Regression Analysis of Time Trends in Perinatal Mortality in Germany, 1980–1993

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Numerous investigations have been carried out on the possible impact of the Chernobyl accident on the prevalence of anomalies at birth and on perinatal mortality. In many cases the studies were aimed at the detection of differences of pregnancy outcome measurements between regions or time periods. Most authors conclude that there is no evidence of a detrimental physical effect on congenital anomalies or other outcomes of pregnancy following the accident. In this paper, we report on statistical analyses of time trends of perinatal mortality in Germany. Our main intention is to investigate whether perinatal mortality, as reflected in official records, was increased in 1987 as a possible effect of the Chernobyl accident. We show that, in Germany as a whole, there was a significantly elevated perinatal mortality proportion in 1987 as compared to the trend function. The increase is 4.8% ($p = 0.0046$) of the expected perinatal death proportion for 1987. Even more pronounced levels of 8.2% ($p = 0.0458$) and 8.5% ($p = 0.0702$) may be found in the higher contaminated areas of the former German Democratic Republic (GDR), including West Berlin, and of Bavaria, respectively. To investigate the impact of statistical models on results, we applied three standard regression techniques. The observed significant increase in 1987 is independent of the statistical model used. Stillbirth proportions show essentially the same behavior as perinatal death proportions, but the results for all of Germany are nonsignificant due to the smaller numbers involved. Analysis of the association of stillbirth proportions with the ^{137}Cs deposition on a district level in Bavaria discloses a significant relationship. Our results are in contrast to those of many analyses of the health consequences of the Chernobyl accident and contradict the present radiobiologic knowledge. As we are dealing with highly aggregated data, other causes or artifacts may explain the observed effects. Hence, the findings should be interpreted with caution, and further independent evidence should be sought. *Key words*: Chernobyl accident, perinatal mortality, regression analysis, spatial–temporal analysis, stillbirth, time trend. *Environ Health Perspect* 108:159–165 (2000). [Online 10 January 2000]
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To date, the explosion of the nuclear reactor in Chernobyl, Ukraine, approximately 160 km northwest of Kiev, on 26 April 1986 is the most serious accident in a nuclear power station. The event led to a release of large quantities of radioactive material over a 10-day period. Depending on atmospheric conditions at the time, the extent of contamination in Europe was variable. Ukraine, Belarus, and parts of Russia and Scandinavia were highly contaminated by radioactive fallout (1).

Doses received by the human population involved a number of different pathways: inhalation of activity, direct gamma radiation from the atmosphere, exposure to external radiation from ground-deposited activity, and ingestion of contaminated food. Data on estimated effective dose equivalents in the first year after the accident were reviewed and compiled by the United Nations Scientific Committee on the Effects of Atomic Radiation (2). Outside the former Soviet Union, the highest country-wide mean doses within the first post-Chernobyl year were roughly between 0.5 and 1.0 mSv in Bulgaria, Austria, Greece, and Romania. In Germany, the estimated effective dose

equivalents in the first year after the accident ranged from < 0.1 mSv to 0.2 mSv. However, on a more local or even individual scale, much higher doses than reflected by national mean values are to be expected (3,4).

Petridou et al. (5) recorded all childhood leukemia cases diagnosed throughout Greece since 1 January 1980. They reported that infants exposed *in utero* to ionizing radiation from the Chernobyl accident had 2.6 times the incidence of leukemia as compared to unexposed children (i.e., children born before and 1.5 years after the accident). In addition to the induction of cancer, exposure to ionizing radiation can be detrimental to human germ cells, developing embryos, and fetuses. Therefore, the radiation from Chernobyl might have led to an increase in the number of congenital malformations. Furthermore, it is possible that a general damage to embryos or fetuses may yield an increase in stillbirth, neonatal death, or even infant death. Kulakov et al. (6) studied the effects of the nuclear accident on approximately 7,000 pregnant women who lived in areas near Chernobyl. The study period extended from 3 years before to 5 years after the event. Estimated exposure was up to

100 mSv. An increase in thyroid disorders, anemia, hypertension, and pregnancy complications was noted among the exposed women. The health of offspring was also affected by exposure. Apgar scores declined, perinatal and neonatal mortality increased, and neurologic, somatic, and hematologic disorders increased among children.

Apart from these two positive studies concerning highly contaminated areas, the majority of investigations that focused on possible health effects of the Chernobyl disaster ended in negative results. In a comprehensive review, Little (7) concluded that there is no consistent evidence of a detrimental physical effect of the accident on congenital anomalies or other measured outcomes of pregnancy.

One of the first investigations of the possible impact of the Chernobyl disaster on gestation in Germany was a trend extrapolation of monthly neonatal mortality from the years 1975–1985 to the years 1986 and 1987 (8). This work has been criticized because the results were dependent on the statistical model chosen, a common criticism about extrapolation (9). Most of the published subsequent work on German perinatal mortality or infant death data did not show any peculiar effects (10–14). Recently, Körblein and Küchenhoff (15) investigated perinatal mortality in Germany from 1980 to 1993. Using annual data, a trend analysis based on an exponential function was performed; this analysis showed a significant increase of approximately 5% in 1987. Körblein and Küchenhoff also identified two peaks of cesium concentration in women's bodies that were associated with two peaks of monthly perinatal mortality data, with a delay of 7 months.

Studies on the possible effect of the Chernobyl accident may generally be divided

into two categories. Marked geographic variations in contamination provide an opportunity to compare radiation-related outcome measures between human populations residing in different regions. Another approach is the investigation of possible changes in the frequencies of pertinent variables over time. However, a combination of the two methods may also be applied. This has been done by Grosche et al. (*16*) in the case of the south German state of Bavaria in contrast with the remainder of Germany excluding the former German Democratic Republic (GDR). The power of this study for one-sided tests was 80% for detecting a 25 or 30% increase in perinatal mortality in southern and northern Bavaria, respectively. Therefore, the negative results reported by Grosche et al. (*16*) may only serve to exclude excesses of ≥ 25%. By way of contrast, logistic regression—as will be shown in our study—is considerably more powerful. Using a two-sided test, a power of 80% can be obtained for excesses of approximately 14% for Bavaria alone.

Problems with regional comparisons of infant mortality data were identified and discussed by Landau (*17*). Important characteristics (environmental conditions, social class, etc.) are rarely identical between regions; therefore, some methods of standardization are nearly always necessary to achieve comparability. Of course, similar considerations apply to temporal comparisons. In that case, special care must be taken to avoid possible changes of variable definitions. However, if the population characteristics of interest are relatively stable over time or if the time periods are not too large, problems with this approach seem less pronounced in contrast to regional comparisons.

In this paper we report on statistical analyses of time trends in perinatal mortality in Germany. Because the fetus is most sensitive to radiation during the period of organogenesis in the first trimester of conception, the impact of external radioactivity from the accident on perinatal death, if any, could be expected 6–9 months after the exposure (i.e., in November 1986 to January 1987) (*15*). Taking into account the somewhat delayed internal exposure by contaminated food as well, the major impact of the total internal and external radioactive exposure from the accident could be observed in 1987 (*14*). Thus, our main intention was to investigate whether perinatal mortality in 1987 deviated from a long-term trend as a possible effect of the Chernobyl accident. We restricted methodology in our study to temporal comparisons in the following sense: we modeled the time trend of perinatal mortality allowing for special effects of certain years, and we included, for example, the year 1987 in the models as a dummy variable

(v_{87}). The corresponding null hypothesis states that the perinatal mortality in 1987 does not deviate from the trend as computed from the remaining years. In technical terms this means that the coefficient of the dummy variable v_{87} equals zero. In the usual manner, we then computed confidence intervals and *p*-values for the coefficient of the dummy variable. In addition, to investigate the impact of different statistical models on *p*-values, we applied three standard regression techniques and compared results.

Data and Statistical Methods

In this study we used the official statistics of annual perinatal mortality in Germany, published by the Federal Statistics Office in Wiesbaden and Berlin. For statistical purposes, Germany was divided into East Germany (the former GDR including West Berlin) and West Germany (the former Federal Republic of Germany excluding West Berlin; FRG). Statistical data were available for East Germany as a whole and for the 11 states of West Germany, including West Berlin.

For the absolute numbers in the public records concerning perinatal mortality for each year, we used the following abbreviations: LB (live births), SB (stillbirths), TB = LB + SB (total births), SD (7-day mortality; born alive but died within 7 days of birth), and PD = SB+SD (perinatal death).

The following proportions (relative frequencies) for each year were derived from these absolute frequencies, dividing by the appropriate denominators: SBp = SB/TB (stillbirth proportion), SDp = SD/LB (7-day mortality proportion), PDp = PD/TB (perinatal death proportion).

In Germany the definition of stillbirth was changed in 1979 and in 1994. In 1994 the minimum weight limit in the definition of stillbirth was reduced from 1,000 g to 500 g, entailing a sharp increase in stillbirth proportion from that time on. Therefore, we restricted analysis to the period 1980–1993. In a first step, to make use of the maximum

possible statistical power, we analyzed combined perinatal mortality from the FRG and the former GDR. This combination may seem problematic because somewhat different definitions of stillbirth were employed. However, the difference in the two definitions is basically theoretical: three signs of life (FRG) as opposed to two signs of life (GDR) were used to distinguish live birth from stillbirth. Because we combined stillbirth and neonatal death into perinatal death, this problem is of less importance. After the German reunification, only one definition of stillbirth was used in all of Germany. We assume that combining data from the FRG and the former GDR does not significantly distort our results and conclusions.

Table 1 contains annual perinatal mortality data for all of Germany from 1980 to 1993. Table 2 presents perinatal mortality data for the former FRG excluding Bavaria and West Berlin, for Bavaria on its own, and for the former GDR including West Berlin. The row totals of TB and PD for the three areas in Table 2 are equal to the corresponding entries in Table 1.

To assess the underlying time trends and possible deviations from the trends in the data of Table 1 and Table 2 and to investigate the dependence of results on methods, we applied three standard regression techniques. We used linear polynomial regression (fit of a polynomial), nonlinear regression (fit of an exponential function plus a constant), and linear logistic regression.

In polynomial and nonlinear (exponential function) regression, a summary measure of the distance between observed (*o*) and fitted (*e*) values is the Pearson χ^2 statistic:

$$X^2 = \Sigma(o-e)^2/e.$$

In linear logistic regression, a corresponding appropriate measure is the deviance:

$$D = 2*\Sigma \; o*\ln(o/e).$$

X^2 and D should be χ^2 with degrees of freedom (*df*) equal to the number of independent

Table 1. Perinatal mortality in Germany, 1980–1993.

Year	Live births	Stillbirths	Total births	7-day mortality	Perinatal death	Stillbirth proportion	7-day mortality proportion	Perinatal death proportion
1980	865,789	4,954	870,743	5,582	10,536	0.005689	0.006447	0.012100
1981	862,100	4,855	866,955	5,008	9,863	0.005600	0.005809	0.011377
1982	861,275	4,409	865,684	4,381	8,790	0.005093	0.005087	0.010154
1983	827,933	4,107	832,040	4,001	8,108	0.004936	0.004833	0.009745
1984	812,292	3,803	816,095	3,656	7,459	0.004660	0.004501	0.009140
1985	813,803	3,601	817,404	3,287	6,888	0.004405	0.004039	0.008427
1986	848,232	3,547	851,779	3,252	6,799	0.004164	0.003834	0.007982
1987	867,969	3,602	871,571	3,222	6,824	0.004133	0.003712	0.007830
1988	892,993	3,474	896,467	2,825	6,299	0.003875	0.003164	0.007026
1989	880,459	3,247	883,706	2,723	5,970	0.003674	0.003093	0.006756
1990	905,675	3,202	908,877	2,488	5,690	0.003523	0.002747	0.006260
1991	830,019	2,741	832,760	2,101	4,842	0.003291	0.002531	0.005814
1992	809,114	2,660	811,774	2,039	4,699	0.003277	0.002520	0.005789
1993	798,447	2,467	800,914	1,891	4,358	0.003080	0.002368	0.005441

observations minus the number of estimated parameters in the model. Goodness of fit refers to the Pearson χ^2 in case of polynomial and nonlinear (exponential function) regression, and the deviance in case of linear logistic regression. For the polynomial and nonlinear (exponential function) regression, we estimated the dispersion parameter by the Pearson χ^2 statistic divided by its degrees of freedom. For the linear logistic regression, we estimated the dispersion parameter by dividing the deviance by its degrees of freedom. Overdispersion is present if the dispersion parameter is > 1. To adequately take into account the variability of the data, we recommend the correction for overdispersion by multiplying the covariance matrix by the estimate of the dispersion parameter. Correcting for overdispersion yields p-values or confidence intervals that are not unrealistically small or narrow, respectively.

As Bavaria was the most highly contaminated part of Germany, we investigated a possible relationship between the annual stillbirth and perinatal death proportions and the deposition of radioactive cesium (^{137}Cs) on a regional level in Bavaria. Table 3 summarizes the results of ^{137}Cs measurements in Germany. Measurements of exposure related to the individual rather than to groups on a regional level would have been preferable, but such data does not exist. There are 96 districts (Landkreise) in Bavaria for which official stillbirth and perinatal death proportions (from the Bavarian Statistical Office) and regional

measurements of ^{137}Cs for 1986 are available. We analyzed the association of stillbirths and perinatal mortality (1980–1993) with deposited ^{137}Cs (interpreted as a surrogate exposure variable for 1986/1987) on a district level in Bavaria using simple spatial–temporal linear logistic regression models. According to Grosche et al. (16), there was an increase of stillbirths in Bavaria during the first 2 years after the accident. (However, Grosche et al. did not interpret this finding as a possible consequence of radioactivity.) Thus, we also included the year 1988 in the spatial–temporal analysis, using a relative weight of 0.5 for the cesium surrogate variable associated with this year. This approximately corresponds to the relation of the excess stillbirth proportions in Bavaria in 1988 and 1987. Körblein and Küchenhoff (15) found a nonlinear dependency of the perinatal death proportion on the calculated cesium concentrations in women's bodies. The estimated exponent of the cesium variable is 3.5. Therefore, we additionally computed spatial–temporal logistic regressions using this exponent of the cesium variable.

Computations were performed using SAS 6.12 (18), S-Plus 3.3 (MathSoft, Seattle, WA) (19), and Mathematica 2.2 (Wolfram Research, Inc., Champaign, IL) (20). Pertinent methodologic and technical information was obtained from these references and also from Cox and Snell (21), Hosmer and Lemeshow (22), Agresti (23), and Collet (24). Methodologic issues concerning the

regression techniques that we applied in our investigation have been previously described in detail (18–24).

Results

As a first step, we analyzed perinatal mortality in Germany from 1980 to 1993. The three proportions listed in Table 1 are displayed in Figure 1. The striking decline of perinatal mortality is due to improved antenatal and perinatal care as well as an overall reduction of risk factors. In Figure 1, a slight deviation from the general trend in 1987 is visible for all three proportions (SBp, SDp, and PDp). Because of the vast amount of data available, it is possible that the deviation of PDp in 1987 from the general trend might be statistically significant.

In Table 4 we compiled results of three regression models fit to the PDps of Table 1. Because we estimated four parameters for each model and made use of 14 independent points in time, each model had 10 df. The model found by ordinary linear polynomial regression is a second degree polynomial including the dummy variable v_{87} for the year 1987. A third degree polynomial did not yield a significantly improved fit. The Pearson χ^2 statistic for the second degree polynomial is 18.97 ($p = 0.0407$). This is not an excellent fit, but the coefficient of the dummy variable v_{87} for the year 1987 is quite significant in this model ($p = 0.0259$).

An alternative model that we used to fit the PDps in Table 1 involved an exponential function plus a constant. In contrast to the polynomial approach, the advantage of this model is that the expected PDp will level out with increasing time. This model was used by Körblein and Küchenhoff (15). The results of the nonlinear regression are summarized in Table 4. The Pearson χ^2 is improved to 16.06 ($p = 0.0979$), and the p-value for the coefficient of v_{87} is reduced to 0.0189.

Because we were dealing with binary data, the most appealing method of modeling the PDp from a theoretical point of view was linear logistic regression (25). Results of fitting a linear logistic regression model to

Table 2. Perinatal mortality in the former FRG excluding Bavaria and West Berlin, in Bavaria, and in the former GDR including West Berlin, 1980–1993.

Year	FRG - (Bavaria + West Berlin)		Bavaria		GDR + West Berlin	
	Total birth	Perinatal death	Total birth	Perinatal death	Total birth	Perinatal death
1980	490,310	5,647	115,013	1,327	265,420	3,562
1981	491,074	5,163	117,626	1,213	258,255	3,487
1982	488,354	4,788	117,075	1,015	260,255	2,987
1983	465,968	4,412	113,092	944	252,980	2,752
1984	457,228	4,009	111,617	867	247,250	2,583
1985	458,756	3,634	111,833	858	246,815	2,396
1986	490,840	3,775	118,871	841	242,068	2,183
1987	504,783	3,701	120,084	842	246,704	2,281
1988	531,753	3,482	126,855	767	237,859	2,050
1989	535,244	3,465	127,428	785	221,034	1,720
1990	570,931	3,483	136,529	746	201,417	1,461
1991	567,909	3,338	134,779	683	130,072	821
1992	566,835	3,285	134,330	683	110,609	731
1993	564,567	3,105	134,276	669	102,071	584

Table 3. Measurements of ^{137}Cs deposition (kBq/m^2) in Germany following the Chernobyl accident.

Part of Germany	n	Mean	Median	Minimum	Maximum	Reference
FRG - (GDR + Bavaria)	895	4.7	3.5	DL	57.0	(36)
GDR[a]	1,088	3.2	2.2	DL	47.0	(36)
Bavaria	1,465	14.9	10.3	DL	120.7	(36,37)
Bavaria (means of districts)	96	14.4	10.1	3.1	53.7	

DL, detection limit.
[a]In the GDR, a different sampling scheme, which entails systematic underreporting, was employed so values are not directly comparable.
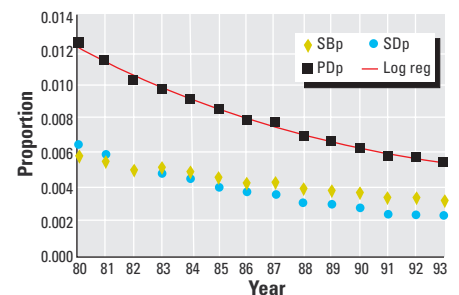

Figure 1. Perinatal death proportions in Germany 1980–1993, including the logistic regression line (Log reg) according to Table 4.

the PDps of Table 1 are shown in Table 4. Within the analyzed time interval from 1980 to 1993, the fit functions of nonlinear regression and linear logistic regression are nearly identical, which is reflected by a similar goodness of fit statistic (deviance = 16.05; p = 0.0982). However, linear logistic regression yields a considerably smaller p-value (p = 0.0046) for the year 1987 as compared to the other two methods. This is due to an alternative inference methodology, Wald χ^2 as opposed to the t-statistic (23).

We also dealt with power considerations connected with the regression analyses. Conditional power functions of the two-sided t-tests for polynomial regression and the two-sided Wald χ^2-tests for the logistic regression for all of Germany and for Bavaria alone are shown in Figure 2. The conditional power is the probability to reject the null hypothesis of no deviation of the parameter for 1987 from the trend computed on the basis of the observations for 1980–1986 and 1988–1993. The conditional power functions show that the Wald χ^2-test is considerably more powerful than the t-test. They also show that for Germany as a whole, there is enough power to detect a 5% increase of PDp with a probability somewhat > 80%. For Bavaria alone, excesses in PDp of ≥ 13.5% could be detected with a power of at least 80%.

Table 5 supplements Table 4 in that it displays expected cases, excess cases, and 95% confidence limits for the excess cases for the year 1987. In 1987, according to the applied regression models, there were approximately 320 cases in excess of the expected perinatal mortality for Germany as a whole. The

lower limits of the 95% confidence intervals are approximately 50–100 additional perinatal deaths.

In a second step we analyzed perinatal mortality in Bavaria alone, the former FRG excluding Bavaria and West Berlin [FRG - (Bavaria + West Berlin)], and the former GDR including West Berlin (GDR + West Berlin) (Figure 3). We only applied linear logistic regression to model the data in Table 2; Figure 4 is a graphic representation of this data and includes the corresponding logistic regression lines. Obviously, a certain part of the elevated perinatal mortality of Germany as a whole in 1987 was attributable to increased levels in Bavaria and the former GDR + West Berlin. In the former GDR + West Berlin, the PDp was elevated as compared to the trend line, not only in 1987 but also in 1988. The estimated increases for the FRG - (Bavaria + West Berlin), for the GDR + West Berlin, and for Bavaria alone are 2.4% (p = 0.2569), 8.2% (p = 0.0458), and 8.5% (p = 0.0702), respectively. In addition, there was an increase in the perinatal death proportion of 7.4% (p = 0.0841) in 1988 in the GDR + West Berlin. Figure 5 shows the data for Bavaria + GDR + West Berlin and the fitted linear logistic regression line.

In a final step, we included dummy variables for 1986, 1987, and 1988 in the regression models to obtain parameter estimates not only for the year of main interest, 1987 but also for the adjacent years 1986 and 1988. Additionally, we performed joint analyses of the combined regions: Bavaria + GDR + West Berlin, and Bavaria + GDR + West Berlin + the remainder of Germany. In

these joint analyses, the regression coefficients in the models are allowed to vary by region to account for structural differences between the regions, but common dummy variables are fit for 1986, 1987, and 1988. This may allow for greater power in the estimation of the increases in these years. The excesses for stillbirth and perinatal death proportions as well as the corresponding 95% confidence limits for the three single regions and the two combined regions are shown in Figure 6. No particular effects were seen in 1986 in any of the five regions, neither for perinatal deaths nor for stillbirths. In 1987 in all regions, perinatal deaths were elevated, but significantly so only in Bavaria + GDR + West Berlin and all of Germany. Nonsignificantly elevated perinatal death proportions were present in 1988 for the GDR + West Berlin and for the GDR + West Berlin + Bavaria. Stillbirth proportions were significantly elevated in 1987 for Bavaria and for the GDR + West Berlin + Bavaria, whereas in 1988, significantly elevated stillbirth proportions were present for the GDR + West Berlin and also for GDR + West Berlin + Bavaria. The only
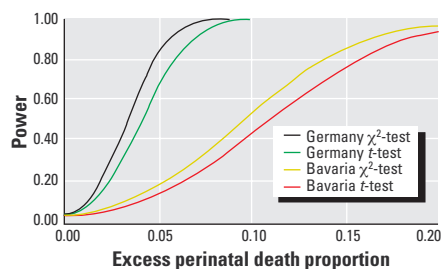

Figure 2. Conditional power functions of the two-sided t-tests of polynomial regression and the two-sided Wald χ^2-tests of the logistic regression for excess perinatal death proportions for all of Germany and for Bavaria alone.

Figure 3. Map of Germany divided into the three regions: Bavaria, the former GDR including West Berlin, and the former FRG excluding West Berlin and Bavaria.

Table 4. Models and parameter estimates of regression analyses applied to German perinatal mortality data 1980–1993.

Regression	Model	Goodness of fit	Parameter estimate	p-Value
Linear polynomial regression	$y = a + b*t + c*t^2 + d*v_{87}$	18.97	a = 0.012848	< 0.0001
			b = -0.000871	< 0.0001
			c = 0.000025	< 0.0001
			d = 0.000371	0.0259
Nonlinear regression	$y = a + b*\exp(-c*t) + d*v_{87}$	16.06	a = 0.003041	< 0.0001
			b = 0.010033	< 0.0001
			c = 0.102380	< 0.0001
			d = 0.000365	0.0189
Linear logistic regression	$y = \{1+\exp[-(a + b*t + c*t^2 + d*v_{87})]\}^{-1}$	16.05	a = -4.321936	< 0.0001
			b = -0.081003	< 0.0001
			c = 0.001255	< 0.0001
			d = 0.047628	0.0046

Abbreviations: t, time (years); v_{87}, dummy variable for 1987; H$_0$, null hypothesis. The v_{87} = 1 for 1987 and zero for other years. For each model, df = 10; two-sided p-values for H$_0$: parameter = 0 were corrected for overdispersion. Computations were performed using SAS 6.12 software (SAS Institute, Cary, NC).

Table 5. Number of expected perinatal death cases, percent excesses, excess cases, and 95% confidence limits (CL) for absolute excess cases for all of Germany in 1987.

Model	Expected	Percent excess	Excess	CL
Linear polynomial regression	6,501	5.0	323	[48, 599]
Nonlinear regression	6,506	4.9	318	[65, 571]
Linear logistic regression	6,509	4.8	315	[96, 541]

significantly reduced estimate in this spatial–temporal (multiple test) consideration is the stillbirth proportion for the remainder of Germany in 1988.

In addition, we analyzed the association of stillbirth and perinatal death proportions with deposited ^{137}Cs in Bavaria on a district level. The results are summarized in Table 6. Assuming that 1988 was affected approximately half as much as 1987, we found a significant (p = 0.0021) association of the stillbirth proportions in 1987 and 1988, with deposited ^{137}Cs as a surrogate variable for the total individual internal and external exposure in the years 1986 and 1987. We determined the slope in the corresponding linear logistic regression as 0.72%/(1 kBq/m²) with a 95% confidence interval of 0.26–1.17. Restricting consideration of the surrogate cesium variable to 1987 alone yields practically the same estimate, however, with somewhat reduced precision. The estimate of 0.72%/(1 kBq/m²) entails a theoretical increase of 43% in the stillbirth proportion with the ^{137}Cs deposition of 50 kBq/m² under the specific conditions of the contamination in Bavaria. There are also more basic aspects of this phenomenon: In the 10 most highly affected districts (mean = 37.2 kBq/m²), the stillbirth proportion increased by approximately 45% above the expected level in 1987 (57 observed against 39.4 expected cases; p = 0.0157). In the combined

Figure 4. Perinatal mortality in the former FRG excluding Bavaria and West Berlin (FRG), the former GDR including West Berlin, (GDR), and Bavaria, 1980–1993, including the logistic regression lines (Log reg).

Figure 5. Perinatal mortality in Bavaria, the former GDR, and West Berlin combined, 1980–1993, including the logistic regression line (Log reg).

three most highly contaminated districts, Augsburg City (53.7 kBq/m²), Berchtesgaden (50.3 kBq/m²), and Garmisch Partenkirchen (40.5 kBq/m²), the excess stillbirth proportion in 1987 exceeded 100% (32 observed against 15.1 expected cases; p = 0.0004). No significant effect was observed in the 10 districts with the lowest contamination. The perinatal death proportion in Bavaria in 1987 and 1988 is not significantly related to the cesium fallout from the Chernobyl accident. Only if we use the results of Körblein and Küchenhoff (*15*) and regress perinatal death proportions on $Cs^{3.5}$ rather than on Cs^1, we get significant results. With this modification, a highly significant association is obtained for the stillbirth proportion (Table 6). To account for as much variation as possible in the dependent variable because of structural differences between the districts, a less parsimonious and less conservative approach is to allow for linear logistic trends for each of the 96 districts instead of using only one trend for all of Bavaria. This approach minimizes confounding, yields a maximum power in the estimation of the corresponding cesium parameters, and results in slightly higher estimates, lower p-values, and tighter confidence intervals as compared with the results in Table 6. Our observation should not be mistaken for extrapolations beyond the presumable range of exposures, as has been done with Körblein and Küchenhoff's finding (*26*). A gender-specific analysis for Bavaria and corresponding analyses for the former GDR and the remainder of Germany are in progress.

Discussion

We investigated annual perinatal mortality in Germany for the years 1980–1993, with emphasis on a possible impact of the Chernobyl disaster on data for 1987 and eventually for 1988. In Germany as a whole,

Figure 6. Excesses and 95% confidence limits for the perinatal death and stillbirth proportions in Germany in 1986, 1987, and 1988. Abbreviations: A, FRG excluding Bavaria and West Berlin; B, GDR including West Berlin; C, Bavaria; D, Bavaria, the former GDR, and West Berlin; E, all of Germany.

there is a significantly (p = 0.0046) elevated perinatal mortality proportion in 1987 in comparison to an appropriately chosen trend function. The increase measures approximately 5% of the expected perinatal death proportion for 1987.

To assess the underlying time trends in perinatal death proportions and to investigate the dependence of results on methods, we applied three standard regression techniques. Theoretically as well as practically, it seems meaningful to model perinatal deaths as binomially distributed random variates. Consequently, parametric methods that yield quantitative effect estimates were applied. Because polynomial regression and nonlinear regression (fit of an exponential function plus a constant) have been applied to the data by other researchers (*15, 27*) and because, according to Cox (*25*), linear logistic regression is the most appealing method for binomial variables, we compared linear polynomial regression (fit of a polynomial), nonlinear regression (fit of an exponential function plus a constant), and linear logistic regression. Logistic regression with the corresponding Wald χ^2 statistic appeared to be the most powerful method among the given alternatives.

In the pertinent reports and papers on perinatal or infant mortality in Germany (*10–14,16*), the slight increases in perinatal mortality in Germany in 1987 and 1988 have not been identified. One reason for this is that the straightforward yet powerful methodology that we employed has not been used in these investigations. Recently, Körblein and Küchenhoff (*15*) reported significant increases in German perinatal mortality in 1987 relative to an exponential plus constant trend model, but their results are still under debate (*16,26*).

We also found a significant relationship between stillbirths in 1987 and some in 1988 and the ^{137}Cs contamination in 1986 on a regional level in Bavaria. There are indications that, similar to the situation in Bavaria, radioactivity might have led to elevated perinatal mortality in the former GDR, which is noticeable on a regional level (*4*). The partitioning of Germany into the former FRG (excluding Bavaria and West Berlin), the area of the former GDR including West Berlin, and Bavaria alone, yields excess perinatal mortality in 1987 of 2.4%, 8.2%, and 8.5%, respectively. Figure 6 shows that combining Bavaria, the GDR, and West Berlin yields further significant results for perinatal deaths and stillbirths in 1987 or 1988. In the GDR + West Berlin, perinatal mortality rose above the expected results by 7.4% in 1988. This could in fact be due in part to less efficient control and insufficient exclusion of contaminated food.
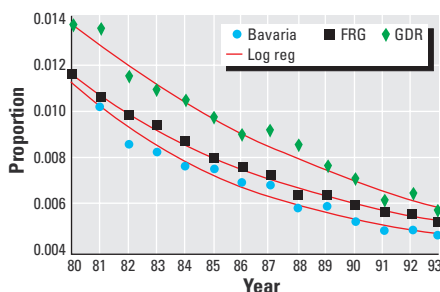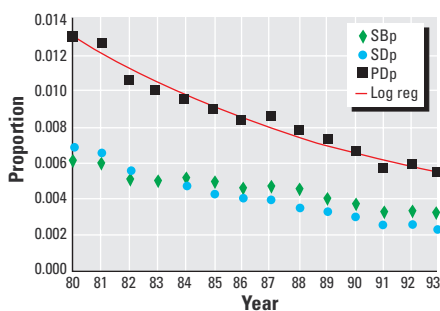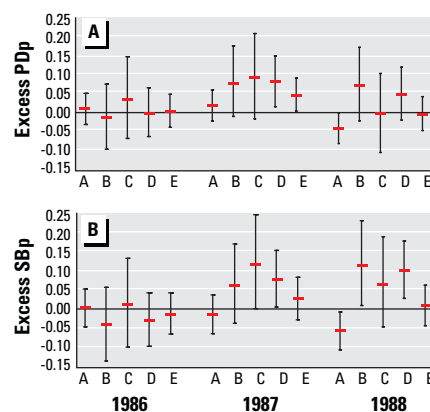
Table 6. Spatial–temporal linear logistic regression of stillbirth proportions and perinatal death proportions on the mean values of deposited ^{137}Cs (kBq/m^2) in the 96 districts of Bavaria, 1980–1993.

Log odds of model	SBp			PDp		
	Parameter estimate (Cs)	p-Value	CL	Parameter estimate (Cs)	p-Value	CL
$icpt + t + Cs*v_{87}$	7.00×10^{-3}	0.0053	$(2.08 \times 10^{-3}, 1.19 \times 10^{-2})$	2.12×10^{-3}	0.2916	$(-1.82 \times 10^{-3}, 6.05 \times 10^{-3})$
$icpt + t + Cs*v_{87} + 0.5*Cs*v_{88}$	7.16×10^{-3}	0.0021	$(2.61 \times 10^{-3}, 1.17 \times 10^{-2})$	1.28×10^{-3}	0.4936	$(-2.38 \times 10^{-3}, 4.94 \times 10^{-3})$
$icpt + t + Cs^{3.5}*v_{87}$	7.26×10^{-7}	< 0.0001	$(3.76 \times 10^{-7}, 1.08 \times 10^{-6})$	3.94×10^{-7}	0.0141	$(7.95 \times 10^{-8}, 7.08 \times 10^{-7})$
$icpt + t + Cs^{3.5}*v_{87} + (0.5*Cs)^{3.5}*v_{88}$	7.33×10^{-7}	< 0.0001	$(3.85 \times 10^{-7}, 1.08 \times 10^{-6})$	3.95×10^{-7}	0.0136	$(8.11 \times 10^{-8}, 7.08 \times 10^{-7})$

Abbreviations: CL, 95% confidence limits; Cs, ^{137}Cs; $icpt$, intercept; t, time in years coded as 1–14.

Table 7. Pertinent results and corresponding interpretations.

Result	Interpretation
A significant (relative) increase of perinatal mortality in Germany in 1987 and significant associations of the SBps and PDps with the ^{137}Cs contamination on a district level in Bavaria in 1987/1988 are found.	If this effect is a consequence of the radioactivity from the Chernobyl accident, it cannot be explained by conventional radiobiologic theory. The assumption of a threshold dose of 50 mSv for the induction of stillbirths and neonatal deaths may not be appropriate, or the threshold may be lower than 50 mSv, or individual extreme exposures in the population were higher and more frequent than anticipated.
The deviation of the perinatal mortality from the trend in 1987 is not seen so clearly in the three subregions of Germany: Germany - (Bavaria + GDR + West Berlin), GDR + West Berlin, and Bavaria.	The power of the trend analyses for excesses < 10% is insufficient in the subregions.
The differential effect between Germany - (Bavaria + GDR + West Berlin), GDR + West Berlin, and Bavaria is more pronounced for stillbirths than for perinatal deaths.	Radioactivity induces more stillbirths than neonatal deaths. Neonatal deaths that comprise approximately 50% of the perinatal deaths in Germany are more subject to differing quality and progress of social and medical care than stillbirths are and are thus more variable.
In the former GDR, the perinatal death and stillbirth proportions were also elevated in 1988.	There is less efficient control and elimination of contaminated food. Contaminated food (preserved) was imported into the GDR from the former Soviet Union, or a (random) discontinuity in the decrease of perinatal mortality may explain this effect.
In Bavaria and other affected parts of Europe the effect is stronger for male than for female stillbirths.	There is evidence that the developing male embryo or fetus is more vulnerable against intrauterine irradiation than the developing female embryo or fetus (*38*).

There is evidence that contaminated food (preserved) was imported to the GDR from the former Soviet Union (*28*). Table 7 summarizes pertinent results and interpretations.

Effects similar to those observed in Germany are also present in official data available by the respective central statistics offices in northern, eastern, and southern European countries such as Sweden, Poland, Hungary, and Greece. A synoptic European analysis has recently been published (*29*).

Our analyses add evidence for elevated stillbirth or perinatal death proportions in Bavaria or Germany to some (*8,15,27*) but not all (*10–14*) results in this field. Similar analyses in other exposed and nonexposed countries are certainly warranted. As an obvious limitation of our ecologic type of study, we must emphasize that, in principle, no causal inference (*30*) is possible on the basis of such highly aggregated data. Alternative causes of the observed excesses in stillbirths and perinatal mortality other than radioactive exposure cannot be ruled out. If the observed effects were attributable to the increased radioactivity in Germany after the Chernobyl accident, biologic hypotheses that can be tested with experimental data and with analytical epidemiologic data would then be helpful. Implicit in the hypothesis is an effect on the ovum and sperm or on the embryo at a certain stage of development. This should be studied to predict in what periods of time the excess perinatal mortality or excess stillbirth proportions would be expected and for what dose.

Studies of the survivors of the atomic bombing of Hiroshima and Nagasaki, Japan, who were exposed to ionizing radiation *in utero* have demonstrated a significant increase in perinatal loss and the vulnerability of the developing fetal brain to injury (*31*). The epidemiologic data are, however, too sparse to settle unequivocally the nature of the dose–response function and, in particular, whether there is a threshold to damage. In Belarus, geographic differences in reproductive health and immune status that were apparent may be related to radiation exposure after the Chernobyl accident (*32*). Petrova et al (*32*) conducted a retrospective analysis on pregnancies that occurred between 1982 and 1990 and compared the results between pregnancy outcomes before and after the meltdown for individuals residing in heavily exposed and lightly exposed oblasts. Neonates born in heavily contaminated areas (Mogilev and Gomel) of the Republic of Belarus were at risk for congenital malformations and neonatal death. No such effect was seen in a retrospective analysis of spontaneous miscarriages, congenital anomalies, and perinatal mortality in the two largest obstetric hospitals of Kiev between 1969 and 1990 (*33*). Several epidemiologic studies following the Chernobyl accident were conducted in Scandinavian countries. In Finland, there was a significant rise in preterm births among children who were exposed to radiation during the first trimester, but Harjulehto et al. (*34*) observed no increase in the incidence of malformations or perinatal deaths. These findings are consistent with a higher incidence of spontaneous abortions in Norway found for pregnancies conceived during the first 3 months after the accident. The rate of legal abortions was unchanged (*35*).

In conclusion, our investigation shows a relative increase in perinatal death proportions in 1987, the year after the Chernobyl accident, in all of Germany. There is a trend for stronger effects in the more affected parts of Germany, and this effect is seen for stillbirths as well. Spatial–temporal analyses of the proportion of stillbirths or perinatal deaths with the cesium deposition after the Chernobyl accident in Bavaria on a district level reveal significant exposure–response relationships. Our findings are in contrast to those of many other studies in this field and contradict the generally accepted radiobiologic theory. Therefore, because an ecologic study has many weaknesses with respect to causal interpretation, the results should be considered with caution, and independent evidence should be sought.

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