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Evaluation of the impact of Chernobyl on the prevalence of congenital anomalies in 16 regions of Europe

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Background	Surveillance data from population-based congenital anomaly registers in 16 regions of Europe (mainly Western Europe) were analysed to assess the impact of the Chernobyl accident on the prevalence of selected congenital anomalies.
Methods	Three cohorts of pregnancies were defined: those exposed during the first month following Chernobyl (External Exposure Cohort), the first year (Total Exposure Cohort) and the two subsequent years (Control Cohort). Expected numbers of congenital anomalies in these cohorts were calculated from 1980–1985 baseline rates. Registries were grouped into three exposure categories according to first-year exposure estimates.
Results	There was no overall or dose-related increase in prevalence in the two exposed cohorts for Down's Syndrome, neural tube defects, other central nervous system defects or eye defects. There was a statistically significant overall 22% (95% CI : 13–31%) excess of Down's Syndrome in the Control Cohort, with no dose-response relationship.
Conclusions	Chernobyl had no detectable impact on the prevalence of congenital anomalies in Western Europe, suggesting that in retrospect the widespread fear in the population about the possible effects of exposure on the unborn fetus was not justified. An increasing prevalence of Down's Syndrome in the 1980s, probably unrelated to Chernobyl, merits further investigation.

Keywords	Chernobyl, congenital anomalies, epidemiology, Down's Syndrome, neural tube defects
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Post-Chernobyl surveillance of congenital anomalies in Western Europe is important to address both scientific and public health concerns. There is scientific interest in the mutagenic and teratogenic effects of low-level radiation of different types. There is public health interest in informing the public of the existing empirical evidence regarding health risks. The level of public concern was demonstrated by the increase in induced abortion and decrease in conceptions during the immediate post-Chernobyl period documented in some countries,[1] with the implication that this related to fear of congenital malformation.

The EUROCAT network of congenital anomaly registers has been engaged in the surveillance of congenital anomalies since 1980, covering approximately 10% of all births in the participating countries.[2] Shortly after the Chernobyl accident on 26 April 1986, preliminary analyses were done[3–5] to address the urgency of concern at the time, with the intention of repeating the analyses when fully confirmed and validated data would become available and when a longer post-Chernobyl period could be surveyed. In this paper, we present this revised analysis concentrating, as before, on Down's Syndrome as a reliably diagnosed and ascertained potential mutagenic effect, and central nervous system and eye anomalies as the anomalies most strongly associated with *in utero* exposure to radiation, although at higher doses, in the literature.[6,7]

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Table 1 Population coverage and characteristics of 16 registries

	Study period	Births 1986	Exposure[a]	Inclusion of induced abortions[b]
Florence (I)	1980–1990	8440[c]	High	Yes
Emilia Romagna (I)	1980–1990	22 760	High	No
Glasgow (UK)	1980–1990	12 940	High	Yes
Liverpool (UK)	1980–1988	20 620	High	Yes
Zagreb (C)	1983–1990	6810[c]	High	No
Strasbourg (F)	1982–1990	13 010	Medium	Yes
Marseille (F)	1985–1990	23 440	Medium	Yes
Dublin (IRL)	1980–1990	21 540	Medium	NA
Galway (IRL)	1981–1990	3140	Medium	NA
Luxembourg	1980–1989	2560[d]	Medium	No
Belfast (UK)	1980–1989	28 150	Medium	Yes
West Flanders (B)	1980–1990	7960	Low	No
Hainaut (B)	1980–1990	8330[c]	Low	Yes
Odense-Funen (DK)	1980–1990	4830	Low	Yes
Paris (F)	1981–1990	35 020	Low	Yes
Groningen (NL)	1981–1990	11 860[c]	Low	Yes

[a] Based on total adult effective doses in the first year,[18] High = 200–700 microSv, Medium = 97–190 microSv, Low = 29–55 microSv.

[b] Whether induced abortions following prenatal diagnosis are registered. Where marked NA, induced abortion is illegal and not practised to any significant extent during study period.

[c] These registries subsequently expanded their population coverage, but in this analysis only the pre-Chernobyl population coverage was included in order to improve comparability over time.

[d] Luxembourg expanded population coverage to over 4000 births (the whole country) in 1989 and the expanded population was included in this study.

Material and Methods

Table 1 shows the study period and population coverage of registries participating in this study. The system of registration in each registry has been described elsewhere.[2] Cases of congenital anomaly are ascertained among live births, late fetal deaths of ⩾20 weeks gestational age (including stillbirths and late spontaneous abortions) and among induced abortions following prenatal diagnosis of malformation. Registries not registering induced abortions are indicated in Table 1.

Cases, with anomalies coded according to ICD-9[8] and BPA[9] codes and divided into Down's syndrome (ICD-9 7580) and six categories of central nervous system and eye anomalies, excluding those diagnosed with congenital infections or chromosomal or Mendelian syndromes (where the anomaly was a usual finding for that syndrome): (1) neural tube defects (ICD-9 7400–7420); (2) arhinencephaly including holoprosencephaly and cyclopia (ICD-9/BPA 74226, plus review of paper records to include cyclopia coded to 75980); (3) microcephaly and brain reduction (ICD-9 7421 and 7422), excluding those associated with neural tube defects or arhinencephaly; (4) hydrocephaly (ICD-9 7423) excluding those associated with neural tube defects; (5) anophthalmos and micropthalmos (ICD-9 7430/7431) excluding those associated with arhinencephaly/holoprosencephaly; and (6) congenital cataract (ICD-9/BPA 74332).

For central nervous system and eye malformations, an approximate sensitive period for teratogenic effects during embryonic and fetal life was assigned, taking into account the heterogeneity of the malformation categories to be analysed. The sensitive period for neural tube defects and arhinencephaly was designated as up to 5 weeks post-conception, and for hydrocephaly, microcephaly, an/microphthalmia and cataract up to 16 weeks post-conception.[6,10] For Down's Syndrome, the time immediately prior to conception was taken to be most relevant to exposure.

External gamma radiation due to radioiodine attenuated rapidly after the first month following Chernbobyl.[11–13] Caesium, because of its long half-life, accumulated in the food chain, and whole body counts and measurements of breast milk indicate that exposure continued to increase and reached its maximum in some of these areas only in March to April 1987, one year after Chernobyl.[14–17] Three exposure cohorts were defined: (1) Cohort E (External Exposure Cohort) corresponded to pregnancies exposed during some or all of their assigned sensitive period in the period of maximum external radiation in the first month following the Chernobyl accident, i.e. in May 1986. (2) Cohort T (Total Exposure Cohort) corresponded to pregnancies exposed during some or all of their sensitive period either during the period of maximum external exposure, or during the period of maximum internal exposure, extending to one year after Chernobyl. Cohort T includes Cohort E. (3) Cohort C (Control Cohort) corresponded to pregnancies occurring when the exposure to Chernobyl radiation had largely subsided in the two years subsequent to Cohort T.

The date of conception of malformed cases was estimated from the date of birth and gestational age at birth. When the gestational age was unknown (2.5% of cases), it was estimated as the average gestational age of all cases from 1980 to 1985, for the same anomaly and the same type of birth (live, still or induced abortion). Cases were assigned to the three exposure cohorts according to their months of conception, as indicated in Table 2.

The denominator figures for the three cohorts were taken from the monthly number of births in each registry area, 38 weeks following the period of conception of interest. The months of birth assigned to each cohort are shown in Table 2.

Baseline or 'expected' rates in each registry were calculated for 1980–1985 pre-Chernobyl. Baseline rates are total prevalences, including cases among live births, stillbirths and induced abortions following prenatal diagnosis in the numerator and the total number of births in the denominator. These baseline rates when applied to the calculated number of births in each of the three cohorts, gave the expected number of cases.

The EUROCAT registries were grouped into 'high', 'medium' and 'low' exposure classes according to published exposure information.[18] The classification was based on relative total adult effective doses in the first year. 'Low' exposures ranged from 29 to 55 microSv. 'Medium' exposures ranged from 97 to 190 microSv. 'High' exposures ranged from 200 to 700 microSv.

Ratios of Expected (E) to Observed (O) numbers of cases are given with their 95% CI (exact limits for Observed numbers below 30). The principal hypothesis test was for all registries combined. The presence of a 'dose-response' effect from low to high exposure categories was also examined, but inspection of data showed that no formal testing was necessary. We did not

Table 2 Definition of cohorts by month of conception and month of birth

	Down's Syndrome	Neural tube defects/arhinencephaly	Other
Cohort E (External)			
Conception	May 1986	April/May 1986	Jan–May 1986
Birth	Feb 1987	Jan/Feb 1987[a]	Oct 1986–Feb 1987
Cohort T (Total)			
Conception	May 1986–April 1987	April 1986–March 1987	April 1986–March 1987
Birth	Feb 1987–Jan 1988	Jan 1987–Dec 1987	Jan 1987–Dec 1987
Cohort C (Control)			
Conception	May 1987–April 1989[b]	April 1987–March 1989[b]	April 1987–March 1989[b]
Birth	Feb 1988–Jan 1990[c]	Jan 1988–Dec 1989[c]	Jan 1988–Dec 1989[c]

[a] Number of births adjusted to reflect the reduced number of days in February.

[b] Truncated for registries with study periods ending in 1988 or 1989, to ensure that all conceptions reaching livebirth, stillbirth or induced abortion were included in the study period.

[c] Truncated for registries with study periods ending in 1988 or 1989.

statistically examine heterogeneity between individual registries because of the generally low expected numbers in individual centres. For neural tube defects, due to the considerable differences in the epidemiology of the condition in the British Isles and in continental Europe,[19] these two geographical areas are analysed separately.

A 'Cohort E seasonality ratio' is given as the ratio of the prevalence of a malformation in the month(s) of conception included in Cohort E (Table 2), and the prevalence in other months of the year, during the pre-Chernobyl period (1980–1985). If this ratio is above one, more cases would be expected in Cohort E than calculated using average baseline rates. In order to maintain transparency of analysis, results were not corrected for this seasonality effect, but the 'seasonality ratios' are given to aid interpretation.

Results

There were no overall excesses, or dose-related excesses, in Cohorts E and T for any malformation category (Table 3). Cohort E 'seasonality ratios' (Table 4), indicate some seasonality, particularly for hydrocephaly and congenital cataract, but not to an extent that would have obscured any overall excess in Cohort E. British Isles centres had a deficit of neural tube defects in Cohorts E and T (Table 3).

In Cohort C, there was an overall excess of Down's Syndrome (O/E = 1.22, 95% CI : 1.13–1.31) (Table 3). This was not dose related, the greatest excess being observed in the low and medium exposure groups (Table 3).

There was an overall deficit of hydrocephaly in Cohort C (O/E = 0.81, 95% CI : 0.68–0.93), particularly in the higher exposure groups (Table 3). There was also an overall deficit of congenital cataract in Cohort C (O/E = 0.66, 95% CI : 0.44–0.95), also more marked in the higher exposure groups.

Individual registry results are given in Table 5, indicating excesses and deficits of nominal 5% statistical significance. The excess of Down's Syndrome in Funen County (Denmark) in Cohorts T and C is slightly overestimated due to known under-ascertainment of induced abortions following prenatal diagnosis in the baseline period (1980–1985). Individual registry results are given because of the local public health interest in such a presentation, and because of potential heterogeneity between areas due to unknown exposure determinants or registration artefacts. However, the results of such analysis must be interpreted in the light of extensive multiple testing and thus the potential for spuriously significant results.

Discussion

There was no widespread increase in the selected congenital anomalies in the immediate post-Chernobyl exposure period (Cohort E), or in the period during which internal exposure was at its highest (Cohort T). However, some results are worthy of further comment.

Firstly, there is evidence that Down's Syndrome increased in prevalence after Chernobyl. Although this increase was already starting in a few regions in the first year after Chernobyl, it became most marked and widespread among conceptions in the second and third year following Chernobyl, with an overall 22% (95% CI : 13–31%) excess during these 2 years. We could find no dose-response relation to presumed exposure. There was an increase in the proportion of births to older (>35 years) mothers during the study period, from approximately 10% in the baseline period, to 12% in Cohort C. This can be calculated to result in at least a 7% excess in observed numbers of Down's Syndrome in Cohort C due to changes in maternal age profile alone. Increasing numbers over time of terminations of pregnancy after prenatal diagnosis can also inflate later prevalence rates, since some of these cases would formerly have been 'lost' to registration systems as undiagnosed or unreported spontaneous abortions. The proportion of induced abortions among Down's Syndrome cases increased from 9% in the baseline period to 18% in Cohort C. We can calculate that this would only result in an approximately 2% excess in observed numbers in Cohort C. Thus we cannot readily explain the excess Down's Syndrome in Cohort C, but further investigation of trends in prevalence, as well as clustering in time and space, during the 1980s and 1990s is necessary,[20–22] with finer maternal age stratification.

Our Down's Syndrome results are consistent with most other published reports.[13,23–25] In contrast, Sperling *et al.*,[26] observed a cluster of Down's Syndrome in Berlin (which would have been classified among our 'high' exposure regions) limited to

Table 3 Observed, Observed/Expected (O/E) ratio and 95% CI for six congenital anomaly categories in three post-Chernobyl cohorts, registries combined[a]

	Cohort E (External)			Cohort T (Total)			Cohort C (Control)		
	O	O/E	95% CI	O	O/E	95% CI	O	O/E	95% CI
Down's syndrome									
All registries (16 regs)	24	0.94	(0.60–1.40)	302	0.98	(0.87–1.09)	710	1.22	(1.13–1.31)
High exposure (5 regs)	4	0.56	(0.15–1.43)	73	0.81	(0.62–1.00)	153	0.99	(0.83–1.15)
Medium exposure (6 regs)	13	1.15	(0.61–1.97)	133	1.01	(0.84–1.18)	307	1.20	(1.07–1.33)
Low exposure (5 regs)	7	1.00	(0.40–2.06)	96	1.13	(0.90–1.36)	250	1.44	(1.26–1.62)
All registries IA+[b] (12 regs)	23	1.07	(0.68–1.61)	260	1.01	(0.89–1.13)	595	1.24	(1.14–1.34)
All registries IA–[b] (4 regs)	1	0.25	(0.01–1.39)	42	0.84	(0.58–1.09)	115	1.10	(0.90–1.30)
Neural tube defects									
British Isles (5 regs)	29	0.61	(0.41–0.88)	178	0.62	(0.53–0.71)	236	0.48	(0.42–0.54)
Continental Europe (11 regs)	25	1.21	(0.78–1.79)	120	0.94	(0.77–1.11)	226	0.86	(0.75–0.97)
Cont. Europe, high exp (3 regs)	4	0.93	(0.25–2.39)	20	0.74	(0.42–1.07)	39	0.71	(0.49–0.94)
Cont. Europe, med exp (3 regs)	10	1.88	(0.90–3.47)	35	1.10	(0.74–1.47)	63	0.95	(0.71–1.18)
Cont. Europe, low exp (5 regs)	11	1.00	(0.50–1.78)	65	0.94	(0.71–1.17)	124	0.87	(0.72–1.03)
Cont. Europe, IA+[b] (7 regs)	19	1.17	(0.70–1.83)	105	1.05	(0.85–1.25)	194	0.94	(0.81–1.07)
Cont. Europe IA–[b] (4 regs)	6	1.39	(0.51–3.03)	15	0.55	(0.27–0.83)	32	0.56	(0.37–0.75)
Hydrocephaly									
All registries (16 regs)	36	0.83	(0.58–1.14)	121	1.12	(0.92–1.32)	168	0.81	(0.68–0.93)
High exposure (5 regs)	10	0.78	(0.33–1.44)	30	0.94	(0.61–1.28)	37	0.67	(0.46–0.89)
Medium exposure (6 regs)	17	0.92	(0.54–1.48)	54	1.20	(0.88–1.52)	62	0.69	(0.52–0.87)
Low exposure (5 regs)	9	0.72	(0.33–1.37)	37	1.18	(0.80–1.57)	69	1.08	(0.82–1.33)
Microcephaly									
All registries (16 regs)	26	0.87	(0.57–1.28)	74	1.00	(0.78–1.23)	123	0.86	(0.71–1.01)
High exposure (5 regs)	6	0.61	(0.23–1.34)	25	1.03	(0.67–1.53)	48	1.08	(0.77–1.38)
Medium exposure (6 regs)	8	0.63	(0.27–1.25)	25	0.81	(0.52–1.20)	39	0.64	(0.44–0.85)
Low exposure (5 regs)	12	1.61	(0.83–2.82)	24	1.29	(0.82–1.92)	36	0.94	(0.63–1.25)
Arhinencephaly									
All registries (16 regs)	0	0.00	(0.00–2.43)	14	1.51	(0.83–2.54)	24	1.34	(0.86–1.99)
High exposure (5 regs)	0	0.00	(0.00–10.85)	3	1.43	(0.29–4.17)	5	1.42	(0.46–3.30)
Medium exposure (6 regs)	0	0.00	(0.00–5.59)	5	1.28	(0.42–2.99)	9	1.15	(0.53–2.19)
Low exposure (5 regs)	0	0.00	(0.00–7.10)	6	1.84	(0.68–4.01)	10	1.51	(0.73–2.78)
An/microphthalmia									
All registries (16 regs)	11	1.03	(0.51–1.85)	27	1.03	(0.68–1.50)	37	0.73	(0.52–1.01)
High exposure (5 regs)	1	0.33	(0.01–1.84)	2	0.27	(0.03–0.96)	10	0.78	(0.38–1.44)
Medium exposure (6 regs)	7	1.38	(0.55–2.83)	17	1.37	(0.80–2.20)	12	0.48	(0.25–0.85)
Low exposure (5 regs)	3	1.18	(0.24–3.44)	8	1.26	(0.54–2.47)	15	1.14	(0.64–1.88)
Congenital cataract									
All registries (16 regs)	7	0.72	(0.29–1.49)	23	0.97	(0.61–1.45)	29	0.66	(0.44–0.95)
High exposure (5 regs)	0	0.00	(0.00–1.19)	3	0.40	(0.08–1.16)	8	0.68	(0.29–1.34)
Medium exposure (6 regs)	3	0.56	(0.12–1.63)	15	1.15	(0.65–1.90)	15	0.58	(0.33–0.96)
Low exposure (5 regs)	4	3.15	(0.86–8.06)	5	1.57	(0.51–3.66)	6	0.94	(0.34–2.04)

[a] Cohort E: exposure during May 1986; Cohort T: exposure during May 1986–April 1987; Cohort C: control cohort of conceptions May 1987–April 1989.

[b] IA+: registries recording induced abortion following prenatal diagnosis (see Table 1). IA–: registries not recording induced abortions.

those exposed immediately before conception in the first month following Chernobyl. There is always a certain probability that such clusters could arise somewhere in Europe by chance, hence the interest in a systematic surveillance of a larger and pre-specified European population. The plausibility of the relationship of the Berlin cluster to Chernobyl would depend on the assumptions that the highest sensitivity to radiation for non-disjunction in the oocyte is just prior to conception, that exposure of the germ cells in the first month after Chernobyl was much higher than in the subsequent year, and that the amount or type of exposure in Berlin was more likely to lead to an increase in trisomies there than elsewhere. Whether or not radiation could cause human Down's syndrome, and whether, if so, maximum sensitivity is likely to be during maternal fetal life, or during resumption of meiosis pre-conception, is a subject of current research.[27,28]

Table 4 Cohort E (external) 'seasonality ratios'[a] (95% CI)

Down's syndrome	1.12 (0.93–1.31)
Neural tube defects, British Isles	1.10 (0.98–1.22)
Neural tube defects, Continent	1.08 (0.85–1.31)
Hydrocephaly	0.80 (0.69–0.91)
Microcephaly	0.94 (0.78–1.10)
Arhinencephaly	1.69 (0.84–3.03)
An/microphthalmia	1.04 (0.75–1.33)
Congenital cataract	1.64 (1.21–2.06)

[a] Seasonality ratios are the ratio of prevalence in the months of conception included in Cohort E (Table 2) and the prevalence in other months of the year, 1980–1985.

Most other published studies of the impact of Chernobyl on the prevalence of central nervous system and eye anomalies[1,12,13,25] have concluded, as we do, that there has been no detectable change or pattern of change in prevalence which might be related to Chernobyl. On the other hand, there were reports from some regions of Turkey, but not others, of an increase in neural tube defects.[1] We consider that these 'clusters', as well as individual centre excesses we found during the exposure period (Cohorts E and T), such as neural tube defects in Odense, microcephaly in Groningen and eye anomalies in Strasbourg cannot be interpreted as related to Chernobyl unless and until some information comes to light which would suggest that these areas were more highly exposed than the other areas

Table 5 Observed (O) and expected (E) numbers of 6 categories of congenital anomaly in 16 registries in three cohorts[a] post-Chernobyl

	Down's Syndrome						**Neural tube defects**					
	Cohort E		Cohort T		Cohort C		Cohort E		Cohort T		Cohort C	
Registry	O	E	O	E	O	E	O	E	O	E	O	E
High exposure												
Florence (I)	0	1.0	9	12.8	17	25.9	0	1.5	9	9.0	15	18.4
Emilia Romagna (I)	1	2.3	22	31.6	70	63.9	3	2.1	8	13.4	17	27.2
Glasgow (UK)	2	1.2	18	14.3	32	27.5	6	7.5	29	46.4	50	90.1
Liverpool (UK)	1	2.1	15⁻	24.8	12⁻	22.8	3	9.6	26	59.6	36	60.8
Zagreb (C)	0	0.6	9	6.7	22	13.8	1	0.7	3	4.5	7	9.1
Medium exposure												
Strasbourg (F)	0	1.1	17	13.7	56*	28.5	4	1.8	11	11.4	11⁻	23.8
Marseille (F)	2	2.5	42*	30.0	100*	61.7	6	3.2	24	18.9	50	38.7
Dublin (IRL)	7	3.3	31	37.9	52⁻	70.5	8	12.2	43	74.0	64	138.0
Galway (IRL)	1	0.5	5	6.0	12	10.6	1	1.1	6	6.7	6	12.0
Luxemburg	0	0.3	1	3.3	9	8.8	0	0.3	0	1.5	2	4.1
Belfast (UK)	3	3.5	37	41.5	78	76.5	11	17.4	74	100.0	80	193.1
Low exposure												
West Flanders (B)	0	0.7	10	8.6	14	18.4	2	1.3	4	7.8	6⁻	17.2
Hainaut (B)	0	0.6	9	7.2	19	14.8	0	1.3	8	7.8	17	16.2
Odense-Funen (DK)	1	0.2	9*	3.0	26*	6.4	4*	1.0	9	6.0	9	12.7
Paris (F)	4	4.6	58	56.5	162*	115.1	4	5.7	38	35.9	76	73.2
Groningen (NL)	2	0.8	10	9.6	29*	18.5	1	1.8	6	11.5	16	22.4

	Hydrocephaly						**Microcephaly**					
	Cohort E		Cohort T		Cohort C		Cohort E		Cohort T		Cohort C	
Registry	O	E	O	E	O	E	O	E	O	E	O	E
High exposure												
Florence (I)	2	1.6	5	3.9	7	7.9	1	0.8	3	2.0	9	4.1
Emilia Romagna (I)	5	4.1	16	10.6	13	21.5	3	1.7	6	4.5	16*	9.1
Glasgow (UK)	2	2.7	7	6.6	5⁻	12.9	2	3.1	7	7.6	14	14.8
Liverpool (UK)	1	3.7	2⁻	9.1	7	9.2	0	1.6	3	3.9	3	3.9
Zagreb (C)	0	0.7	0	1.7	5	3.4	0	2.5	6	6.2	6	12.6
Medium exposure												
Strasbourg (F)	1	3.8	6	9.6	11⁻	20.2	0	2.1	3	5.4	6	11.4
Marseille (F)	3	4.2	17	10.0	23	20.4	1	2.5	7	6.0	13	12.2
Dublin (IRL)	5	4.5	13	11.1	13	20.6	5	3.0	6	7.3	6⁻	13.7
Galway (IRL)	1	0.4	2	0.9	0	1.6	0	0.3	0	0.7	2	1.3
Luxemburg	1	0.5	2	1.1	2	3.0	0	0.0	1	0.0	0	0.0
Belfast (UK)	6	5.0	14	12.3	13⁻	23.7	2	4.7	8	11.4	12⁻	22.1

Table 5 continued

	Hydrocephaly						Microcephaly					
	Cohort E		Cohort T		Cohort C		Cohort E		Cohort T		Cohort C	
Registry	O	E	O	E	O	E	O	E	O	E	O	E
Low exposure												
West Flanders (B)	2	1.1	7	2.8	4	6.2	1	0.5	2	1.2	4	2.7
Hainaut (B)	0	1.1	2	2.8	6	5.8	0	1.4	2	3.5	6	7.2
Odense-Funen (DK)	0	0.7	2	1.9	3	4.1	1	0.5	2	1.4	3	3.0
Paris (F)	5	8.4	23	20.7	55	42.2	4	3.9	10	9.5	21	19.4
Groningen (NL)	2	1.2	3	3.0	1⁻	5.9	6*	1.2	8*	3.0	2	5.9

	Arhinencephaly						An/Microphthalmia					
	Cohort E		Cohort T		Cohort C		Cohort E		Cohort T		Cohort C	
Registry	O	E	O	E	O	E	O	E	O	E	O	E
High exposure												
Florence (I)	0	0.0	0	0.2	3*	0.3	1	0.2	1	0.5	3	1.0
Emilia Romagna (I)	0	0.1	1	0.6	0	1.2	0	0.8	0	2.0	0	4.1
Glasgow (UK)	0	0.1	2	0.7	1	1.3	0	1.2	0	2.8	1	5.5
Liverpool (UK)	0	0.1	0	0.7	1	0.7	0	0.9	1	2.2	3	2.2
Zagreb (C)	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	3	0.0
Medium exposure												
Strasbourg (F)	0	0.1	3	0.7	1	1.6	3	0.8	9*	2.0	2	4.1
Marseille (F)	0	0.2	0	1.0	3	2.0	3	1.7	4	4.0	7	8.2
Dublin (IRL)	0	0.1	0	0.4	2	0.8	0	0.7	0	1.7	3	3.2
Galway (IRL)	0	0.1	0	0.5	0	1.0	0	0.0	1	0.0	0	0.0
Luxemburg	0	0.0	0	0.2	0	0.5	0	0.1	0	0.2	0	0.5
Belfast (UK)	0	0.2	2	1.0	3	2.0	1	1.8	3	4.5	0⁻	8.8
Low exposure												
West Flanders (B)	0	0.0	0	0.0	0	0.0	0	0.2	1	0.6	1	1.3
Hainaut (B)	0	0.1	1	0.7	2	1.4	1	0.6	3	1.6	3	3.3
Odense-Funen (DK)	0	0.1	0	0.5	2	1.1	0	0.1	0	0.4	3	0.8
Paris (F)	0	0.2	3	1.2	5	2.5	2	1.4	4	3.5	4	7.0
Groningen (NL)	0	0.1	2	0.8	1	1.6	0	0.2	0	0.4	4*	0.8

	Congenital Cataract					
	Cohort E		Cohort T		Cohort C	
Registry	O	E	O	E	O	E
High exposure						
Florence (I)	0	0.1	1	0.3	1	0.6
Emilia Romagna (I)	0	0.6	0	1.4	1	2.9
Glasgow (UK)	0	1.0	1	2.5	5	4.8
Liverpool (UK)	0	1.4	1	3.4	0	3.4
Zagreb (C)	0	0.0	0	0.0	1	0.0
Medium exposure						
Strasbourg (F)	2	0.7	8*	1.7	6	3.6
Marseille (F)	1	2.1	2	5.0	1⁻	10.2
Dublin (IRL)	0	1.1	4	2.7	7	5.1
Galway (IRL)	0	0.2	0	0.5	0	1.0
Luxemburg	0	0.0	0	0.0	0	0.0
Belfast (UK)	0	1.2	1	3.0	1⁻	5.8
Low exposure						
West Flanders (B)	0	0.0	0	0.0	0	0.0
Hainaut (B)	1	0.1	1	0.2	0	0.4
Odense-Funen (DK)	0	0.1	1	0.2	0	0.4
Paris (F)	3	0.7	3	1.6	4	3.3
Groningen (NL)	0	0.5	0	1.2	2	2.4

under study in ways relevant to potential teratogenic effects[29] which might not be reflected by the usual estimates of exposure. Even then the differences in outcome attributable to exposure would be difficult to explain. Some or all of these clusters might be chance events, given the multiple statistical tests carried out, or they may be due to a change in risk factors or in case ascertainment unrelated to the Chernobyl accident. Microcephaly in particular has been difficult to ascertain in a consistent fashion in time and space.[30]

Only a large increase in neural tube defect prevalence related to Chernobyl could have been detected in the British Isles, against the background of a rapidly declining prevalence since the early 1960s and throughout the 1980s.[19] Deficits in hydrocephaly and eye defects in the second and third year following Chernobyl, combined with our finding of a 'seasonality effect' for these anomalies, indicate the interest of further investigation of time-space clustering, particularly in relation to their potential infective origin.

No data is available on the impact of Chernobyl on the rate of early spontaneous abortions. If there was a greater impact on pregnancies with malformed fetuses than those with non-malformed fetuses, then an effect of Chernobyl on the overall malformation rate would be masked.

Limitations of this surveillance approach to assessing the impact of Chernobyl have been discussed in more detail elsewhere[30]. Most importantly, it is crucial that data on terminations of pregnancy should be made available to congenital anomaly registers, if they are to answer environmental concerns. Four of the registers with data analysed in this report did not register induced abortions, including two of the most highly exposed areas, and the validity of their results would depend on there being little change in the frequency of induced abortion during the study period in those areas, and in particular no change in prenatal screening uptake due to Chernobyl itself.

When reporting the results of surveillance related to a very widespread exposure, it is important to remember that a small rise in prevalence below the limits of detection of the study could still represent an excess of children born with congenital anomalies of public health importance across Europe as a whole. Nevertheless, on an individual basis, we would have to conclude that the rise in induced abortions[1], presumably representing the termination of wanted pregnancy due to fear of malformation, might have been avoided if the women could have benefited from 'hindsight' as shown by our results, and is therefore a tragic consequence of Chernobyl.

In conclusion, we find no evidence of a generalized detectable increase in the prevalence of congenital anomalies among conceptions or early pregnancies in the first month or first year following Chernobyl. An increase in Down's Syndrome prevalence in the late 1980s, apparently unrelated to Chernobyl, needs further investigation.

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