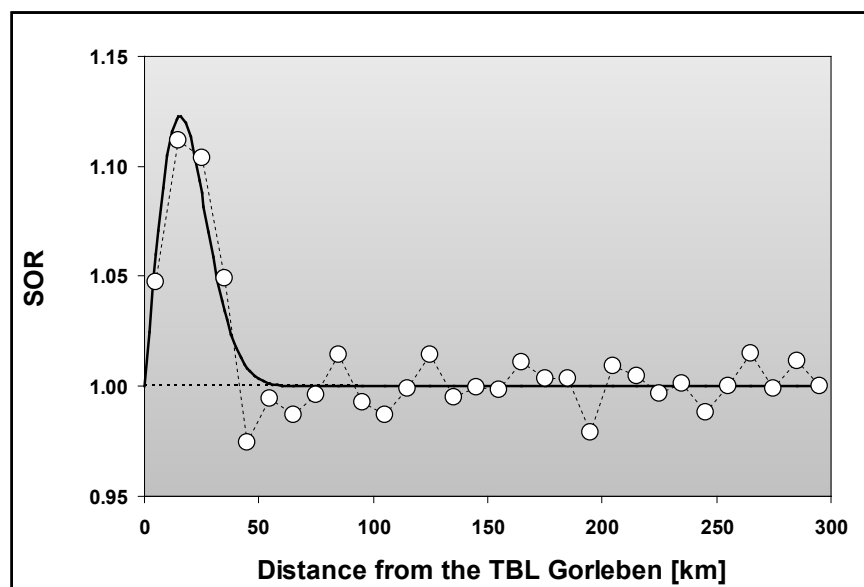

Figure 1
Rayleigh function for the evaluation of distance trends from the TBL Gorleben

In Figure 1, the distance law 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 is demonstrated. The F-test p-value

is 0.0090, which means that the Rayleigh curve significantly improves the fit to the data compared to the intercept-only model. A distinct increase in the human sex odds at birth within 40 km distance from Gorleben compared to far distances can clearly be stated. In this approach, approximately 23.5 million births are considered.

3.2 Chemical Plants

We performed the same analysis described under section 2.3 on chemical sites in Germany. Results of this first screening approach can be found in the Proceedings of the iEMSs Conference 2012 [Voigt et al., 2012, submitted]. In this paper we also considered the influence of chemical accidents on the sex odds. We therefore took a closer look at the live birth sex odds in the vicinity of Hoechst – Griesheim, where an accident took place in 1993. During this accident approximately 11.8 tons of chemical mixtures containing mostly chlorinated nitroarenes were emitted leading to serious contaminations in Schwanheim/Goldheim, a nearby housing area. Numerous inhabitants of the contaminated area complained of irritation of eyes, skin and mucous membranes, headache and nausea, and 92 persons with moderate symptoms were reported to the National Health Department [Heudorf et al., 1994].
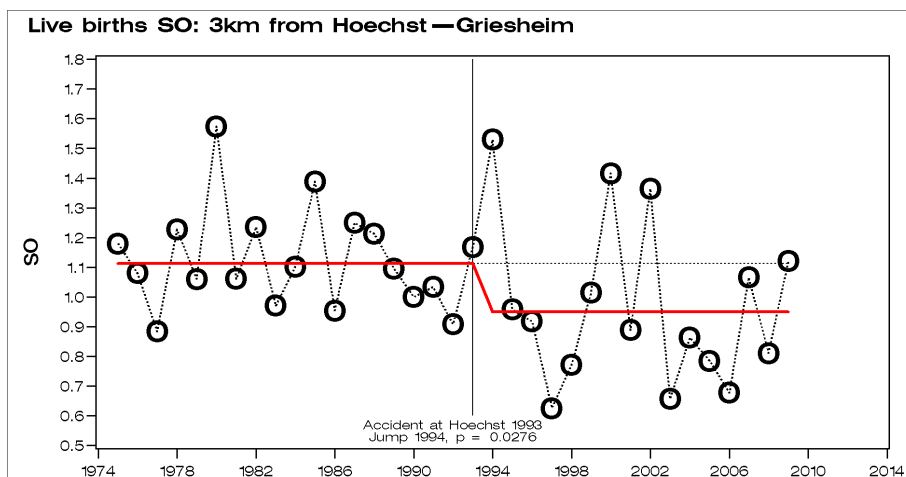

Figure 2
Sex odds 3 km from Hoechst-Griesheim

We therefore looked at the live birth sex odds in the vicinity of Hoechst – Griesheim (see Figure 2). Here we detected a remarkable decrease in sex odds after the chemical accident. The p-value 0,0276 indicates a considerable significant effect. For this graphical output 5.203 live births were considered from 1975 to 2009.

4. Summary and Outlook

Some environmental hazards can alter the sex ratio at birth. In a recently published review article [Terrell et al, 2011] 100 studies were evaluated including several studies on ionizing radiation and chemicals. Most of these studies are non-ecological ones. The range of cases only was between tens and thousands,

which clearly are much too small numbers in order to detect genuine determinants of the secondary sex odds in humans.

In our ecological studies we take a look at a huge number of cases. The studies on sex odds with respect to accidents with ionizing radiation clearly indicated strong effects in the direction of an increase in sex odds [Scherb and Voigt, 2009, 2011, 2012]. We made one investigation around a chemical plant where a major chemical accident took place in 1993. Here we found a significant effect on the sex odds, say a decrease in sex odds. Both increase and decrease in the human sex odds at birth provide a strong indication that there is an impact of man-made facilities on the human genome. Further background concerning this issue is given by Sperling et al. [2012].

We demonstrated that the indicator "sex odds at birth" is a strong one showing the influence of ionizing radiation and chemicals on human health. Furthermore, we support the importance of ecological studies in this respect, as the data are available and the datasets are much larger as in cohort and case-control studies. The latter cost a lot of money and also have several deficiencies, e.g. missing data only to name one.

We are continuing our research in this area trying to prove that nuclear facilities as well as chemical sites pose a risk to the environment and to human health. Complete data sets in Germany as well as French birth statistics will be analyzed in the near future.

Bibliography

Ein-Mor E, Mankuta D, Hochner-Celnikier D, Hurwitz A, Haimov-Kochman R (2010) Sex ratio is remarkably constant. Fertil Steril 93 (6):1961-1965.

Heudorf U, Neumann HG, Peters M (1994) Accident in the Hoechst AG company 22 February 1993. 2. Public health evaluation. Gesundheitswesen 56 (7):405-410.

Kusmierz R, Voigt K, Scherb H (2010) Is the human sex odds at birth distorted in the vicinity of nuclear facilities (NF)? A preliminary geo-spatial-temporal approach. In: Greve K, Cremers AB (eds) Integration of Environmental Information in Europe, Bonn, 2010. Shaker Verlag, Aachen, pp 616-626.

Kusmierz R, Scherb H, Voigt K (2012) Overview on data sources for modelling epidemiological effects of environmental pollution. In: Seppelt R, Voinov AA, Lange S, Bankamp D (eds) International Environmental Modelling and Software Society (iEMSs) 2012, Leipzig, Germany, 2012.

Neel JV, Schull WJ (1991) The children of atomic bomb survivors: a genetic study. National Academy, Washington, D.C., USA.

Scherb H, Voigt K (2009) Radiation-Induced Genetic Effects and the Chernobyl Nuclear Power Plant Accident. Acta Paediatrica 98:51-51.

Scherb H, Voigt K (2011) The human sex odds at birth after the atmospheric atomic bomb tests, after Chernobyl, and in the vicinity of nuclear facilities. Environ Sci Pollut Res Int 18 (5):697-707. doi:10.1007/s11356-011-0462-z

Scherb H, Voigt K (2012) 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 Environ Sci Pollut Res Int 19 (4): 1335-1340. doi:DOI: 10.1007/s11356-011-0644-8.

Sperling K, Neitzel H, Scherb H (2012) Evidence for an increase in trisomy 21 (Down syndrome) in Europe after the Chernobyl reactor accident. Genet Epidemiol 36:48-55.

Terrell ML, P. HK, Macrus M (2011) Can environmental or occupational hazards alter the sex ration at birth? A systematic review. Emerging Health Threats Journal 4 (7109). doi:DOI: 10.3402/ehtj.v4i0.7109

Voigt K, Scherb H, Kusmierz R Chemicals' risks versus radiation risks with respect to the alteration of human sex odds: a preliminary evaluation approach. In: Seppelt R, Voinov A, Lange S, Bankamp D (eds) International Environmental Modelling and Software Society (iEMSs) 2012, Leipzig, Germany, 2012.