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# Childhood Leukaemia Following the Chernobyl Accident: The European Childhood Leukaemia–Lymphoma Incidence Study (ECLIS)

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**The objective of the European Childhood Leukaemia–Lymphoma Incidence Study (ECLIS) is to investigate trends in incidence rates of childhood leukaemia and lymphoma in Europe, in relation to the exposure to radiation which resulted from the accident at the Chernobyl nuclear power plant in April 1986. In this first report, the incidence of leukaemia in children aged 0–14 is presented from cancer registries in 20 European countries for the period 1980–1988. Risk of leukaemia in 1987–1988 (8–32 months post-accident) relative to that before 1986, is compared with estimated average dose of radiation received by the population in 30 geographic areas. The observed changes in incidence do not relate to exposure. The period of follow-up is so far rather brief, and the study is planned to continue for at least 10 years.**
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## INTRODUCTION

On 26 April 1986, an accident occurred at the Chernobyl nuclear power plant, about 100 km west of Kiev in the Ukraine. One reactor core and part of its containment building were destroyed, allowing radioactive particles to be released into the atmosphere. Releases continued for 9 days after the accident. Exposure to populations living beyond the immediate vicinity of the plant has been extensively reviewed by the United Nations Scientific Committee on the Effects of Atomic Radiation in its 1988 report [1].

There were three successive 'plumes' of material affecting (1) the eastern part of what was then the USSR, Poland and Sweden, (2) Central Europe, especially Austria, Bavaria, northern Italy and part of Switzerland, and finally (3) Romania and Bulgaria.

Most exposure was due to radioactive iodine ($^{131}$I) and caesium ($^{134}$Cs, $^{137}$Cs). Iodine, which has a half-life of about 8 days, was only important in the first weeks following the accident, while the contribution of caesium to exposure, particularly $^{137}$Cs which has a half-life of 30 years, will continue to be important for many years. Humans were exposed externally, from deposition of radionuclides on the ground, and internally from the ingestion of contaminated food (e.g. milk, leafy vegetables, grains); in the first year, more than two-thirds of dose resulted from ingestion of contaminated food [1, 2].

There have been many reports on the likely long-term consequences of the accident at Chernobyl, and the appropriate methods of surveillance—reports from international organisations include those from WHO [3], the CEC [4] and IAEA [2]. These reports, and independent evaluations of likely consequences to populations outside the immediate vicinity of the accident, e.g. [5–7] suggest that any excess cancer resulting from the levels of exposure to radioactivity from the accident will be undetectable against the expected background incidence. Nevertheless, it is acknowledged that there is considerable public disquiet about the size of the risk to health. In addition, there are already reports of a raised incidence of leukaemia in young children [8], excess infant mortality [9] and excess premature births among malformed children [10] in sub-national areas where exposure to radiation from the Chernobyl accident was higher than the national average. Even if the occurrence of leukaemia cases was entirely random, their spatial and/or temporal clustering is to be expected, and so too are further reports linking such observations to the Chernobyl accident. Finally, existing knowledge of risk of cancer during the short-term period after exposure is imprecise, because the Japanese

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life-span study did not begin until 5 years after exposure to radiation from the atomic bombs. For all of these reasons, surveillance of exposed populations for the excess occurrence of malignant disease is justified, provided that it can be undertaken with due consideration of the cost and effort involved in relation to the probable statistical power of any study.

We report here the study design and preliminary results of a project to monitor incidence rates of childhood leukaemia and lymphoma in Europe, the ECLIS study.

## MATERIALS AND METHODS

*Radiation exposure*

The estimated dose from the first year and from the first 4 years of exposure in different regions of Europe have been obtained from UNSCEAR (Table 1). In this paper, the term 'dose' is used to denote the individual committed effective dose equivalent resulting from exposure in a given time period. These estimates were based on direct measurements carried out in 34 countries in the first year. Doses from external exposures were calculated, making assumptions about average shielding by buildings and average time spent indoors. Doses from internal contaminations were based on radioactivity of various foodstuffs and assumptions about average consumption. The measurements indicated the general climatic and geographical factors which prevailed during the first year following the accident. After the first year, the contributions to external and internal doses resulting from deposited radioactive materials (mainly $^{137}Cs$) were estimated from models derived by UNSCEAR from fallout measurement experience.

Average doses were estimated for all European countries. However, in several countries where the distribution of exposures was very uneven, doses were estimated for 2–4 subregions where they were more homogenous. Figure 1 shows the countries and subregions for which these dosimetric estimates were produced.

For second and subsequent years, the projected contribution to exposure from ingestion was relatively smaller than that from external radiation. The transfer factors used to calculate internal exposures were higher in the more southerly latitudes because of the more advanced stage of the agricultural cycle in spring, when the accident occurred.

*Table 1. Radiation doses in European countries from the Chernobyl accident (estimates prepared by UNSCEAR): effective dose (μSv)*

| European countries | First year | 0–4 years |
|---|---|---|
| Austria | 670 | 1101 |
| Bulgaria | 760 | 900 |
| Region 1 | 720 | 790 |
| Region 2 | 800 | 1020 |
| Czechoslovakia | 350 | 440 |
| Region 1 | 275 | 320 |
| Region 2 | 355 | 450 |
| Region 3 | 340 | 390 |
| Denmark | 30 | 55 |
| Finland | 460 | 730 |
| France | | |
| Region 3 | 150 | 210 |
| ex-German Democratic Republic | 210 | 340 |
| Region 1 | 260 | 370 |
| Region 2 | 340 | 540 |
| Region 3 | 175 | 290 |
| Federal Republic of Germany | 130 | 200 |
| Region 1 | 67 | 100 |
| Region 2 | 130 | 200 |
| Region 3 | 490 | 780 |
| Hungary | 230 | 285 |
| Region 1 | 280 | 370 |
| Region 2 | 175 | 203 |
| Italy | | |
| Region 1 | 374 | 485 |
| Netherlands | 57 | 90 |
| Norway | 230 | 330 |
| Poland | 270 | 370 |
| Slovenia | 620 | 1045 |
| Sweden | 150 | 270 |
| Region 1 | 390 | 960 |
| Region 2 | 85 | 100 |
| Region 3 | 105 | 150 |
| Switzerland | 270 | 320 |
| Region 2 | 315 | 380 |
| Region 3 | 205 | 240 |
| Region 4 | 120 | 145 |
| United Kingdom | 27 | 32 |
| Region 1 | 12 | 14 |
| Region 2 | 105 | 140 |
| Region 3 | 190 | 250 |
| ex-USSR* | 260 | 350 |
| Region 1 | 1960 | 2680 |
| Region 3 | 445 | 630 |
| Region 4 | 140 | 190 |

* Belarus, Estonia, Lithuania, Russian Federation.

*Cancer data*

Data on cases of leukaemia and lymphoma occurring in children aged less than 15 years are supplied from population-based cancer registries in all of the countries listed in Table 1, although for some of the geographic regions only part of the population was covered by participating registries (France, region 3; Italy, region 1; Switzerland, regions 2–4; ex-USSR, regions 3 and 4). A map and a full list of participating centres is given in Annex A. These registries record data either for all cancers, or only for paediatric cancers or leukaemia/lymphoma cases, from geographically defined populations, and use multiple source reporting, including death certificates, as recommended by IARC/IACR [11]. All participants were required to have collected data according to these criteria for a period of at least 6 years prior to the accident (i.e. since 1980), although there were two general exceptions to this condition:

(1) For some regions, important contributions to the incidence data were provided by registries which had begun subsequent to 1980, and these were included, most notably two large paediatric cancer registries in France.
(2) For certain parts of the Russian Federation, and for Belarus, special retrospective verification of recorded leukaemia cases was considered necessary.

Data are submitted each year in the form of a case listing, with, for each case: date of incidence, date of birth, sex, place and type (urban/rural) of residence, place of birth (if available), basis of diagnosis (e.g. clinical examination, haematology/cytology, histology) and diagnosis. Diagnosis was noted as site (for

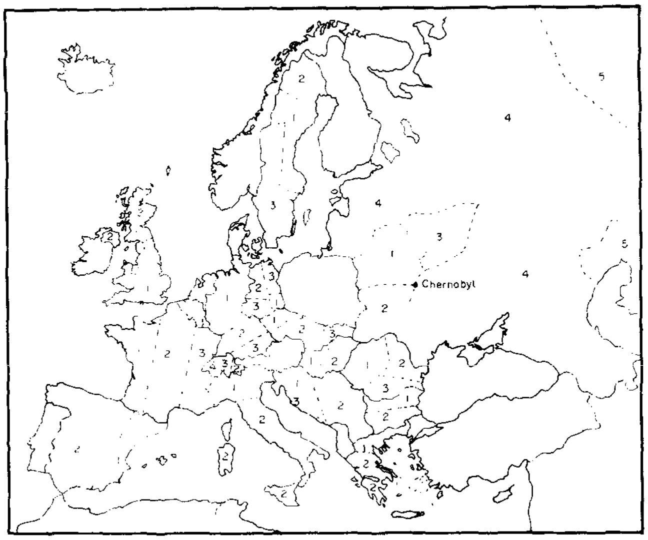


**Fig. 1. Division of Europe by country, or by subregions within countries, for the purpose of dose assessment (Source: UNSCEAR, 1988 [1]). (Within a country, the numbers refer to the regions used for dose estimation, and do not imply any ranking.)**

lymphomas) and morphology, and was either already coded according to the International Classification of Diseases—Oncology [12, 13], or converted from local codes to ICD-0.

The estimated size of the population-at-risk—children aged 0–14—was also supplied for each area every year, by district and type (urban/rural) of residence, sex and with maximum available detail on age (single year, if possible).

*Analysis*

Incidence rates were calculated for all forms of leukaemia and lymphoma, and for subgroups as defined by the ICD-0 morphology codes [14]. Rates were calculated per million person-years for age-groups 0, 1–4, 5–9 and 10–14, and the cumulative rate (0–14) was calculated as a summary index (this is effectively a direct standardisation, with the same weighting applied to each individual year of age [15]).

The main objective of this preliminary analysis was to see whether there was any evidence of a change in incidence of leukaemia in the first 3 years following the Chernobyl accident. In each country or region, the observed number of cases and incidence rate for the period 1987–1988 (8–32 months post-accident) were therefore compared with the expected value. In this preliminary analysis, the expected values were based on the average incidence rate in the 6 years pre-accident (1980–1985).

The excess risk [difference between the observed incidence rates (1987–1988) and those expected], and the excess relative risk [(observed rate/expected rate) − 1], were considered as a function of the first-year dose given in Table 1.

## RESULTS

*Radiation exposure*

Table 1 shows the estimated radiation doses in the first year and first 4 years of exposure for the countries and subregions participating in the study. Outside the former USSR, the highest first-year dose exposures were for south-eastern, central and northern Europe. The highest country average (760 μSv) in Bulgaria is about one third of the natural background annual dose (2400 μSv), a level which corresponds with the average first-year dose in Belarus (region 1 of the former-USSR).

*Leukaemia*

Figure 2 illustrates the incidence of all leukaemia in children (aged 0–14) by sex in the 18 countries for which data were available for the period 1980–1985. The cumulative rates are generally in the range 400–700 per million, although somewhat lower in Poland. With a few exceptions, rates are slightly higher in boys than in girls; however, since there appears to be no difference in leukaemogenicity of radiation between the sexes, further results are presented for both sexes combined.

Acute lymphocytic leukaemia accounted for 72–83% of leukaemia cases in almost all of the registries, with the exception of Poland (54.2% in 1980–1985), where the percentage of unspecified leukaemias was also high. Since chronic lymphocytic leukaemia is extremely rare in children, and for all other forms of leukaemia the risk is known to be enhanced by exposure to radiation, further analysis was for leukaemia as a whole.

Table 2 represents some indicators of quality of data in the different countries, as a guide to interpretation of results, for the baseline period (1980–1985) and for 1987–1988. For several registries, there have been improvements in the quality of data, as reflected by these three indicators. The largest change, for Austria, is based on data from a single year (1987), for which there was a lower than expected incidence (Table 3). The data from Poland suggest some improvement in quality (lower percentages of unspecified leukaemia and DCO cases), and the possibility that some of the increase in incidence (rates were 13% higher in 1987–1988 than in 1980–1985) is due to improved ascertainment should be considered.

Table 3 presents the number of cases registered, by region, in 1980–1985 and 1987–1988, together with the cumulative incidence rates per million. The expected number of cases in 1987–1988 is also shown, based on the age-specific rates from the baseline period (1980–1985).

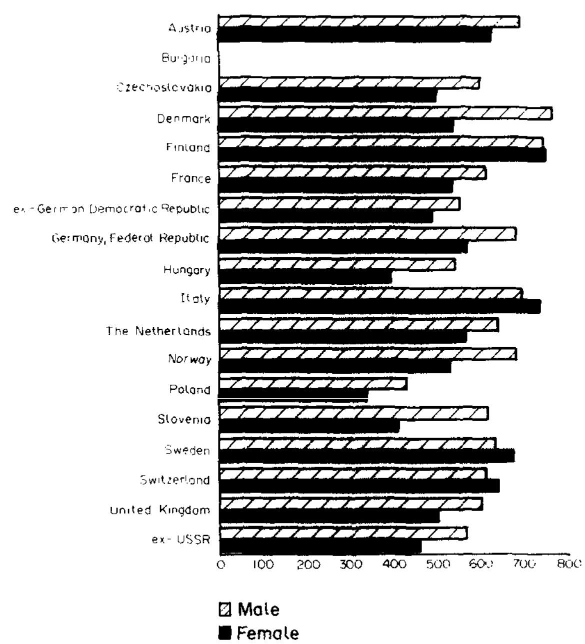


**Fig. 2. Cumulative incidence of leukaemia per million, aged 0–14 years, by sex, between 1980 and 1985.**

*Table 2. Indicators of data quality*

| European countries | % Unspecified* 80–85 | % Unspecified* 87–88 | % Histology† 80–85 | % Histology† 87–88 | % DCO‡ 80–85 | % DCO‡ 87–88 |
|---|---|---|---|---|---|---|
| Austria | 8.3 | 1.9§ | 85.0 | 94.2§ | 14.7 | 5.8§ |
| Czechoslovakia | 5.9 | 4.8 | 98.7 | 99.0 | — | — |
| Denmark | 1.6 | 0.0 | 99.6 | 98.9 | — | — |
| Finland | 3.5 | 2.5 | 97.5 | 96.3 | — | — |
| France | 1.6 | 0.0 | 99.6 | 98.4 | — | — |
| ex-GDR | 0.9 | 3.6 | 98.1 | 99.5 | — | — |
| FRG | 0.9 | 1.3 | 84.7 | 95.7 | — | — |
| Hungary | 0.0 | 0.0 | 100 | 100 | — | — |
| Italy | 2.5 | 0.0 | 98.8 | 100 | — | — |
| Netherlands | 0.0 | 0.0 | 100 | 100 | — | — |
| Norway | 3.6 | 0.0§ | 99.0 | 93.1§ | 0.5 | 6.9§ |
| Poland | 19.6 | 11.2 | 69.3 | 67.8 | 5.8 | 3.7 |
| Sweden | 4.3 | 2.5 | 84.3 | 96.8 | — | — |
| Switzerland | 2.4 | 2.7 | 99.2 | 97.3 | — | — |
| England and Wales | 1.8 | 1.0 | 98.4 | 97.4 | — | — |
| Scotland | 2.3 | 2.1 | 91.6 | 90.6 | — | — |
| Estonia and Lithuania | 9.8 | 2.5 | 97.9 | 97.5 | 2.1 | 2.5 |
| Slovenia | 4.4 | 3.2 | 100 | 100 | — | — |

* Percentage of leukaemia cases of 'Unspecified' type [14].
† Percentage of cases diagnosed from bone marrow or peripheral blood.
‡ Percentage of cases registered from death certificate only (—:data not available).
§ 1987 data only.

For the entire study population for which data were available for 1987–1988, 3679 cases were observed, compared with 3533.2 expected on the basis of the 1980–1985 rates. This small increase in overall incidence (4.1%) is statistically significant ($\chi^2 = 6.0$, $P < 0.05$). However, there is no association between the change in incidence, and estimated first-year dose for the individual regions. In Fig. 3, excess risk and in Fig. 4, excess relative risk are plotted against first-year dose equivalent for the 30 countries or subregions shown in Table 3. Weighted least squares regression lines have been fitted with weights equal to 1/variance in order to diminish the effect of observations from very small populations [the two outlying points correspond to Sweden (region 2) with 9 cases in 1987/88 and Switzerland (region 3) with 4 cases]. Excess risk shows a small non-significant decline with increase in estimated unit dose ($b = -0.012$, $P = 0.87$), as does the excess relative risk ($b = -3.3 \times 10^{-5}$, $P = 0.79$).

A little over half of the leukaemia cases observed in 1987–1988 were aged less than five years at diagnosis ($n = 1923$); this is a significant increase on the number expected, based on pre-accident rates (RR = 1.066, $P < 0.01$). Once again, however, the weighted least squares regression showed no association between dose and excess risk ($b = -0.64 \times 10^{-3}$, $P = 0.95$) or excess relative risk ($b = +0.55 \times 10^{-5}$, $P = 0.98$).

## DISCUSSION

Almost all studies and reports dealing with the possible consequences of the accident at the Chernobyl nuclear power plant conclude that, although a substantial number of cancers may be induced by the radioactive material released, any increase in rates outside the regions in the USSR close to the reactor site will not be detectable against the normal incidence of cancer in the general population. Using the estimate of excess relative risk of leukaemia for exposures under the age of 20 from the BEIR V report [16], and assuming that excess risk at 2–5 years is the same as that at 5–10 years (to which the BEIR data apply), we estimated that the overall increase in incidence of leukaemia for the area covered by the ECLIS study will be about 0.8% with the most marked increase in Belarus (5.8%) [17]. These estimates were, however, based on the first-year effective dose equivalent. Doses in the subsequent years would be less, with the main decline being in internal radiation. The total effective dose equivalent was estimated to be about three times that of the first-year dose [1]. For cancer cases occurring over several years, a rather more complex calculation is required, estimating the cumulated dose for each individual year of birth cohort. It is unknown, of course, whether the excess risk resulting from a dose cumulated over several years would be the same as the much higher/shorter duration exposures in Hiroshima and Nagasaki, on which the BEIR V estimates are based. However, it does seem that, unless the estimates of relative risk in relation to dose, or estimated doses, are considerably in error, no excess incidence should be detectable anywhere, with the possible exception of Belarus. It has, however, been acknowledged that surveillance is required, provided that this can be undertaken in a relatively cost-effective manner by using existing data collection systems, if only because a bland reassurance that nothing could be found is likely to be treated with scepticism by a substantial proportion of the European populations most exposed to the Chernobyl fallout.

In the context of monitoring the possible effects of exposure to low levels of radioactivity, there are several advantages to the study of leukaemia, and of cancers in childhood. Leukaemia is one of the earliest malignant neoplasms to demonstrate an increase in incidence following radiation exposure (2–10 years), and provides the largest relative increase of any cancer, at least at low to moderate exposure levels [16]. The relative risk of radiation-induced leukaemia is probably higher for those exposed as children than as adults [18, 19], and pre-natal

*Table* 3

| | Baseline (1980–1985) | | Observed (1987–1988) | | Expected (1987–1988)* |
|---|---|---|---|---|---|
| | Cases | Cumulative rate | Cases | Cumulative rate | Cases |
| Austria | 374 | 657 | 52† | 588† | 58.4 |
| Bulgaria | | | | | |
| Region 1 } Region 2 } | Not available | | | | |
| Czechoslovakia | | | | | |
| Region 1 | 211 | 526 | 70 | 555 | 64.5 |
| Region 2 | 210 | 565 | 71 | 616 | 65.2 |
| Region 3 | 405 | 548 | 149 | 617 | 132.9 |
| Denmark | 253 | 652 | 89 | 783 | 76.4 |
| Finland | 285 | 745 | 81 | 638 | 94.7 |
| France | | | | | |
| Region 3 | 257 | 573 | 126 | 598 | 122.2 |
| Germany | | | | | |
| ex-GDR | | | | | |
| Region 1 | 157 | 571 | 47 | 512 | 52.2 |
| Region 2 | 143 | 506 | 51 | 539 | 47.6 |
| Region 3 | 378 | 507 | 126 | 492 | 128.6 |
| ex-FRG | | | | | |
| Region 1 | 1512 | 604 | 486 | 619 | 475.8 |
| Region 2 | 471 | 586 | 161 | 618 | 151.7 |
| Region 3 | 243 | 493 | 88 | 542 | 80.1 |
| Hungary | | | | | |
| Region 1 | 222 | 450 | 88 | 575 | 66.6 |
| Region 2 | 205 | 464 | 71 | 535 | 61.9 |
| Italy | | | | | |
| Region 1 | 244 | 714 | 60 | 669 | 63.7 |
| Netherlands | 687 | 603 | 200 | 561 | 215.5 |
| Norway | 197 | 604 | 29† | 550† | 31.7 |
| Poland | 1431 | 350 | 516 | 396 | 498.9 |
| Slovenia | 91 | 515 | 31 | 558 | 628.2 |
| Sweden | | | | | |
| Region 1 | 65 | 679 | 25 | 830 | 20.6 |
| Region 2 | 10 | 500 | 9 | 1458 | 3.0 |
| Region 3 | 320 | 657 | 123 | 781 | 103.5 |
| Switzerland | | | | | |
| Region 2 | 67 | 624 | 20 | 836 | 15.0 |
| Region 3 | 20 | 789 | 4 | 496 | 6.4 |
| Region 4 | 38 | 562 | 13 | 578 | 12.7 |
| United Kingdom | | | | | |
| Region 1 | 2076 | 554 | 701 | 563 | 688.9 |
| Region 2 | 203 | 517 | 92 | 737 | 64.5 |
| Region 3 | 61 | 636 | 21 | 679 | 19.7 |
| ex-USSR | | | | | |
| Region 1 } Region 3 } | Not available | | | | |
| Region 4 | 235 | 514 | 79 | 493 | 82.1 |

* Based on age-specific incidence 1980–1985.
† 1987 data only.

exposure to radiation may carry an even higher risk for childhood leukaemia [20, 21]. Some uncertainty, moreover, underlies the dose–response relationship for leukaemia in children (and adults), because of lack of data from the first 5 years following exposure in the studies of survivors of the atomic bombs in Japan. An additional consideration in the choice of childhood leukaemia was the fact that, for several countries or regions, the only cancer registries with data for the period of interest were restricted to childhood cancer (e.g. Federal Republic of Germany) or leukaemia/lymphoma (e.g. The Netherlands), or that such data were available for more extensive geographical areas, or were of better quality than comparable data for all cancers (e.g. Hungary, Austria, France). In Austria, for example, the national cancer registry files were compared sys-

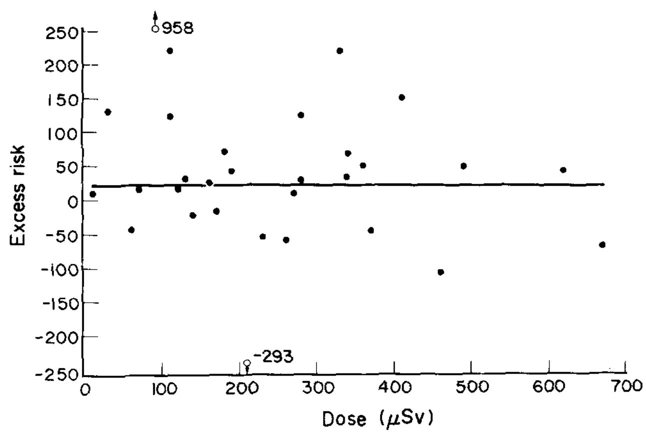


**Fig. 3. Excess risk of leukaemia (observed cumulative rate − expected cumulative rate) vs. dose for 30 countries/regions (expected rate is that observed in 1980–1985).**

tematically with other sources of data on childhood leukaemia (notably from clinical trials series) to produce a combined list of incident cases.

In view of the high level of contamination by $^{131}I$, thyroid cancer has been a particular concern following the Chernobyl accident, and prophylactic iodide was widely administered in several countries. However, the latency period for thyroid cancer following exposure to radiation is thought to be much longer than for leukaemia. Moreover, there are problems in the uniform registration of thyroid cancer, because of the high prevalence of undiagnosed thyroid nodules in the general population, and the consequent potential for biases due to changes in the level of ascertainment. There is certainly less possibility for cases of leukaemia in the population to be unrecognised, although changes in incidence could still result from changes in the efficiency of case-finding. Although in some registries, there was evidence of improvement in some of the indicators of data quality, there was little suggestion of an association between the quality of diagnostic information and the completeness of registration, as indicated by increases in incidence data. A recent report from three districts in the Ukraine [22] suggests that enhanced surveillance and reporting of cancers after 1986 was responsible for abrupt increases in incidence of leukaemia and other cancers in the age groups 65+.

The data presented in this report relate only to childhood leukaemia. However, the distinction between non-Hodgkin lymphoma (NHL) and acute lymphocytic leukaemia (ALL) in childhood is somewhat arbitrary [23, 24], based upon the percentage of lymphoblasts in the bone marrow (> 25% in ALL), and NHL may progress to a leukaemic form. For this reason, data on childhood lymphoma have been collected from most centres, so that any trends in leukaemia incidence can be compared with simultaneous changes in the incidence of NHL.

The original objective of the ECLIS study was the surveillance of leukaemia (and lymphoma) incidence in countries outside the USSR. Within the former Soviet Union, a special follow-up was initiated, with a centralised register (the All Union Distributed Registry) containing medical and dosimetric information on some 530 000 individuals, including 230 000 clean-up workers, and 300 000 members of the population living in the 'special control zones' of the Russian Federation, Ukraine and Belarus which received the highest exposures [25]. It includes some 35 000 people evacuated from the zone 30 km around the reactor site, who received doses of around 400 mGy. A decision has been made recently to include incidence data from the former USSR in the ECLIS study, provided that they fulfil the criteria for the study. To date, only those from Lithuania and Estonia have been analysed. Aggregate data (numbers of leukaemia cases by age group and sex) have been received for Belarus, and do not suggest any change in incidence between 1987 and 1988 and 1980 and 1985, although since the individual records were unavailable, they are not at present included.

The data analysis comprises a comparison of population-level exposure (radiation) and outcome (leukaemia), and in common with all such ecological analyses, is subject to the limitation that cause and effect at the individual level may not be the same as those for group data [26]. However, because we are interested in changes in risk over time within areas, rather than variation between areas, the probably unequal distribution of other determinants of risk for childhood leukaemia between the different regions of Europe, for example, differences in the levels of background radiation [27], is not a concern. In this study, we are, clearly, not able to control for the change in exposure to such risk factors within the different regions over time and, as the study duration increases, the observed incidence will be based on data increasingly distant in time from the comparison, pre-accident, period. Future analyses will, therefore, examine the effect of country-specific pre-accident time trends in incidence on expected incidence post-accident.

The estimates of average radiation dose used in the analysis are those produced by UNSCEAR [1], which are in general rather similar to the earlier estimates from OECD [28]. It must be remembered that these estimates are derived from complex models involving as input measures of environmental isotopes (mainly $^{137}Cs$), and a variety of assumptions about ground deposition, uptake by plants, food consumption, etc. In the absence of direct measurement, this is the only feasible methodology, although measurements close to the reactor site suggest that in the contaminated areas, the environmental transfer models (by assuming no modification of the diet) may overestimate dose [2].

In this report, we have examined data on leukaemia cases occurring up to the end of 1988 (some 32 months after the accident). This is too early to have observed any effect, even if one were anticipated at the low estimated exposure levels. At least 5 years of post-accident data are required for a meaningful analysis. At that time, it will be important to examine incidence rates specific for birth cohorts, to separate, for example, children

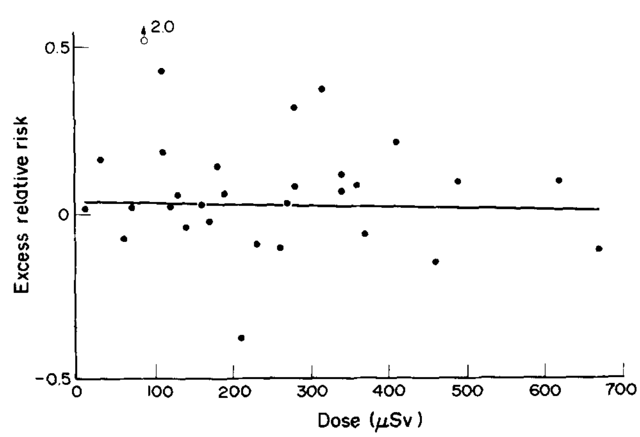


**Fig. 4. Excess relative risk of leukaemia [(observed cases/expected cases) − 1] vs. dose for 30 countries/regions (expected cases calculated from rates observed in 1980–1985).**

exposed *in utero*, and those never exposed, even *in utero*, to radiation within 12 months of the accident (born after January 1988).

The longer the timespan of the study, the more likely is it that discrepancies will arise between place of residence at time of diagnosis, and place of residence since the time of the accident. They will lead to a misclassification of populations by estimated average dose. However, with the large geographical units under consideration, there is unlikely to be much cross-boundary movement within 5 years. Its extent can be gauged by comparing the place of birth and place of residence variables in the listings of leukaemic cases, although time of migration of such cases is unknown, and it will not be possible to allocate person-years according to average level of dose.

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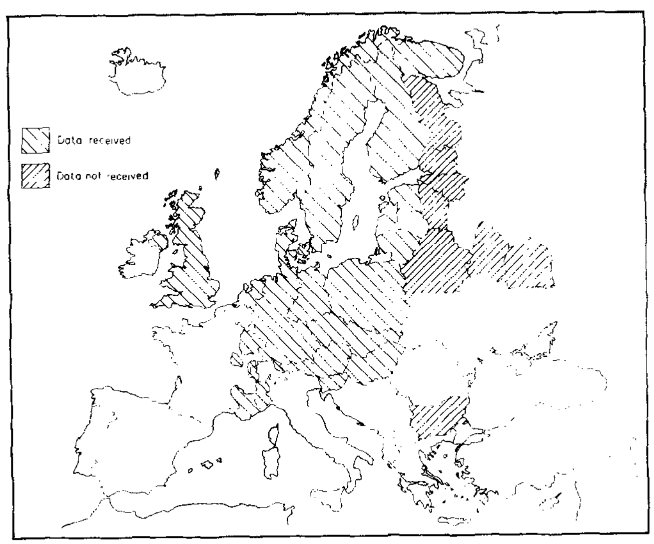


**Annex A. European Childhood Leukaemia–Lymphoma Incidence Study—Coverage by geographic area.**