# Title page

**The secondary sex ratio in Italy over the past eighty years (1940 to 2019) and potential impact of radiological contamination after atmospheric nuclear testing and after Chernobyl: temporal change-point analysis using Markov Chain Monte Carlo**

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# Abstract

In Europe, the male to female ratio at birth (secondary sex ratio: SSR; sex odds: SO) is 1.04-1.06, is influenced by many factors and is declining in industrialized countries. This study was carried out to identify possible impacts of fallout by atomic bomb tests or by the Chernobyl event on SSR in Italy. Italy is a country without commercial nuclear power generation for the last four decades and thus nearly free of radiological confounders. Counts of annual male and female live births in Italy are provided by the World Health Organization (WHO) and by the Italian Istituto Nazionale di Statistica (ISTAT). This study included 57.7 million live births (1940-2019) with overall SSR 1.05829. The Italian SSR trend was modelled with linear and non-linear logistic regression. Trend changes, i.e., periods with level shifts were estimated with Markov Chain Monte Carlo (MCMC). Two distinct idealized level shifts were identified superimposed on a uniform secular downward trend. The first one is seen towards the end of the 1960s with a jump sex odds ratio (SOR) 1.00681, p<0.0001. The second one occurred in 1987 with SOR 1.00474, p<0.0001. In each of the 3 periods separated by the two jumps, SSR uniformly decreased with trend SOR per 100 years of 0.98549, p<0.0001. In conclusion, the secular trend in the Italian SSR showed two marked level shifts, at the end of the 1960s and from 1987 onward. These follow the release of radioactivity by atmospheric atomic bomb tests during the 1960s and by Chernobyl in 1986 and corroborate the hypothesis that ionizing radiation increases SSR.

**Keywords:** Atmospheric atomic bomb tests; Chernobyl, ecological study; gender proportions; ionizing radiation; nuclear accidents; radiation induced genetic effects.

# Introduction

Understanding the geographic and secular trend variations of the SSR has been considered one of the most elusive concepts in life science [[1](#_ENREF_1), [2](#_ENREF_2)]. However, for obvious biologic, social, and demographic reasons the analysis of the ratio of male to female offspring at birth (m/f, secondary sex ratio: SSR, sex odds: SO) can be considered a simple and non-invasive way to asses and monitor the reproductive health of a population [[3-5](#_ENREF_3)]. Except in societies where selective abortion skews the sex ratio [[6](#_ENREF_6)], approximately 104 to 106 boys are born for every 100 girls. Generally, the human sex ratio at birth is remarkably constant in large populations [[7](#_ENREF_7)] and slightly decreasing in industrialized countries [[8](#_ENREF_8)], and this has been linked to many factors including increasing air pollution [[9](#_ENREF_9)]. Radiation is one of few stressors known to elevate the sex ratio while dropping total births [[10](#_ENREF_10), [11](#_ENREF_11)]. For example, in dentists the offspring sex ratio was 1.13 among male dentists, 1.50 for female dentists, and 1.44 when both parents were dentists, possibly due to x-ray exposure [[12](#_ENREF_12)]. Smoking is shown to increase the sex ratio [[13](#_ENREF_13), [14](#_ENREF_14)] in a dose-dependent manner possibly partly due to elevated radionuclides in tabaco [[15](#_ENREF_15)]. After the atomic bombing of Japan [[4](#_ENREF_4), [16](#_ENREF_16)], following the global atmospheric nuclear weapons tests [[17-19](#_ENREF_17)], after the Windscale fire [[20](#_ENREF_20), [21](#_ENREF_21)], and after the Chernobyl accident [[22](#_ENREF_22), [23](#_ENREF_23)] long-lasting significant elevations (jumps or level shifts) in the sex ratio have been found. Even in Cuba, the sex ratio rose immediately after Chernobyl, presumably due to contaminated food imports from the former USSR [[24](#_ENREF_24), [25](#_ENREF_25)].

In contrast to those numerous sex odds increases after Chernobyl, Peterka et al. [[26](#_ENREF_26)] reported a unique proportion of strongly reduced male live births in November 1986 compared to all other monthly male birth proportions covering 50 years from 1950 to 1999 in the Czech Republic. They hypothesized a possible selective effect of the Chernobyl accident on male fetuses during the third month of prenatal development leading to a loss of the male gender at birth. Although such an effect restricted to only one month seems counterintuitive with respect to general environmental and biological variability, another effect particularly strong in a certain month has been reported by Sperling et al. [[27](#_ENREF_27)] and Zatsepin et al. [[28](#_ENREF_28)]: peak occurrences of Down’s syndrome in January 1987 in Berlin and Belarus. From this point of view, it would not be surprising that specific effects caused by acute post- or periconceptional exposure at relatively high doses could be somewhat different from chronic pre-, peri-, or post-conceptional exposure after relatively low and protracted doses in the years following the Chernobyl accident. The prenatal irradiation of parents and the direct radiation of fetuses may have opposing effects [[10](#_ENREF_10)]. The finding by Peterka et al. was later supported by an ecological dose-response relation [[29](#_ENREF_29)], but could not be confirmed with monthly Bavarian (German) data [[30](#_ENREF_30)].

Astolfi and Zonta [[31](#_ENREF_31)] analyzed the data on 2.8 million births in Italy by duration of gestation from last menstrual period, birth order, maternal age, maternal education, and sex: higher risks of preterm births were associated with male sex. Parrazini et al. analyzed trends in SSR between 1950 and 1990 in 29 countries from five continents. Among the 29 countries considered, the proportion of males declined in 16, increased in six, and remained stable in seven [[32](#_ENREF_32)]. Ulizzi and Zonta have used a stepwise multiple regression to analyze the covariation over time of the sex ratio with stillbirth rate, maternal age, firstborn proportion, and birth order. They found that a quadratic function of the firstborn proportion and mother's age was a predictor of the SSR [[33](#_ENREF_33)]. Zonta et al. considered SSR in four Italian regions with different degrees of industrialization. In less favorable environments, selection against male newborns was almost twice that against female newborns [[34](#_ENREF_34)].

Increased sex ratios have been observed in many circumstances in the vicinity of all kinds of nuclear facilities [[35-39](#_ENREF_35)]. Therefore, it may be concluded that the sex ratio is a useful, however neglected sentinel indicator for possibly detrimental changes in the environment inducing sub-clinical or yet unnoticed clinical effects. Italy, which is a country without noteworthy nuclear power generation since nearly 4 decades, is an interesting country for studying the sex ratio since possible confounding exposures by regular effluents from nuclear facilities and nuclear incidents with presumable subsequent health effects [[40-43](#_ENREF_40)] can be excluded. The present study investigates whether the secular sex ratio trend in Italy over eighty years from 1940-2019 is subject to any disturbances due to enhanced environmental ionizing radiation after the atmospheric atomic bomb tests and after the Chernobyl event.

# Data and statistical methods

*Gender specific birth counts*

Freely available Italian annual live birth counts by gender for the years 1950 through 2014 were obtained from the World Health Organization (WHO) ‘Health For All Data Base’ (HFADB, <https://gateway.euro.who.int/en/datasets/european-health-for-all-database/>). Counts for 1940 to 1949 can be downloaded from the ‘The Human Mortality Database’ (<https://www.mortality.org/>). Most recent monthly data (January 2015 to December 2019) are provided on the internet by the ‘Italian National Institute of Statistics’ (ISTAT, [http://demo.istat.it/ index\_e.html](http://demo.istat.it/%20index_e.html)). The data compiled and analyzed are presented in Table 1 and Figure 1. Note, the data values in Table 1 for the year 2019 are complete but provisional. The potential (minuscule) error introduced by this inaccuracy is considered negligible.

*Radiological contamination*

Increased environmental radioactivity across Italy due to the atmospheric atomic weapons tests and Chernobyl have been documented in detail by UNSCEAR in its Report 2000 Annex C-Corr and Annex J, respectively [[44](#_ENREF_44), [45](#_ENREF_45)]. The overall Cs-137 depositions in Italy due to the nuclear tests are in the order of magnitude of 2 to 6 kBq/m2 (mean 4.0) and in the order of magnitude of additional 2 to 4 kBq/m2 (mean 3.0) after Chernobyl. According to different sources, 10 kBq/m2 Cs-137 translates to an air dose-rate of 0.144 mSv/a [[46](#_ENREF_46)] or of 0.224 mSv/a [[47](#_ENREF_47)]. Considering further radionuclides contained in fallout, e.g., Cs-134 with an air dose per unit of deposition density 2.7 times greater than that of Cs-137 [[47](#_ENREF_47)], it is conceivable that fallout deposition in Italy entailed an additional 0.40 mSv/a (20%) at the beginning of the 1970ies and additionally 0.30 mSv/a (15%) from 1987 onward after Chernobyl. The half-lives of Cs-134 and Cs-137 are 2.07 and 30.2 years, respectively. Adding cumulatively 10% to 20% to the 2 mSv/a [[48](#_ENREF_48)] natural background radiation in Italy due to global anthropogenic radionuclide deposition (excluding radon and medical sources) allows the estimation of a dose-specific SOR per mSv/a by associating the additional doses with the sex odds jump heights.

*Data analysis and statistical methods*

The Italian birth counts, and the annual sex ratios compiled in Table 1 and displayed in Figure 1 were analyzed with focus on the possibility that the sex ratio increased because of

the atomic bomb tests and after Chernobyl, when radioactive precipitation affected Italy in the periods between 1955 to 1985 [[44](#_ENREF_44), [49](#_ENREF_49)] and from 1986 [[45](#_ENREF_45), [50](#_ENREF_50)], respectively. To this end, a robust hierarchical Bayesian changepoint model (SAS procedure MCMC) was employed to determine and estimate possible sex ratio jumps in the two overlapping 30-years periods 1955 to 1985 and 1970 to 2000, respectively.

Ordinary linear logistic regression and non-linear logistic regression based on the inversely variance weighted logit transform was used to assess the time trend in the probability of boys among live births (m+f), and to investigate whether there were significant changes (drops or jumps) in the trend functions. This involves considering the male proportion pm among all male (m) and female (f) births: pm = m/(m+f). Pertinent parameters in this context are the sex odds SO = pm/(1- pm) = m/f and the sex odds ratio (SOR), which is the ratio of two sex odds of interest, e.g., the sex odds in exposed populations divided by the sex odds in non-exposed populations. The variance of the natural logarithm of the sex odds is estimated by m-1+f-1 [[51](#_ENREF_51)]. The required Binomial distributional assumption, possible heterogeneity, and autocorrelation issues have been considered in detail in [[36](#_ENREF_36), [52](#_ENREF_52)]. For trend analyses of birth counts and sex odds, Poisson regression (SAS GENMOD) and linear as well as non-linear logistic regression using SAS procedures LOGISTIC and NLIN were applied, respectively. The estimation of possible change-points in the sex ratio trends was carried out by Bayesian Markov chain Monte Carlo (SAS MCMC). Figures were produced with SAS procedure SGPLOT. Software employed was MS-Excel-365 (2016), R 3.5.1, Wolfram MATHEMATICA 11.3, and mostly SAS/STAT software 9.4 (SAS Institute Inc: SAS/STAT User’s Guide, Cary NC: SAS Institute Inc, 2014).

# Results

Table 2 presents the results of the MCMC changepoint model. In the overall secular Italian sex ratio trend 1940 to 2019, two unique distinct idealized level shifts are found: (1) in rounded 1970, 95%-HPDI (1968, 1972), and (2) in 1987, 95%-HPDI (1985, 1988). The corresponding jump parameters estimated by this approach on the natural log scale are 0.00451, 95%-HPDI (0.00284, 0.00628), and 0.00303, 95%-HPDI (0.00103, 0.00541), respectively. These jump parameters are somewhat conservative as the employed MCMC approach was specified with the assumption of piecewise constant trends in the periods 1955 to 1985 and 1970 to 2000, respectively.

With the estimated idealized level shifts in 1970 and 1987 in the Italian sex ratio trend, a logistic regression model was set up for the male proportion with each of the change-point effects (jumps or level shifts) coded as a temporal dummy variable that is 0 before and 1 after the corresponding change-point in 1970 and in 1987, respectively. The sex ratios from 1940 to 2019 in Italy and their interrupted optimum logistic regression line, which accounts for the identified jumps are presented in Figure 2. The first jump in 1970 is described by a jump SOR of 1.00681, 95%-CI (1.00474, 1.00888), p < 0.0001. The second jump in 1987 is characterized by a jump SOR of 1.00474, 95%-CI (1.00246, 1.00702), p < 0.0001. These estimates are less conservative as the underlying overall secular downward trend is accounted for.

An alternative to MCMC and to logistic regression employing the MCMC change-points is inversely variance weighted nonlinear regression. The following nonlinear function was fit to the natural logarithm of the Italian sex odds data and displayed as the thick gray curve in Figure 2 for comparison:

The parameter estimates for are *a*=0.0569, *b*=0.0073, *c*=0.0052, *t0*=-0.00017, *t1*=29.74, *t2*=45.62, *s1*=0.68590, and *s2*=0.1285, where *t* runs from 0 to 79 representing the years from 1940 through 2019. Function illustrates that the first level shift around 1970 extends over an approximate 5-year period (s1/s2=5.34) whereas the second level shift occurred abrupt from 1986 to 1987 within one year.

Assuming cumulative increases of the background radiation in Italy from 1970 and from 1987 onward of 20%, i.e. 0.4 mSv/a, and 15%, i.e. 0.3 mSv/a, respectively, yields an SOR per mSv/a of 1.0165, 95%-CI (1.0118, 1.0211), p-value < 0.0001.

# Discussion

This study has shown two distinct and unique sex ratio level shifts around 1970 and in 1987 in the Italian sex ratio trend 1940 to 2019. While the second jump from 1987 can be attributed to the one-time event Chernobyl in 1986 [[23](#_ENREF_23), [25](#_ENREF_25)], the first level shift around 1979 is only a simplifying idealization. Table 2 shows that this temporal change-point estimate has a (rounded) 5-year-wide 95%-HPDI of (1968, 1972). To visualize the stretched first level shift, we added a non-linear logistic regression line to Figure 2. The increasing number of atomic bomb tests during the 1960ties may not have impacted all countries uniformly. It is possible that some major single events coincident with unfavorable meteorological conditions led to the specific temporal exposure pattern, which is now reflected by the SO trend in Italy. The radioactive decay naturally decreasing radiation exposure after cessation of the radiological releases may partly explain the dominating piecewise downward trends of the SO, despite the upward level shifts.

The SAS-MCMC procedure employed is a general-purpose Markov chain Monte Carlo (MCMC) simulation procedure that is designed to fit Bayesian models. In essence, Bayesian statistics treats parameters as unknown random variables with specified prior distributions, and it makes inferences based on the posterior distributions of the parameters. Hierarchical Bayes changepoint models avoid sophisticated analytic and numerical high dimensional integration procedures. The desired marginal posterior densities are obtained utilizing the Gibbs sampler [[53](#_ENREF_53)]. An important advantage of this approach is the capability of providing 95% highest posterior density intervals (95%-HPDI) for the parameters involved including the time point of the change-point. A confidence interval for the time point of the change-point, i.e., the time point of the level shift cannot be computed with other methods that easily.

The roughly estimated SOR of 1.0165 per mSv/a derived from the association of the additional radiation exposure and the extent of the level shifts agrees in principle and in the order of magnitude with findings based on municipality/district-level data in Austria and Germany before and after Chernobyl: SOR of 1.0145 per mSv/a (1.0021–1.0271), p-value 0.0218 [[16](#_ENREF_16), [22](#_ENREF_22)]. However, a major limitation of the present study is the lacking spatial stratification of the Italian secular sex odds trend according to differently radiologically impacted subregions of Italy. However, a corresponding spatiotemporal approach [[30](#_ENREF_30)] could be the topic of future refined investigation motivated by the present study.

Ever since the discovery that significantly more male than female births occur in nature [[54](#_ENREF_54)], the study of the secondary sex ratio has been accompanied by important developments in science [[2](#_ENREF_2)]. To asses the radiological impact on the sex ratio in animals, genetic and ecological studies have been carried out after Chernobyl and Fukushima: For example, Mousseau et al. observed: ‘*… declines in population sizes of birds in Chernobyl including changes in adult sex ratios (more males than females)’* [[55](#_ENREF_55)]. Investigations of the human sex ratio in the children of the atomic-bomb survivors initially yielded positive evidence [[4](#_ENREF_4)], which was later dismissed [[56](#_ENREF_56)]. Indeed, from the 1960s onward, the sex ratio was not considered an indicator of genetic damage. While UNSCEAR in 1958 stressed that a disturbed sex ratio is an obvious criterion for genetic detriment [[5](#_ENREF_5)], the UNSCEAR 2013 report showed practically no evidence of changes in offspring sex ratios of parents exposed to radiation [[57](#_ENREF_57)], despite the updated and strengthened evidence at that time [[11](#_ENREF_11), [22](#_ENREF_22)]. Ultimately, the UNSCEAR 2017 report does not consider the sex ratio any longer [[58](#_ENREF_58)]. Therefore, the sex ratio is an unfairly neglected sentinel indicator of chemical or physical environmental changes that cause genetic health effects gone.

In this paper, 57.7 million gender-specific annual births in Italy from January 1940 to September 2019 showed distinct sex ratio increases around 1970 and from 1986/1987 onward. Extrapolating the base-line sex ratio from 1940 through 1969, which is indicated by the broken straight line in Figure 2 suggests the assumption that today the sex ratio in Italy is approximately 1.2 % higher than it would be without the presumable cumulative radiological depositions of the ‘nuclear age’. A simplifying conservative assumption is that due to their fathers’ more vulnerable X-chromosomes more girls are lost after increasing ionizing radiation exposure at population level [[38](#_ENREF_38), [59](#_ENREF_59)]. Two possibilities with the same outcome may be considered: (1) girls get not conceived because of dysfunctional or impaired paternal X-chromosomes and (2) fewer female embryos and fetuses survive pregnancy, for the same reason. For a discussion and classification of the comprehensive empirical sex ratio investigations from conception to birth by Orzack et al. [[59](#_ENREF_59)] see Austad [[60](#_ENREF_60)]: “*If the sex ratio at or near conception is indeed a Mendelian 50:50, as these extensive data indicate, but is a slightly male-biased 51.3% at birth, then if anything, during much of gestation female fetuses turn out to be the (slightly) frailer sex.*” From this point of view, it is plausible that additional radiation exposure around conception and during pregnancy would increase the secondary sex ratio by compromising conceptions and the development of female zygotes, embryos, and fetuses. Since about 200,000 girls are currently born in Italy per year (see Table 1), this means that in Italy approximately 2400 girls (1.2%) are lost annually due to cumulative environmental radiation exposure after the above-ground atomic bomb tests and after the Chernobyl event.

These findings call for intensifying bio-physical research in exposure mechanisms and exposure pathways of natural or artificial ionizing radiation. Biological, epidemiological, and medical research should aim to clarify the genetic and carcinogenic consequences of increased radiation in the environment. Since radiation-induced genetic effects occur without spectacular incidents or accidents [[61](#_ENREF_61)], an implication of this study for the legislator, the nuclear industry, and the nuclear and radio-pharmaceutical medicine is that even greater care must be imposed when processing, employing, and disposing radioactive materials. Beyond these practical considerations, the disturbed sex ratios in Italy are of theoretical interest in as much as in evolutionary biology changes in the effective mutation rate can be estimated from changes in the secondary sex ratio [[62](#_ENREF_62)]. Indeed, Preston et al. stated “*New approaches for the estimation of hereditary risk have been developed with the use of human data whenever feasible, although the current estimates of heritable radiation effects still are based on mouse data because of an absence of effects in human studies*.” [[63](#_ENREF_63)] In the light of these and many similar findings, the claim of an absence of hereditary risk effects in human studies should be reconsidered.

# Conclusions

The secular secondary sex ratio trend of Italy 1940 to 2019 discloses two distinct level shifts, the first one at the end of the 1960ties and the second one from 1987 onward. These level shifts are temporally associated with the releases of radioactivity by the atmospheric atomic bomb tests during the 1960s and by Chernobyl in 1986. This finding strengthens previous evidence that elevated environmental ionizing radiation increases secondary sex ratios at population levels.

**Abbreviations**

µSv/h Micro-Sieverts per hour

95%-CI 95%-confidence interval

95%-HPDI 95%-highest posterior density interval

Bq Becquerel (1 nuclear decay per second)

Cs-137 Cesium-137

HFADB Health for all data base (WHO)

ISTAT Italian National Institute of Statistics

kBq/m2 Kilo-Becquerel per square meter

MCMC Markov chain Monte Carlo

mSv/a Milli-Sieverts/annum or milli-Sieverts/year

OR Odds ratio

p p-value

SAS Statistical Analysis System, software produced by SAS Institute Inc.

SO sex odds

SOR sex odds ratio

UNSCEAR United Nations Scientific Committee on the Effects of Atomic Radiation

USA United States of America

USSR Union of Soviet Socialist Republics

WHO World Health Organization

**Declarations**

*Ethical Approval and Consent to participate*Not applicable. Ethics approval and consent to participate are not required and not necessary, since only publicly available data and previously published information is being used.

*Consent for publication*Not applicable. Only anonymous data is being used.

*Availability of supporting data*   
The employed data has exclusively been published previously and/or it is contained in the Tables and in the Figures included in this paper.

*Competing interests*   
The authors declare that they have no conflicts of interest.

*Funding*   
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**Legends of Tables and Figures**

**Table 1.** Annual live births in Italy by gender and sex ratio, 1940 – 2019; sources: <https://www.mortality.org/> 1940-1949, <https://gateway.euro.who.int/> 1950-2014, <http://demo.istat.it/> 2015-2019; values in 2019 are provisional.

**Table 2.** Markov chain Monte Carlo (MCMC) analyses for the determination of change points in the secular Italian sex ratio trend 1940 to 2019; time points of change-point estimates (jumps) and corresponding HPDI intervals highlighted.

**Figure 1.** Live birth counts by gender with sex-specific trends according to polynomial Poisson regression models (SAS procedure GENMOD).

**Figure 2.** Secondary sex ratio in Italy (1940-2019); black solid line: linear logistic regression model accounting for idealized optimum jumps in 1970 and 1987; light gray thick line: non-linear logistic regression model allowing for smooth changes 1968-1972 and 1985-1987.

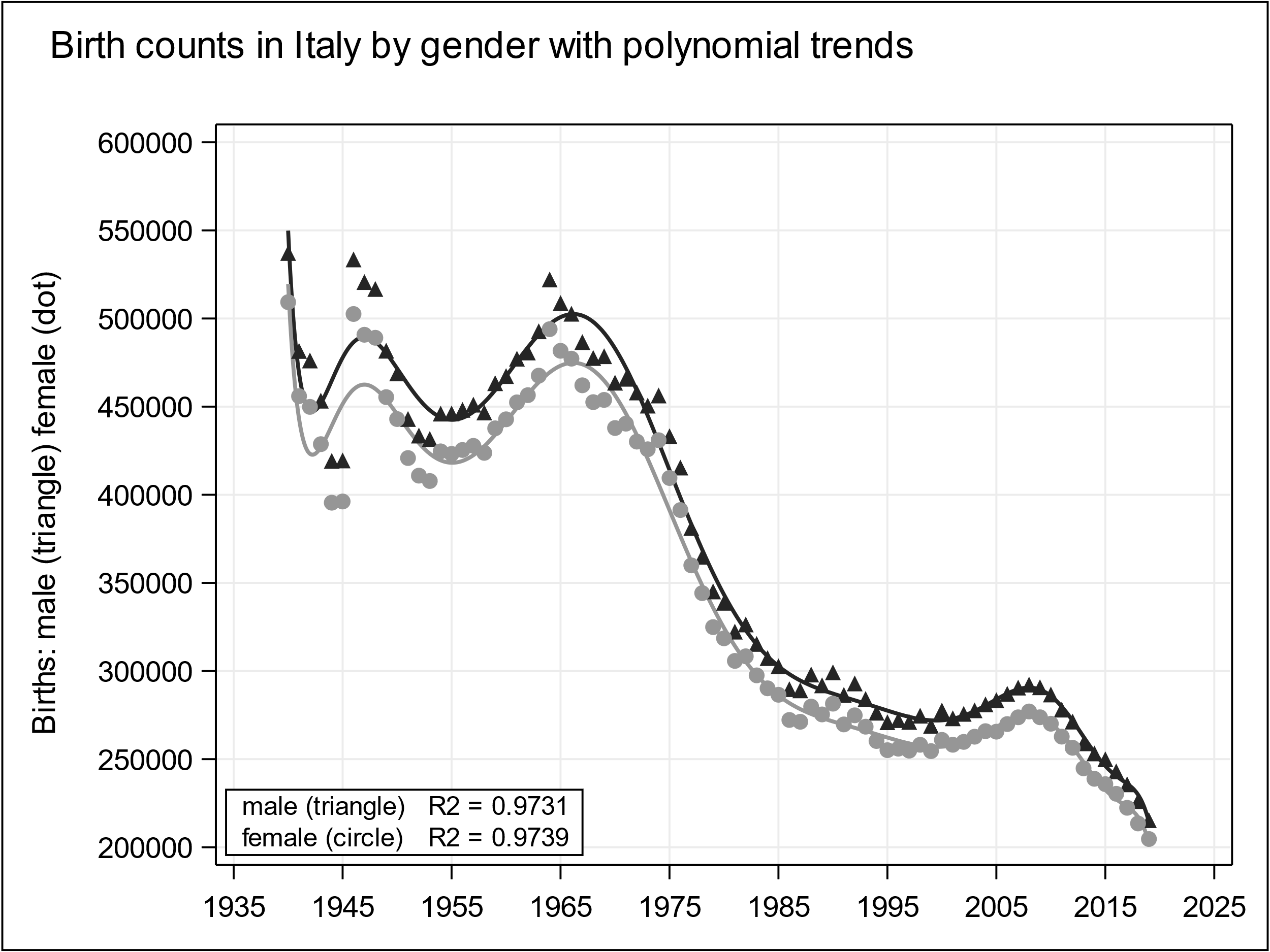
**Tables and Figures**

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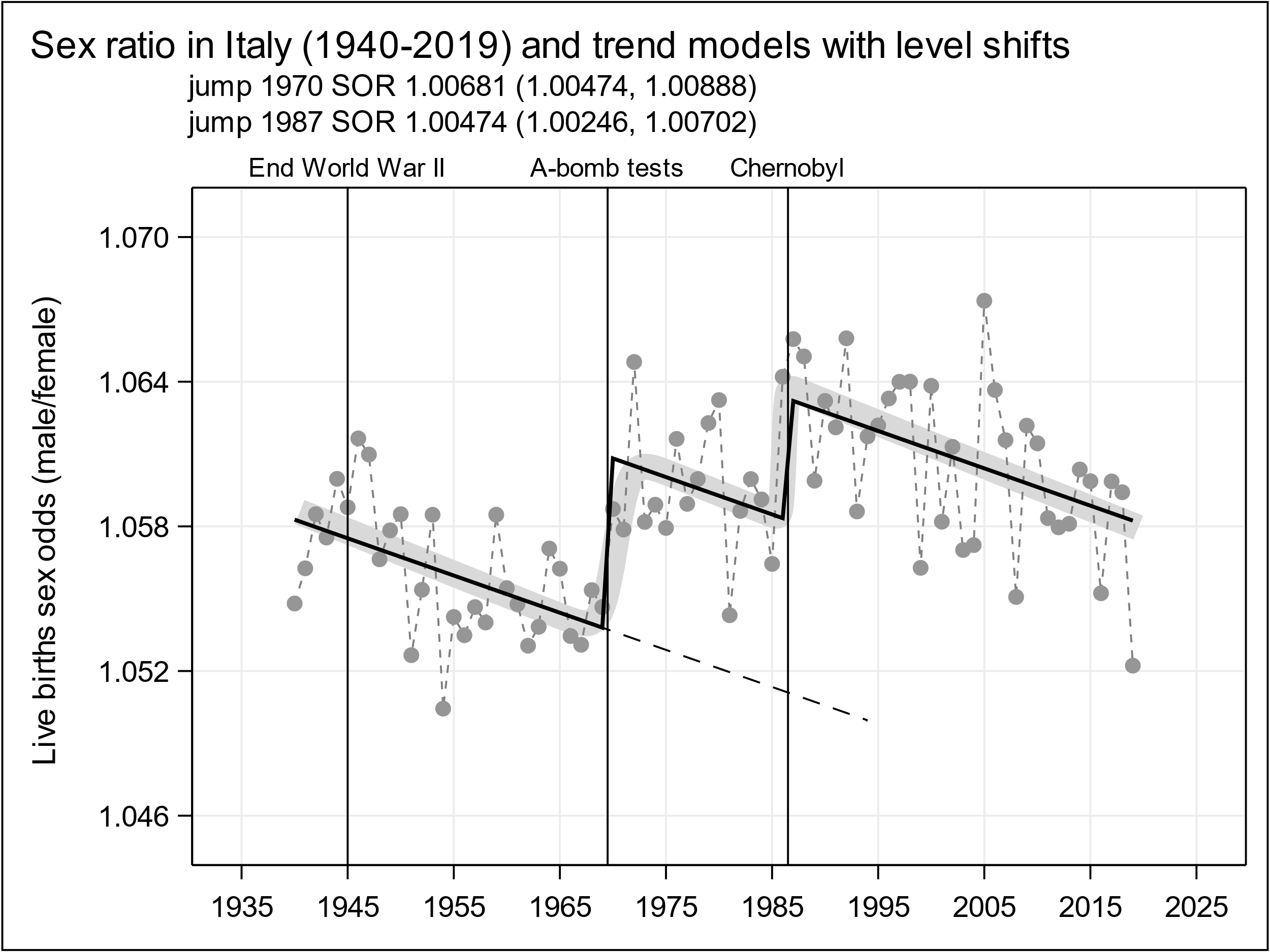
|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **year** | **male** | **female** | **sex ratio** | **year** | **male** | **female** | **sex ratio** |
| 1940 | 537,194 | 509,285 | 1.0548 | 1980 | 338,712 | 318,566 | 1.0632 |
| 1941 | 481,599 | 455,947 | 1.0563 | 1981 | 322,360 | 305,753 | 1.0543 |
| 1942 | 476,192 | 449,871 | 1.0585 | 1982 | 326,438 | 308,356 | 1.0586 |
| 1943 | 453,386 | 428,719 | 1.0575 | 1983 | 315,389 | 297,547 | 1.0600 |
| 1944 | 419,233 | 395,513 | 1.0600 | 1984 | 307,358 | 290,202 | 1.0591 |
| 1945 | 419,485 | 396,193 | 1.0588 | 1985 | 302,703 | 286,530 | 1.0564 |
| 1946 | 533,540 | 502,558 | 1.0616 | 1986 | 289,726 | 272,246 | 1.0642 |
| 1947 | 520,709 | 490,781 | 1.0610 | 1987 | 289,051 | 271,214 | 1.0658 |
| 1948 | 516,775 | 489,076 | 1.0566 | 1988 | 298,029 | 279,827 | 1.0650 |
| 1949 | 481,742 | 455,404 | 1.0578 | 1989 | 291,881 | 275,387 | 1.0599 |
| 1950 | 468,860 | 442,945 | 1.0585 | 1990 | 299,276 | 281,485 | 1.0632 |
| 1951 | 443,005 | 420,844 | 1.0527 | 1991 | 286,463 | 269,712 | 1.0621 |
| 1952 | 433,598 | 410,849 | 1.0554 | 1992 | 292,964 | 274,877 | 1.0658 |
| 1953 | 431,664 | 407,814 | 1.0585 | 1993 | 284,161 | 268,426 | 1.0586 |
| 1954 | 446,054 | 424,635 | 1.0504 | 1994 | 276,367 | 260,298 | 1.0617 |
| 1955 | 446,144 | 423,189 | 1.0542 | 1995 | 270,964 | 255,100 | 1.0622 |
| 1956 | 448,181 | 425,427 | 1.0535 | 1996 | 272,153 | 255,950 | 1.0633 |
| 1957 | 451,142 | 427,764 | 1.0547 | 1997 | 271,133 | 254,825 | 1.0640 |
| 1958 | 446,679 | 423,789 | 1.0540 | 1998 | 274,683 | 258,160 | 1.0640 |
| 1959 | 463,308 | 437,709 | 1.0585 | 1999 | 268,895 | 254,568 | 1.0563 |
| 1960 | 467,370 | 442,822 | 1.0554 | 2000 | 277,599 | 260,943 | 1.0638 |
| 1961 | 477,219 | 452,438 | 1.0548 | 2001 | 273,194 | 258,170 | 1.0582 |
| 1962 | 480,738 | 456,519 | 1.0531 | 2002 | 275,732 | 259,806 | 1.0613 |
| 1963 | 492,754 | 467,582 | 1.0538 | 2003 | 277,719 | 262,738 | 1.0570 |
| 1964 | 522,158 | 493,962 | 1.0571 | 2004 | 281,102 | 265,887 | 1.0572 |
| 1965 | 508,775 | 481,683 | 1.0562 | 2005 | 283,489 | 265,599 | 1.0674 |
| 1966 | 502,724 | 477,216 | 1.0535 | 2006 | 287,099 | 269,917 | 1.0637 |
| 1967 | 486,653 | 462,119 | 1.0531 | 2007 | 290,611 | 273,754 | 1.0616 |
| 1968 | 477,612 | 452,560 | 1.0554 | 2008 | 292,312 | 277,054 | 1.0551 |
| 1969 | 478,635 | 453,831 | 1.0547 | 2009 | 290,798 | 273,775 | 1.0622 |
| 1970 | 463,592 | 437,880 | 1.0587 | 2010 | 286,701 | 270,104 | 1.0614 |
| 1971 | 465,832 | 440,350 | 1.0579 | 2011 | 278,121 | 262,789 | 1.0583 |
| 1972 | 458,043 | 430,160 | 1.0648 | 2012 | 271,317 | 256,453 | 1.0580 |
| 1973 | 450,593 | 425,817 | 1.0582 | 2013 | 259,008 | 244,784 | 1.0581 |
| 1974 | 456,345 | 430,962 | 1.0589 | 2014 | 253,269 | 238,852 | 1.0604 |
| 1975 | 433,235 | 409,510 | 1.0579 | 2015 | 249,950 | 235,830 | 1.0599 |
| 1976 | 415,448 | 391,331 | 1.0616 | 2016 | 243,080 | 230,358 | 1.0552 |
| 1977 | 381,158 | 359,945 | 1.0589 | 2017 | 235,733 | 222,418 | 1.0599 |
| 1978 | 364,841 | 344,202 | 1.0600 | 2018 | 226,217 | 213,530 | 1.0594 |
| 1979 | 345,158 | 324,920 | 1.0623 | 2019 | 215,387 | 204,697 | 1.0522 |
| **Total** | **18,447,373** | **17,454,121** | **1.0569** | **Total** | **11,227,144** | **10,586,487** | **1.0605** |

**Table 2.** Markov chain Monte Carlo (MCMC) analyses for the determination of change points in the secular Italian sex ratio trend 1940 to 2019; time points of change-point estimates (jumps) and corresponding HPDI intervals highlighted.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **MCMC change-point estimation in**  **periods** | **Posterior Summaries and Intervals** | | | | | |
| **parameter** | **n** | **mean** | **standard deviation** | **95% highest posterior density interval (HPDI)** | |
|
| **1955 - 1985** | intercept | 1000 | 1.05490 | 0.00067 | 1.05380 | 1.05640 |
| jump | 1000 | 0.00451 | 0.00088 | 0.00284 | 0.00628 |
| time point | 1000 | **1969.60** | 0.96030 | **1967.80** | **1971.90** |
| **1970 - 2000** | intercept | 1000 | 1.05960 | 0.00077 | 1.05830 | 1.06140 |
| jump | 1000 | 0.00303 | 0.00113 | 0.00103 | 0.00541 |
| time point | 1000 | **1986.10** | 0.82780 | **1985.00** | **1987.90** |

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**Figure 1.** Live birth counts by gender with sex-specific trends according to polynomial Poisson regression models (SAS procedure GENMOD).

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**Figure 2.** Secondary sex ratio in Italy (1940-2019); black solid line: linear logistic regression model accounting for idealized optimum jumps in 1970 and 1987; light gray thick line: non-linear logistic regression model allowing for smooth changes 1968-1972 and 1985-1987.

**References**

[1] D. Pavic, Secular trends and geographical variations in sex ratio at birth, Early Hum Dev 91(12) (2015) 811-5.

[2] E. Brian, M. Jaisson, The Descent of Human Sex Ratio at Birth. A Dialogue between Mathematics, Biology and Sociology, Springer Netherlands, Dordrecht, 2007.

[3] M.L. Terrell, H.K. P., M. Macrus, Can environmental or occupational hazards alter the sex ratio at birth? A systematic review, Emerging Health Threats Journal 4(7109) (2011).

[4] W.J. Schull, J.V. Neel, Radiation and the sex ratio in man, Science 128(3320) (1958) 343-8.

[5] UNSCEAR, Report of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), General Assembly Official Records: Thirteenth session Supplement No. 17 (A/3838); ANEX H:The genetic effects of radiation, 1958. <http://www.unscear.org/unscear/en/publications/1958.html>; accessed October 27, 2020.

[6] C. Zhou, X.L. Wang, X.D. Zhou, T. Hesketh, Son preference and sex-selective abortion in China: informing policy options, Int J Public Health 57(3) (2012) 459-65.

[7] E. Ein-Mor, D. Mankuta, D. Hochner-Celnikier, A. Hurwitz, R. Haimov-Kochman, Sex ratio is remarkably constant, Fertil Steril 93(6) (2010) 1961-5.

[8] V. Grech, Sex ratios at birth in the British Isles over the past sixty years, European Journal of Pediatrics 172(4) (2013) 525-528.

[9] A.J.F.C. Lichtenfels, J.B. Gomes, P.C. Pieri, S.G. El Khouri Miraglia, J. Hallak, P.H.N. Saldiva, Increased levels of air pollution and a decrease in the human and mouse male-to-female ratio in São Paulo, Brazil, Fertility and Sterility 87(1) (2007) 230-232.

[10] W.H. James, Ionizing radiation and offspring sex ratio, J Epidemiol Community Health 51(3) (1997) 340-1.

[11] H.O. Dickinson, L. Parker, K. Binks, R. Wakeford, J. Smith, The sex ratio of children in relation to paternal pre-conceptional radiation dose: a study in Cumbria, northern England, J Epidemiol Community Health 50(6) (1996) 645-52.

[12] H. Ghasemi, S.R. Mirdehghan, M. Namdari, F. Bayat, Offspring sex ratio of Iranian dentists, Environ Health Prev Med 21(6) (2016) 446-449.

[13] N.G. Beratis, A. Asimacopoulou, A. Varvarigou, Association of secondary sex ratio with smoking and parity, Fertility and Sterility 89(3) (2008) 662-667.

[14] M. Voigt, M. Hermanussen, U. Wittwer-Backofen, C. Fusch, V. Hesse, Sex-specific differences in birth weight due to maternal smoking during pregnancy, European Journal of Pediatrics 165(11) (2006) 757-761.

[15] C. Papastefanou, Radioactivity of tobacco leaves and radiation dose induced from smoking, Int J Environ Res Public Health 6(2) (2009) 558-67.

[16] H. Scherb, K. Voigt, R. Kusmierz, Ionizing radiation and the human gender proportion at birth-A concise review of the literature and complementary analyses of historical and recent data, Early Human Development 91(12) (2015) 841-850.

[17] V. Grech, Atomic bomb testing and its effects on global male to female ratios at birth, Int J Risk Saf Med 27(1) (2015) 35-44.

[18] H. Scherb, Letter to the Editor, Int J Risk Saf Med 27(2) (2015) 107-10.

[19] A. Korblein, Human sex ratio at birth after atmospheric weapons testing, Early Hum Dev 100 (2016) 33-4.

[20] V. Grech, Births and male:female birth ratio in Scandinavia and the United Kingdom after the Windscale fire of October 1957, Int J Risk Saf Med 26(1) (2014) 45-53.

[21] H. Scherb, R. Kusmierz, K. Voigt, Letter to the editor, Int J Risk Saf Med 26(3) (2014) 173-4.

[22] H. Scherb, K. Voigt, Trends in the human sex odds at birth in Europe and the Chernobyl Nuclear Power Plant accident, Reproductive Toxicology 23(4) (2007) 593-599.

[23] H. Scherb, K. Voigt, 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) (2011) 697-707.

[24] S.J. Venero Fernandez, R.S. Medina, J. Britton, A.W. Fogarty, The association between living through a prolonged economic depression and the male:female birth ratio--a longitudinal study from Cuba, 1960-2008, Am J Epidemiol 174(12) (2011) 1327-31.

[25] H. Scherb, R. Kusmierz, K. Voigt, Increased sex ratio in Russia and Cuba after Chernobyl: a radiological hypothesis, Environ Health 12 (2013) 63.

[26] M. Peterka, R. Peterkova, Z. Likovsky, Chernobyl: prenatal loss of four hundred male fetuses in the Czech Republic, Reproductive Toxicology 18(1) (2004) 75-9.

[27] K. Sperling, Pelz, J., Exogeneous and endogenous risk factors for maternal non-disjunction of chromosome 21, BJMG 6 (2003) 5-10.

[28] P. Zatsepin, P. Verger, E. Robert-Gnansia, B. Gagniere, R.D. Khmel, G.I. Lazjuk, Cluster of Down's syndrome cases registered in January 1987 in the Republic of Belarus as a possible effect of the Chernobyl accident, International Journal of Radiation Medicine Special Issue(6) (2004) 57-71.

[29] M. Peterka, R. Peterkova, Z. Likovsky, Chernobyl: relationship between the number of missing newborn boys and the level of radiation in the Czech regions, Environ Health Perspect 115(12) (2007) 1801-6.

[30] H. Scherb, K. Voigt, Analytical ecological epidemiology: exposure-response relations in spatially stratified time series, Environmetrics 20(6) (2009) 596-606.

[31] P. Astolfi, L.A. Zonta, Risks of preterm delivery and association with maternal age, birth order, and fetal gender, Hum Reprod 14(11) (1999) 2891-4.

[32] F. Parazzini, C. La Vecchia, F. Levi, S. Franceschi, Trends in male:female ratio among newborn infants in 29 countries from five continents, Human Reproduction 13(5) (1998) 1394-1396.

[33] L. Ulizzi, L.A. Zonta, Factors affecting the sex ratio in humans: multivariate analysis of the Italian population, Hum Biol 67(1) (1995) 59-67.

[34] L.A. Zonta, P. Astolfi, L. Ulizzi, Early selection and sex composition in Italy: a study at the regional level, Hum Biol 68(3) (1996) 415-26.

[35] H. Scherb, R. Kusmierz, K. Voigt, Human sex ratio at birth and residential proximity to nuclear facilities in France, Reprod Toxicol 60 (2016) 104-111.

[36] H. Scherb, R. Kusmierz, M. Sigler, K. Voigt, Modeling human genetic radiation risks around nuclear facilities in Germany and five neighboring countries: A sex ratio study, Environmental Modelling and Software 79 (2016) 343–353.

[37] H. Scherb, V. Grech, Trends in births and the birth sex ratio in the vicinity of the Mainz research reactor in Germany, Early Hum Dev 141 (2020) 104869.

[38] H. Scherb, R. Kusmierz, K. Voigt, Secondary sex ratio and trends in the associated gender-specific births near nuclear facilities in France and Germany: Update of birth counts, Reprod Toxicol 89 (2019) 159-167.

[39] H. Scherb, The Human Secondary Sex Odds in the Vicinity of the Nuclear Power Plant Leibstadt in Switzerland, 2002 to 2019, Journal of Womens Health Care and Management 2(1) (2020) 1-3.

[40] P. Kaatsch, C. Spix, R. Schulze-Rath, S. Schmiedel, M. Blettner, Leukaemia in young children living in the vicinity of German nuclear power plants, Int J Cancer 122(4) (2008) 721-6.

[41] R. Wakeford, Childhood leukaemia and nuclear installations: the long and winding road, Br J Cancer 111(9) (2014) 1681-3.

[42] NLGA, Niedersächsisches Landesgesundheitsamt (NLGA). Fachgespräch Sekundäres Geschlechterverhältnis in der Umgebung des Transportbehälterlagers (TBL) Gorleben am 12. März 2012. Editor: Niedersächsisches Landesgesundheitsamt, Roesebeckstr. 4 - 6, 30449 Hannover. <http://www.nlga.niedersachsen.de/download/65642/Sekundaeres_Geschlechterverhaeltnis_in_der_Umgebung_des_Transportbehaelterlagers_TBL_Gorleben_-_Fachgespraech_am_12_Maerz_2012.pdf>. Accessed November 1, 2019, 2012.

[43] International Atomic Energy Agency (IAEA), Nuclear Safety Review for the Year 2001; Printed by the IAEA in Austria, July 2002. <https://inis.iaea.org/collection/NCLCollectionStore/_Public/33/039/33039369.pdf>. Accessed 29 August, 2019.

[44] UNSCEAR. Report 2000. United Nations Scientific Committee on the Effects of Atomic Radiation, ANNEX C Exposures to the public from man-made sources of radiation, <http://www.unscear.org/docs/publications/2000/UNSCEAR_2000_Annex-C-CORR.pdf>. Accessed 29 January, 2020.

[45] UNSCEAR. Report 2000. United Nations Scientific Committee on the Effects of Atomic Radiation, Annex J, Exposure and effects of the Chernobyl accident, <http://www.unscear.org/docs/publications/2000/UNSCEAR_2000_Annex-J.pdf>. Accessed 29 January, 2020.

[46] H. Scherb, E. Weigelt, Congenital Malformation and Stillbirth in Germany and Europe Before and After the Chernobyl Nuclear Power Plant Accident, Environmental Science and Pollution Research, Special Issue 1 (2003) 117-125.

[47] S. Mikami, H. Tanaka, H. Matsuda, S. Sato, Y. Hoshide, N. Okuda, T. Suzuki, R. Sakamoto, M. Andoh, K. Saito, The deposition densities of radiocesium and the air dose rates in undisturbed fields around the Fukushima Dai-ichi nuclear power plant; their temporal changes for five years after the accident, Journal of Environmental Radioactivity 210 (2019) 105941.

[48] Commission of the European Communities. Exposure of the population to natural radiation. Directorate-General for Social Affairs. Directorate of Health Protection, (1974). <http://aei.pitt.edu/49301/1/B0028.pdf>, Accessed January 20, 2020.

[49] W.E. Bost, H.E. Voress, RADIOACTIVE FALLOUT; A BIBLIOGRAPHY OF THE WORLD'S LITERATURE. TID-3086 (SUPPL 2), ORO Rep (1965) 1-246.

[50] E. Cardis, D. Krewski, M. Boniol, V. Drozdovitch, S.C. Darby, E.S. Gilbert, S. Akiba, J. Benichou, J. Ferlay, S. Gandini, C. Hill, G. Howe, A. Kesminiene, M. Moser, M. Sanchez, H. Storm, L. Voisin, P. Boyle, Estimates of the cancer burden in Europe from radioactive fallout from the Chernobyl accident, International Journal of Cancer 119(6) (2006) 1224-1235.

[51] Y.M. Bishop, S.E. Fienberg, P.W. Holland, Discrete Multivariate Analysis, Springer-Verlag New York 1975.

[52] H. Scherb, K. Voigt, 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), Environ Sci Pollut Res Int 19(4) (2012) 1335-40.

[53] B.P. Carlin, A.E. Gelfand, F.M.S. Adrian, Hierarchical Bayesian Analysis of Changepoint Problems, Journal of the Royal Statistical Society. Series C (Applied Statistics) 41(2) (1992) 389-405.

[54] A. Bouckaert, [Dr. John Arbuthnot, inventor of statistical testing], Hist Sci Med 30(4) (1996) 459-66.

[55] T.A. Mousseau, A.P. Moller, Genetic and ecological studies of animals in Chernobyl and Fukushima, J Hered 105(5) (2014) 704-9.

[56] W.J. Schull, J.V. Neel, A. Hashizume, Some further observations on the sex ratio among infants born to survivors of the atomic bombings of Hiroshima and Nagasaki, Am J Hum Genet 18(4) (1966) 328-38.

[57] UNSCEAR. Report 2013, Volume II. United Nations Scientific Committee on the Effects of Atomic Radiation, REPORT TO THE GENERAL ASSEMBLY,SCIENTIFIC ANNEX B: Effects of radiation exposure of children, <https://www.unscear.org/unscear/publications/2013_2.html>. Accessed November 5, 2019.

[58] UNSCEAR. Report 2017. United Nations Scientific Committee on the Effects of Atomic Radiation, Report to the General Assembly, SCIENTIFIC ANNEXES A and B, <https://www.unscear.org/unscear/en/publications/2017.html>. Accessed November 5, 2019.

[59] S.H. Orzack, J.W. Stubblefield, V.R. Akmaev, P. Colls, S. Munne, T. Scholl, D. Steinsaltz, J.E. Zuckerman, The human sex ratio from conception to birth, Proc Natl Acad Sci U S A 112(16) (2015) E2102-11.

[60] S.N. Austad, The human prenatal sex ratio: A major surprise, Proc Natl Acad Sci U S A 112(16) (2015) 4839-40.

[61] I. Schmitz-Feuerhake, C. Busby, S. Pflugbeil, Genetic radiation risks: a neglected topic in the low dose debate, Environmental Health and Toxicology 31 (2016) e2016001.

[62] M. Kim, H.C. Jeong, S.K. Baek, Sex-ratio bias induced by mutation, Phys Rev E 99(2-1) (2019) 022403.

[63] R. Julian Preston, J.D. Boice Jr, A. Bertrand Brill, R. Chakraborty, R. Conolly, F. Owen Hoffman, R.W. Hornung, D.C. Kocher, C.E. Land, R.E. Shore, G.E. Woloschak, Uncertainties in estimating health risks associated with exposure to ionising radiation, Journal of Radiological Protection 33(3) (2013) 573-588.