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Childhood leukaemia near nuclear sites in Belgium, 2002–2008

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This paper describes an ecological study investigating whether there is an excess incidence of acute leukaemia among children aged 0–14 years living in the vicinity of the nuclear sites in Belgium. Poisson regression modelling was carried out for proximity areas of varying sizes. In addition, the hypothesis of a gradient in leukaemia incidence with increasing levels of surrogate exposures was explored by means of focused hypothesis tests and generalized additive models. For the surrogate exposures, three proxies were used, that is, residential proximity to the nuclear site, prevailing winds and simulated radioactive discharges, on the basis of mathematical dispersion modelling. No excess incidence of acute leukaemia was observed around the nuclear power plants of Doel or Tihange nor around the nuclear site of Fleurus, which is a major manufacturer of radioactive isotopes in Europe. Around the site of Mol-Dessel, however, two- to three-fold increased leukaemia incidence rates were found in children aged 0–14 years living in the 0–5, 0–10 and the 0–15 km proximity areas. For this site, there was evidence for a gradient in leukaemia incidence with increased proximity, prevailing winds and simulated radioactive discharges, suggesting a potential link with the site that needs further investigation. An increased incidence of acute leukaemia in children aged 0–14 years was observed around one nuclear site that hosted reprocessing activities in the past and where nuclear research activities and radioactive waste treatment are ongoing. ***European Journal of Cancer Prevention* 27:184–191 Copyright © 2018 The Author(s). Published by Wolters Kluwer Health, Inc.**

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Introduction

The possible health risks associated with living in the vicinity of large nuclear installations have been the subject of public concern for several decades. Early in 2008, these concerns were boosted worldwide by the publication of the German ‘KiKK’ survey (Kinderkrebs in der Umgebung von Kernkraftwerken), a large scale case–control study that showed a significant increase in leukaemia incidence among children living within 5 km of nuclear power plants (NPPs) in Germany (Kaatsch *et al.*, 2008; Spix *et al.*, 2008). The incidental gaseous release of I-131 that occurred in August 2008 at the Institute for Radio-Elements in Fleurus (Belgium), one of the world’s major players in the production chain of radioiodines, further fuelled these concerns locally.

In response to both the publication of the KiKK-study and the incident at Fleurus, the Minister for Social Affairs and Public Health commissioned a nationwide epidemiological study to explore the health risks associated with living in the vicinity of nuclear sites in Belgium. As it was the first study of its kind in Belgium, a multidisciplinary research group decided that this study was to adopt an ecological approach using data that were readily available and that it should focus on acute leukaemia in children aged 0–14 years and on thyroid cancer.

The current paper presents the results for acute leukaemia in children aged 0–14 years. The investigation particularly focuses on the question of whether the leukaemia incidence is higher than expected in the vicinity of the nuclear sites in Belgium. In addition, the hypothesis of a gradient in leukaemia incidence with increasing levels of surrogate exposures is explored. The results for thyroid cancer have been reported in Bollaerts *et al.* (2014, 2015).

Materials and methods

Nuclear sites and proximity areas

The nuclear sites under study are the four Belgian nuclear facilities of class 1, corresponding to the highest

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radiological risk (Belgian Federal Government, 2001), that is, Doel, Mol-Dessel, Fleurus, Tihange and the French nuclear facility of Chooz, which is located at ± 3 km from the Belgian border. Doel, Tihange and Chooz are electricity-generating NPPs. Doel and Tihange started up in 1975 and Chooz in 1967. The nuclear site of Fleurus has produced radionuclides for medicine and industry since 1971. Finally, the site of Mol-Dessel started up in 1956 and hosts a combination of nuclear activities, that is, scientific and technological research, applied research and metrology, operational waste management, the Belgian Underground Research Laboratory and the production of fuel assemblies for pressurized-water reactors based on uranium oxide (UO_2) and mixed oxides (MOX). An additional facility that produced MOX fuel for NPPs has been being dismantled since 2006 [see Bollaerts *et al.* (2014), for a detailed description of the sites].

Proximity areas were constructed as aggregations of communes with their centroid within the circle of radius r around the site. Communes are the smallest administrative level for which age-specific and sex-specific cancer incidence data are available. Belgium has 589 communes with an average surface area of 52 km^2 and an average population of 18 256 inhabitants. As the choice of the proximity area is to a certain extent arbitrary, and as it has been shown that the model results can depend on this choice (Urquhart, 1991), different proximity areas were studied, that is, 0–5, 0–10, 0–15 and 0–20 km radius. A map with the five nuclear sites and their 20 km proximity areas is shown in Fig. 1.

Health outcome

Data on acute leukaemia incidence in children aged 0–14 years were obtained from the Belgian Cancer Registry (BCR). The BCR is a national population-based registry. The incidence year and place of residence are defined at the year of cancer diagnosis. Data were available from 2002 to 2008 for Flanders (the northern part from Belgium) and from 2004 to 2008 for Brussels-Capital Region and Wallonia (the southern part of Belgium). The nuclear sites of Doel and Mol-Dessel are situated in Flanders, whereas the nuclear sites of Tihange and Fleurus are situated in Wallonia.

The corresponding population data were obtained from the population registers of the Federal Public Service (FPS) Economy, Directorate-General Statistics and Economic Information for every year from 2002 to 2008.

Covariates

Urban–rural status

The urban–rural status of every commune was determined on the basis of the index of urbanization as proposed by Mérenne *et al.* (1997). They distinguish four categories: (a) 'agglomeration', (b) 'suburb', (c) 'residential zone of commuters' and (d) 'not urban area'. Classification was carried out according to well-defined criteria, including the concentration of commerce and services, the population density, the built area and the commuting flows. For the current study, the urban–rural status was dichotomized as 'urban area' (categories 1–3) and 'not urban area' (category 4).

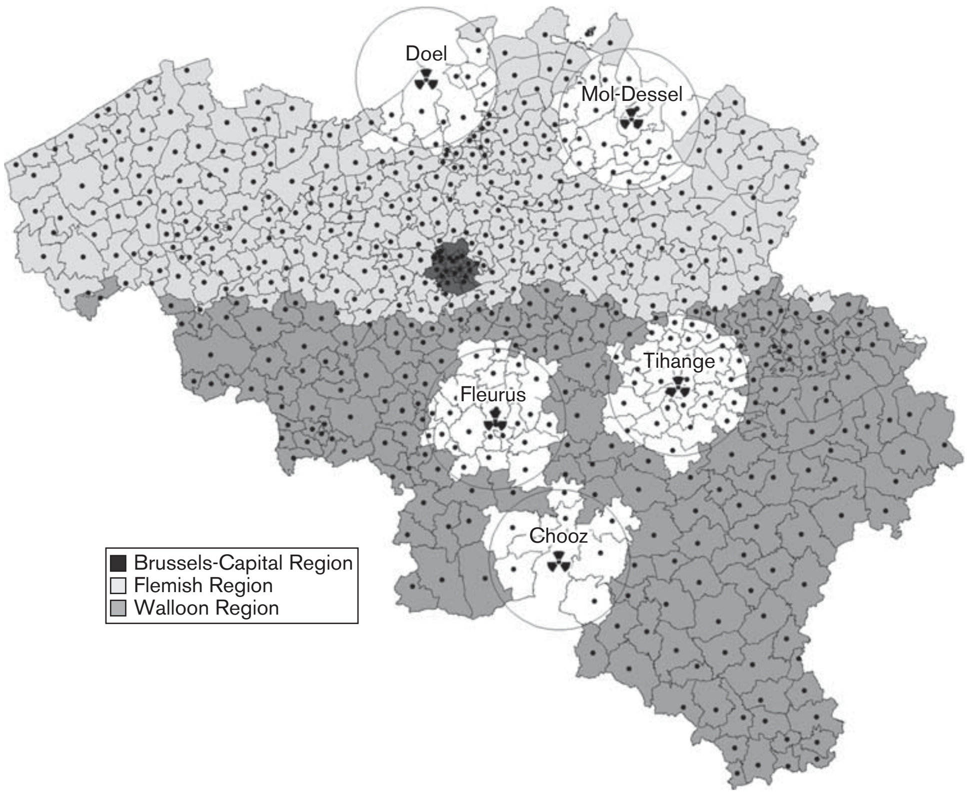
Socioeconomic status

The socioeconomic status (SES) at the commune level was calculated on the basis of the annual wealth index (WI) as used by the Belgian Federal Public Service (FPS) Economy. For every year, the FPS Economy calculates the annual commune-specific WI as the ratio between the average income per inhabitant within the commune and the national average income per inhabitant multiplied by 100.

Surrogate exposures

For all communes within the proximity areas, two different measures of surrogate exposure to radionuclide gaseous discharges were determined, that is, (i) residential proximity to the nuclear site and (ii) prevailing wind directions. Residential proximity was calculated as the distance between the location of the nuclear sites and the communes' centroids. Prevailing wind directions were defined as the frequency (in %) of the wind blowing from the site towards the commune. To this end, wind direction data collected by the Federal Agency of Nuclear Control survey stations around the four Belgian nuclear sites for the period 2003–2008 were converted into 16-sector compass roses. Measurements were discarded when the wind velocity was below 0.2 m/s because low wind velocity is associated with continuously changing wind directions. Finally, simulated radioactive discharges on the basis of mathematical dispersion modelling were calculated for one site, that is, the site of Mol-Dessel that showed significant results for incidence, distance and prevailing winds (see later). The radionuclide Ar-41 was chosen as it is the most relevant for exposure from this site. The exposures from Ar-41 were simulated using Hotspot (University of California, Lawrence Livermore National Laboratory – UC LLNL, Hotspot version 2.07, *http://www.llnl.gov/nai/technologies/hotspot/*, 2005–2012) for standard releases (total activity: 10^{15} Bq), assuming average meteorological conditions (wind speed: 3 m/s; annual percentage rain fall: 5%) and a site-specific effective release height of 80 m. Hotspot provides analytical solutions to the transport and diffusion equations for short duration (puffs) or continuous (plumes) releases of atmospheric pollutants. The model assumes that dispersion in the upwind and cross-wind direction takes the form of a Gaussian curve, with the maximum concentration in the centre of the plume. The model further assumes that a steady state exists in the radioactive discharges and the meteorological conditions. The simulated exposures were first expressed as a function of distance from the source. By multiplying these simulations by the wind direction frequencies (in %), the final exposure simulations at every commune's centroid were obtained.

Fig. 1



Map of Belgium showing the nuclear sites, the communes' centroids and the 20 km radius proximity areas (white) around the nuclear sites.

Statistical analyses

Incidence of acute childhood leukaemia around nuclear sites

Poisson regression models were constructed, regressing the number of acute childhood leukaemia cases on proximity to the nuclear sites and covariates. To account for overdispersion, the quasi-likelihood approach was adopted with a Pearson-based overdispersion parameter φ (McCullagh and Nelder, 1989). The covariates accounted for were sex, 5-year age groups, SES on the basis of the WI and the 'urban–rural' status of the commune. As the WI was strongly fluctuating over time and over communes, SES was measured as the average life span WI calculated for every given incidence year and age group. In particular, for a given year i ($i=2000$, 2001, …2008) and age group j ($j=1, 2, 3$), the average life span WI was calculated as follows:

$$\overline{\mathrm{WI}}_{i(j)} = (K+1)^{-1} \times \sum_{K=0}^{K} \mathrm{WI}(\text{year}\, i-k) \text{ with } K = 5(j-1)+2.$$

Model construction was performed by forward selection, consecutively adding sex, age groups, interaction between sex and age groups, urban–rural status and the linear trend of SES on the basis of the WI. Significance tests were performed using Wald tests at $\alpha=0.05$.

The effects of proximity to the nuclear sites were reported as rate ratios (RRs), with Belgium as the common reference population for all comparisons. The 95% confidence intervals (95% CIs) were obtained from the large sample distribution of log (RR). To investigate whether the results depend on the size of the circular proximity area, the RRs were calculated for the 0–5, 0–10, 0–15 and 0–20 km proximity area. Statistical power for finding an excess of cases was calculated for the 0–5, 0–10, 0–15 and 0–20 km proximity area by Monte Carlo simulations (Appendix A, Supplemental digital content 1, *http://links.lww.com/EJCP/A89*). Analyses were carried out for the four sites separately (single-site analyses) and the four Belgian nuclear sites together (multisite analyses).

Association between surrogate exposures and incidence of acute childhood leukaemia around nuclear sites

Focused hypothesis tests (Elliott *et al.*, 2000) were used to test the hypothesis of a positive gradient in acute leukaemia with increasing levels of surrogate exposure. The following focused hypothesis tests were carried out: (a) the conditional form of Stone's test fixing the total number of cases observed within the proximity area (Bithell, 1995) using the inverse residential distance from nuclear site, prevailing winds and simulated discharges as surrogates of exposure, (b) the conditional form of Bithell's Linear Risk Score (Bithell, 1995) test with these surrogates of exposure as scores θ_i and (c) the conditional form of Bithell's LRS test with corresponding ranks. *P*-values were obtained by Monte Carlo simulation from the multinomial distribution with $R = 5000$ iterations. Finally, the focused hypotheses tests were complemented by estimating the shape of the exposure–response relationships. To this end, generalized additive models (Wood, 2006) were used. In particular, the Poisson regression model described above is extended by allowing the previously assumed constant RR to vary smoothly as a function of exposure. The smooth function is taken to be a B-splines basis of 10 B-splines of third degree with a second-order discrete smoothness penalty to control for overfitting (Eilers and Marx, 1996). More extended descriptions of the statistical methodology can be found in the study by Bollaerts *et al.* (2015).

Results

Childhood leukaemia incidence around nuclear sites

The final Poisson regression models (Table 1) included as covariates sex, age groups and the linear trend of SES on the basis of the average life span WI. The urbanization index and the interaction between sex and age groups were found not to be significant in the model construction and were excluded from the final model. The overdispersion parameters φ were close to 1, indicating the absence of overdispersion and underdispersion. The Poisson models showed no excess in acute childhood leukaemia (0–14 years) in any of the proximity areas near the NPPs of Doel and Tihange, or near the Fleurus' site. On the Belgian territory around the NPP of Chooz, no cases of acute leukaemia were reported in the period 2004–2008; this site was excluded from further analyses. The RRs around Mol-Dessel were significant for the 0–5, 0–10 and 0–15 km proximity area, but not for the 0–20 km proximity area. The multisite analyses around the four Belgian sites together showed no significant results.

Association between surrogate exposures and childhood leukaemia incidence around nuclear sites

None of the focused hypothesis tests as a function of (i) residential proximity to the site and (ii) prevailing winds was significant for the NPP of Doel and Tihange, the site of Fleurus or the multisite analyses (Table 2). For the NPPs of Doel and Tihange, the site of Fleurus and the four Belgian nuclear sites together, the estimated exposure–response curves as a function of (i) residential proximity and (ii) prevailing winds showed no indications of a gradient in acute childhood leukaemia with increasing levels of surrogate exposure (results not shown). In contrast, for the site of Mol-Dessel, the results of the focused hypothesis tests were predominantly significant (Table 2).

For Mol-Dessel, the estimated exposure–response curves as a function of (i) distance, (ii) prevailing winds and (iii) simulated Ar-41 discharges on the basis of mathematical modelling (Fig. 2) may all be indicative of a gradient in acute childhood leukaemia incidence at 0–14 years with increasing levels of exposure, although some of the curves show strong fluctuations. This gradient is largely driven by the data from one commune, which has a commune-specific RR of 6.81 [95% CI: 2.28–20.32] on the basis of three cases of acute childhood leukaemia. The communes with the second and the third highest incidence rates showed RRs of 3.74 [95% CI: 0.98–14.27] and 4.39 [95% CI: 1.46–13.17], respectively. They are the three communes lying in the dominant wind direction of the Mol-Dessel nuclear site. A map of the communes within the 20 km proximity area around the nuclear site of Mol-Dessel and a table with the RRs and 95% CIs of acute leukaemia incidence 0–14 years by commune in this 20 km proximity area are presented in Appendices B, Supplemental digital content 2, *http://links.lww.com/EJCP/A90* and C, Supplemental digital content 3, *http://links.lww.com/EJCP/A91*, respectively.

Table 1 Rate ratios and 95% confidence intervals of acute leukaemia incidence (0–14 years) for the 0–5, 0–10, 0–15 and 0–20 km proximity area around each nuclear site and the four Belgian nuclear sites together

Proximity area around the nuclear site	Observed number of cases	Person-years at risk	RR (95% CI[a]) adjusted for age and sex	RR (95% CI[a]) adjusted for age, sex and SES
Doel (2002–2008)				
0–5 km	[b]	[b]	[b]	[b]
0–10 km	[c]	74 494	0.31 (0.05–2.08)	0.35 (0.05–2.34)
0–15 km	[c]	146 810	0.32 (0.08–1.22)	0.36 (0.09–1.38)
0–20 km	32	886 699	0.81 (0.57–1.14)	0.84 (0.59–1.19)
Tihange (2004–2008)				
0–5 km	[c]	28 592	0.80 (0.12–5.38)	0.75 (0.11–5.03)
0–10 km	[c]	77 286	0.30 (0.05–2.01)	0.29 (0.04–1.95)
0–15 km	[c]	126 029	0.36 (0.09–1.43)	0.35 (0.09–1.38)
0–20 km	10	269 732	0.86 (0.47–1.58)	0.81 (0.44–1.48)
Fleurus (2004–2008)				
0–5 km	[c]	30 200	0.77 (0.12–5.13)	0.65 (0.10–4.33)
0–10 km	15	279 496	1.24 (0.75–2.04)	1.05 (0.63–1.75)
0–15 km	21	38 5015	1.27 (0.83–1.94)	1.12 (0.73–1.73)
0–20 km	22	502 760	1.01 (0.67–1.53)	0.91 (0.60–1.48)
Mol-Dessel (2002–2008)				
0–5 km	5	45 422	**2.58 (1.10–6.04)**	**2.70 (1.15–6.33)**
0–10 km	11	147 671	1.76 (0.99–3.13)	**1.82 (1.02–3.25)**
0–15 km	15	188 031	**1.90 (1.15–3.11)**	**1.96 (1.19–3.22)**
0–20 km	21	463 902	1.06 (0.69–1.62)	1.09 (0.71–1.61)
Four Belgian nuclear sites together [2002-(2004)-2008]				
0–5 km	7	104 214	1.57 (0.67–3.05)	1.49 (0.64–2.90)
0–10 km	28	581 680	1.22 (0.75–1.61)	1.05 (0.70–1.51)
0–15 km	40	865 237	1.08 (0.77–1.48)	1.04 (0.74–1.41)
0–20 km	85	2 160 499	0.89 (0.70–1.12)	0.87 (0.68–1.09)

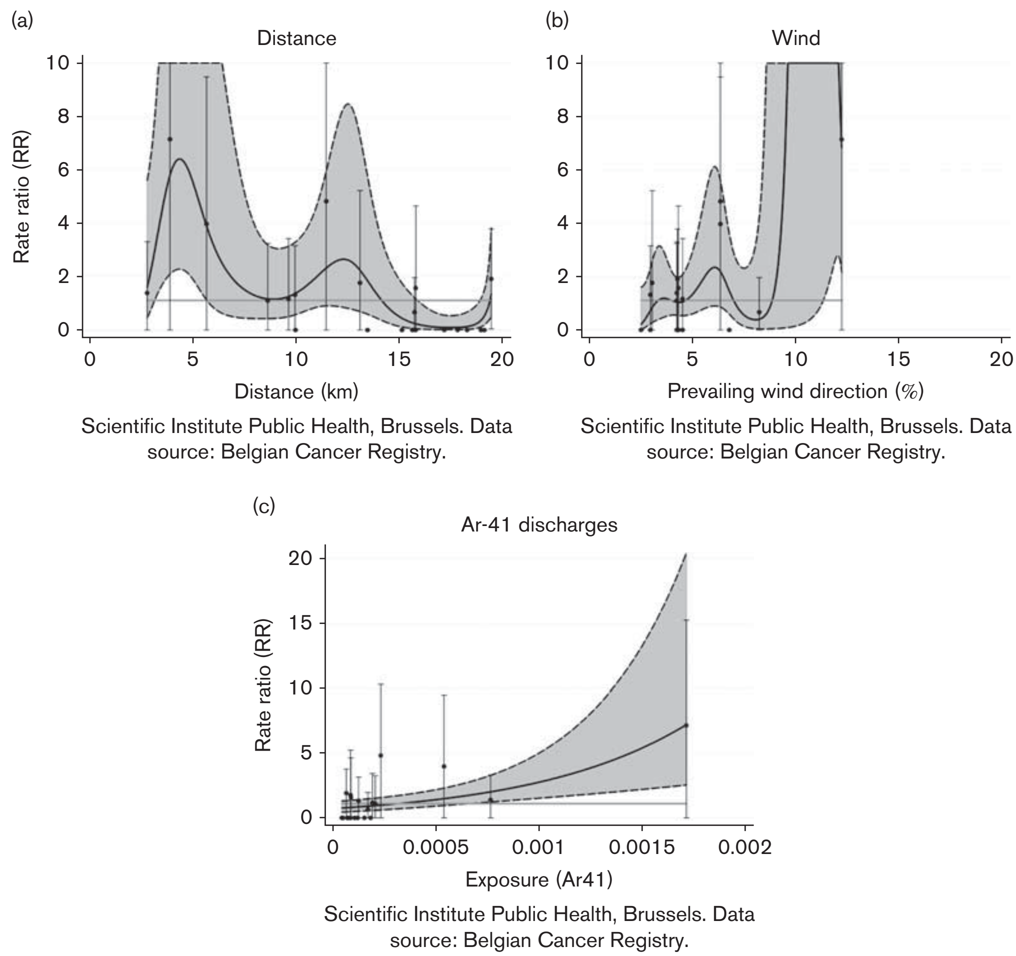
CI, confidence interval; RR, rate ratio; SES, socioeconomic status. Values in bold indicate significantly increased incidence.
[a]95% CI accommodated for overdispersion.
[b]Around the nuclear facilities of Doel, there are no communes with their centroid within the 0–5 km proximity area.
[c]Observed number of cases below 5. For privacy reasons, only numbers greater than or equal to 5 are reported.

Table 2 ***P*-values of Stone's test, Bithell's linear risk score test and Bithell's linear risk score test with corresponding ranks as a function of different measures of surrogate exposure, that is, (i) residential proximity to the nuclear site, (ii) prevailing winds and (iii) simulated radioactive discharges by Ar-41 on the basis of mathematical modelling (only for the site of Mol-Dessel)**

	Proximity			Wind			Ar-41		
	Stone	LRS	LRS^r	Stone	LRS	LRS^r	Stone	LRS	LRS^r
Doel	0.72	0.84	0.86	0.56	0.35	0.53			
Mol-Dessel	< 0.01*	< 0.01*	< 0.01*	0.42	0.01*	0.03*	0.70	< 0.01*	< 0.01*
Fleurus	0.35	0.14	0.12	0.11	0.13	0.41			
Tihange	0.24	0.89	0.91	0.18	0.62	0.47			
Four Belgian nuclear sites together	0.92	1.00	0.99	0.72	0.88	0.93			

LRS, Bithell's linear risk score test; LRS^r, Bithell's linear risk score test with corresponding ranks.
*Significant at $\alpha = 0.05$.

Fig. 2



Rate ratios (RR) and pointwise 95% confidence intervals (grey area) of acute childhood leukaemia incidence (0–14 years) within the 20 km proximity area around the nuclear site of Mol-Dessel as a smooth function of (a) residential proximity to the nuclear site, (b) prevailing winds and (c) simulated Ar-41 discharges. The dashed lines represent the constant RR. The dots (bars) represent the RR (95% CI) for the individual communes within the 20 km proximity area.

Discussion and conclusion

Summary of the findings

This study was designed to detect whether there is evidence of an increased incidence of acute leukaemia in children aged 0–14 years around the Belgian nuclear sites. Around the NPPs of Doel and Tihange and around the nuclear site of Fleurus, no statistical evidence for an increased incidence of acute leukaemia in children aged 0–14 years or an association with the nuclear site was observed. Around the site of Mol-Dessel, however, children aged 0–14 years living in the 0–5, 0–10 and the 0–15 km proximity areas around the site had two- to three-fold increased leukaemia rates. Furthermore, statistically significant associations were found as a function of distance, prevailing winds and the simulated radioactive discharges, potentially indicating a link with the nuclear site. When combining the four Belgian nuclear sites in one analysis, no increased incidence of acute childhood leukaemia was observed.

Childhood leukaemia incidence around nuclear sites

An increase in the incidence of acute childhood leukaemia in the 5 km perimeter closest to the nuclear sites was also observed in the recent French (Sermage-Faure *et al.*, 2012) and German (Kaatsch *et al.*, 2008) case–control studies. More specifically, the German study (KiKK, 1980–2003) found an odds ratio (OR) of 2.19 (lower 95% confidence limit 1.41, on the basis of 37 cases) in children younger than 5 years of age. The French study (Geocap, 2002–2007) reported an OR of 1.9 [95% CI (1.0–3.3), on the basis of 14 cases] for the 0–14-year age category, whereas results for the 0–4 year olds were not significant [OR of 1.6, 95% CI (0.7–4.1), on the basis of six cases]. It is noteworthy that the age ranges for increased leukaemia incidence differ among the studies, that is, 0–14-year-old children in the Belgian and French studies and 0–4-year-old children in the German study. From a medical point of view, however, there is no reason why these results would be inconsistent or there would be a need to focus only on children younger than 5 years of age. Childhood leukaemia is known to have a peak incidence between 2 and 4 years, but children as a whole may be considered as a vulnerable population and latency times may be different as a function of individual characteristics and inducing agents. In contrast to these studies, a British case–control study (Bithell *et al.*, 2013) found little evidence for increased incidences of childhood leukaemia and non-Hodgkin lymphoma in the 5 km perimeter around their NPPs. A Swiss cohort study (CANUPIS, i.e. Childhood Cancer and Nuclear Power Plants in Switzerland) (Spycher *et al.*, 2011) observed non-significant results both in the 0–15-year and in the 0–4-year age categories when using exposure at the time of diagnosis. Finally, a Finnish cohort and case–control study (Heinävaara *et al.*, 2010) could not find indications of an increased incidence of childhood leukaemia in the vicinity of the NPPs. In contrast to the German and French studies that reported increased risks around NPPs, the Belgian study showed an increased risk around one nuclear site that hosts both industrial and research activities, where reprocessing activities have taken place from 1966 until 1974 and where nuclear and radioactive waste treatment is still ongoing.

Association between surrogate exposures and childhood leukaemia incidence around nuclear sites

The current study is the first to investigate the association between acute childhood leukaemia incidence and three surrogate measures of exposure, that is, (i) residential proximity to the nuclear site (distance), (ii) prevailing wind directions and (iii) simulated radioactive discharges on the basis of mathematical dispersion modelling. In addition to several measures of surrogate exposure, different focused hypothesis tests were used. Their combined use yields more complete and robust results. To our knowledge, surrogate exposure modelling has only been used in two French studies (Evrard *et al.*, 2006; Sermage-Faure *et al.*, 2012), where geographical zoning on the basis of the modelling of gaseous discharges was used. In the French studies, no association was observed between childhood leukaemia incidence and geographical zoning. In our study, in contrast, two of the three focused hypothesis tests for radioactive discharges yielded significant results, that is, the Bithell's linear and the Bithell's linear rank test, and the exposure–response model may be indicative for a potential association with the nuclear site. However, the results are strongly influenced by the data from one commune and, hence, need to be interpreted with caution.

Covariates

As the doses attributable to current routine releases have been shown to be too low to explain the increased childhood leukaemia incidences as observed in recent studies (Dionan *et al.*, 1987; Stather *et al.*, 1988; COMARE, 1996; Laurier *et al.*, 2000; Nord-Cotentin Radioecology Group (GRNC), 2000; Strahlenschutzkommission (SSK), 2009; Lane *et al.*, 2013), alternative hypotheses need to be considered such as population mixing, that is the influx of outside workers to rural regions where nuclear installations are being set-up and where local individuals are not immune to pathogens brought along with the incomers (Kinlen hypothesis) (Kinlen, 2011, 2012; Janiak, 2014). Indeed, the site of Mol-Dessel, which hosts a conglomerate of industries and institutes with high-end activities in science and technology, has attracted thousands of individuals from all over the world over the years and still does. As such, we have adjusted the analyses for the commune's socioeconomic (income) and urban–rural status as rough proxies for population mixing that were available from the registers. The results, however, remained similar. This does not firmly exclude a potential effect of population mixing. Such an investigation would require migration data.

Interpretation of the results and study limitations

In conclusion, we found a two- to three-fold increased risk of acute leukaemia for children living in the 0–5, 0–10 and 0–15 km proximity areas around the site of Mol-Dessel. There was, however, no evidence of such findings around the other nuclear sites, and the point estimates for Doel and Tihange were below 1. The statistical power for each site investigation was not much different and adjusting the results for socioeconomic and urban–rural status did not change these findings. The activities at the Mol-Dessel site are of a more varying nature compared with the NPPs and some less controlled releases took place in the past. From a biological point of view, the site of Mol-Dessel is thus the most plausible for an increased incidence of childhood leukaemia.

The results of both the single-site and the multisite analyses are presented. Multisite studies are generally preferred to single-site studies as they have greater statistical power and provide a broader context for the interpretation of results, that is, comparing risks between sites of similar characteristics (Laurier *et al.*, 2014). For the current study and at the cost of reduced statistical power, we have chosen to also carry out single-site analyses as the exposure of the sites under study is not homogeneous, which is a 'conditio sine qua non' for a multisite analysis. Notably, the site of Fleurus and the site of Mol-Dessel host particular types of activities (Bollaerts *et al.*, 2015), and are not comparable to the NPPs. The statistical power for each site separately was low. This may result in false negative (i.e. small exposure effects may be non-significant), but not in false positive results (i.e. significant results are truly significant). We also opted to use the whole of Belgium (not excluding the proximity area of interest) as a reference population, providing a common reference for all comparisons despite the potential dilution of the relative risk estimates.

The study was a first approach to exploring the health risks associated with living in the vicinity of the nuclear sites in Belgium and was based on data that were readily available. The study was carried out at a low cost, but with the limitations inherent to this approach:

(1) An ecological approach was adopted using cancer incidence data aggregated at the level of the commune. Ecological studies are purely descriptive and do not allow one to infer causal relationships on the origin of the clusters. They also do not provide information at the individual level.
(2) Data in the BCR are available for the year of cancer diagnosis and the place of residence of the incident case at the time of diagnosis. Hence, migration phenomena, that is, individuals moving away from or towards the nuclear sites for different reasons, cannot be taken into account. Also, reconstruction of the exposure history of the children (place of birth, residential history, antenatal exposures,…) is not possible.
(3) Several risk factors have been proposed for childhood leukaemia [International Agency for Research on Cancer (IARC) Working Group on the Evaluation of Carcinogenic Risks to Humans, 2002; Buffler *et al.*, 2005; Greaves, 2006; Caughey and Michels, 2009; Kinlen, 2011] including Down syndrome, sex, chemotherapeutic drugs, ionizing radiation, high birth weight, exposure to 50 Hz electric and magnetic fields (ELF-EMF), population mixing, exposure to infectious agents and immune function. We adjusted for some potential risk factors, but for others, the information was lacking in the routinely collected information of registries and surveys; this would require the set-up of new studies at individual level.
(4) A main limitation of the current study is the large geographical level at which health data are currently available in Belgium (i.e. the level of the commune). This may lead to bias towards the null value as well as away from the null value, and thus lead to both spurious increased risk and missing true excess risk (Jurek *et al.*, 2005). Therefore, we recommend making cancer incidence data available at smaller geographical levels (i.e. the statistical sector with an average surface of 1.5 km^2) and repeating the study when data are available over a longer time period.

Acknowledgements
Conflicts of interest
There are no conflicts of interest.

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