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Sex-specific Infant Mortality Trends in Switzerland (1950 - 2022) and Test of the Null Hypotheses of No Trend Changes after the Chernobyl Accident in 1986

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Abstract

Background: In Switzerland after the Chernobyl accident in April 1986, the cumulative radiation dose up to 2005 was around 3,500 Sieverts, corresponding to 25 µSv/year per person. Stillbirths, perinatal mortality, and congenital malformations increased in a dose-dependent and sex-specific manner in numerous countries affected by Chernobyl fallout. Less attention has been paid to the gender specific infant mortality rate. The aim of this report is to study the secular sex-specific infant mortality trends in Switzerland (1950 - 2022) and to test the null hypotheses of no trend changes after the Chernobyl accident in 1986.

Methods: Counts of annual live births (LB) and infant deaths (ID) under 1-year of age by gender for Switzerland from 1950 to 2022 were obtained from the human mortality database. Time trend analyses of total, female, and male ID proportions employing logistic regression were carried out. Possible level-shifts in the annual mortality rates and in the ID vs LB sex odds ratios (SOR) from 1987 onward were estimated and tested.

Results: The overall ID proportion in the period 1950 - 2022 was 1.13% (female 0.99%, male 1.27%), i.e., 69,905 total ID in 6,186,134 total LB (female 29,677 vs 3,010,130 and male 40,228 vs 3,176,004). In Switzerland, total female and male infant mortality rates abruptly increased in 1987 relative to the monotone secular downward trends as estimated from the period 1950 - 1986. The jump OR in 1987 with 95% confidence interval and p value for the total (female + male) mortality was 1.175 (1.102, 1.253) p value < 0.0001; females: 1.187 (1.095, 1.287) p value < 0.0001; males 1.167 (1.078, 1.262) p value 0.0001. The relatively stable infant mortality SOR in the period 1950 to 1986 of 1.307 (1.283, 1.331) decreased continuously in the period after 1986 to a value of 1.134 in 2022, according to a 10-year sex period interaction OR of 0.960 (0.939, 0.982) p value 0.0003.

Conclusion: The jumps in the infant mortality rates in Switzerland in 1987 and the changing annual infant Mortality vs LB SOR during the post-Chernobyl period indicate possible sex-differential radio contamination impacts and corroborate previous findings of increased sex-linked detrimental radiation induced genetic effects after Chernobyl.

Keywords: Radioactive contamination, Radiation induced genetic effects, Sex-linked mutation, Time trend analyses

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Introduction

The World Health Organization in 1957 emphasized "Man's most precious trust is his genetic heritage, upon which must depend the health and orderly development of future generations" [1]. It is well known that ionizing radiation may induce cancer and a variety of detrimental genetic effects [2-10]. Since nutrition is a key driver in human health [11], detrimental reproductive effects like increases in stillbirths, perinatal mortality, ID, congenital malformations, reduced birth weight, and distorted birth sex ratios [12-15] may be caused by Chernobyl fallout contaminating food and tap water. More recently, distinct genetic effects have been reported in the vicinity of a Swiss nuclear power plant after an INES-2 accident [16] and around a radiologically contaminated military training ground in Germany [17]. In these incidents, underestimated risks of far-reaching neutron radiation may play a crucial role. According to official estimates in Switzerland, the cumulative radiation dose mainly by internal contamination up to 2005 due to Chernobyl was 3,500 sieverts [18]. As the Swiss population between 1986 and 2005 counted on average 7 million, Chernobyl fallout caused 0.5 mSv in total per person, or 25 µSv/year. A conservative estimation in a recent report [19, 20] based on updated radiation cancer risks [2, 21] concluded that the collective dose of 25 µSv/year and person may have caused 400 additional fatal cancer cases in Switzerland. While radioactivity decreases according to the corresponding half-lives of the involved nuclides, radiation induced biological effects may be long-lasting, nevertheless. For example, a study of atomic bomb survivors demonstrated that the excess thyroid cancer risk associated with childhood exposure has persisted for more than 50-years after exposure [22]. From this perspective, it would be no surprise if infant mortality had increased in Switzerland after Chernobyl. And this increase might be long-lasting as far as genetic material or genetic information had been compromised. Since no or little attention has been paid to the gender specific infant mortality rate yet [23], the aim of this report is to study the long-term sex-specific and sex adjusted infant mortality trends in Switzerland with focus on possible sex dependent trend changes after Chernobyl.

Methods

The sex-specific infant mortality rate is defined as the number by sex of resident newborns in a defined geographic area (country, state, county, etc.,) dying under 1-year of age, divided by the number of LB for the same sex and area, usually for a calendar year. Sex-specific counts of annual LB and infant mortality under 1-year of age for Switzerland from 1950 - 2022 were obtained from the freely accessible **human mortality database**. Table 1 lists the LB counts and the numbers of ID in age category zero (0) by gender and year. The overall ID proportion is approximately 1%: 69,905 ID in 6,186,134 LB. The ascertainment error of infants being born in the calendar year before the calendar year of their death is considered negligible in the present context. Parsimonious time trend analyses employing logistic regression for total, female, and male ID proportions were carried out. The following most parsimonious albeit well suited and well-fitting models (1) and (2) in SAS notation were applied to the total and the sex-specific data in table 1, respectively.

Model 1:

ID/LB = t d1970*t d1970*t2 d1987 / scale=d

Model 2:

ID/LB = t d1970*t d1970*t2 d1987 sex sex*d1987*t / scale=d

In model 1 and model 2, time in years is denoted by t. For convenient numerical representations and interpretation of estimates and OR, t is measured in 10-years. Additionally, t and its powers as factors of the model variables are centered at the corresponding change-points in the years 1970 and 1987, respectively. $d_{year}(t)$ is a dummy variable which is 0 for t < year, and 1 else. $t_{year}(t)$ is the product of (t-year)/10 with $d_{year}(t)$. d_{year} and t_{year} serve to effectively model jumps and kinks in trends, respectively. The distinct years 1970 and 1987 were selected a-priori for the following reasons: (1) In Italy adjacent to Switzerland, a local maximum in 1970 of the birth sex ratio after the atomic bomb tests in the 1950/60ies has been identified as a possible radiation induced genetic effect [8, 24]; (2) increased stillbirth rates and sex ratio shifts were seen across Europe after the Chernobyl accident from 1987 onward [5, 25]. Model 1 and model 2 were derived by backward selection from corresponding initially full models containing all powers of t up to the third order and all 2nd and 3rd order interactions of those powers of t with the change-point dummy variables d_{1970} and d_{1987}. A similar data analysis would be employing (over-dispersed) Poisson regression or better negative binomial regression in place of logistic regression. This is especially important for determining how changes in sex ratios relate to changes in absolute numbers in the corresponding numerators and/or denominators [26]. However, in the present context focused on ID proportions, logistic regression is the method of choice. The Wald-Chi^2 statistic was used to test whether potential level shifts (jumps or kinks) from 1970 and 1987 were different from zero. A p value < 0.05 was taken to represent a statistically significant result. The code/data-analysis/output for this paper was generated using SAS software, mainly SAS-PROCs LOGISTIC and SGPLOT. Copyright © 2021 SAS Institute Inc. Cary, NC, USA. All Rights Reserved. SAS On Demand Release 3.1.0. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc.

Results and Discussion

Table 2 and table 3 compile the estimates, standard errors, OR, p values, and according 95% confidence limits of model 1 and model 2 applied to the total and sex-specific data in table 1, respectively. Figure 1 displays the total counts (gray dots), the predicted model fit (red line), and the corresponding null-model (dotted line). The gap between the predicted line and the line of the null model corresponds to 1989 (1239, 2696) excess total female and male ID from 1987 to 2022. Analogously, figure 2 and figure 3 show the results of fitting model 1 to the female and male data in table 1, respectively. In figure 2, the gap between the predicted and dotted lines indicates 924 (506, 1304) excess female ID from 1987 to 2022; and in figure 3 this gap corresponds to 1071 (542, 1560) excess male ID. The legends in figure 1, figure 2 and figure 3 contain additionally the respective excess counts with 95% confidence limits for the first 7 - years (1987 - 1983) after the Chernobyl accident. Those 7 - year periods played a role in institutional discussions [19]. Whereas the highly significant main effect 'sex' in table 3 with OR 1.307 (1.283, 1.331) means that in the period 1950 - 1986 approximately 30% more infant boys than infant girls died in the first year of their life, the highly significant interaction effect "sex*d_{1987}*t" means a significant gradual reduction of this gender gap by approximately 4% per 10-years: OR 0.960 (0.939, 0.982). Table 4 represents a dichotomized version of this observation: the annual infant mortality vs LB SOR (male/female) decreased significantly by 7.7%, p value 0.0001 in the post-Chernobyl aera compared to before. Figure 4 a is graphical representation of this finding.

Table 2: Parameters, estimates, and pertinent statistics of model 1 for the annual total counts of table 1.

Parameter	Estimate	Standard error	P value
Intercept	- 4.8173	0.0258	< 0.0001
t	- 0.3753	0.0093	< 0.0001
t_{1970}	- 0.1529	0.0221	< 0.0001
t^2_{1970}	0.0619	0.0036	< 0.0001
d_{1987}	0.1612	0.0326	< 0.0001
OR			
Effect	Estimate	95% confidence limits	
		Lower	Upper
t	0.687	0.675	0.700
t_{1970}	0.858	0.822	0.896
t^2_{1970}	1.064	1.056	1.071
d_{1987}	1.175	1.102	1.253

Table 3: Parameters, estimates, and pertinent statistics of the sex-adjusted model 2 for the annual female and male counts of table 1.

Parameter	Estimate	Standard error	P value
Intercept	- 4.9642	0.0233	< 0.0001
t	- 0.3756	0.0082	< 0.0001
t_{1970}	- 0.1493	0.0194	< 0.0001
t^2_{1970}	0.0656	0.0033	< 0.0001
sex	0.2676	0.0094	< 0.0001
d_{1987}	0.1634	0.0286	< 0.0001
sex*d_{1987}*t	- 0.0405	0.0113	0.0003
OR			
Effect	Estimate	95% confidence limits	
		Lower	Upper
t	0.687	0.676	0.698
t_{1970}	0.861	0.829	0.895
t^2_{1970}	1.068	1.061	1.075
sex	1.307	1.283	1.331
d_{1987}	1.177	1.113	1.245
sex*d_{1987}*t	0.960	0.939	0.982

In Switzerland, infant mortality rates are subject to significant level shifts after 1986, the year of the Chernobyl accident and a chemical accident near Basel [27]. In addition, the relatively high infant Mortality vs LB SOR (male/female) of 1.3 decreased significantly from 1987 onward. So, the question arises, whether ID level-shifts and divergent trends in sex ratios of ID versus sex ratios of LB in Switzerland after Chernobyl are sentinel indicators of radiation-induced distortions of the human genome [1, 8, 12]. The identified sex-differential radiation

Table 1: Total and sex-specific infant mortality (< 1-year) and LB in Switzerland 1950 to 2022.

Year	Death at age < 1			LB		
	Female	Male	Total	Female	Male	Total
1950	1101	1541	2642	41115	43661	84776
1951	1039	1428	2467	39694	42209	81903
1952	1026	1407	2433	40649	42900	83549
1953	1051	1422	2473	40458	42571	83029
1954	991	1289	2280	41027	42714	83741
1955	992	1269	2261	41523	43808	85331
1956	972	1300	2272	42663	45249	87912
1957	877	1202	2079	44237	46586	90823
1958	859	1174	2033	44490	46931	91421
1959	837	1224	2061	45248	47725	92973
1960	832	1161	1993	46185	48187	94372
1961	873	1213	2086	48581	50657	99238
1962	953	1258	2211	50870	53452	104322
1963	936	1298	2234	53746	56247	109993
1964	894	1248	2142	55034	57856	112890
1965	857	1139	1996	54187	57648	111835
1966	788	1088	1876	53323	56415	109738
1967	765	1113	1878	52402	55015	107417
1968	738	952	1690	51191	53939	105130
1969	683	891	1574	49990	52530	102520
1970	618	876	1494	47981	51235	99216
1971	559	821	1380	46850	49411	96261
1972	498	718	1216	44163	47179	91342
1973	472	681	1153	42438	45080	87518
1974	427	626	1053	41021	43486	84507
1975	343	500	843	38055	40409	78464
1976	338	459	797	36499	37700	74199
1977	317	395	712	35300	37529	72829
1978	239	376	615	34648	36727	71375
1979	252	358	610	35134	36852	71986
1980	275	392	667	35944	37717	73661
1981	227	330	557	35682	38065	73747
1982	261	313	574	36589	38327	74916
1983	235	325	560	35686	37973	73659
1984	225	308	533	36177	38533	74710
1985	222	293	515	36719	37965	74684
1986	224	297	521	37416	38904	76320
Total 1950 - 1986	**23,796**	**32,685**	**56,481**	**1,592,915**	**1,679,392**	**3,272,307**
1987	233	291	524	37318	39187	76505
1988	220	330	550	39120	41225	80345
1989	262	334	596	39502	41678	81180
1990	258	316	574	41025	42914	83939
1991	222	315	537	41876	44324	86200
1992	226	331	557	42492	44418	86910
1993	216	249	465	40730	43032	83762
1994	181	245	426	40386	42594	82980
1995	178	237	415	40113	42090	82203
1996	163	227	390	40299	42708	83007
1997	186	201	387	39284	41300	80584
1998	153	224	377	38521	40428	78949
1999	146	215	361	38152	40256	78408
2000	169	217	386	38056	40402	78458
2001	154	211	365	35172	37123	72295
2002	146	180	326	35054	37318	72372
2003	143	166	309	34946	36902	71848
2004	130	181	311	35742	37340	73082
2005	131	179	310	35334	37569	72903
2006	141	183	324	35605	37766	73371

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2007	141	155	296	36310	38184	74494
2008	139	169	308	37142	39549	76691
2009	142	196	338	37879	40407	78286
2010	158	147	305	39179	41111	80290
2011	135	168	303	39182	41626	80808
2012	144	156	300	39729	42435	82164
2013	136	183	319	40136	42595	82731
2014	142	194	336	41437	43850	85287
2015	138	201	339	41910	44649	86559
2016	158	148	306	42951	44932	87883
2017	132	178	310	42508	44873	87381
2018	133	154	287	42838	45013	87851
2019	134	149	283	42049	44123	86172
2020	138	175	313	41615	44299	85914
2021	122	158	280	43716	45928	89644
2022	131	180	311	39907	42464	82371
Total 1987 - 2022	**5,881**	**7,543**	**13,424**	**1,417,215**	**1,496,612**	**2,913,827**
Total 1950 - 2022	**29,677**	**40,228**	**69,905**	**3,010,130**	**3,176,004**	**6,186,134**

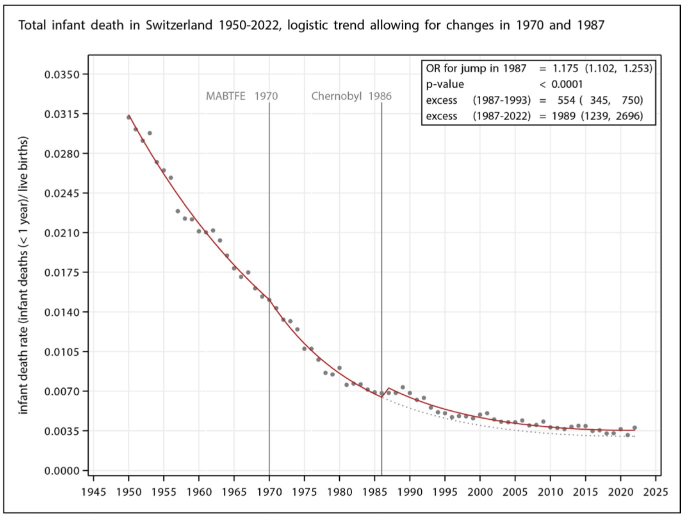

Figure 1: Total (male + female) ID rate in Switzerland and red solid linear logistic trend line according to model 1; the dotted line indicates the trend under the null hypothesis of no trend change from 1986 onward; MABTFE means assumed "Maximum Atomic Bomb Test Fallout Effect" in 1970 [24].

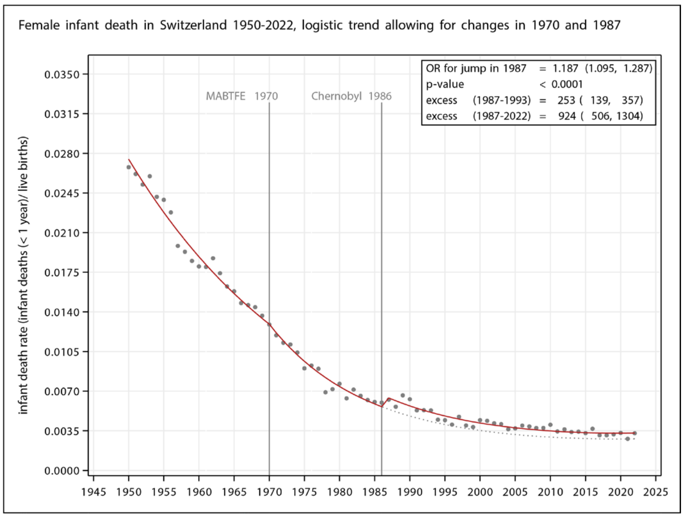

Figure 2: Female ID rate in Switzerland and red solid linear logistic trend line according to model 1; the dotted line indicates the trend under the null hypothesis of no trend change from 1986 onward; MABTFE means assumed "Maximum Atomic Bomb Test Fallout Effect" in 1970 [24].

effect on ID in Switzerland could be related to a finding on congenital malformations in Bavaria/Germany [15, 28]. As with malformations in Germany, this genetic phenomenon seen in Switzerland may be interpreted as follows: Uncontaminated, girls present a lower level of postnatal fatal risk than boys since the genetically more vulnerable girls had already been vanishing more likely during pregnancy [8]. This 'vulnerable female effect' might also explain the natural secondary sex ratio of 1.05: The primary human sex ratio seems to be 1.0 [29, 30], and the vulnerable female embryonal and fetal life entails a deficit of girls at birth. As during pregnancy, after birth again, contaminated girls prove to be more vulnerable since the female infant mortality increased by nearly 7.7% relative to the male infant mortality in the post-Chernobyl period in Switzerland. These findings corroborate previous observations demonstrating elevated genetic sex-linked detriment in humans under escalated radiological conditions [13, 16, 17, 25]. Finally, it is necessary to emphasize, that the genetic effects identified in Switzerland from 1970 and/or 1986 onward must not necessarily be due to atomic bomb fallout or Chernobyl alone. Considerable parts of the Swiss population live within 35 km around major nuclear facilities from which persistent radiological effluents may induce cumulating detrimental albeit subclinical genetic health effects predominantly affecting potential fathers and their vulnerable female offspring [17, 25, 31, 32].

Conclusion

The hypothesis that minute ionizing radiation exposure entails disproportional fewer female births and somewhat more previously damaged female offspring by compromising the emergence of viable babies and infants in a gender-biased manner should be investigated more thoroughly. Disproportionately lesser female births and more congenitally damaged female offspring and infants would manifest as increased birth sex ratios and decreased ID sex ratios, which is exactly what can be observed at the country-level in radioactively contaminated parts of Europe after 1986 - probably due to the Chernobyl accident, even more as no alternative explanations for these undeniable statistical effects have been offered yet.

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Conflict of Interest

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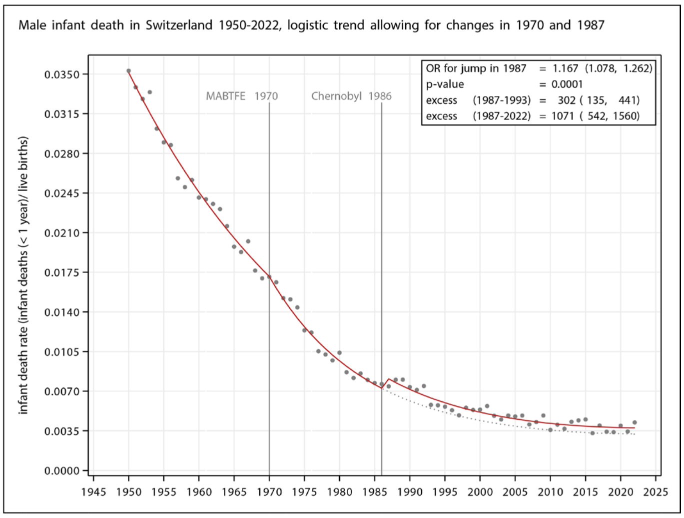

Figure 3: Male ID rate in Switzerland and red solid linear logistic trend line according to model 1; the dotted line indicates the trend under the null hypothesis of no trend change from 1986 onward; MABTFE means assumed "Maximum Atomic Bomb Test Fallout Effect" in 1970 [24].

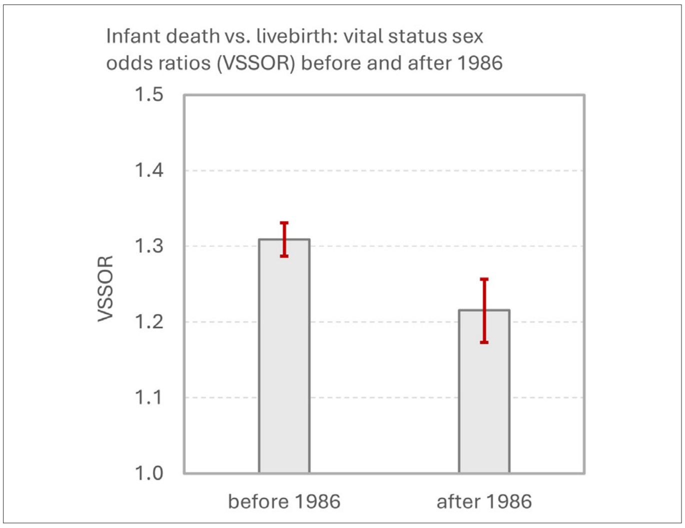

Figure 4: Before vs After 1986 comparison of the vital status SOR (VSSOR) in Switzerland: ID sex odds divided by sex odds of the LB surviving the first year of live, i.e., LB-ID, the difference is significant with a period vital status SORR (PVSSORR) of 1.077 (1.04, 1.12); p value = 0.0001, (Table 4).

Table 4: Births in Switzerland 1950 - 2022 by sex, vital status in the first year of life, and period; sex*vital status*period 2 × 2 × 2 table; pertinent statistics for assessing the significance of the corresponding sex OR ratio (SORR) sex*vital status*period interaction [33] (Figure 4).

Periods, odds, OR, ORR, and inference statistics	Period: Before vs After Chernobyl			
	Before 1987		From 1987	
	ID	LB - ID	ID	LB - ID
Male	32,685	1,646,707	7,543	1,489,069
Female	23,796	1,569,119	5,881	1,411,334
Sex odds (SO: male/female)	1.3736	1.0494	1.2826	1.0551
Vital status SOR (VSSOR: ID/(LB - ID))	1.3088		1.2156	
Period vital status SORR (PVSSORR)	1.0767			
Natural logarithm (Ln) (PVSSORR)	0.0739			
Variance of Ln (PVSSORR)	0.0004			
Standard error	0.0194			
Wald-Chi-square	14.4368			
P value (Probability greater Chi-square)	0.0001			

None.

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