



## Childhood leukemia near nuclear sites in Belgium: An ecological study at small geographical level

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### ABSTRACT

**Background:** A previous investigation of the occurrence of childhood acute leukemia around the Belgian nuclear sites has shown positive associations around one nuclear site (Mol-Dessel). In the following years, the Belgian Cancer Registry has made data available at the smallest administrative unit for which demographic information exists in Belgium, i.e. the statistical sector. This offers the advantage to reduce the potential misclassification due to large geographical scales.

**Methods:** The current study performed for the period 2006–2016 uses Poisson models to investigate (i) the incidence of childhood acute leukemia within 20 km around the four Belgian nuclear sites, (ii) exposure-response relationships between cancer incidence and surrogate exposures from the nuclear sites (distance, wind direction frequency and exposure by hypothetical radioactive discharges taking into account historical meteorological conditions). All analyses are carried out at statistical sector level.

**Results:** Higher incidence rate ratios were found for children <15 years (7 cases, RR = 3.01, 95% CI: 1.43;6.35) and children <5 years (< 5 cases, RR = 3.62, 95% CI: 1.35;9.74) living less than 5 km from the site of Mol-Dessel. In addition, there was an indication for positive exposure-response relationships with the different types of surrogate exposures.

**Conclusion:** Results confirm an increased incidence of acute childhood leukemia around Mol-Dessel, but the number of cases remains very small. Random variation cannot be excluded and the ecological design does not allow concluding on causality. These findings emphasize the need for more in-depth research into the risk factors of childhood leukemia, for a better understanding of the etiology of this disease.

### 1. Introduction

The possible health risks associated with living around nuclear installations have been a public concern for several decades. This was particularly boosted by the German KiKK study which showed an increased risk of cancer, especially leukemia, in children living in the vicinity of the German nuclear power plants [1,2].

In Belgium, the Minister of Social Affairs and Public Health commissioned, in 2008, an ecological study to assess the possible cancer risks for populations living near the Belgian nuclear sites with facilities of the highest radiologic risk. Higher incidence of childhood acute leukemia (CL) was observed around one nuclear site with combined industrial and research activities (Mol-Dessel) for the period 2002–2008 [3]. However, this observation was based on only 7 years of data and

**Abbreviations:** BCR, Belgian Cancer Registry; CI, confidence interval; CL, childhood acute leukemia; IMA, Inter Mutualistic Agency; NPP, nuclear power plants; RR, incidence rate ratios.

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potential exposure misclassification due to the large geographical scale at which cancer incidence data was available (the communes) could not be excluded. In 2012, the Minister commissioned a second ecological study at smaller geographical level and over a longer period.

This paper describes results from an ecological study performed at the level of the statistical sectors, which are subdivisions of communes, and including 11 years of data (2006–2016). The statistical sector, defined by the Belgian statistical office (Statbel) on the basis of social, economic and urban characteristics, is the smallest Belgian administrative unit. Such data has the advantage of reducing the risk of misclassification of the exposure and ecological bias thanks to a smaller within-area variation [4–6].

More specifically, the study investigates whether there is a higher incidence of CL within 20 km around the Belgian nuclear sites and, in a second phase, whether there is evidence for exposure-response relationships in cancer incidence with increasing surrogate exposures from the nuclear sites.

## 2. Material and methods

### 2.1. Geographical data, population and cancer data

Belgium counts 19,782 statistical sectors with an average surface area of 1.5 km<sup>2</sup> and an average population of 573 inhabitants in 2016 (ranging from 1 to 8,288). In comparison, there are 589 communes in Belgium, with averaged area of 50 km<sup>2</sup> and population count of 19,130 inhabitants.

Information on the statistical sector of residence was available in data collected by the InterMutualistic Agency (IMA) which gathers demographic, socio-economic and reimbursement data concerning the members of the health insurance funds, and reliable from 2006 onwards. Population data were provided by sex, 5-year age groups (0–4, 5–9 years and 10–14 years) and statistical sector at December 31<sup>st</sup> for every year from 2006 to 2016. In 2016, the IMA collected information on a population of 11,106,119 people, including 1,871,509 children (< 15 years). Given the obligatory health insurance in Belgium, the IMA data can be considered quasi population-based.

CL cases, provided by the Belgian Cancer Registry (BCR), a national population-based registry, were selected according to the ICD-O-3 codes (see Supplementary Material). Children diagnosed with acute lymphoid or myeloid leukemia between 2006 and 2016 and aged < 15 years at the time of diagnosis were included in the study, together with information on the sex, age at diagnosis (by 5-year age groups), year of diagnosis, and statistical sector of residence the year of diagnosis (after coupling with IMA data). The BCR has an estimated >95% overall completeness [7] thanks to linkage of data from different sources and source types (paediatric centres, pathology/clinical biology, hospitals/health insurance) [8].

### 2.2. Nuclear sites

Belgium has four nuclear sites with facilities of the highest radiologic risk (defined as Class I facilities). Doel and Tihange are electricity-generating nuclear power plants (NPP). Mol-Dessel primarily consists of the Belgian Nuclear Research Centre and hosts a combination of nuclear activities (applied research and metrology, scientific and technological research and operational waste management). Fleurus primarily consists of the Institute for radioelements, a major production site of radioiodine for usage in diagnostic and therapeutic nuclear medicine (see [9] for a detailed description of the sites).

### 2.3. Surrogate exposures and covariates

Three surrogate exposures were considered: (i) the distance between the nuclear site and the centroid of the statistical sector; (ii) the wind direction frequency which corresponds to the percentage of time that the

dominant wind blows from the nuclear site towards the statistical sector, calculated using wind speed and directions data collected by the Federal Agency for Nuclear Control using survey stations and provided for the period 2006–2016; and (iii) an exposure by hypothetical radioactive discharges estimated on the basis of a mathematical dispersion model [10], taking into account historical meteorological conditions (see Supplementary Material for more details). We only performed this modelling for the one site with increased incidence and significant associations with distance and with wind frequency (i.e. Mol-Dessel, see 3.1 Incidence of childhood leukemia around the nuclear sites).

A socio-economic index, based on data derived from the 2001 Belgian census [11], was defined for the statistical sectors. Five variables from this survey, each representing an objective dimension of deprivation, were selected to construct the index, defined as the first component of a principal component analysis [12] of those variables (unemployment rate, percentage of people ≥ 18 years without higher education, percentage of households without a car, percentage of households without basic conveniences and percentage of households renter-occupied). Next to the index, we used income data derived from fiscal statistics on net taxable income provided by Statbel. Because income varies strongly over time, we used this information on a yearly basis, for the year preceding the cancer diagnosis. Finally, the latest update of the degree of urbanization defined by Eurostat for the Belgian communes was used as an indicator of urbanization [13] (see Supplementary Material for a detailed description of these variables).

### 2.4. Statistical methods

To investigate whether there is a higher incidence of CL around the nuclear sites, incidence rate ratios (RR) were obtained from a zero-inflated model [14] with Poisson distribution including the distance from the nuclear site (defined as 0–5 km, >5–10 km, >10–15 km and >15–20 km, as well as 0–10 km, 0–15 km and 0–20 km), age, sex, incidence year, socio-economic index, median household income and degree of urbanization. Over-(under)dispersion of the data was assessed using the Pearson Chi-2 estimator. The final model was selected using a backward elimination based on the Akaike Information Criterion (AIC) of the models.

The statistical power of the analyses for 5 and 20 km distances from the nuclear sites was calculated using Monte Carlo simulations for alternative hypotheses defined in line with the literature, i.e. RR of 1.1, 1.2, 1.5, 2 and 3 (see Supplementary Material).

Generalized additive models [15] were used to investigate the shapes of the exposure–response relationships between CL incidence and each surrogate exposure in the 20 km around the sites. The model described above was extended by allowing the previously assumed constant RR to vary smoothly as a function of exposure. This function was a B-splines basis of 10 B-splines of third degree with a second-order discrete smoothness penalty to control for overfitting [16]. This investigation was complemented by three tests of the hypothesis of positive gradients in CL incidence with levels of exposure: the conditional form of Stone's test [17], Bithell's Linear Risk Score test [18] with these exposures as scores (LRS), and with corresponding ranks (LRS rank). P-values were obtained with Monte Carlo simulations from the multinomial distribution with 5,000 iterations (see [19] for a more detailed description of the statistical methods).

### 2.5. Supplementary analyses

Supplementary analyses were performed to investigate in further details the incidence of childhood leukemia around the nuclear sites. In line with the literature, we considered two additional potential confounders for which data were available at the level of the commune or statistical sector: radon [20] and NO<sub>2</sub> as a marker of outdoor air pollution [21] (see Supplementary Material).

In the main analysis, distances were calculated from the first research

reactor in Mol-Dessel. However, this reactor has not been in continuous operation and a second reactor has become more important over time. We performed a sensitivity analysis by calculating distances from the latter (several hundred meters apart from the first reactor).

Data of the present study (2006–2016) were not completely independent of data from our previous work (period 2002–2008 and with the communes as geographical entities) [3]. Therefore, we ran an extra analysis without years of overlap (i.e. for the period 2009–2016).

Finally, we assessed whether the observed RR around the nuclear sites were exceptional or not as compared to other areas in Belgium. To this purpose, the centroid of every statistical sector ( $i = 1; 2; \dots; 19,782$ ) was considered consecutively as the middle point of a circle with radius 5 km, and we used Poisson models described above to calculate the corresponding RR estimates ( $N = 19,782$ ).

### 3. Results

Over the period 2006–2016, 884 CL cases aged < 15 years were registered at the BCR. For 855 cases, a coupling with IMA data was possible. 808 cases for whom valid information on statistical sector was available were included in the analyses (405 cases aged < 5 years). The 47 cases with non-valid statistical sector appear to be geographically randomly distributed, based on the commune of residence (see Supplementary Material).

The 0–5 km and >5–10 km circles around the Belgian nuclear sites included the centroids of, respectively, 296 statistical sectors (median surface  $Q_2$ : 0.44 km<sup>2</sup>;  $Q_1$ : 0.27 km<sup>2</sup> –  $Q_3$ : 0.88 km<sup>2</sup>) and 657 statistical sectors (median surface  $Q_2$ : 0.47 km<sup>2</sup>;  $Q_1$ : 0.26 km<sup>2</sup> –  $Q_3$ : 1.17 km<sup>2</sup>). The detailed distribution of statistical sector sizes around the nuclear sites is given in Table A.1.

#### 3.1. Incidence of childhood leukemia around the nuclear sites

RR adjusted for age, sex, socio-economic index and median household income, and their 95% confidence interval (CI) were obtained for the 0–5 km, >5–10 km, >10–15 km and 15–20 km distances from the nuclear sites in children aged < 15 and < 5 years, specifically (Table 1). In the vicinity of the nuclear sites of Doel, Tihange and Fleurus, non-

significant RR were observed. Around Mol-Dessel, compared with children living more than 5 km from the site, a higher RR was found for children aged < 15 years (RR = 3.01, 95% CI: 1.43;6.35) and < 5 years (RR = 3.62, 95% CI: 1.35;9.74). These RR estimates were higher than, respectively, 96.6% and 95.8% of the 5-km circles zones (see 2.5 Supplementary analyses). Multisite analyses showed a higher RR for children < 15 years living less than 5 km from the sites (RR = 1.65, 95% CI: 1.07;2.55) (Table 2). This result became non-significant when the site of Mol-Dessel was excluded (RR = 1.34, 95% CI: 0.79;2.28) (Table 2). In children < 5 years, RR was non-significant for all sites together (RR = 1.37, 95% CI: 0.70;2.65) and when Mol-Dessel was excluded (RR = 0.55, 95% CI: 0.18;1.71). The additional results for the 0–5 km, 0–10 km, 0–15 km and 0–20 km distances are given in Table A.2 (see Supplementary Material).

In the statistical power investigation for 5 km distances around the sites, the analyses of all sites together showed a sufficient power (i.e. more than 80%) to detect a  $RR \geq 2$ , while in the single-sites analyses, a RR of at least 3 can be detected with a power >80% around Tihange and Fleurus only (Table A.3). All-sites and single-sites analyses showed a sufficient statistical power to detect a  $RR \geq 1.5$  within 20 km except around the sites of Tihange and Mol-Dessel (64 and 67%, respectively).

Additional adjustment for radon or outdoor air pollution (NO<sub>2</sub>) exposures did not change the results (see Fig. A.1 and Fig. A.2 in Supplementary Material). RR estimates resulted in small changes when calculating distances from the second Belgian reactor of Mol-Dessel: RR = 2.80 (95% CI: 1.32;5.90) for children aged < 15 living less than 5 km from the reactor (data not shown). For the period 2009–2016 (Table A.4), results around Doel, Tihange, Fleurus and for the > 5 km circles around Mol-Dessel remained non-significant. Within 5 km around Mol-Dessel, children aged < 5 years showed similarly increased RR (RR = 3.55, 95% CI: 1.13;11.17). In children < 15 years, the results became non-significant (RR = 1.70, 95% CI: 0.55;5.30). These RR estimates were higher than, respectively, 94.5% and 74.3% of the 5-km circles zones (see 3.5 Supplementary analyses).

**Table 1**

Incidence rate ratios (RR) and 95% confidence intervals (CI) according to 0-5 km, >5-10 km, >10-15 km and >15-20 km statistical sectors distances from each nuclear site for the period 2006-2016 in children < 15 years and < 5 years.

Distance from the nuclear site	Age < 15 years				Age < 5 years				
	PY	O	E	RR (95% CI)	PY	O	E	RR (95% CI)	
Doel	0–5 km	6,742	<5	0.3	0.00 (0.00;Inf)	2,044	<5	0.1	0.00 (0.00;Inf)
	>5–10 km	46,181	<5	<5	0.48 (0.07;3.40)	13,510	<5	1.0	0.00 (0.00;Inf)
	>10–15 km	273,808	7	12.0	0.57 (0.27;1.20)	83,741	<5	<10	0.33 (0.08;1.31)
	>15–20 km	1,024,598	42	46.3	0.93 (0.68;1.27)	351,172	21	25.1	0.85 (0.55;1.32)
Tihange	0–5 km	78,706	5	3.5	1.46 (0.61;3.52)	24,737	<5	<5	1.71 (0.55;5.31)
	>5–10 km	68,617	7	3.0	1.68 (0.70;4.04)	19,907	<5	<5	x
	>10–15 km	129,585	7	5.6	1.24 (0.59;2.62)	38,301	<5	<5	0.72 (0.18;2.90)
	>15–20 km	289,633	13	12.8	1.02 (0.59;1.77)	91,512	5	6.5	0.76 (0.31;1.84)
Mol-Dessel	0–5 km	54,485	7	2.3	3.01 (1.43;6.35)	15,699	<5	<5	3.62 (1.35;9.74)
	>5–10 km	111,785	7	4.8	1.46 (0.69;3.08)	31,962	<5	<5	1.77 (0.66;4.76)
	>10–15 km	157,078	8	6.7	1.19 (0.59;2.39)	44,934	<5	<5	1.25 (0.47;3.37)
	>15–20 km	308,632	19	13.3	1.43 (0.90;2.26)	90,534	9	6.5	1.40 (0.72;2.73)
Fleurus	0–5 km	158,110	9	7.0	1.33 (0.69;2.58)	50,879	<5	<5	0.55 (0.14;2.21)
	>5–10 km	391,779	15	17.5	0.88 (0.52;1.47)	129,614	7	9.3	0.75 (0.35;1.60)
	>10–15 km	288,696	17	12.6	1.36 (0.84;2.20)	87,747	11	6.3	1.77 (0.97;3.22)
	>15–20 km	274,893	10	11.9	0.82 (0.44;1.54)	81,867	6	5.9	1.01 (0.45;2.26)

PY: person-years, O: observed and E: expected number of cases, RR (95% CI): incidence rate ratios and their 95% confidence intervals based on a zero-inflated Poisson model, adjusted for age, sex, socioeconomic index and median income of the place of residence.

x: no estimate because of missing covariate values (socioeconomic index and median income).

Age at diagnosis, statistical sector at the end of the year of diagnosis.

For privacy protection (risk of identification of individuals), observed number of cases < 5 are not provided (as well as their corresponding expected number of cases).

**Table 2**

Incidence rate ratios (RR) and 95% confidence intervals (CI) for all sites and all sites except Mol-Dessel according to 0-5 km, >5-10 km, >10-15 km and >15-20 km statistical sectors distances from the nuclear sites for the period 2006-2016 in children < 15 years and < 5 years.

Distance from the nuclear site	Age < 15 years		Age < 5 years		
	PY	RR (95% CI)	PY	RR (95% CI)	
All sites	0-5 km	298,043	1.65 (1.07;2.55)	93,359	1.37 (0.70;2.65)
	>5-10 km	618,362	1.04 (0.71;1.52)	194,993	0.78 (0.43;1.43)
	>10-15 km	849,167	1.05 (0.76;1.45)	254,723	1.04 (0.65;1.65)
	>15-20 km	1,897,756	1.01 (0.81;1.27)	615,085	0.94 (0.68;1.30)
All sites except Mol-Dessel	0-5 km	243,558	1.34 (0.79;2.28)	77,660	0.55 (0.18;1.71)
	>5-10 km	506,577	0.95 (0.61;1.47)	163,031	0.97 (0.53;1.78)
	>10-15 km	692,089	1.02 (0.71;1.46)	209,789	0.89 (0.51;1.55)
	>15-20 km	1,589,124	0.93 (0.72;1.20)	524,551	0.92 (0.64;1.31)

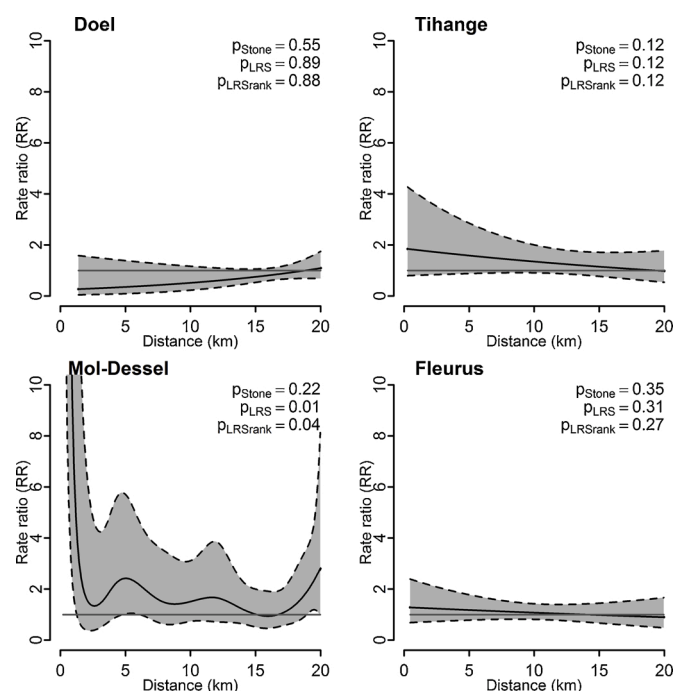
PY: person-years, RR (95% CI): incidence rate ratios and their 95% confidence intervals based on a zero-inflated Poisson model, adjusted for age, sex, socioeconomic index and median income of the place of residence.

Age at diagnosis, statistical sector at the end of the year of diagnosis.

Observed number of cases are not provided (as well as their corresponding expected number of cases) because this would allow to calculate single-site observed number of cases which are not provided in Table 1 for privacy protection (risk of identification of individuals).

**3.2. Relationship between incidence of childhood leukemia and surrogate exposures**

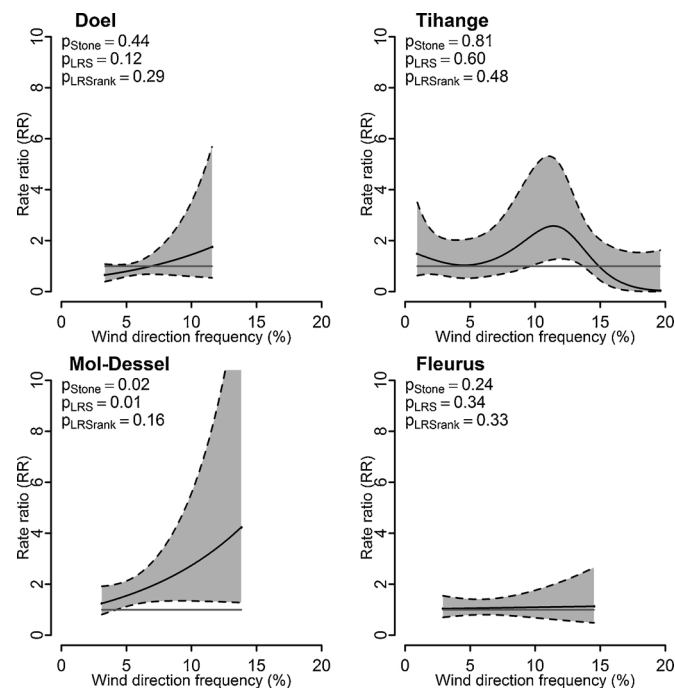
For the nuclear sites of Doel, Tihange and Fleurus, none of the exposure-response relationships between CL incidence and distance (Fig. 1) or wind direction frequency (Fig. 2) showed significant results. For the site of Mol-Dessel, the results of the exposure-response relationships investigation showed predominantly significant results for all surrogate exposures investigated, except for Xenon-133 (Fig. 3) and may indicate a positive gradient between CL incidence and surrogate exposures.



**Fig. 1.** Exposure-response relationship with distance from the site. Incidence rate ratios (RR) and 95% confidence intervals (dotted lines) of childhood leukemia incidence within the 20 km around the nuclear sites as a smooth function of the distance from the site and corresponding p-values of the Stone's test, the Bithell's Linear Risk Score test (LRS) and the Bithell's Linear Risk Score test with rank (LRS rank) for the period 2006-2016 in children < 15 years.

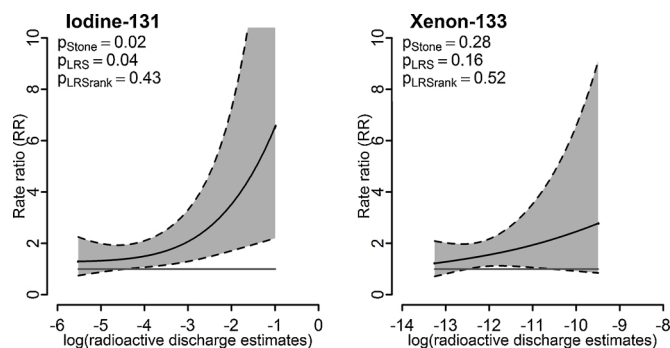
**4. Discussion**

In the investigation of the incidence of childhood acute leukemia around Belgian nuclear sites, no evidence was found for more incident cases of childhood leukemia near the nuclear power plants of Doel and Tihange, nor the nuclear site of Fleurus. A significantly higher incidence was observed in the close vicinity of Mol-Dessel, a research and industrial nuclear site. In addition, there was an indication for positive exposure-response relationships with the different types of surrogate exposures considered. The results of this second investigation



**Fig. 2.** Exposure-response relationship with wind direction frequency. Incidence rate ratios (RR) and 95% confidence intervals (dotted lines) of childhood leukemia incidence within the 20 km around the nuclear sites as a smooth function of the wind direction frequency and corresponding p-values of the Stone's test, the Bithell's Linear Risk Score test (LRS) and the Bithell's Linear Risk Score test with rank (LRS rank) for the period 2006-2016 in children < 15 years.





**Fig. 3.** Exposure-response relationship with hypothetical radioactive discharge estimates. Incidence rate ratios (RR) and 95% confidence intervals (dotted lines) of childhood leukemia incidence within the 20 km around the nuclear site Mol-Dessel as a smooth function of the hypothetical radioactive discharge estimates and corresponding p-values of the Stone's test, the Bithell's Linear Risk Score test (LRS) and the Bithell's Linear Risk Score test with rank (LRS rank) for the period 2006–2016 in children < 15 years.

(2006–2016) confirm results of the first investigation (2002–2008) that also observed increased risks nearby Mol-Dessel. RR in children < 15 years are slightly higher for 2006–2016 as compared to 2002–2008 (5 cases, RR = 2.70, 95% CI: 1.15;6.33) [3].

The above results show that the number of cases remains very small and results unstable. This was confirmed by an extra analysis including only non-overlapping years (2009–2016, statistical sectors), which gave non-significant results in children < 15 years and RR similar to 2006–2016 in children < 5 years. As such, we cannot exclude random variation as possible explanation for our findings.

Higher incidence of childhood acute leukemia was also found when considering the four nuclear sites together but these results became non-significant when the site of Mol-Dessel was excluded. Multi-site analyses offer a greater statistical power than single-site analyses. We have however chosen for single-site investigations because the four Belgian nuclear sites give rise to non-homogeneous exposures: as compared to the two nuclear power plants of Doel and Tihange, the sites of Fleurus and Mol-Dessel host particular types of industrial and research activities, these activities being of a more varying nature in Mol-Dessel [9]. It was of interest to investigate whether the observed incidence pattern could be compatible with levels of radiation exposure from this site. However, levels of radioactivity of the surrounding air measured by the Federal Agency for Nuclear Control are often below the detection limit of the routine environmental monitoring in Belgium. Therefore, the surrogate exposure was based on strictly hypothetical and modelled estimates, not on radiation doses. This surrogate exposure is radio-ecologically more plausible than distance or wind direction (which assume that the risk would decrease with distance independently of the direction, or inversely) but the potential bias of measurement error may be more pronounced because it combines distance and wind direction uncertainties.

Based on the available evidence, our estimations of risk would be expected after exposures to high doses of radiation such as levels received after nuclear accidents, and levels of radiation met during routine operations are not expected to cause an excess risk of childhood leukemia [22]. Moreover, they are lower than levels of radiation coming from other sources (e.g., cosmic, terrestrial or medical irradiation).

Most of the studies on childhood leukemia and nuclear sites concern nuclear power plants. Our results are in line with the German KiKK [1,2] and French GEOCAP [23] studies which showed higher risks of leukemia in children < 5 years living less than 5 km from a nuclear power plant. Studies in Great Britain [24], Switzerland [25], Finland [26] and Canada [27] showed very little or, for most of them, no association.

Contrary to our investigations on thyroid cancer incidence [28], we did not apply Bayesian hierarchical models [29] to calculate smoothed

incidence rate ratios. In this study, low observed information (i.e. small number of cases due to very low incidence rates and small populations) led to non-robust results due to a very strong dependence of the estimates with regard to the prior structure specification. In general, smoothing methods produce more stable estimates by avoiding chance variations related to small numbers [4]. In our case, results are based on very small numbers and we cannot exclude that areas identified as high-risk areas are false positive findings. However, smoothing methods have been shown to perform poorly in terms of their abilities to detect areas with true excess in case of low observed information since risk estimates in the latter might be smoothed away [4,5,30].

The study presents some drawbacks related to its ecological design, such as misclassification of the exposure and ecological bias [6]. These limitations cannot completely be ruled out but were reduced through the use of data aggregated at a small geographical level [6]. In this context, it is noteworthy that we could not account for several known individual risk factors, including high doses of ionizing radiation received for medical purposes [31], genetic anomalies [32] or high birth weight [33, 34]. It seems less likely that these potential individual risk factors have been biasing our estimates because, to the authors' knowledge, their distribution is not expected to be associated with the proximity to the nuclear sites. This also includes personal mobility before the time of diagnosis (although children are less prone to this phenomenon than adults) e.g. commuting between the residential and daytime locations (school, nurseries) as well as change of residence. In our case, residential history before diagnosis was not available at the level of the statistical sectors. However, we observed that of 829 cases for whom the commune of birth was available, 73.1% still lived in the same commune at time of diagnosis. 87.5% of the cases did not migrate between communes in the two years prior to diagnosis. Including residential history would certainly improve the exposure assessment but strong correlations between exposure estimates in successive dwellings have often been observed [35]. Exposure estimated at a single address, being the residential address at birth or at diagnosis, may thus be equally relevant.

We could also not consider infections and immunological characteristics as potential individual risk factors. Following the "population mixing hypothesis" by Kinlen [36,37], the immune system of children residing in isolated areas meets a less diverse range of infectious agents, rendering them more likely to develop leukemia once exposed to novel infections from inward migrants. The three communes in the close vicinity of the Mol-Dessel site are, however, classified as intermediate density areas in the urbanization index, and not as isolated areas. Nevertheless, it could be of interest to better describe population density as well as quantify inward migration in these areas [38,39].

In this investigation at small-area level and including more years of follow-up, higher incidences of childhood leukemia were observed around one nuclear site in Belgium. Results are based on very small numbers and random variation cannot be excluded as an explanation. Moreover, because of its ecological design, this study does not allow inferring causal relationships on the origin of variations in incidence. Therefore, more in-depth research into the risk factors of childhood leukemia may be useful to come to a better overall understanding of the etiology of this disease.

## Contributions

Claire Demoury: acquisition of data, analysis and interpretation of data, drafting the article, final approval of the version to be published

Christel Faes: substantial contributions to conception and design, revising it critically for important intellectual content, final approval of the version to be published

Harlinde De Schutter: substantial contributions to conception and design, analysis and interpretation of data, revising it critically for important intellectual content, final approval of the version to be published

Sylviane Carbonnelle: analysis and interpretation of data, revising it

critically for important intellectual content, final approval of the version to be published

Michael Roszkamp: analysis and interpretation of data, revising it critically for important intellectual content, final approval of the version to be published

Julie Francart: analysis and interpretation of data, revising it critically for important intellectual content, final approval of the version to be published

Nancy Van Damme: analysis and interpretation of data, revising it critically for important intellectual content, final approval of the version to be published

Lodewijk Van Bladel: substantial contributions to conception and design, revising it critically for important intellectual content, final approval of the version to be published

An Van Nieuwenhuysse: substantial contributions to conception and design, revising it critically for important intellectual content, final approval of the version to be published

Eva M. De Clercq: substantial contributions to conception and design, revising it critically for important intellectual content, final approval of the version to be published

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The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## CRedit authorship contribution statement

**Claire Demoury:** Conceptualization, Software, Formal analysis, Writing - original draft, Writing - review & editing. **Christel Faes:** Methodology, Writing - review & editing. **Harlinde De Schutter:** Conceptualization, Writing - review & editing. **Sylviane Carbonnelle:** Conceptualization, Writing - review & editing. **Michael Roszkamp:** Resources, Writing - review & editing. **Julie Francart:** Resources, Writing - review & editing. **Nancy Van Damme:** Resources, Writing - review & editing. **Lodewijk Van Bladel:** Conceptualization, Writing - review & editing. **An Van Nieuwenhuysse:** Conceptualization, Writing - review & editing, Supervision. **Eva M. De Clercq:** Conceptualization, Writing - review & editing, Supervision, Project administration.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.canep.2021.101910>.

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