Reproductive Toxicology 100 (2021) 137–142

Contents lists available at ScienceDirect

Reproductive Toxicology

journal homepage: www.elsevier.com/locate/reprotox

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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A R T I C L E I N F O

Keywords:
Atmospheric atomic bomb tests
Chernobyl
Ecological study
Gender proportions
Ionizing radiation
Nuclear accidents
Radiation induced genetic effects

A B S T R A C T

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.

1. Introduction

Understanding the geographic and secular trend variations of the SSR has been considered one of the most elusive concepts in life science [1,2]. 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]. Except in societies where selective abortion skews the sex ratio [6], approximately 104–106 boys are born for every 100 girls. Generally, the human sex ratio at birth is remarkably constant in large populations [7] and slightly decreasing in industrialized countries [8], and this has been linked to many factors including increasing air pollution [9]. Radiation is one of few stressors known to elevate the sex ratio while dropping total births [10,11]. 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]. Smoking is shown to increase the sex ratio [13,14] in a dose-dependent manner possibly partly due to elevated radionuclides in tobacco [15]. Following the atomic bombing of Japan [4,16], the global

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/m^2, 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.

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https://doi.org/10.1016/j.reprotox.2021.01.012
Received 19 October 2020; Received in revised form 5 January 2021; Accepted 25 January 2021
Available online 1 February 2021
0890-6238/

atmospheric nuclear weapons tests [17–19], the Windscale fire [20,21] and the Chernobyl accident [22,23], long-lasting and 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 [24,25].

In contrast to those numerous sex odds increases after Chernobyl, Peterka et al. [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] and Zatsepin et al. [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]. The finding by Peterka et al. was later supported by an ecological dose-response relation [29], but could not be confirmed with monthly Bavarian (German) data [30].

Astolfi and Zonta [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]. 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]. 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].

Increased sex ratios have been observed in many circumstances in the vicinity of all kinds of nuclear facilities [35–39]. The sex ratio may therefore serve as a useful (albeit currently neglected) sentinel indicator for possible 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] can be excluded. The present study investigates whether the secular sex ratio trend in Italy over eighty years from 1940 to 2019 is subject to any disturbances due to enhanced environmental ionizing radiation after the atmospheric atomic bomb tests and after the Chernobyl event.

Table 1
Annual live births in Italy by gender and sex ratio, 1940 – 2019.

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**

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.

2. Data and statistical methods

2.1. 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 1940–1949 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). The data compiled and analyzed is presented in Table 1 and Fig. 1. Note that 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.

2.2. 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 [44,45]. The overall Cs-137 depositions in Italy due to the nuclear tests are in the order of magnitude of 2–6 kBq/m^2 (mean 4.0) and in the order of magnitude of additional 2–4 kBq/m^2 (mean 3.0) after Chernobyl. According to different sources, 10 kBq/m^2 Cs-137 translates to an air dose-rate of 0.144 mSv/a [46] or of 0.224 mSv/a [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], 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%–20% to the 2 mSv/a [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.

2.3. Data analysis and statistical methods

The Italian birth counts, and the annual sex ratios compiled in Table 1 and displayed in Fig. 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 1955–1985 [44,49] and from 1986 [45,50], 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 1955–1985 and 1970–2000, 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 p_m among all male (m) and female (f) births: $p_m = m/(m + f)$. Pertinent 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 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]. The required Binomial distributional assumption, possible heterogeneity, and autocorrelation issues have been considered in detail in [36,52]. 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).

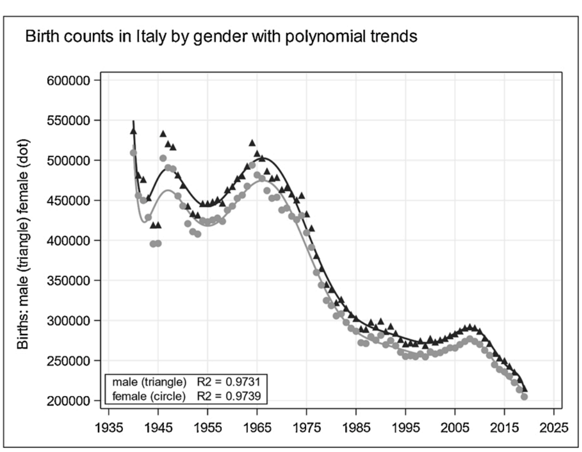

Fig. 1. Live birth counts by gender with sex-specific trends according to polynomial Poisson regression models (SAS procedure GENMOD).

3. Results

Table 2 presents the results of the MCMC changepoint model. In the overall secular Italian sex ratio trend 1940–2019, 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 1955–1985 and 1970–2000, 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 1940–2019 in Italy and their interrupted optimum logistic regression line, which accounts for the identified jumps are presented in Fig. 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 $z(t)$ was fit to the natural logarithm of the Italian sex odds data and displayed as the thick gray curve in Fig. 2 for comparison:

$$z(t) = a + \frac{b}{\exp\left(\frac{t_1 - t}{s_1}\right) + 1} + \frac{c}{\exp\left(\frac{t_2 - t}{s_2}\right) + 1} + t * t_0$$

The parameter estimates for $z(t)$ are $a = 0.0569$, $b = 0.0073$, $c = 0.0052$, t_0=-0.00017, $t_1 = 29.74$, $t_2 = 45.62$, $s_1 = 0.68590$, and $s_2 = 0.1285$, where t runs from 0 to 79 representing the years from 1940 through 2019. Function $z(t)$ illustrates that the first level shift around 1970 extends over an approximate 5-year period ($s_1/s_2 = 5.34$) whereas the second level shift occurred abrupt from 1986 to 1987 within one

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**

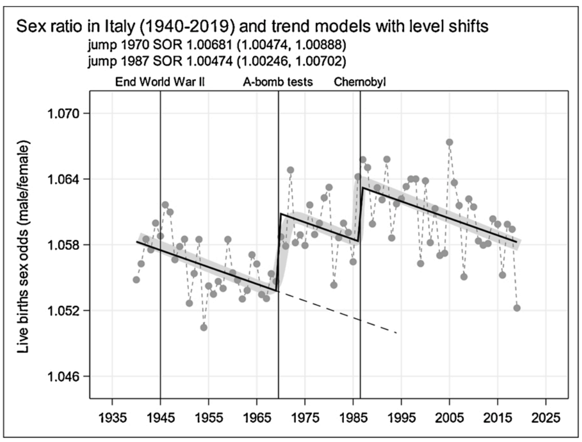

Fig. 2. Secondary sex ratio in Italy (1940-2019); black solid line: linear logistic regression model accounting for idealized optimum jumps in 1970 and 1987; light gray thick line: non-linear logistic regression model allowing for smooth changes 1968-1972 and 1985-1987.

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.

4. Discussion

This study has shown two distinct and unique sex ratio level shifts around 1970 and in 1987 in the Italian sex ratio trend 1940–2019. While the second jump from 1987 can be attributed to the one-time event Chernobyl in 1986 [23,25], 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 Fig. 2. The increasing number of atomic bomb tests during the 1960s 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]. 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 [16,22]. 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] 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], the study of the secondary sex ratio has been accompanied by important developments in science [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]. Investigations of the human sex ratio in the children of the atomic-bomb survivors initially yielded positive evidence [4], which was later dismissed [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], the UNSCEAR 2013 report showed practically no evidence of changes in offspring sex ratios of parents exposed to radiation [57], despite the updated and strengthened evidence at that time [11,22]. Ultimately, the UNSCEAR 2017 report does not consider the sex ratio any longer [58].Therefore, the gender ratio is an unjustifiably neglected sentinel indicator for chemical or physical environmental changes. This neglect leads to genetic health effects being overlooked.

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 Fig. 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 [38,59]. Two possibilities with the same outcome may be considered: (1) girls are 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] see Austad [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], 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]. 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] In the light of these and many similar findings, the claim of an absence of hereditary risk effects in human studies should be reconsidered.

5. Conclusions

The secular secondary sex ratio trend of Italy 1940–2019 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.

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.

Funding

The authors declare that they had no funding for this study.

Conflict of interest

The authors declare no conflict of interest.

Declaration of Competing Interest

The authors report no declarations of interest.

References

[1] D. Pavic, Secular trends and geographical variations in sex ratio at birth, Early Hum. Dev. 91 (12) (2015) 811–815.

[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, Emerg. Health Threats J. 4 (7109) (2011).

[4] W.J. Schull, J.V. Neel, Radiation and the sex ratio in man, Science 128 (3320) (1958) 343–348.

[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. Accessed 27 October 2020, http://www.unscear.org/unscear/en/publications/1958.html.

[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) 459–465.

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

[8] V. Grech, Sex ratios at birth in the British Isles over the past sixty years, Eur. J. Pediatr. 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, Fertil. Steril. 87 (1) (2007) 230–232.

[10] W.H. James, Ionizing radiation and offspring sex ratio, J. Epidemiol. Community Health 51 (3) (1997) 340–341.

[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) 645–652.

[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, Fertil. Steril. 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, Eur. J. Pediatr. 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) 558–567.

[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 Hum. Dev. 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) 107–110.

[19] A. Korblein, Human sex ratio at birth after atmospheric weapons testing, Early Hum. Dev. 100 (2016) 33–34.

[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) 173–174.

[22] H. Scherb, K. Voigt, Trends in the human sex odds at birth in Europe and the Chernobyl Nuclear Power Plant accident, Reprod. Toxicol. 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) 1327–1331.

[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, Reprod. Toxicol. 18 (1) (2004) 75–79.

[27] K. Sperling, J. Pelz, 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, Int. J. Radiat. Med. 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) 1801–1806.

[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) 2891–2894.

[32] F. Parazzini, C. La Vecchia, F. Levi, S. Franceschi, Trends in male:female ratio among newborn infants in 29 countries from five continents, Hum. Reprod. 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) 415–426.
[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, Environ. Model. Softw. 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, J. Womens Health Care Manage. 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) 721–726.
[41] R. Wakeford, Childhood leukaemia and nuclear installations: the long and winding road, Br. J. Cancer 111 (9) (2014) 1681–1683.
[42] NLGA, in: Niedersächsisches Landesgesundheitsamt (Ed.), Niedersächsisches Landesgesundheitsamt (NLGA). Fachgespräch Sekundäres Geschlechterverhältnis in der Umgebung des Transportbehälterlagers (TBL) Gorleben am 12, Roesebeckstr., Hannover, 2012, 4-6, 30449, März 2012 http://www.nlga.niedersachsen.de/download/65642/Sekundaeres_Geschlechterverhaeltnis_in_der_Umgebung_des_Transportbehaelterlagers_TBL_Gorleben_-_Fachgespraech_am_12_Maerz_2012.pdf (Accessed 1 November 2019).
[43] International Atomic Energy Agency (IAEA, Nuclear Safety Review for the Year 2001; Printed by the IAEA in Austria, 2002. July https://inis.iaea.org/collection/NCLCollectionStore/_Public/33/039/33039369.pdf. (Accessed 29 August 2019).
[44] UNSCEAR Report, United Nations Scientific Committee on the Effects of Atomic Radiation, ANNEX C Exposures to the Public from Man-made Sources of Radiation, 2000 (Accessed 29 January 2020), http://www.unscear.org/docs/publications/2000/UNSCEAR_2000_Annex-C-CORR.pdf.
[45] UNSCEAR Report, United Nations Scientific Committee on the Effects of Atomic Radiation, Annex J, Exposure and Effects of the Chernobyl Accident, 2000. Accessed 29 January 2020, http://www.unscear.org/docs/publications/2000/UNSCEAR_2000_Annex-J.pdf.
[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, J. Environ. Radioact. 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. Accessed January 20, 2020, http://aei.pitt.edu/49301/1/B0028.pdf.
[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, Int. J. 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) 1335–1340.
[53] B.P. Carlin, A.E. Gelfand, F.M.S. Adrian, Hierarchical bayesian analysis of changepoint problems, J. R. Statist. Soc. Ser. C (Appl. Statist.) 41 (2) (1992) 389–405.
[54] A. Bouckaert, Dr. John Arbuthnot, inventor of statistical testing, Hist. Sci. Med. 30 (4) (1996) 459–466.
[55] T.A. Mousseau, A.P. Moller, Genetic and ecological studies of animals in Chernobyl and Fukushima, J. Hered. 105 (5) (2014) 704–709.
[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) 328–338.
[57] UNSCEAR Report, 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, 2013. Accessed 5 November 2019, https://www.unscear.org/unscear/publications/2013_2.html.
[58] UNSCEAR Report, United Nations Scientific Committee on the Effects of Atomic Radiation, Report to the General Assembly, SCIENTIFIC ANNEXES A and B, 2017. Accessed 5 November 2019, https://www.unscear.org/unscear/en/publications/2017.html.
[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) 4839–4840.
[61] I. Schmitz-Feuerhake, C. Busby, S. Pflugbeil, Genetic radiation risks: a neglected topic in the low dose debate, Environ. Health Toxicol. 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, J. Radiol. Prot. 33 (3) (2013) 573–588.