INTRODUCTION
The European Childhood Leukaemia-Lymphoma Incidence Study (ECLIS) aims to monitor trends in the incidence of these diseases in European populations in relation to estimated exposures to radioactive material released at the time of the Chernobyl accident. Thirty-six cancer registries in 23 countries are collaborating in ECLIS, coordinated by the International Agency for Research on Cancer (IARC).

DATA AND METHODS

Populations-at-risk and childhood leukaemia incidence data
Registries provided listings of cases of childhood leukaemia for a period from 1980 up to the most recent complete year of registration (at least 1991), and estimates of the populations-at-risk broken down by sex and single years of age.

Radiation exposure assessment
Estimates of levels of radiation exposure due to the Chernobyl accident were obtained from the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). The countries participating in ECLIS are shown in figure 1. For countries with wide variations in exposure levels, sub-regions were used. The estimated mean effective dose equivalents at 1, 4 and 70 years after the accident are shown for the study areas in figure 2. An individual dose was imputed for each child-at-risk, based on age, year of follow-up and place of residence, under the following assumptions:

- the leukaemogenic effect of the exposures due to the accident has a latency of at least one year
- the effective dose to the foetus is equivalent to that of a free-living individual
- the total leukaemogenic dose is cumulative, starting from conception (Fig. 3)
Fig. 1: Europe, showing (shaded) areas for which data on exposures populations-at-risk and leukaemia incidence were available.

Note: the numbered regions within countries, for example Germany, represent areas for which regional dose estimates and cancer registry data were used. The numbering does not indicate ranking. Unnumbered regions in other countries, for example France, show the locations of regional cancer registries, whose data were pooled with exposure regions.
Fig. 2: Effective dose equivalents (mSv) due to Chernobyl accident by region
Source: UNSCEAR, 1988

Belarus
Sweden (1)
Austria
Slovenia
Germany (6)
Finland
Bulgaria
Russia
Romania
Germany (2)
Italy
Czech Republic (2)
Germany (1)
Poland
Germany (3)
Norway
Hungary (1)
Switzerland (2)
Czech Republic (3)
Slovakia
Germany (5)
Czech Republic (1)
United Kingdom (3)
France
Baltic republics*
Switzerland
Hungary (2)
Sweden (3)
United Kingdom (2)
Germany (4)
Switzerland (4)
Netherlands
Sweden (2)
Denmark
United Kingdom (1)

0-1 year 1-4 years 4-70 years
Fig. 3: Illustration of the method of calculation of dose.

The box in the upper graph contains all points \((t,a)\) representing subjects aged 2 at any time in 1989. The method of estimating the effective dose at \((t,a)\) consists of integrating the dose rate curve \(s\)
Statistical methods

Poisson regression models with terms for sex, age or birth cohort, region of residence and calendar year were used to establish the null distribution of childhood leukaemia in Europe since 1980. Likelihood ratio tests were then applied by adding parameters for dose.

RESULTS

The estimated doses were generally very small, with 91 million person-years-at-risk at a cumulative dose of less than 0.06 mSv and 58 person-years-at-risk at more than 0.3 mSv. The highest doses were in Belarus, with an estimated dose of 2 mSv in the first year following the accident.

In all study regions combined, there was an increase in the overall age-standardised rate of childhood leukaemia in the period 1980-86, during which the leukaemogenic dose attributable to the Chernobyl accident was zero (average annual change +0.6%). Thereafter, there was no evidence of an increase in this gradient (average annual change +0.4%). Table II shows observed and expected cases by cumulative dose. There was no indication of heterogeneity between the dose categories ($\chi^2=0.98, 3df$), or of a trend in incidence with dose when fitted as a continuous variable ($\chi^2=0.85, 1df$).

Table I: Observed and expected cases of childhood leukaemia and observed/expected ratios by dose category

<table>
<thead>
<tr>
<th>Cumulative excess dose (mSv)</th>
<th>Observed cases</th>
<th>Expected cases</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>15004</td>
<td>15004.0</td>
<td></td>
</tr>
<tr>
<td>0.01 - 0.05</td>
<td>3870</td>
<td>3862.2</td>
<td>1.002</td>
</tr>
<tr>
<td>0.06 - 0.12</td>
<td>2172</td>
<td>2151.7</td>
<td>1.009</td>
</tr>
<tr>
<td>0.13 - 0.29</td>
<td>2022</td>
<td>2037.7</td>
<td>0.992</td>
</tr>
<tr>
<td>0.30 +</td>
<td>2752</td>
<td>2764.5</td>
<td>0.995</td>
</tr>
</tbody>
</table>

This lack of effect of dose was also seen in the individual age groups (table II). The data are categorised by approximate birth cohort in table III. Of
Table II: Observed (O) and expected (E) cases of childhood leukaemia by age at diagnosis and estimated cumulative excess radiation dose due to the Chernobyl accident

<table>
<thead>
<tr>
<th>Cumulative dose (mSv)</th>
<th>0</th>
<th>1 - 4</th>
<th>5 - 9</th>
<th>10 - 14</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>O</td>
<td>E</td>
<td>O</td>
<td>E</td>
</tr>
<tr>
<td>0</td>
<td>775</td>
<td>775.0</td>
<td>6796</td>
<td>6796.0</td>
</tr>
<tr>
<td>0.01 - 0.05</td>
<td>513</td>
<td>506.3</td>
<td>2054</td>
<td>2048.8</td>
</tr>
<tr>
<td>0.06 - 0.12</td>
<td>43</td>
<td>53.7</td>
<td>1063</td>
<td>1084.3</td>
</tr>
<tr>
<td>0.13 - 0.29</td>
<td>6</td>
<td>7.6</td>
<td>977</td>
<td>952.7</td>
</tr>
<tr>
<td>0.30 +</td>
<td>13</td>
<td>7.3</td>
<td>982</td>
<td>990.2</td>
</tr>
<tr>
<td>$\chi^2$ (1 d.f.)</td>
<td>0.26</td>
<td>0.12</td>
<td>0.72</td>
<td>0.28</td>
</tr>
</tbody>
</table>

Table III: Observed (O) and expected (E) cases of childhood leukaemia by approximate birth cohort and estimated cumulative excess radiation dose due to the Chernobyl accident

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>O</td>
<td>E</td>
<td>O</td>
<td>E</td>
</tr>
<tr>
<td>0</td>
<td>12083</td>
<td>12083.1</td>
<td>2921</td>
<td>2921.0</td>
</tr>
<tr>
<td>0.01 - 0.05</td>
<td>852</td>
<td>872.7</td>
<td>1381</td>
<td>1340.4</td>
</tr>
<tr>
<td>0.06 - 0.12</td>
<td>691</td>
<td>651.1</td>
<td>925</td>
<td>938.5</td>
</tr>
<tr>
<td>0.13 - 0.29</td>
<td>617</td>
<td>647.1</td>
<td>1006</td>
<td>997.5</td>
</tr>
<tr>
<td>0.30 +</td>
<td>937</td>
<td>926.2</td>
<td>1426</td>
<td>1461.7</td>
</tr>
<tr>
<td>$\chi^2$ (1 d.f.)</td>
<td>0.02</td>
<td>0.36</td>
<td>0.72</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Particular interest is the 1987 cohort, which includes children who received the largest exposures in utero. The trend in risk with dose for this cohort was not statistically significant ($\chi^2=0.72$, 1 df).
DISCUSSION

Although we observed a small increase in the risk of childhood leukaemia in Europe during the 1980s and early 1990s, there was no evidence of an association between risk and the estimated doses received due to the Chernobyl accident (after allowance for the effects of sex, age or birth cohort, calendar year and region of residence). However, at this stage of follow-up, the study has low statistical power to detect such a trend. If the excess risks per unit dose estimated from the atomic bomb survivors are applied to the childhood population-at-risk in Europe following the accident, then the power of the study is about 50%. This may even overstate the statistical power, since the protracted low-dose exposures concerned differ in quality, and probably also in leukaemogenic effect, from the acute high-dose exposures experienced by the atomic bomb survivors.

The study has been analysed as a cohort study, it should be clear that the allocation of dose to individuals was determined by a function of place of residence and time since the accident. The actual exposure of individuals within the study populations was unknown, and imputed values from estimated population averages were used. Migration between study regions would give rise to exposure misclassification, which would attenuate any estimated dose effect. However, inter-regional migration of children in the five years of observation is unlikely to have been of a sufficient scale to have affected the results of the study.

A possible source of bias in the studies of cancer risk following radiation exposure is differential ascertainment of cases which is correlated with exposure, due to an increased interest in and improved detection of cases in heavily exposed populations. In contrast to thyroid cancer, which can exist for long periods in a latent form, this seems unlikely for childhood leukaemia.

The study will continue data collection for a period of ten years following the accident, so that the further potential of the excess radiation exposure can be studied.