Environmental Research 188 (2020) 109681

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Cancer incidence in the vicinity of a waste incineration plant in the Nice area between 2005 and 2014

Eugènia Mariné Barjoan[a,*], Nadège Doulet[a], Amel Chaarana[a], Julie Festraëts[a], Agnès Viot[a], Damien Ambrosetti[b,c], Jean-Luc Lasalle[d], Nicolas Mounier[e], Laurent Bailly[a], Christian Pradier[a]

[a] Université Côte d'Azur, Public Health Department, Centre Hospitalier Universitaire de Nice, France
[b] Université Côte d'Azur, Anatomo-Pathology Laboratory, Centre Hospitalier Universitaire de Nice, France
[c] Centre de Regroupement Informatique et Statistique en Anatomie et Cytologie Pathologique (CRISAP PACA), France
[d] Santé Publique France, Regional Office Provence-Alpes-Côte d'Azur and Corsica, France
[e] Université Côte d'Azur, Clinical Hematology Department, Centre Hospitalier Universitaire de Nice, France

ARTICLE INFO

Keywords:
Cancer
Incidence
Trends
Waste incineration plant
EU directive

ABSTRACT

Introduction: Few studies on cancer incidence have been conducted since the adoption of the EU 2000/76/EC waste incineration directive which aimed to limit dioxin emission levels to less than 0.1 ng TEQ/m^3 before December 31, 2005.
Objective: To measure cancer incidence among the population exposed to atmospheric emissions from the waste incineration plant near the town of Nice (South-Eastern France), compared to the unexposed population of the Alpes-Maritimes department (A-M).
Methods: All primary invasive cancers and haematological malignancies diagnosed among AM residents between 2005 and 2014 were recorded. The exposed surface was modeled on an average dioxin deposition model $\geq$4.25 ng/m^2/year. Each case was geolocated and assigned to one of 36 predefined geographic units of exposed area, or one of 462 units in the unexposed area. The adjusted incidence rate, the standardized incidence ratio and the Comparative Morbidity Figure were calculated for two periods: 2005–2009/2010-2014.
Results: We recorded 80,865 new cancers in the A-M population. Between 2005 and 2009, we observed a higher incidence among exposed women of acute myeloid leukaemia, myelodysplastic syndromes and myeloma and, among exposed men, of soft tissue sarcomas, myeloma and lung cancer. Between 2010 and 2014, there was no excess incidence among women, while among men incidence of myeloma and lung cancer remained higher.
Conclusion: Only among men, the incidence of myeloma and lung cancer remained higher in the exposed area during the second period. The EU directive resulting in the limitation of atmospheric emissions from incinerators could explain the decrease in incidence of cancers with protracted latency. Consideration of other risk factors and further data collection will be necessary to validate this hypothesis.

1. Introduction

Incineration remains the main means of disposal of solid domestic waste in France. Up to 2005, this was the leading source of pollution, namely due to the emission of dibenzo-p-dioxins and dibenzofurans (PCDD/F) (T. Coudon et al., 2019a, 2019b; Serveau et al., 2015) with proven toxicity to human health (Baan et al., 2009; IARC, 1997).

In 1991, France adopted the 1989 EU waste incineration directive (Journal Officiel République française, 1991). It concerned IUOMs (Unité d'incinération des ordures ménagères, i.e. domestic waste incineration unit) with a capacity of at least 6 tonnes per hour but it did not mention any limit value for dioxin emissions. The UIOM of the city of Nice complied with the directive in 1997. At that time, dioxin levels measured in France for household waste incinerators respecting the operating conditions set by the 1991 decree ranged between 1 and 10 ng/m3.

In December 2005, incinerators within EU member states were expected to have complied with the standards established in the European Community December 4, 2000 waste incineration directive (EU, 2000/76/EC) which cut dioxin emission levels down to less than 0,1 ng TEQ/m^3 (Journal Officiel de la Communauté Européenne, 2000; Journal Officiel République française 2002). Several epidemiological studies

* Corresponding author. Centre Hospitalier Universitaire, Hôpital Archet1, Département de Santé Publique, Rte St Antoine de Ginestière Niveau 1 CS23079, 06202, NICE cedex 3, France.
E-mail address: marine-barjoan.e@chu-nice.fr (E. Mariné Barjoan).

https://doi.org/10.1016/j.envres.2020.109681
Received 12 February 2020; Received in revised form 30 April 2020; Accepted 10 May 2020
Available online 20 May 2020
0013-9351/

conducted among residents living close to older generation incinerators have demonstrated a link between residing in the vicinity of an incinerator and the occurrence of certain malignancies (Comba et al., 2003; Elliott et al., 2000; Floret et al., 2003; Knox, 2005; Viel et al., 2000). However, a report by the World Health Organisation (WHO) concluded that the results of these studies should be interpreted with caution as they were conducted before 2007, when concomitant environmental factors were present, and in the absence of causality criteria (World Health Organization. Regional Office for Europe, 2007). Two recent meta-analyzes highlight the importance of the type of incinerator when analyzing the results (Negri et al., 2020; Tait et al., 2019). Thus Negri et al. reach the conclusion that although the link between certain cancers and incinerators has been demonstrated for 1st and 2nd generation incinerators (incinerators active before 2006), no analysis is available for 3rd generation incinerators.

The most recent epidemiological studies, which were all conducted on data from before 2005, showed that residing in an area exposed to smoke plumes from incinerators was associated with certain malignancies, namely non-Hodgkin's lymphoma (Viel et al., 2011), soft tissue sarcoma (Zambon et al., 2007), breast cancer, multiple myeloma (Daniau et al., 2009), leukaemia (Bertazzi et al., 2001), or lung cancer (Biggeri et al., 1996). In 2005, an epidemiological study was conducted in France by the French public health surveillance institute (Institut de Veille Sanitaire, InVS), in partnership with the French agency for health and food safety (Agence nationale de sécurité sanitaire, de l'alimentation, de l'environnement et du travail, ANSES), to estimate soil contamination with dioxins and the impact of consumption of local products among populations living in the vicinity of domestic waste incinerators (Fréry et al., 2009). It showed that residents living close to furnaces complying with the standards of the time did not display higher concentrations of dioxins, lead or cadmium; however, excess impregnation was found among residents living close to highly polluting older installations and consuming large quantities of local animal products (eggs, animal fat and milk products).

The Nice Côte d'Azur Metropolis (NCA) is equipped with a domestic waste incineration facility in the North-Eastern suburb of l'Ariane, a highly densely populated area through which run major roads, and which includes shared plots where olive oil is commonly produced and consumed. Over the past years, local residents' organisations have raised the issue of potential health-related risks. To assess these risks, the NCA authorities approached Nice University Hospital (Centre Hospitalo Universitaire de Nice) to conduct an epidemiological investigation focusing on the occurrence of cancer within the area exposed to the smoke plume arising from the facility.

The main objective of this study was to assess cancer incidence among the population exposed to atmospheric emissions from the Ariane waste disposal facility and to determine whether the number of cases among this population exceeded that recorded among the remaining population of the A-M.

2. Methods

This is a descriptive ecological study of the spatial distribution of cancer incidence between 2005 and 2014 among the population living in the area exposed to the atmospheric emissions of the Ariane waste disposal facility and among the A-M population. A multidisciplinary steering committee was set up, bringing together various administrations, residents' organisations, and the Nice University Hospital Public health department. The study was approved by the Ethics Committee and by the French National Commission for Data Protection and Privacy (CNIL, Authorisation N°913023).

The Ariane UIOM is located in the furthest North-eastern part of the city of Nice, at the entrance of the Paillon valley, through which runs the Paillon River descending from the relatively rugged hills of the hinterland. The unit comprises four furnaces in operation since 1977 (furnaces 1 & 2), 1982 (furnace n°3) and 1998 (furnace n°4). The Ariane unit achieved compliance with European standards in December 2005.

The study included all patients diagnosed with an invasive tumour between January 2005 and December 2014 who resided in the A-Ms area at the time of diagnosis. According to International association of cancer registries guidelines (Jensen et al., 1991), the date of incidence is the date of the first pathology report or, for cases lacking a histological diagnosis, that of admission for the first diagnostic investigation. Cutaneous basal-cell carcinomas were excluded. All other cancers were included in the analysis, and more specifically lung, laryngeal, breast, liver, bladder, soft tissue sarcoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, multiple myeloma and the various forms of leukaemia. We also analysed cases of myelodysplastic and chronic myeloproliferative syndromes. Non-Hodgkin's small-cell lymphomas, which are indolent forms of lymphoma, were analysed separately, due to their longer latency period. NHL were thus studied according to criteria put forward in 2018 by the French public health surveillance institute (InVS) (Salel et al., 2019). Following the analysis of the various forms of leukaemia, only acute myeloid leukaemia was included (Bertazzi et al., 2001; Monnereau et al., 2013).

Lastly, we compared our incidence rates to those recorded between 2003 and 2007 in the Bas-Rhin (East), Loire Atlantique (West, Atlantic) and Hérault (South, Mediterranean) cancer registers which have similar socio-geographic characteristics (Forman et al., 2014), as well as those observed for France in 2012 (Binder Foucard et al., 2013).

2.1. Case sources

Cancer cases were extracted from the ongoing and validated CRISAP PACA cancer observatory [Centre de Regroupement Informatique et Statistique en Anatomie Pathologique en Provence–Alpes–Côte d'Azur], a database managed by the Public Health Department, Nice University Hospital, since 2005, in which histological findings are coded by the pathologists (Bailly et al., 2009). Cases for which no histological diagnosis was available were obtained via the Medical Information Departments of the A-M and nearby public and private healthcare institutions (CIM-10 main or associated discharge diagnosis coded C00 to C97) and haematology laboratories [Extraction criteria as described in the Recommendations for recording haematological malignancies in cancer registries published by French cancer registries network (FRANCIM:Réseau Français des registres du cancer (https://www.encr.eu/node/382)] and InVS (Salel et al., 2019). Data were collected from patients' medical records by two Clinical Research Associates familiar with the extraction of medical data and by a physician for haematological malignancies. The organ, the histological characteristics and the behaviour of the tumour were recoded as CIM 0–3 (Fritz et al., 2000), based on the pathologists' ADICAP electronic coding procedure (Martin, 1991).

2.2. Study area

The exposed area was defined as the geographical zone exposed to atmospheric fallout from the smoke plume arising from the Ariane incinerator; the non-exposed, i.e. reference area, was the remainder of A-M department. The most accurate statistical analysis unit selected was the IRIS, i.e. the acronym for aggregated units for statistical information, a subdivision of localities into "districts", the smallest geographical areas for which census data are available which include approximately 2000 residents.

An initial study was conducted by the Joint Research Unit N° 7300 of Nice Sophia-Antipolis University, investigating the air flow over the catchment area where the Ariane waste management incinerator unit is located, taking into account the height of the stack and the specific characteristics of the valley that leads towards the Alps (unpublished data). The results showed that the emissions flowed mainly towards the city of Nice, i.e. towards the South-West. The steering committee then assigned the NUMTECH company to model the scattering of atmospheric emissions generated by the UIOM. Before modelling the scattering of the smoke plume, prior calculations had been made by POLDEN INSAVALOR, an affiliate of the Institute for applied science in Lyon, which illustrated the main trends in the UIOM operation over three separate periods (1977–1986, 1986–1998 and 1998–2004). Flows were calculated for each period and type of pollutant (dust, metals, dioxins) by multiplying estimated concentrations by the average incinerated tonnage and by the theoretical volume of smoke emitted per incinerated ton. Actual population exposure was recalculated by weighting the results of each operation scenario, according to the duration of each of these scenarios. As the site characteristics include a specific topography and the occurrence of complex meteorological phenomena, it was decided to use a complete modelling chain including 3D meteorological modelling and 3D dispersion modelling of the atmospheric pollutants emitted by the UIOM. This chain involves RAMS (a prognostic meteorological model) (Pielke et al., 1992), CALMET (a diagnostic meteorological model) (Hernández et al., 2014), and CALPUFF (a Lagrangian puff modelling system) (Scire et al., 2000) models.

Dispersion mapping of mean annual concentrations of each pollutant were thus obtained, over which the IRIS unit contours were superimposed. To identify the IRIS units corresponding to the exposed area, the dioxin emission map was used, as dust was shown not to be an accurate indicator because calculated emission concentrations provided values well below those advised by WHO (PM2,5 : 10 μg/m^3/year, 25 μg/m^3/24 h on average, PM10 : 20 μg/m^3/year, 50 μg/m^3/24 h on average), and below values obtained in French towns (Chanel et al., 2016), and lastly, below those obtained in the A-M by AirPACA in 2011, regardless of the source. As for metals, there was an overlap between metal and dioxin dispersal, whether for air or for soil concentrations. The final criterion selected to determine the exposure zone was established by InVS (Daniau et al., 2009): a mean dioxin deposit of at least 4.25 ng/m^2/year, with two exposure levels within the exposed area: a perimeter with deposits ≥17.9 ng/m^2/year and a second perimeter with deposits ranging from 4.25 to 17.8 ng/m^2/year. These thresholds correspond to the 50th and 90th percentiles of the exposure distribution, respectively (Fig. 1).

The final exposure zone included 23 IRIS units completely exposed to the smoke plume and 21 IRIS units that were partly located in the exposed zone. Among the 21 partially exposed IRIS units, 8 were not retained because the exposed areas were sparsely populated or uninhabited.

The population of the exposed zone according to the INSEE (The National Institute for Statistics and Economic Studies) 2008 census, distributed over the 36 IRIS units, included 87,462 inhabitants [47,199 women (53.9%); 40,263 men (46.1%)]. The population of the remaining A-M department (unexposed area) numbered 996,512 [524,898 women (52.7%); 417,614 men (47.3%)]. The A-M department is home to a large proportion of elderly residents: 11.6% of the A-M population was aged over 75, while in France this age group consists of 8.6% of the overall population. The age distribution of the population in the exposed area is, however, similar to that of the remainder of the A-M ($p = 0.8853$).

Each patient's address at the time of diagnosis was obtained and geolocated in order to determine the exposure status. Addresses were provided by histology labs for 80% of patients and by healthcare institutions for 20% through matching on surname, given name, date of birth and date of diagnostic confirmation.

Each address was processed using a geographical information system (ARCGIS 10®) which located each patient within each of the IRIS units. It was thus possible to geolocate 99.6% of patients from the exposed area, while for the remaining 334 the place of residence was estimated based on the location where the diagnosis was established.

2.3. Statistical analysis

Results were expressed as world standard population age-adjusted rates (Bray et al., 2017) and for 100,000 population. This paper focuses on cancer cases suspected of being associated with waste incinerator emissions among men and women according to the period and area of exposure.

We conducted a global analysis over the ten-year period, which was subsequently subdivided into two five-year periods: 2005–2009 and 2010–2014. The first period follows the upgrading of the UIOM unit.

The Breslow-Day interaction test revealed a significant interaction between these two periods and the exposed area, showing that the impact of the exposed area differs between these two periods.

A standardized incidence ratio (SIR) was calculated to investigate an excess risk of disease in the exposed area compared to the reference area (Breslow et al., 1987). For each type of cancer, the ratio of the numbers of observed to expected cases in the exposed area was calculated.

For certain cancer sites, the number of observed cases every year was less than 10. In such cases the SIR was compared to 1 using the normal approximation of the Poisson distribution.

For cancers with significant excess rates, a Comparative Morbidity Figure (CMF) was computed, i.e. the ratio of the standardized incidence rates (SIR) in each of the two areas, to assess whether the observed rates differed significantly between the exposed area and the remaining A-M territory.

Calculations initially focused on all the patients with an address or postal code that was known or estimated from the laboratory or institution responsible for the diagnosis, and, subsequently, after excluding those whose postal code had been estimated. Since there was no significant difference regarding the results, the first group was selected for completeness.

Sensitivity tests were performed using different definitions of areas exposed to the UIOM unit smoke plume:

- Area with deposits ≥17.9 ng/m^2/year versus area with deposits ranging from 4.25 to 17.8 ng/m^2/year
- Area with deposits ≥17.9 ng/m^2/year versus unexposed area
- Area with deposits ≥17.9 ng/m^2/year versus remaining area with deposits ranging from 4.25 to 17.8 ng/m^2/year including only completely exposed IRIS units
- Area with deposits ranging from 4.25 to 17.8 ng/m^2/year including only completely exposed IRIS units versus the reference area, i.e. the remaining A-M department (unexposed area)

Results were validated by recalculating the yearly incidence rate for each type of cancer based on the yearly population estimate (between 2005 and 2014) provided by INSEE, applying the variation in percentage of population between each year and 2008 per age group, gender and area.

A threshold of 5% was considered statistically significant. All statistical tests were performed using the SAS© software package.

3. Results

Between 2005 and 2014 in the A-M, 81,594 new cases of cancer were recorded; of these, 729 were excluded from the final analysis. Medical records were not available for 594 of these, information was not consistent with a diagnosis of invasive tumour for another 118 patients, and place of residence could not be found for 17 patients.

The final statistical analysis was conducted on 80,865 cancer cases [37,844 women (46.8%) and 43,021 men (53.2%) residing in the A-M department], including 71,097 (87.9%) from the CRISAP PACA database, 8,413 (10.4%) from hospital information systems and 1,355 (1.7%) from the ONCOPACA network (the Oncology Provence-Alpes-Côte d'Azur Network). In the exposed area, 6,165 cancer cases were recorded (2,964 women [48.1%] and 3,201 men [51.9%]), while in the non-exposed area 74,700 cancer cases were recorded (39,820 men [53.3%] and 34,880 women [46.7%]). In the A-M department, among

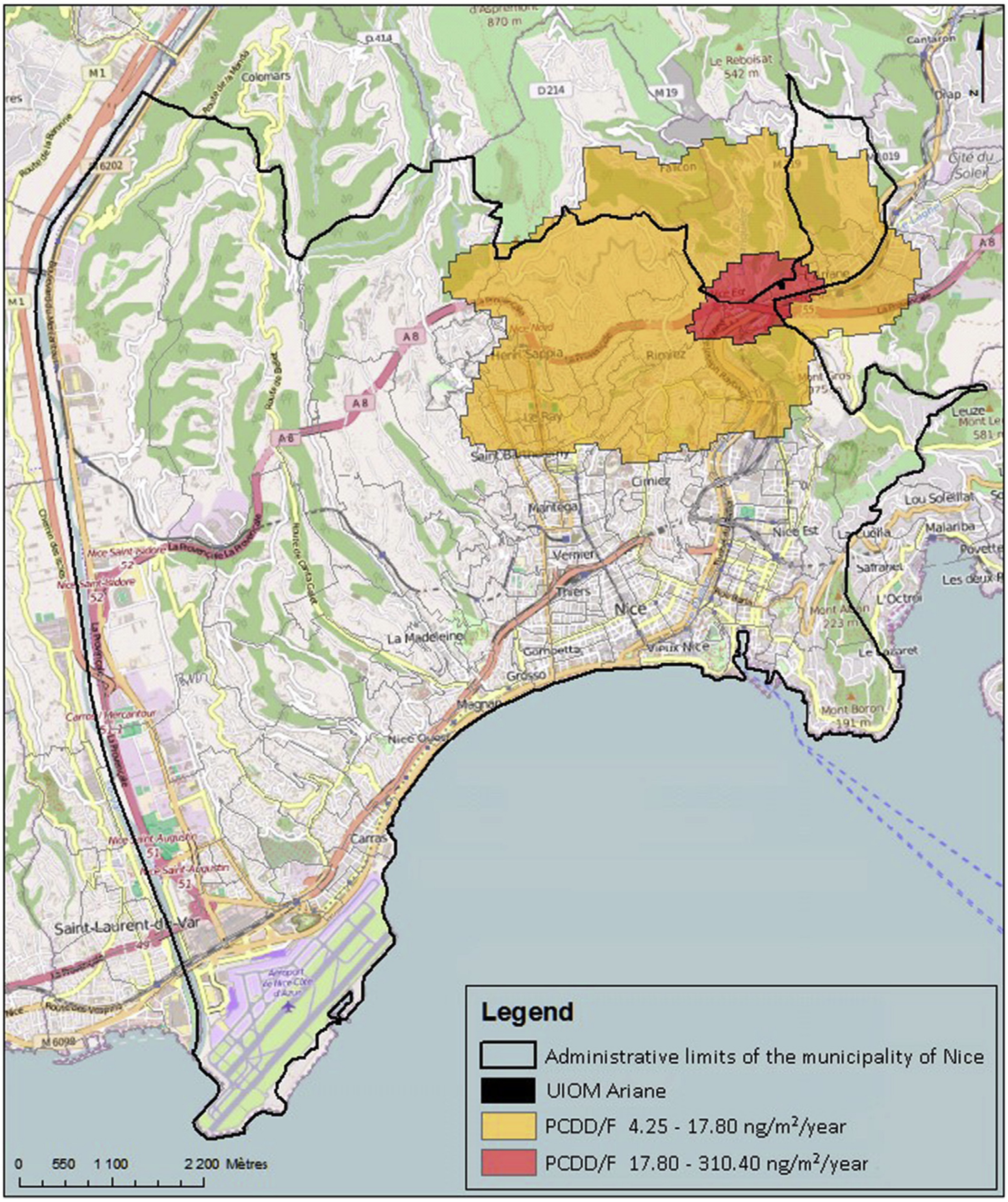

Fig. 1. The study area.

men, prostate, lung, skin (excluding melanoma) and colon cancer accounted for 56% of cases; among women, breast, skin (excluding melanoma) and colon cancer accounted for 51% of cases. Overall, the rate of histological confirmation was 95.1% for all cancers; in 2.6% of cases the primary tumour could not be identified.

Among women living in the exposed area, there was a significantly higher number of cases of acute myeloid leukaemia (27 observed *versus* 16 expected cases), multiple myeloma (51 observed *versus* 33 expected cases) and myelodysplastic syndromes (37 observed *versus* 24 expected cases) over the 10-year study period.

Breaking down the analysis by period shows that these excess cases are related to an over-incidence observed only during the 2005–2009 period for acute myeloid leukaemia (SIR = 1.81 [1.03–2.93]; CMF = 2.01 [1.04–3.89]), multiple myeloma (SIR = 1.64 [1.09–2.37]; CMF = 1.64 [1.02–2.63]) and myelodysplastic syndromes (SIR = 2.58 [1.70–3.76]; CMF = 1.99 [1.12–3.52]). Between 2010 and 2014, no significant excess incidence was observed for either of these three conditions (Figs. 2 and 3).

The test for interaction between period and exposure was statistically significant in men for acute myeloid leukaemia ($p = 0.035$), non-Hodgkin's lymphomas without indolent forms ($p = 0.029$) and for all non-skin cancers ($p = 0.001$). In women, we observed a significant interaction for myelodysplastic syndromes ($p < 0.001$) and for all cancers except skin cancer ($p = 0.022$).

There were no excess rates of non-Hodgkin's lymphoma among women in the exposed area, regardless of the group considered (NHL excluding small cell lymphoma or indolent forms, NHL according to FRANCIM criteria, and NHL small cell lymphoma or indolent forms). Table 1.

Among men living in the exposed area, there was a significant excess incidence of multiple myeloma (64 observed *versus* 34 expected cases) and lung cancer (415 observed *versus* 342 expected cases) over the 10-year period. The breakdown analysis shows this excess incidence rate concerned both 5-year periods for multiple myeloma (2005–2009:

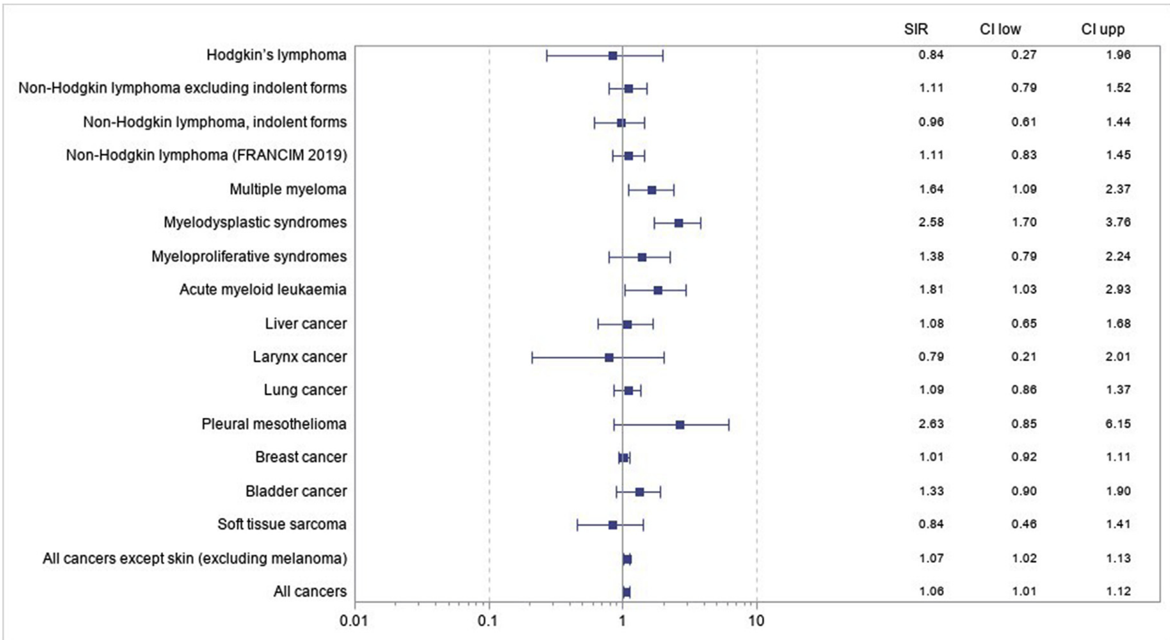

Fig. 2. Standardized Incidence Ratios for women: 2005–2009.

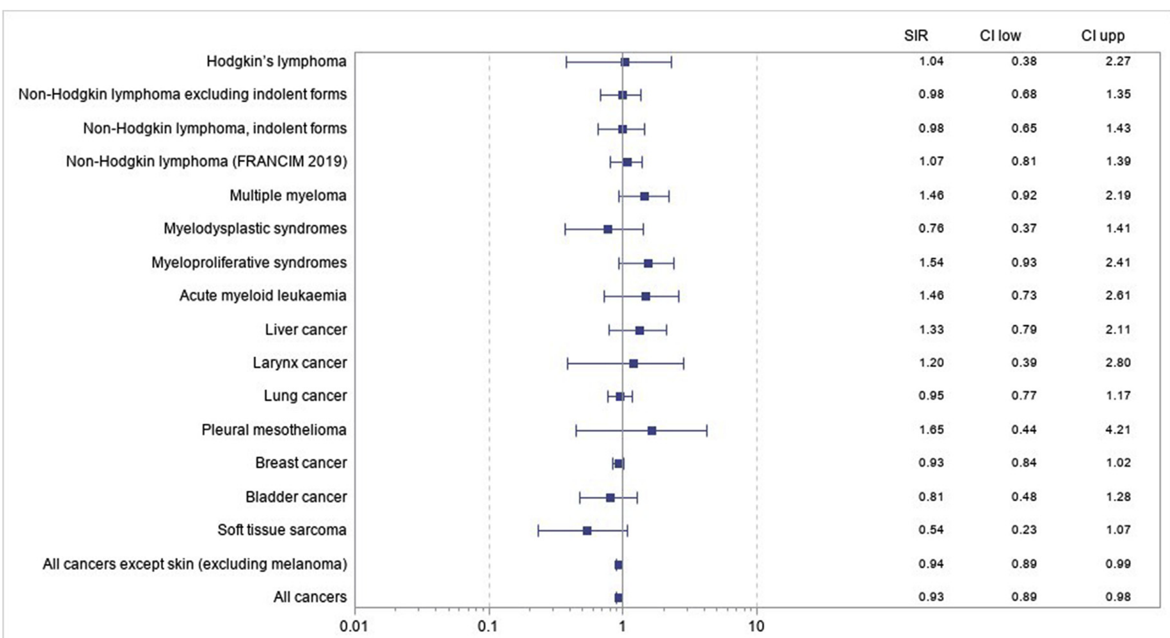

Fig. 3. Standardized Incidence Ratios for women: 2010–2014.

SIR = 2.04[1.39–2.90]; CMF = 1.86[1.21–2.86]), 2010–2014: SIR = 1.76[1.21–2.47]; CMF = 1.72[1.14–2.59]) and lung cancer (2005–2009: SIR = 1.19[1.03–1.36]; CMF = 1.26 [1.08–1.48]), 2010–2014: SIR = 1.24[1.08–1.41]; CMF = 1.22[1.05–1.43]). In contrast, the excess incidence of soft tissue sarcoma observed in 2005–2009 did not persist between 2010 and 2014.

Furthermore, observed cases of AML (SIR = 1.84 [1.07–2.95]) and of small cell or indolent forms of NHL (SIR = 1.45 [1.02–1.99]) exceeded the expected numbers in the exposed area and only during the 2005–2009 period; however, comparison of incidence rates did not show excess incidence in that area.

There were fewer cases of NHL, excluding non-indolent forms, during the 2005–2009 period in the exposed area (SIR = 0.68 [0.46–0.98] confirmed by a significantly lower incidence rate (CMF = 0.58 [0.36–0.91]). When applying the FRANCIM criteria, the lower incidence is no longer statistically significant (SIR = 0.76 [0.55–1.02]). In both cases no significant difference regarding the SIR was observed between 2010 and 2014 (Figs. 4 and 5, Table 2).

Table 3 shows a summary of age-standardized rates per 100,000 persons for the world population among men and among women, according to the period and exposure zone for cancer suspected to be associated with waste incinerator fumes.

We also undertook additional sensitivity analyses by changing the definition of the exposure zone. Regardless of the chosen definition for exposure (area restricted to IRIS units located in the UIOM's immediate vicinity, area including the partially exposed IRIS units, area excluding

Table 1
Age-standardized incidence rates (world) according to tumour site per period and gender, in areas exposed and unexposed to the Nice UIOM.

	MEN				WOMEN			
	Unexposed 2005–2009	Unexposed 2010–2014	Exposed 2005–2009	Exposed 2010–2014	Unexposed 2005–2009	Unexposed 2010–2014	Exposed 2005–2009	Exposed 2010–2014
Non-Hodgkin lymphoma (FRANCIM, 2019)	16.81	16.78	11.42	23.47	9.77	11.26	11.87	12.49
Non-Hodgkin lymphoma excluding indolent forms	12.99	13.14	7.49	17.70	7.12	8.01	7.77	7.92
Non-Hodgkin lymphoma, indolent forms	6.52	6.77	9.25	10.00	4.36	5.20	4.22	5.14
Multiple myeloma	3.42	4.45	6.36*	7.65*	2.95	2.76	4.83*	3.29
Myelodysplastic syndromes	2.52	2.40	3.36	2.39	1.34	1.45	2.66*	0.82
Acute myeloid leukaemia	2.47	2.45	4.27	1.04	1.72	1.69	3.46*	2.82
Lung cancer	42.78	42.63	54.04*	52.09*	14.35	19.76	16.12	19.59
Soft tissue sarcoma	4.79	4.30	8.92*	3.19	4.22	3.93	3.79	2.00
All cancers except skin (excluding melanoma)	493.79	480.70	501.15	495.12	392.07	414.32	431.74	392.63
All cancers	540.2	532.56	546.0	540.63	421.45	448.20	459.41	421.97

* p-value < 0,005 exposed versus unexposed.

all the partially exposed IRIS units), results were consistent.

Lastly, compared with the national French rates or those in nearby regions with available population cancer registries, incidence rates observed among men in unexposed areas for myeloma, myelodysplastic syndromes and acute myeloid leukaemia were similar to those observed in French registers; in contrast, they were lower for lung cancer and myelodysplastic syndromes and higher for soft tissue sarcomas. In women, incidence rates observed in unexposed areas were comparable regarding myeloproliferative syndromes, multiple myeloma and lung cancer and slightly lower for acute myeloid leukaemia.

4. Discussion

Our study shows a significantly higher incidence of multiple myeloma, lung cancer and soft-tissue sarcoma among male residents of the exposed area during the 2005–2009 period. Among women, during the same period, there was a significantly higher incidence of acute myeloid leukaemia, myelodysplastic syndromes and multiple myeloma. During the 2010–2014 period, only multiple myeloma and lung cancer among men in the exposed area retained a significantly higher incidence.

This study is one of the first in Europe to describe cancer incidence over a 10-year period in the vicinity of a domestic waste incinerator following the 2000 European Directive (Journal Officiel de la Communauté Européenne, 2000). To our knowledge, most European studies of this type published to this date focused on cases diagnosed prior to 2005 and for first or second generation UIOM (Negri et al., 2020).

For the 2005–2009 period, our results are generally in line with those of the literature: Viel (Viel et al., 2000) showed an excess incidence of soft-tissue sarcoma in residents living close to an incinerator that released fumes containing up to 16.3 ng I-TEQ/m3 of dioxins. A French study of 135,000 cancer cases diagnosed between 1990 and 1999 near incinerators also suggested a positive correlation for both genders with soft-tissue sarcoma and multiple myeloma (Daniau et al., 2009). In Italy, a descriptive study conducted on a population living in concentric areas near a waste incinerator between 1990 and 2005 showed excess rates of leukaemia in women, although no spatial trend was found (Federico et al., 2009). We did not observe a higher incidence of NHL, in contrast with some authors (Floret et al., 2003; Knox, 2005; Viel et al., 2000). However, we found a lower incidence of NHL during 2005–2009 among men living in the exposed area. No specific factor was identified that might account for this result. Nevertheless, when applying the 2019 FRANCIM classification criteria,

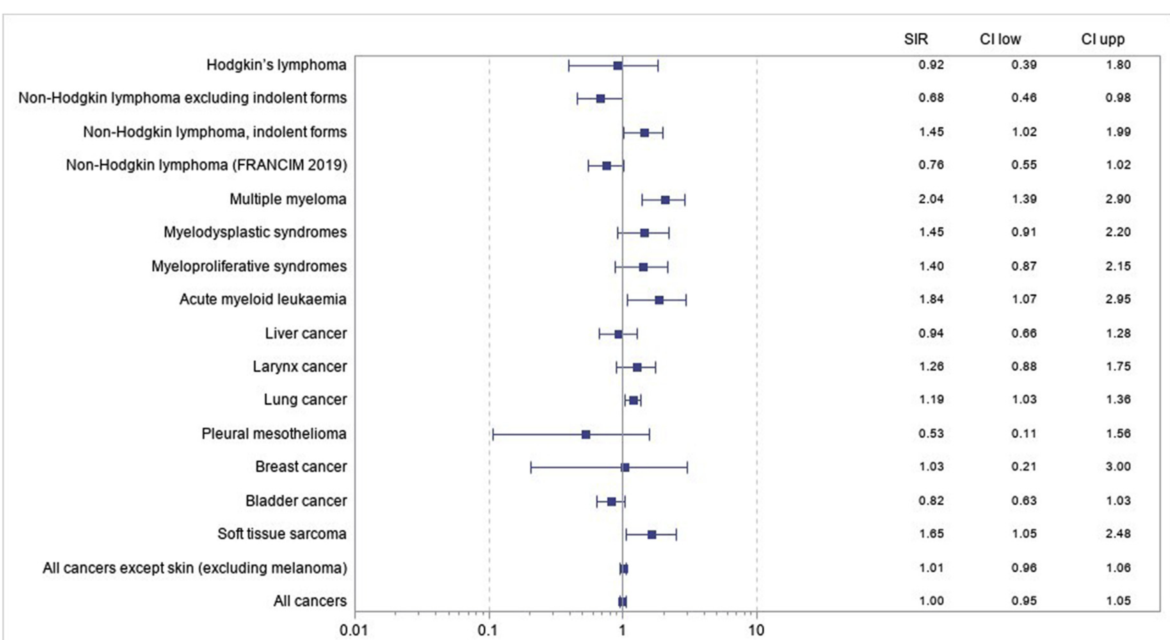

Fig. 4. Standardized Incidence Ratios for men: 2005–2009.

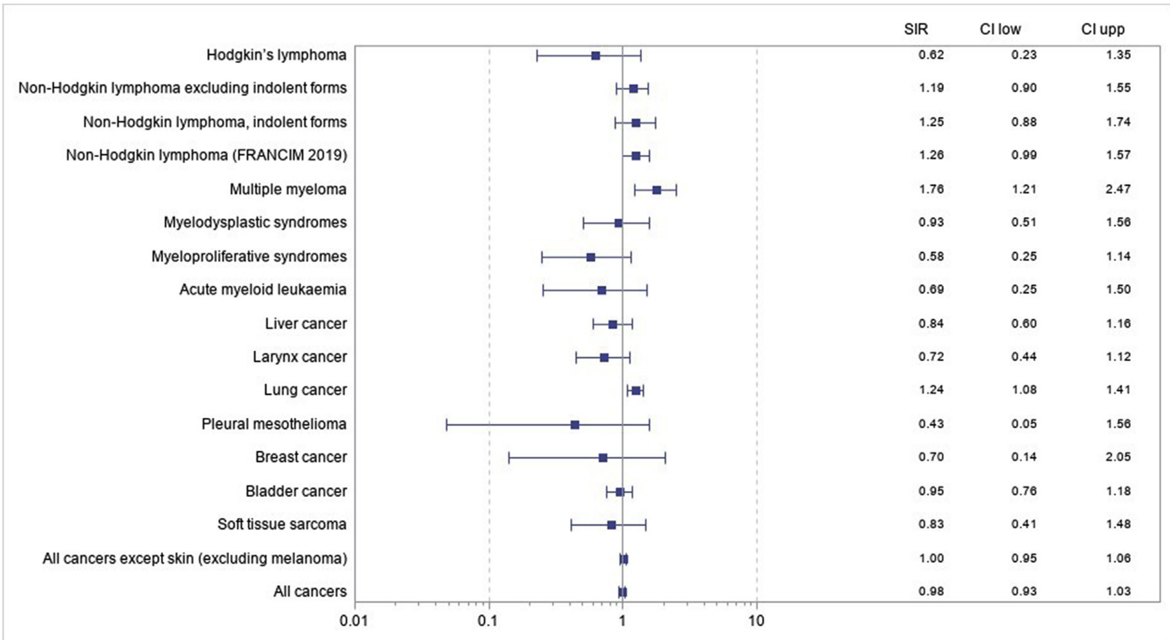

Fig. 5. Standardized Incidence Ratios for men: 2010–2014.

the incidence becomes similar in both areas. NHL are known to represent a heterogeneous group of conditions, each with its own epidemiology and aetiology (Morton et al., 2014). In 2001, the classification of lymphomas was modified in the 3rd edition of the ICD-O, based on research conducted by Harris (Harris et al., 1994). Analysing trends over time has become difficult since comparison with prior coding is no longer possible.

Our study suggests that, as time passes since the upgrading of the Ariane UIOM according to European standards, some of the excess incidence rates have disappeared. This is the case, among women, for acute myeloid leukaemia and myelodysplastic syndromes for which the median delay of emergence of secondary forms is 3–5 years; the trend is less obvious for multiple myeloma. The excess number of cases of multiple myeloma among men also disappeared. Although causal relationships cannot be established, these results could be explained by the reduced emission of pollutants from the UIOM stacks. Several studies demonstrated that waste incinerating plants equipped with recent, adequate technology emit less than 0.1 ng I-TEQ/m3 PCDD/F and that soil, and plasma concentrations among neighbouring residents had dropped significantly (Consonni et al., 2012; Marquès et al., 2018; Nadal et al., 2019; Zubero et al., 2017). In France, the CITEPA [A centre for the study of atmospheric pollution] (Serveau et al., 2015) observed that this reduction had begun in the early 2000s and intensified after 2005. Dioxins are estimated to last 7–11 years in soils, which would support a trend towards a uniform distribution in exposed and non-exposed areas, providing there was no input from other sources.

In contrast, excess incidence of multiple myeloma and lung cancer among men persisted in the exposed area between 2010 and 2014. Similar findings have been reported regarding multiple myeloma in male patients (Daniau et al., 2009). This could be because this malignancy can have a very long latency period (20 years) (Cesana et al., 2002; Mouhieddine et al., 2019), and also be due to improved diagnostic procedures over the past years (Mateos and Landgren (2016)). An increased incidence of myeloma was observed in both areas. It may be that extending data collection beyond 2014 could reveal a fall in incidence rate in the exposed area, resulting in a comparable incidence rate with the non-exposed area. Lung cancer is also characterized by a long latency (Pirie et al., 2013; Vineis et al., 2007). Its main, well known risk factor remains tobacco (Agudo et al., 2012; Doll and Hill (1952); Gilhodes et al., 2015; Shopland, 1995); however, its association with dioxins has been described (Baan et al., 2009), as well as that with other environmental exposures (García-Pérez et al., 2013; Wong et al., 2019). Tobacco use could not be investigated in this study. Besides, other risk factors could also have played a role, e.g. the vicinity of a major highway (the France-Italy motorway and a busy urban road network), population density and social characteristics which contribute to health inequality. As a follow-up of this observational study, etiological investigations are needed to determine the role of these various risk factors (Porta et al., 2009). Our results should be interpreted with caution. First, this type of study may be subject to selection bias. However, we believe case identification has been thorough thanks to the multiple information sources we used (Bailly et al., 2011). Data quality control provided the equivalent of a population cancer registry (Parkin et al., 1994). The rate of histological confirmation and the proportion of cancers without a known primary focus is close to that of French cancer registries (Bray et al., 2017).

Second, the exposure area is difficult to define and may be a source of classification bias. Several authors have analysed and discussed the importance of the model applied for the determination of the exposure zone (Ashworth et al., 2013; Cordioli et al., 2013; Goria et al., 2007; Zambon et al., 2007). Most studies of this type have considered a concentric exposure zone around the source or on the basis of administrative units (Forastiere et al., 2011; Ranzi et al., 2011; Zambon et al., 2007). However, conclusions of the European experts' report (WHO Regional Office for Europe, 2007) state that studies based on distance are unlikely to provide accurate assessments given their major limitations. A recent paper concluded that emissions modelling appears to be the most suitable method to determine their area of impact (Coudon et al., 2019a, 2019b). In the present study, the historical summary of the incinerator's emissions provided a more accurate model of the atmospheric fallout of the smoke plume. Moreover, all cases were geolocated, it was thus possible to conduct the investigation at the IRIS unit level and accurately determine the level of exposure for each case. Partially exposed IRIS units were discussed among a multi-disciplinary steering committee.

Furthermore, during the study period, changes in diagnostic procedures for malignant hemopathies and/or in coding (namely for non-Hodgkin's lymphomas ICD-O-3 version 2000), as well as diagnosis and

Table 2
Comparison of incident cases according to pathology, gender and area between 2005 and 2009.

	Men				Women			
	N[a] exposed area	N[a] unexposed area	SIR[b] (CI 95%)[c]	CMF[d] (CI 95%)[c]	N[a] exposed area	N[a] unexposed area	SIR[b] (CI 95%)[c]	CMF[d] (CI 95%)[c]
Hodgkin's lymphoma	8	105	0.92 (0.39, 1.80)		5	68	0.84 [0.27–1.96]	
Non-Hodgkin lymphoma excluding indolent forms	29	516	0.68 (0.46–0.98)	0.58 (0.36–0.91)	39	415	1.11 (0.79–1.52)	
Non-Hodgkin lymphoma, indolent forms	38	320	1.45 (1.02–1.99)	1.42 (0.97–2.08)	23	285	0.96 (0.61–1.44)	
Non-Hodgkin lymphoma (FRANCIM, 2019)	42	672	0.76 (0.55, 1.02)		53	563	1.11 (0.83, 1.45)	
Multiple myeloma	31	185	2.04 (1.39, 2.90)	1.86 (1.21, 2.86)	28	203	1.64 (1.09, 2.37)	1.64 (1.02, 2.63)
Myelodysplastic syndromes	22	183	1.45 (0.91, 2.20)		27	125	2.58 (1.70, 3.76)	1.99 (1.12, 3.52)
Myeloproliferative syndromes	21	182	1.40 (0.87, 2.15)		16	137	1.38 (0.79, 2.24)	
Acute myeloid leukaemia	17	110	1.84 (1.07, 2.95)	1.72 (0.92, 3.22)	16	106	1.81 (1.03, 2.93)	2.01 (1.04, 3.89)
Liver cancer	38	495	0.94 (0.66, 1.28)		19	208	1.08 (0.65, 1.68)	
Larynx cancer	36	350	1.26 (0.88, 1.75)		4	60	0.79 (0.21, 2.01)	
Lung cancer	202	2076	1.19 (1.03, 1.36)	1.26 (1.08, 1.48)	77	830	1.09 (0.86, 1.37)	
Pleural mesothelioma	3	69	0.53 (0.11, 1.56)		5	23	2.63 (0.85, 6.15)	
Breast cancer	3	36	1.03 (0.21, 3.00)		449	5238	1.01 (0.92, 1.11)	
Bladder cancer	69	1027	0.82 (0.63, 1.03)		30	271	1.33 (0.90, 1.90)	
Soft tissue sarcoma	23	168	1.65 (1.05, 2.48)	1.86 (1.11, 3.12)	14	194	0.84 (0.46, 1.41)	
All cancers except skin (excluding melanoma)	1440	17,664	1.01 (0.96, 1.06)		1385	15,105	1.07 (1.02, 1.13)	1.10 (1.04, 1.17)
All cancers	1601	19,765	1.00 (0.95, 1.05)		1515	16,728	1.06 (1.01, 1.12)	1.09 (1.03, 1.15)

[a] Cases.
[b] Standard Incidence Ratio.
[c] Confidence Interval.
[d] Comparative Morbidity Figure.

Table 3
Comparison of incident cases according to pathology, gender and area between 2010 and 2014.

	Men				Women			
	N[a] exposed area	N[a] unexposed area	SIR[b] (CI 95%)[c]	CMF[d] (CI 95%)[c]	N[a] exposed area	N[a] unexposed area	SIR[b] (CI 95%)[c]	CMF[d] (CI 95%)[c]
Hodgkin's lymphoma	6	116	0.62 (0.23, 1.35)		6	63	1.04 (0.38, 2.27)	
Non-Hodgkin lymphoma excluding indolent forms	55	561	1.19 (0.90–1.55)		36	435	0.98 (0.68–1.35)	
Non-Hodgkin lymphoma, indolent forms	36	350	1.25 (0.88–1.74)		27	329	0.98 (0.65–1.43)	
Non-Hodgkin lymphoma (FRANCIM, 2019)	76	734	1.26 (0.99, 1.57)		56	618	1.07 (0.81, 1.39)	
Multiple myeloma	33	228	1.76 (1.21, 2.47)	1.72 (1.14, 2.59)	23	189	1.46 (0.92, 2.19)	
Myelodysplastic syndromes	14	181	0.93 (0.51, 1.56)		10	159	0.76 (0.37, 1.41)	
Myeloproliferative syndromes	8	168	0.58 (0.25, 1.14)		19	146	1.54 (0.93, 2.41)	
Acute myeloid leukaemia	6	106	0.69 (0.25, 1.50)		11	89	1.46 (0.73, 2.61)	
Liver cancer	38	552	0.84 (0.60, 1.16)		18	160	1.33 (0.79, 2.11)	
Larynx cancer	20	341	0.72 (0.44, 1.12)		5	49	1.20 (0.39, 2.80)	
Lung cancer	213	2111	1.24 (1.08, 1.41)	1.22 (1.05, 1.43)	92	1142	0.95 (0.77, 1.17)	
Pleural mesothelioma	2	56	0.43 (0.05, 1.56)		4	29	1.65 (0.44, 4.21)	
Breast cancer	3	52	0.70 (0.14, 2.05)		439	5594	0.93 (0.84, 1.02)	
Bladder cancer	84	1073	0.95 (0.76, 1.18)		18	268	0.81 (0.48, 1.28)	
Soft tissue sarcoma	11	161	0.83 (0.41, 1.48)		8	172	0.54 (0.23, 1.07)	
All cancers except skin (excluding melanoma)	1428	17,542	1.00 (0.95, 1.06)		1298	16,154	0.94 (0.89, 0.99)	0.95 (0.89, 1.01)
All cancers	1600	20,055	0.98 (0.93, 1.03)		1449	18,152	0.93 (0.89, 0.98)	0.94 (0.89, 0.99)

[a] Cases.
[b] Standard Incidence Ratio.
[c] 95% Confidence Interval.
[d] Comparative Morbidity Figure.

coding of sarcomas, which are very heterogeneous, could have altered the results and thus precluded comparison with former studies. Lastly, the lack of information on residential background, which was collected in a recent cohort study (Danjou et al., 2019), and on the history of the UIOM employees may have led to classification errors; since such information is very difficult to obtain in this type of study, it was assumed that residential mobility did not differ between the two areas among patients with cancer. Moreover, this concerned very few patients.

However, because of this potential bias, sensitivity analyses were performed by altering the exposure area, without obtaining different results (Spiegelman, 2010).

Lastly, the methodology applied in this study does not allow to conclude to a causal relationship between the observed associations since the over-incidence of cancers could have been due to exposure to other pollutants and socio-behavioural factors which we were not able to measure. The association between lung cancer and tobacco use or the presence of other polluting agents (road traffic, cement factory …) and socio-demographic factors will be investigated in a further study. As recommended by Tait et al., (2019) in a recent meta-analysis, in addition to comparing results on the basis of incinerator characteristics, data collection should be ongoing and should include potential confounders. Six-monthly measurements of soil deposits in various sites near the incinerator will be available in forthcoming analyses.

5. Conclusion

Our study shows a statistically significant correlation between residing during a specific period in an area exposed to the smoke plume of the UIOM and the occurrence of certain types of cancer. Most excess incidence rates observed for the 2005–2009 period disappeared during the 2010–2014 period. These correlations have already been observed with the same types of cancer in other studies conducted before the application of the 2000 EU Directive (Journal Officiel de la Communauté Européenne, 2000).

If we are correct in assuming that the incinerator upgrade in compliance with EU standards is effective, it may be that the incidence of these malignancies, which have a protracted latency period between environmental exposure and occurrence (Tait et al., 2019), will diminish in the coming years, as described by Forastière.

Author contribution

Eugènia Mariné-Barjoan: Project Manager, author, Nadège Doulet: Data manager, Amel Chaarana: Statistician, Julie Festraëts: Geographer, Agnès Viot: Data manager, Damien Ambrosetti: Supervision, Review, Jean-Luc Lasalle: Supervision, Review, Nicolas Mounier: Review, Laurent Bailly: Review, Christian Pradier: Supervision, Review.

Appendix A

Details of 95%CI formula for SIR

$$SIR = \frac{O}{E} \qquad SIR_{inf} = \frac{O}{E}\left(1 - \frac{1}{9O} - \frac{z_{a/2}}{3\sqrt{O}}\right)^3$$

$$SIR_{sup} = \frac{O+1}{E}\left(1 - \frac{1}{9(O+1)} - \frac{z_{a/2}}{3\sqrt{O+1}}\right)^3$$

Details of 95% CI formula for CMF

$$\mathrm{CMF}_{\substack{\mathrm{inf}\\ \mathrm{sup}}} = e^{\ln\mathrm{CMF} \pm z_{a/2}\sqrt{\mathrm{var}[\ln \mathrm{CMF}]}}$$

$$z_{a/2} = 1.96$$

Declaration of competing interest

The authors declare that they have no competing financial interests.

Acknowledgements

Members of Steering committe [D Chouvy (Association des intérêts de l'Abadie, CDIA), C Masson (Association Un cœur pour l'Ariane), JF Michiels (CHU Nice/CRISAP PACA), JF Ascas, Y Lalle, N Lopez, B Vernet (Métropole Nice Côte d'Azur), G Fontes, M Mihoubi, F Peloux-Petiot, J Raibaut (Agence Régionale de Santé, délégation Alpes-Maritimes); L Pascal (Santé publique France, regional office Provence-Alpes-Côte d'Azur and Corsica); Laboratories of CRISAP PACA and contributors [MJ Carayon (ACP Tzarewitch), F Dupré (CHPG Monaco), C Penot-Rivollet (Laboratoire Saint Laurent du Var), JF Roussel (CHPG Monaco), C Sattonnet (DIAG), D Semplici (MEDIPATH), I Peyrottes (CAL)]; Hospital and Clinic Medical Information Departments [H Bonnet (CH Draguignan), V Bonniol (IAT), G Daideri (CAL), D Desse (CH Grasse), PL Genillier (CH Cannes), M Lehmann (IAT), G Lesbats (Clinique Parc Impérial), M Ligiardi (Clinique Saint George), M Monguillon (CH Menton), P Staccini (CHU Nice), Y Pinier (CH Fréjus/Saint Raphaël), A Vallet-Anfosso CH Antibes), J Viot (Groupe DOMUSVI); Haematology Laboratory CHU Nice [S Raynaud, I Sudaka]; Clinical and pole services managers and teams [CHU de Nice: J Amiel, G Bernardin, P Boileau, P Brocker, A Bongain, JP Cassuto, C Desnuelle, E Ferrari, JG Fuzibet, X Hébuterne, J Lacour, JF Michiels, P Rohrlich], [CAL: J Santini]; M Poirée (CHU/Lenval)]; CHU Nice (F Ajmia, V Casanova, R Chevrier, M Del Rosso, C Geloen, E Huynh Van, M Houlès, JY Juskiwiesky, V Lacroix-Hugues, M Licari, R Marignol, A Morisot, MC Paumelin, M Pellegrini, B Prouvost Keller, S Saulnier, C Senesi, D Van Giesel, J Valbousquet), ONCOPACA Netwoork [P Poggi, M Taouqi], and all the doctors, secretaries, clinica research officers, archivists of CH Antibes, Cannes, Grasse, CAL and CHU de Nice, Palais Clinic, Institut Arnaut Tzanck, Parc Impérial Clinic, Saint George Clinic; NUMTECH society, POLDEN INSAvalor society; P Carrega (Université Nice Côte d'Azur, Sophia Antipolis); JP Daurès (Université de Montpellier-Faculté de médecine) and especially the CHU Nice Public Health Department staff and Brigitte Dunais for the translation.

CAL: Centre de lutte contre le cancer Antoine Lacassagne, CH: Centre Hospitalier, CHU: Centre Hospitalier Universitaire de Nice, CHPG: Centre Hospitalier Princesse Grace. This work was funded by NCA Metropole Nice Côte d'Azur and supported by the Regional Health Agency (ARS PACA).

Appendix B

Multiple myeloma. Men	
France 2012	4.2
Loire Atlantique 2003-2007	3.8
Hèrault 2003-2007	3.4
Bas Rhin 2003-2007	4.7
AM Unexposed 2005-2014	3.9(3.5–4.4)
AM Exposed 2005-2014	7.1(5.1–8.9)
Age-standardized incidence rates (world) /100,000	

Multiple myeloma. Women	
France 2012	2.9
Loire Atlantique 2003-2007	2.2
Herault 2003-2007	2.1
Bas Rhin 2003-2007	3.1
AM Unexposed 2005-2014	2.9 (2.5-3.2)
AM Exposed 2005-2014	4.1 (2.7-5.4)
Age standardized incidence rates (world) / 100,000	

Acute myeloid leukaemia. Men	
France 2012	2.6
Loire Atlantique 2003-2007	2.3 (1.9-2.8)
Herault 2003-2007	3.1 (2.5-3.7)
Bas Rhin 2003-2007	3.2 (2.4-4.0)
AM Unexposed 2005-2014	2,5 (2.1-2.9)
AM Exposed 2005-2014	2,7 (1.3-4.0)
Age standardized incidence rates (world) / 100,000	

Acute myeloid leukaemia. Women	
France 2012	2.3
Loire Atlantique 2003-2007	2.2 (1.8–2.7)
Herault 2003-2007	2.3 (1.8–2.8)
Bas Rhin 2003-2007	1.9 (1.3-2.5)
AM Unexposed 2005-2014	1.7(1.4–2.0)
AM Exposed 2005-2014	3.1 (1.4–3.6)
Age standardized incidence rates (world) / 100,000	

Lung cancer. Men	
France 2012	51.7
Loire Atlantique 2009-2013	47.,2 (45.2–49.1)
Herault 2009-2013	52.8 (50.6–55.0)
Bas Rhin 2009-2013	47.1 (44.4–49.7)
AM Unexposed 2005-2014	42.7 (41.3–44,1)
AM Exposed 2005-2014	53,1 (47.4–58.7)
Age-standardized incidence rates (world) / 100,000	

Lung cancer. Women	
France 2012	18.6
Loire Atlantique 2009-2013	14.7(13.6–15.7)
Herault 2009-2013	20.8 (19,4–22.2)
Bas Rhin 2009-2013	15.2 (13.7–16.7)
AM Unexposed 2005-2014	17.1(16.2–17.9)
AM Exposed 2005-2014	17.9 (14.8–21.0)
Age-standardized incidence rates (world) / 100,000	

Soft tissue sarcoma. Men	
Loire Atlantique 2003-2007	2.7
Herault 2003-2007	2.3
Bas Rhin 2003-2007	2.9
AM Unexposed 2005-2014	4.6 (4.0-5.2)
AM Exposed 2005-2014	6.1 (3.7–8.5)
Age-standardized incidence rates (world) / 100,000	

Soft tissue sarcoma. Women	
Loire Atlantique 2003-2007	1.9
Herault 2003-2007	1.5
Bas Rhin 2003-2007	1.8
AM Unexposed 2005-2014	4.0 (3.5–4.6)
AM Exposed 2005-2014	2.7 (1.4-4.0)
Age-standardized incidence rates (world) / 100,000 habitants	

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