International Journal of Hygiene and Environmental Health 222 (2019) 22–29

Contents lists available at ScienceDirect

International Journal of Hygiene and Environmental Health

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

Cancers in France in 2015 attributable to occupational exposures

Claire Marant Micallef[a,*], Kevin D. Shield[a], Jérôme Vignat[a], Isabelle Baldi[b], Barbara Charbotel[c], Béatrice Fervers[d], Anabelle Gilg Soit Ilg[e], Pascal Guénel[f], Ann Olsson[g], Lesley Rushton[h], Sally J. Hutchings[i], Enora Cléro[j], Dominique Laurier[j], Pascale Scanff[j], Freddie Bray[a], Kurt Straif[k], Isabelle Soerjomataram[a]

[a] Section of Cancer Surveillance, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372, Lyon, CEDEX 08, France
[b] Equipe Santé Environnement, Centre de recherche INSERM U 897, Université de Bordeaux, Bât. ISPED - Case 11, 146, rue Léo-Saignat, Bordeaux, France
[c] Université Lyon 1, UMRESTTE, UMR_T9405, Service des maladies professionnelles, Hospices Civils de Lyon, 8, avenue Rockefeller, 69008, Lyon, France
[d] Centre Léon Bérard, Université de Lyon, Département cancer environnement, 28 rue Laennec, 69008, Lyon, France
[e] Santé publique France, Direction Santé Travail, 12, rue du Val d'Osne, 94 415, Saint-Maurice cedex, France
[f] Centre de recherche en Epidémiologie et Santé des Populations (CESP), Cancer and Environment team, Université Paris-Sud, Université Paris-Saclay, 16, avenue Paul Vaillant Couturier, 94800, Villejuif, France
[g] Section of Environment and Radiation, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372, Lyon, CEDEX 08, France
[h] Department of Epidemiology and Biostatistics, Imperial College London, Level 2, Faculty Building, South Kensington Campus, London, SW7 2AZ, United Kingdom
[i] Manchester University, Population Health, Health Services Research & Primary Care, School of Health Sciences, University of Manchester, Oxford Road, Manchester, M13 9PL, UK
[j] Direction of Health and Environment, Institute for Radiological Protection and Nuclear Safety, 31, avenue de la Division Leclerc 92260, Fontenay-aux-Roses, 92260, France
[k] Section of Evidence Synthesis and Classification, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372, Lyon, CEDEX 08, France

ARTICLE INFO

Keywords:
Occupation
Carcinogen
Cancer
Risk
Comparative risk assessment/attributable fractions

ABSTRACT

Background: Recent and comprehensive estimates for the number of new cancer cases in France attributable to occupational exposures are lacking.

Objectives: To estimate the number of new cancer cases attributable to occupational exposures, using a newly developed methodology and the most recent data, for a comprehensive set of occupational carcinogens in France in 2015.

Methods: Surveys among employees, the national labor force data, a cohort of agricultural workers, national monitoring of workers exposed to ionizing radiation and job-exposure matrix in France were used. The number and proportion of new cancer cases attributable to established occupational carcinogens (Group 1) was estimated using estimation of lifetime exposure and risk estimates from cohort studies. Cancer data were obtained from the French Cancer Registries Network.

Results: In France in 2015, an estimated 7905 new cancer cases, 7336 among men and 569 among women, were attributable to occupational exposures, representing 2.3% of all new cancer cases (3.9% and 0.4% among men and women respectively). Among men and women, lung cancer was impacted the most, followed by mesothelioma and bladder cancer in men, and by mesothelioma and ovary in women. These cancers contributed to 89% of the total cancers attributable to occupational carcinogens in men, and to 80% in women. The main contributing occupational agent was asbestos among men (45%) and women (60%).

Conclusions: Currently, occupational exposures contribute to a substantial burden of cancer in France. Enhanced monitoring and implementation of protective labor policies could potentially prevent a large proportion of these cancers.

* Corresponding author. International Agency for Research on Cancer, 150 Cours Albert Thomas, 69372, Lyon, CEDEX 08, France.
E-mail addresses: marantmicallefc@iarc.fr (C. Marant Micallef), kevin.david.shield@gmail.com (K.D. Shield), vignatj@iarc.fr (J. Vignat), isabelle.baldi@u-bordeaux.fr (I. Baldi), barbara.charbotel-coing-boyat@univ-lyon1.fr (B. Charbotel), beatrice.fervers@lyon.unicancer.fr (B. Fervers), Anabelle.GILGSOITILG@santepubliquefrance.fr (A. Gilg Soit Ilg), pascal.guenel@inserm.fr (P. Guénel), olssona@iarc.fr (A. Olsson), l.rushton@imperial.ac.uk (L. Rushton), sally.hutchings@postgrad.manchester.ac.uk (S.J. Hutchings), enora.clero@irsn.fr (E. Cléro), dominique.laurier@irsn.fr (D. Laurier), pascale.scanff@irsn.fr (P. Scanff), brayf@iarc.fr (F. Bray), straifk@iarc.fr (K. Straif), SoerjomataramI@iarc.fr (I. Soerjomataram).

https://doi.org/10.1016/j.ijheh.2018.07.015
Received 24 April 2018; Received in revised form 19 July 2018; Accepted 27 July 2018

1. Introduction

Occupational exposures to certain chemical, physical, biological agents and occupational circumstances (e.g. rubber manufacturing industry) are well established risk factors for the development of cancer (Pearce et al., 2015; Siemiatycki et al., 2004). However, still today we observe a large number of carcinogenic agents across various occupational settings. Therefore, up-to-date data on the prevalence of exposure to occupational carcinogens and the cancer cases attributable to these agents are vital information for policy makers for the formulation, prioritization and implementation of targeted prevention strategies to improve working conditions by reducing exposure and ultimately reduce the cancers attributable to these carcinogens (Rushton et al., 2007).

Previous studies have estimated that approximately 3%–14% and 0%–2% of all new cancer cases among men and women respectively are attributable to occupational exposures in high-income countries (Boffetta et al., 2010; Driscoll et al., 2005; Fritschi and Driscoll, 2006; Nurminen and Karjalainen, 2001; Rushton et al., 2010; Steenland et al., 2003). In France 2.3% and 0.3% of all new cancer cases in 2000 among men and women respectively were attributable to occupational exposures; however, this estimate was based on cross-sectional prevalence estimates of exposure from the mid-1990s, and included only selected occupational agents (Boffetta et al., 2010). Furthermore, the most recent estimates from the French National Public Health Agency in 2012, which adjusted for changes in the prevalence of exposure over time, were limited to four Group 1 exposures (asbestos, benzene, trichloroethylene and silica dust) (Gilg Soit Ilg et al., 2016).

Accordingly, the objective of this study was to estimate the number of new cancer cases in France in 2015 attributable to historical exposure to occupational carcinogens with sufficient evidence of a causal relationship with cancer risk in humans (Group 1, as classified by the International Agency for Research on Cancer (IARC)), adjusting for changes in exposure over time. A secondary analysis provides similar estimates, including all Group 1 and 2A occupational carcinogens and cancer sites pairs with at least limited evidence of a causal relationship.

2. Material and methods

Data on the prevalence of occupational exposures and the relative risk (RR) of developing cancer for people ever exposed to occupational agents compared to those never exposed were combined to estimate the Population-Attributable Fraction (PAF) (Shield et al., 2016). Subsequently, the number of new cancer cases attributable to occupational exposures was estimated by applying the PAFs to the estimated new cancer cases in France in 2015.

2.1. Exposures and cancers included

We considered occupational agents classified as carcinogenic (Group 1 of IARC Monographs) or probably carcinogenic to humans (Group 2A of IARC Monographs). To account for differences in the level of evidence across exposure/cancer site pairs, the main analysis included only Group 1 occupational agent and cancer site pairs with sufficient evidence of a causal relationship as determined by the IARC Monographs program volumes 1 to 114 (International Agency for Research on Cancer, 2017; Pearce et al. 2015), whereas the secondary analysis included all Group 1 and Group 2A occupational agent and cancer site pairs with at least limited evidence of a causal relationship. Furthermore, only those occupational exposures which were relevant for France, where exposure data were available, and where an RR estimate was available were included in the study (Marant Micallef et al., 2018). Based on these criteria, 25 agents were included in the main analysis, with these agents causally related to the development of 23 cancer sites, representing 44 occupational agent and cancer site pairs (see Figure S1) (Marant Micallef et al., 2018). Furthermore, the secondary analysis included 34 agents which were causally related to 23 cancers, representing 73 occupational agent and cancer site pairs.

2.2. Estimation of the proportion of the population ever exposed to occupational carcinogens

We used multiple sources of occupational exposure data in order to derive the most comprehensive data which are outlined in Table 1. Briefly, we used the French national survey on occupational exposures among 50,000 employees (SUMER), the French CAREX estimates, the national labor force survey, a French agricultural cohort (AGRICAN), the national monitoring system for workers exposed to ionizing radiation (SISERI), and the Matgéné program combining lifetime self-reported job history of a representative sample of 10,000 French persons with a French-specific job-exposure matrix (JEM).

Solid cancers have been reported to have a distinct latency time as compared to hematological and lymphatic malignancies. Therefore, the risk exposure period (REP), i.e. the time-period during which exposure to occupational carcinogens are considered to have contributed to cancer incidence in 2015, was assumed to be from 1995 to 2015 for hematological cancers (short REP), and from 1965 to 2005 for solid cancers (long REP). This corresponds to a latency time of 0–20 years for the first, and of 10–50 years for the latter (Rushton et al., 2010).

2.2.1. Estimation of the prevalence of the ever exposed population over the short exposure period

To estimate the prevalence of exposure to occupational agents over the short REP, cross-sectional prevalence of exposure from the AGRICAN (Leveque-Morlais et al., 2015), SUMER (Arnaudo et al., 2006), CAREX (Vincent et al., 1999) and national labor force survey databases (Direction des statistiques démographiques et sociales 2016) were applied to the 2015 French population data by age and sex (Institut national de la statistique et des études économiques 2015). For the agents that were included in the Matgéné program (Fevotte et al., 2011), we used the 2007 prevalences of exposure as provided from this database, applied to the 2015 French population. Finally, to assess cumulative exposure to ionizing radiation over the short REP by sex, we simulated a cohort of workers over 1995–2015, using population data combined with the number of workers exposed and their average annual exposure dose reported annually from 1996 to 2015 (Institut de Radioprotection et de Sûreté Nucléaire, 2015) (See note S1 detailing the method to assess cumulative occupational exposure to ionizing radiation).

2.2.2. Estimation of the prevalence of the ever exposed population over the long exposure period

Similarly, several methods were used to estimate the prevalence of exposure over the long REP. The prevalence of ever exposed to pesticides over the long REP was directly obtained from the AGRICAN database (Leveque-Morlais et al., 2015). This was then applied to the number of farmers in France, based on the national labor force survey, to determine the proportion of the French population ever occupationally exposed to pesticides. The cumulative prevalence of exposure to ionizing radiation was assessed over the long REP using the same cohort simulation as for the short REP, but over the period 1965–2005 (see note S1 detailing the method to assess cumulative occupational exposure to ionizing radiation). The same method was used to estimate prevalence of shift workers over the long REP. Finally, for the remaining carcinogens, to take into account the exposure changes over time, the agents were categorized into three groups: (i) agents which have been used with no change since 1965, (ii) agents very little used after 2000 (e.g. asbestos, benzene), and (iii) agents where there has been a moderate decrease in use since 1965 (Table S1 of supplemental material). Based on these categories, age- and sex-specific adjustment factors were applied to the cross-sectional exposure prevalence for these agents obtained from the SUMER, CAREX and the national labor

Table 1
Data sources for exposure to occupational carcinogens.

Data source	Description/Data available	Occupational exposures	Dates
SUMER surveys (Arnaudo et al., 2006)	Random sample of 50,000 salaried workers/Prevalence of exposure to agents	Polycyclic aromatic hydrocarbons 1,3-Butadiene Bis(chloromethyl)ether Beryllium and compounds	1994
		Aromatic amines Arsenic and inorganic arsenic compounds Asbestos Benzene Cadmium compounds Chromium (VI) compounds Dichloromethane Engine exhaust, diesel Ethylene oxide Formaldehyde Nickel compounds Polychlorinated biphenyls Wood dust Cobalt metal with tungsten carbide Lead compounds, inorganic Silica dust Trichloroethylene Perchlorethylene	2003
CAREX database (Vincent et al., 1999)	Based on active population data: estimation of numbers of workers exposed by sector/Numbers of salaried workers exposed to agents	Acid mists, strong inorganic	1990–1993
National labour force survey (Direction des statistiques démographiques et sociales 2016)	Representative survey of people aged ≥15/Numbers of workers by occupation or sector in 2007	Iron and steel founding Rubber manufacturing industry Art glass, glass containers and pressed ware (manufacture of) Painter Hairdresser or barber Shiftwork that involves circadian disruption	2007
AGRICAN study, (Leveque-Morlais et al., 2015)	French cohort of 180,000 farmers/Lifetime exposure to selected pesticides	Lindane Diazinon Malathion	2005
SISERI database, (Institut de Radioprotection et de Sûreté Nucléaire, 2015) Annual reports on occupational exposure to ionizing radiation in France	Exhaustive collection of individual radiation doses received by workers exposed to ionizing radiation/Number of workers and mean radiation dose received for monitored workers	Ionizing radiation	1996 to 2015
Matgéné program (Fevotte et al., 2011)	Job history of 10,000 representative French persons, combined with a job-exposure matrix/Cross-sectional and lifetime prevalence of exposure	Asbestos Benzene Silica dust Trichloroethylene Perchlorethylene Dichloromethane Leather dust	2007

force surveys (see Tables S1 for the detailed categories and corresponding adjustment factors), i.e. we multiplied the cross-sectional prevalences by the adjustment factors to get the prevalence over the long exposure period. The adjustment factors were developed based on lifetime estimates of occupational exposures from the Matgéné program (Fevotte et al., 2011) as compared to the cross-sectional prevalences from the SUMER survey (Arnaudo et al., 2006) for the agents which were ascertained in both surveys. It was assumed that these adjustment factors accounted for all factors that may influence the difference between cross-sectional prevalence estimates and estimates over the long REP, including exposures changes over time. For the agents ascertained in both surveys, the actual age and sex-specific ratios between the two existing estimates were used to estimate the prevalences of exposure over the long REP.

2.3. Relative risk estimates

RR estimates of developing cancer for people ever exposed to the agent compared to people never exposed were obtained from meta-analyses, large cohorts or pooled occupational studies matching French exposure data in terms of exposure levels (see the review by Marant Micallef and colleagues explaining the rationale for the selection of the RRs used (Marant Micallef et al., 2018). In cases where RR estimates were only reported for stratified levels of exposures, a fixed effects meta-analysis was performed to pool the RRs estimates (Fleiss, 1993), as this method was applicable even in the absence of exposure prevalence. The RR estimates related to ionizing radiation were derived from the BEIRVII dose-risk models (National Research Council, 2006), based on the average years of exposure and cumulated doses for workers exposed to ionizing radiation.

2.4. Estimation of the Population-Attributable Fraction

The PAFs for cancers attributable to occupational agents were estimated using two methods. The PAF for the proportion of new mesothelioma cases attributable to asbestos was derived directly from the National Mesothelioma Surveillance Program: this program included a case-control study which was used to estimate this PAF using the Mantel-Haenszel estimation (Lacourt et al., 2014). We used the PAF associated with occupational exposures to asbestos only, not to para-occupational exposures, i.e. exposures occurring indirectly from occupational exposures (for instance, living with relatives occupationally exposed to asbestos). In all other cases, the PAFs for new cancer cases due to a particular occupational exposure were estimated using the method proposed by Levin (Levin, 1953) (see Formula 1). Specifically, this latter method combines data on the proportion of the population ever exposed to occupational carcinogens (P) and the corresponding RR estimates (Marant Micallef et al., 2018).

$$PAF = \frac{P(RR - 1)}{1 + P(RR - 1)} \quad (1)$$

In cases where there were multiple occupational exposures that influenced the risk of a cancer type, the exposure prevalence and/or the PAFs were adjusted. Firstly, in cases where exposure to occupational circumstances (e.g. working in a certain profession) and to an occupational agent overlapped, the agent exposure prevalence was calculated excluding workers with such similarly exposed profession. As an example, in the calculation of the PAF for bladder cancer, exposure as a hairdresser was subtracted from the estimation of the exposure to aromatic amines (See Table S2 for a list of overlapping situational and chemical exposures). Secondly, in cases where multiple exposures increased the risk of a specific cancer, the combined PAF (PAF_T) was estimated using the exposure-specific PAFs (PAF_i) assuming independence between risk factors and assuming the RRs were multiplicative (see Formula 2).

$$PAF_T = 1 - \prod_{i=1}^{n} (1 - PAF_i) \quad (2)$$

2.5. Cancer data

The projected number of new cancer cases by age, sex, and cancer type (ICD-10) in France in 2015 were estimated using 2013 age, sex, and cancer type specific incident rates obtained from the French Cancer Registries Network (FRANCIM) (Santé Publique France, 2017). These incident rates were then applied to 2015 population data to estimate the number of new cancer cases in 2015 (Institut national de la statistique et des études économiques 2015).

3. Results

3.1. Prevalence of French population ever exposed to occupational carcinogens during the REP

In general, the prevalence of being ever exposed to occupational carcinogenic agents over the REP in France in 2015 was higher among men than among women (see Table 2 for the prevalence of exposure to occupational carcinogens). Over the REP relevant for solid cancers (1965–2005), the prevalence of ever exposure among men ranged from 23.5% for exposure to asbestos to 0.03% for exposure to bischloromethylether. Among women, the highest estimated prevalence of ever exposure over the REP was observed for shift work (6.3%), which is classified as 2A, to 0.01% for exposures to bischloromethylether, ionizing radiation, rubber manufacturing industry and polychlorobiphenyls. Furthermore, over the REP relevant for hematological cancers, the prevalence of ever exposure among men ranged from 1.3% for benzene to 0.06% for ethylene oxyde, while among women, it ranged from 1.3% for formaldehyde to 0.01% for lindane and polychlorobiphenyls.

Table 2
Prevalences of exposure (%) by occupational carcinogen over short and long risk exposure periods.

Occupational exposure	Prevalence (%) 1995–2015		Prevalence (%) 1965–2005	
	Men	Women	Men	Women
Group 1 agents				
1,3-butadiene	0.19	0.08	0.97	0.22
Acid mists, strong inorganic			2.53	1.02
Aromatic amines			1.94	0.91
Arsenic			1.11	0.12
Asbestos			23.54	2.47
Benzene	1.26	0.04	7.26	0.84
Beryllium and beryllium compounds			0.24	0.09
Bis(chloromethyl)ether			0.03	0.01
Cadmium and cadmium compounds			1.25	0.26
Chromium (vi) compounds			5.51	0.45
Engine exhaust, diesel			6.93	0.53
Ethylene oxide	0.06	0.04	0.37	0.10
Formaldehyde	0.69	1.30	3.69	4.13
Ionizing radiation	0.73	0.60	0.58	0.48
Iron and steel founding			0.81	0.02
Leather dust			0.60	1.30
Lindane	0.57	0.01	1.13	0.04
Nickel compounds			3.87	0.74
Polycyclic aromatic hydrocarbons			4.10	0.62
Painters			6.09	0.14
Polychlorinated biphenyls	0.08	0.01	0.47	0.01
Rubber manufacturing industry			0.81	0.01
Silica dust, crystalline			14.16	0.97
Trichloroethylene	0.30	0.02	7.57	0.97
Wood dust			14.27	0.83
Group 2A agents				
Art glass manufacture			0.40	0.12
Cobalt metal with tungsten carbide			1.81	0.03
Diazinon	0.71	0.02	1.10	0.03
Dichloromethane (methylene chloride)	0.13	0.08	1.15	0.31
Hairdressers			1.67	2.84
Lead compounds, inorganic			5.96	0.73
Malathion	0.76	0.02	1.13	0.03
Shift work involving circadian disruption				6.34
Perchloroethylene			0.34	0.58

3.2. Cancer cases attributable to occupational carcinogens and population attributable fraction by cancer sites

Of the 346,000 new cancer cases in France in 2015, occupational exposures led to 7905 new cancer cases, representing 2.3% of all new cancer cases (for occupational agent and cancer site pairs with sufficient evidence of a causal relationship; see Table 3). Men were disproportionately affected, with 7336 new cancers cases (3.9% of all cases) that can be attributable to occupational exposures as compared to 569 new cancer cases (0.4% of all new cancer cases) among women. However, the major cancer types that can be associated to occupational agents were similar in both sexes: the most common cancers caused by occupational agents were lung cancers (5621 in men and 294 in women) and mesothelioma (652 in men and 133 in women). In men, bladder (299) and larynx (252) cancers were the following, whereas ovary (62) was the following in women.

The PAF of cancer caused by occupational exposure also varied by cancer site. Mesothelioma was the cancer site which was impacted the most by occupational exposures to asbestos among both men (PAF = 83.1%) and women (PAF = 41.7%). After mesothelioma, nasal cavity (PAF = 32.9%), nasopharyngeal (PAF = 19.9%) and lung (PAF = 19.3%) cancers were the sites most impacted by occupational

Table 3
The number of new cancer cases and population attributable fraction (PAF) in France in 2015 attributable to exposure to occupational carcinogenic agents, by cancer site.[a]

Cancer (ICD10)	Men		Women		Total	
	Number of attributable cases	PAF (%)	Number of attributable cases	PAF (%)	Number of attributable cases	PAF (%)
Nasopharynx (C11, C14)	55	19.9	4	5.4	59	17.0
Nasal cavity (C30.0)	173	32.9	19	7.9	193	25.0
Larynx (C32)	252	8.3	9	2.3	261	7.6
Lung (C33-34)	5621	19.3	294	2.6	5916	14.6
Skin melanoma (C43)	3	0.1	0	0.0	3	0.02
Mesothelioma (C45)	652	83.1	133	41.7	785	71.1
Ovary (C56)	–	–	62	1.3	62	0.02
Kidney (C64-65)	190	2.4	13	0.3	202	1.7
Bladder (C67)	299	2.9	5	0.2	304	2.4
Radio-inducible solid cancers[b]	8	< 0.1	3	< 0.1	11	< 0.1
Non-Hodgkin Lymphoma (C82-83)	28	0.3	0	0.0	28	0.2
Leukemia (C91-96)	55	0.7	27	0.7	82	0.7
All cancers	**7336**	**3.9**	**569**	**0.4**	**7905**	**2.3**

[a] These results are for carcinogenic agents (IARC Monograph Group 1) where there is sufficient evidence of a causal relationship between exposure and the development of cancer in humans.

[b] The radio-inducible solid cancers are cancers of salivary glands (C07-08), esophagus (C15), stomach (C16), colon-rectum (C18-20), liver (C22), pancreas (C25), lung (C33-34), breast (C50), ovary (C56), prostate (C61), kidney (C64-66), bladder (C67), nervous central system (C70-72), thyroid (C73).

agents among men. Similarly, although at different level among women nasal cavity (PAF = 7.9%), nasopharyngeal (PAF = 5.4%) and lung (PAF = 2.6%) cancers were the sites most impacted by occupational agents (Table 3).

3.3. Population attributable fraction and cancer cases attributable to occupational carcinogens by agents

The number of new cancer cases attributable to occupational agents varied between agents (see Fig. 1 and Table 4). Among both men and women, asbestos exposure caused the largest number of cancer cases (3489 cases in men and 344 in women). In men, asbestos was followed by Chromium VI (1133 cases), working as a painter (780 cases) and silica (429 cases). In women, asbestos was followed to a much lesser extent by Chromium VI (42 cases), nickel compounds (40 cases), and beryllium (26 cases).

3.4. Secondary analysis

If analyses were extended to exposure/cancer site pairs where there is limited evidence of a causal relationship, then 12,314 new cancer cases, representing 3.5% of all new cancer cases, were estimated to be attributable to occupational agents in France in 2015 (Table S3 of Supplemental material). As also observed in the main analysis, the occupational exposures disproportionately affected men, with 10,814 new cancer cases among men, representing 5.7% of all new cancer cases among men, and 1500 new cancer cases among women, representing 1.0% of all new cancer cases among women. The inclusion of two exposures/cancer site pairs associated with limited evidence of a causal association in humans had a noticeable impact on the number of attributable cases: exposure to asbestos added 758 attributable colorectal cancer cases in men and 70 in women; and exposure to shift work in women added 669 breast cancer cases (Table S4 of Supplemental material).

4. Discussion

This study presents the first, most comprehensive, estimation for France of the number of new cancer cases attributable to occupational exposures that accounts for the evolution of the exposure over time. Specifically, this study estimated that 7900 new cancer cases, representing approximately 2.3% of all new cancer cases (3.9% among males and 0.4% among women), were attributable to occupational exposures. When extending the analysis to exposure/cancer site pairs

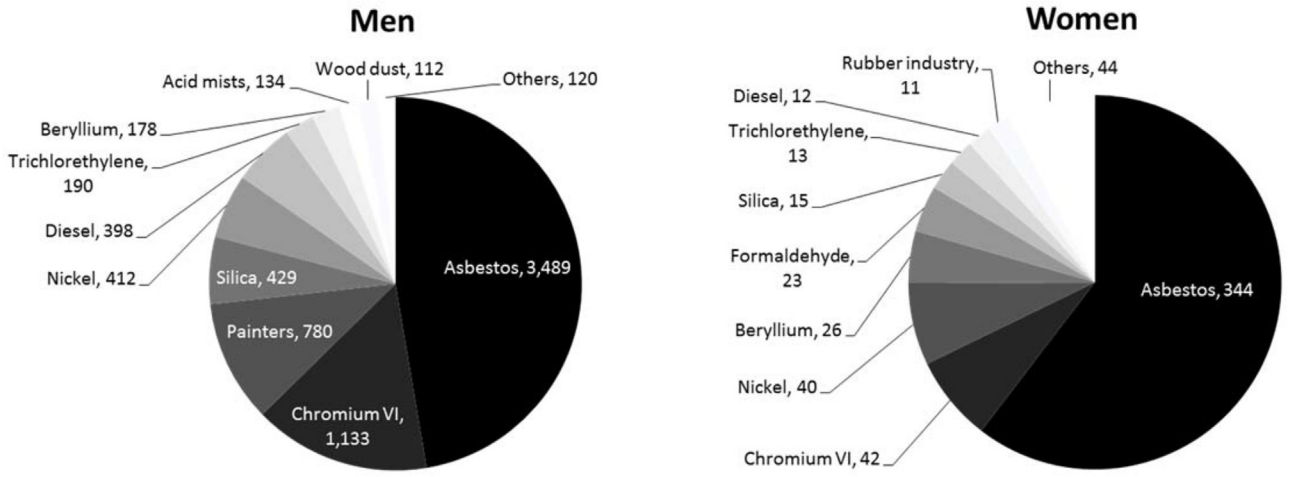

Fig. 1. Agents' contribution to the total number of cancer cases attributable to occupational exposures by sex in France in 2015 (including only agents and cancer sites with sufficient evidence of a causal association in humans).

Table 4
Estimated number of cases (N) and fraction of cancers cases (PAF) attributable to occupational exposures, by exposure.[a]

Agents (Group 1)	Cancer sites (ICD-10)	Men		Women		Total	
		N	PAF (%)	N	PAF (%)	N	PAF (%)
1,3-Butadiene	Leukemias (all) (C91-96)	18	0.4	6	0,2	24	0.3
Asbestos	Larynx (C32)	123	4.1	< 5	0.4	125	3.6
	Lung (C33-34)	2715	9.3	147	1.3	2862	7.1
	Pleural mesothelioma (C45)	652	83.1	133	41.7	785	71.1
	Ovary (C56)			62	1.3	62	1.3
Acid mists	Larynx (C32)	134	4.4	8	1.8	142	4.1
Aromatic amines	Bladder (C67)	5	0.05	0	0	< 10	0.04
Arsenic	Lung (C33-34)	56	0.2	0	0	56	0.1
Benzene	Acute myeloid leukemia (C92.0)	24	1.6	< 5	0.05	25	0.9
Beryllium	Lung (C33-34)	178	0.6	26	0.2	203	0.5
Bischloromethylether	Lung (C33-34)	60	0.2	6	0.05	66	0.2
Cadmium	Lung (C33-34)	69	0.2	6	0.05	75	0.2
Chromium VI	Lung (C33-34)	1133	3.9	42	0.4	1175	2.9
Diesel engine exhaust	Lung (C33-34)	398	1.4	12	0.1	410	1.0
Formaldehyde	Nasopharynx (C11)	11	3.9	< 5	4.4	14	4.0
	Leukemias (all) (C91-96)	13	0.3	20	0.5	33	0.4
Ionizing radiation	Radio-inducible leukemias (C91-96, excl. C91.1)	< 1	0.01	< 1	0.003	< 1	< 0.01
	Radio-inducible solid cancers[b]	8	0.006	< 5	0.003	11	< 0.01
Iron and steel founding	Lung (C33-34)	70	0.2	< 5	0.005	71	0.2
Leather dust	Nasal cavity (C30.0)	< 5	0.6	5	2.2	< 10	1.1
Lindane	Non-Hodgkin lymphoma (C82-85, C96)	28	0.3	0	0.0	28	0.2
Nickel	Nasal cavity (C30.0)	121	23.0	13	5.4	134	17.4
	Lung (C33-34)	291	1.0	27	0.2	318	0.8
Painters	Lung (C33-34)	607	2.1	6	0.05	613	1.5
	Bladder (C67)	173	1.7	< 5	0.04	174	1.4
Polycyclic aromatic hydrocarbons	Lung (C33-34)	14	0.05	< 5	0.01	15	0.04
	Bladder (C67)	83	0.8	< 5	0.1	86	0.7
Polychlorobiphenyls	Skin melanoma (C43)	< 5	0.05	0	0.0	< 5	0.02
Rubber industry	Lung (C33-34)	54	0.2	10	0.08	63	0.2
	Bladder (C67)	41	0.4	< 5	0.05	42	0.3
Silica	Lung (C33-34)	429	1.5	15	0.1	444	1.1
Trichlorethylene	Kidney (C64-65)	190	2.4	13	0.3	202	1.7
Wood dust	Nasopharynx (C11)	46	16.7	< 5	1.2	47	13.5
	Nasal cavity (C30.0)	66	12.5	< 5	0.5	67	8.7

[a] These results are for carcinogenic agents (IARC Monograph Group 1) where there is sufficient evidence of a causal relationship between exposure and the development of cancer in humans.

[b] The radio-inducible solid cancers are cancers of salivary glands (C07-08), esophagus (C15), stomach (C16), colon-rectum (C18-20), liver (C22), pancreas (C25), lung (C33-34), breast (C50), ovary (C56), prostate (C61), kidney (C64-66), bladder (C67), nervous central system (C70-72), thyroid (C73).

with the limited level of evidence of a causal relationship, an estimated 12,300 new cancer cases, representing 3.5% of all new cancer cases (5.7% among males and 1.0% among women), were attributable to occupational exposures.

We found that lung cancers were by far the leading type of cancer among men and women attributable to occupational exposure. Among the main agents related to lung cancers in France, some are still present in the working environment (Chromium VI, silica, diesel engine exhaust) (Vinck and Memmi, 2015). Many occupational carcinogens including Chromium VI, silica or diesel engine exhaust have been suggested to have common exposure route through the respiratory system (Delva et al., 2016; Field and Withers, 2012). Therefore, monitoring of air contaminant concentrations and reduction of exposure in various working environments (Institut National Du Cancer, 2013; World Health Organization, 2013) could prevent a large number of new lung cancer cases and lead to a decrease in occupational related cancers.

4.1. Comparison to other studies

The percentage of all new cancer cases attributable to occupational exposures estimated by this study was higher than that estimated by a previous study for France in 2000, where 1.6% of all new cancer cases were attributable to occupational exposures (2.7% among males and 0.3% among women) (Boffetta et al., 2010). In both studies the largest numbers of new cancer cases were observed for the same cancer sites (i.e., lung cancer in both males and females, followed by mesothelioma and bladder cancers in men). The current study estimated the number of new cancer cases attributable to a wider range of occupational exposures (and also additional cancer sites associated with these exposures), which might explain part of the differences in the estimates. Differences in data sources used, as well as the method to estimate the prevalence of exposure may be other sources of discrepancies. Furthermore, the findings of the current study were similar to the recent estimates of the French National Public Health Agency for 2012 (for the four common agents reported in both studies) (Gilg Soit Ilg et al., 2016).

In other countries the percentage of new cancer cases attributable to occupational agents have ranged from 3% to 14% among men and from 0% to 2% of all new cancer cases among women (Boffetta et al., 2010; Driscoll et al., 2005; Fritschi and Driscoll, 2006; Nurminen and Karjalainen, 2001; Purdue et al., 2015; Rushton et al., 2010). However, direct comparisons between this study and other previous studies are complicated due to differences in the occupational agents and agent/cancer site pairs included, the RR estimates and the methodologies used (Purdue et al., 2015), as well as in the exposure prevalences. A study in the UK in 2010 used a similar methodology to this current study and resulted in similar estimates. Specifically, in the UK in 2010, 4.0% of all new cancer cases, 5.7% among men, and 2.2% among women, were attributable to occupational agents (including pairs with sufficient and limited evidence of a causal association with cancer in humans). Additionally, similar major contributors to the attributable number of cases (asbestos, silica, work as a painter in men, shift work in women) were observed between the current study and those estimated for the UK in 2010 (Rushton et al., 2010).

4.2. Limitations

The estimates of this study are impacted by limitations in the measurements and estimation of exposure to occupational agents, in the estimation of cancer incidence, and in the availability of RR estimates.

As no detailed cancer incidence data were available for year 2015, we used 2013 incidence rates applied to 2015 population to estimate 2015 cancer incidence. Depending on the cancer sites, that may either over- or under-estimate the number of attributable cases for 2015. However, it shouldn't change the conclusion of this work, as cancer incidence is not assumed to have substantially changed between 2013 and 2015.

Data on the exposure to certain important carcinogens in the French population were not available. Specifically, it was not possible to estimate the number of new cancer cases in France attributable to solar radiation, tobacco smoke in the working environment, or dioxins (Marant Micallef et al., 2018). Additionally, exposure to pesticides was assessed using the AGRICAN database, which includes only farmers, but not other workers potentially exposed to pesticides, such as gardeners. The AGRICAN study also does not assess exposure to glyphosate, despite its wide usage in France (Woodburn, 2000). Consequently, our study may underestimate the overall exposure to carcinogens in the French occupational setting. However, to date, glyphosate and the other considered pesticides (except lindane), are associated with cancers with only limited evidence in humans, so this missing data should not impact greatly our main analysis (IARC Monographs, 2017). Furthermore, to take into account historical changes in exposure prevalences, agents were classified into three large categories. Consequently, the corresponding adjustment factors may not be appropriate for each agent within categories, which may lead to some over- or under-estimation of the prevalence of exposure over the long REP. For example, that may explain the high estimated prevalence of exposure to chromium VI in men over the long REP.

Another limitation in this study relates to the risk estimates used. Firstly, for most of the exposures, we used a single risk estimate (of the ever exposed as compared to never exposed), which does not consider different levels of exposure to occupational carcinogens. However, RRs were frequently reported in the literature by percentiles of exposure distribution, and do not necessarily correspond to the categories of occupational exposure in France. As such this may lead to an over- or under-estimation depending on the distribution of exposure to specific agents in France. For agents with a dramatic decrease in exposure levels over the REP such as beryllium and chromium VI, we might have overestimated the PAF in this study. Conversely, to assess the exposure to ionizing radiation and the corresponding relative risk estimates, we used observed average annual exposure doses and a risk model accounting for age and for the exposure dose, which lowers the uncertainty of the estimation for ionizing radiation compared to other exposures.

Furthermore, the RR estimates for some occupational exposures have a large degree of uncertainty. In particular, the RR for the relationship between shift work and breast cancer remains controversial. A recent meta-analysis of cohort studies reported a RR of 0.99 (95%CI = 0.95 to 1.03) for the effect of shift work on breast cancer (Travis et al., 2016). Yet others have argued that different definitions of shift work across the cohorts and imprecise exposure assessment may have hampered pooling of RRs and might bias the result (Knutsson, 2004). In our secondary analysis, including shift work increased the number of cases caused by occupational exposures among women of 669 cases (Table S4 of the Supplemental material).

Lastly, there is limited evidence with which to ascertain whether there is a causal relationship between certain occupational exposures and the risk of developing cancer in humans (Pearce et al., 2015; Purdue et al., 2015; Rushton et al., 2007). Because of this, we performed two distinguished analyses, one including only pairs with sufficient evidence of a causal relationship in humans, and the other one including both pairs with sufficient or limited evidence in humans.

5. Conclusions

Occupational exposures continue to contribute to a substantial number of new cancer cases in France, with many of these carcinogens still currently present in French workplaces. Our study shows that data on occupational carcinogens, in particular over lifetime, are sparse, highlighting the importance of improved monitoring systems or methods to provide better estimate for lifetime exposure of occupational carcinogens. Furthermore, our results largely reflect historical exposure to occupational carcinogenic agents, and do not reflect the burden caused by current exposures. Projection of future cancer burden attributable to current occupational exposures to carcinogens would be of great interest, as recently performed in Australia or in the United Kingdom (Carey et al., 2017; Hutchings and Rushton, 2011).

In combination with costs (such as health care and lost productivity) (Hanly and Sharp, 2014) and the years of life lost due to premature mortality and disability (Soerjomataram et al., 2012), our results can provide an evidence base for the formulation, prioritization and implementation of labor policies aimed at improved occupational conditions and ultimately reduce the overall burden of cancers in France.

Declaration of interest

DL declared he received research support from AREVA, EDF, as a grant to IRSN. All the other authors declare they have no actual or potential competing financial interests.

Funding

This project is funded by the French National Cancer Institute (Institut National Du Cancer) for the project entitled “Définition des priorités pour la prévention du cancer en France métropolitaine: la fraction de cancers attribuables aux modes de vie et aux facteurs environnementaux.” (Grant Number: 2015-002).

Acknowledgements

The authors thank the members of the International Advisory group (D. Maxwell Parkin, Jürgen Rehm and Paolo Vineis) and the members of the steering committee (Catherine Hill, Agnes Rogel, Jean-Nicolas Ormsby, Laure Dossus, and Gwenn Menvielle) for their overall advice in the project “Définition des priorités pour la prévention du cancer en France métropolitaine: la fraction de cancers attribuables aux modes de vie et aux facteurs environnementaux.” We also thank the French Cancer Registries Network which provided the French incidence data. Finally, we acknowledge the contribution of the AGRICAN study team, the Quetelet network, and Hervé Roy from the Institute for Radiological Protection and Nuclear Safety for the provision of some exposure data used in the study (pesticides, SUMER data, and SISERI, respectively).

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ijheh.2018.07.015.

References

Arnaudo, B., Floury, M., Guigon, N., Sandret, N., 2006. Présentation de l'enquête française sumer 2002-2003 menée en France auprès des médecins du travail. Santé, Société et Solidarité 5, 135–138.

Boffetta, P., Autier, P., Boniol, M., Boyle, P., Hill, C., Aurengo, A., et al., 2010. An estimate of cancers attributable to occupational exposures in France. J. Occup. Environ. Med. 52, 399–406.

Carey, R.N., Hutchings, S.J., Rushton, L., Driscoll, T.R., Reid, A., Glass, D.C., et al., 2017. The future excess fraction of occupational cancer among those exposed to

carcinogens at work in Australia in 2012. Cancer epidemiology 47, 1–6.
Delva, F., Andujar, P., Lacourt, A., Brochard, P., Pairon, J.C., 2016. occupational risk factors for lung cancer. Rev. Mal. Respir. 33, 444–459.
Direction des statistiques démographiques et sociales, 2016. Enquête emploi en continu.Direction des statistiques démographiques et sociales.
Driscoll, T., Nelson, D.I., Steenland, K., Leigh, J., Concha-Barrientos, M., Fingerhut, M., et al., 2005. The global burden of disease due to occupational carcinogens. Am. J. Ind. Med. 48, 419–431.
Fevotte, J., Dananche, B., Delabre, L., Ducamp, S., Garras, L., Houot, M., et al., 2011. Matgene: a program to develop job-exposure matrices in the general population in France. Ann. Occup. Hyg. 55, 865–878.
Field, R.W., Withers, B.L., 2012. Occupational and environmental causes of lung cancer. Clin. Chest Med. 33, 681–703.
Fleiss, J.L., 1993. The statistical basis of meta-analysis. Stat Methods in Med 2, 121–145.
Fritschi, L., Driscoll, T., 2006. Cancer due to occupation in Australia. Aust. N. Z. J. Publ. Health 30, 213–219.
Gilg Soit Ilg, A.G.S., Houot, M., Pilorget, C., Imbernon, E., 2016. Estimation de parts de cancers attribuables à certaines expositions professionnelles en France–utilisation des matrices emplois-expositions développées dans le cadre du programme matgéné. Arch. Maladies Prof. 77, 509.
Hanly, P.A., Sharp, L., 2014. The cost of lost productivity due to premature cancer-related mortality: an economic measure of the cancer burden. BMC Canc. 14, 224.
Hutchings, S., Rushton, L., 2011. Toward risk reduction: predicting the future burden of occupational cancer. Am. J. Epidemiol. 173, 1069–1077.
IARC Monographs, 2017. Iarc monographs on the evaluation of carcinogenic risks to humans. Some organophosphate insecticides and herbicides. IARC Monogr. Eval. Carcinog. Risks Hum. 112.
Institut de Radioprotection et de Sûreté Nucléaire, 2015. La radioprotection des travailleurs. Exposition professionnelle aux rayonnements ionisants en france: Bilan 2014. Institut de Radioprotection et de Sûreté Nucléaire, Fontenay-aux-Roses, France.
Institut national de la statistique et des études économiques, 2015. Statistical Operation: Population Estimates. Institut national de la statistique et des études économiques, Paris, France.
Institut National Du Cancer, 2013. Particules fines, dont diesel, et risque de cancer. (Fiches repère). Institut National Du Cancer, Boulogne-Billancourt, France.
International Agency for Research on Cancer, 2017. List of classifications by cancer sites with sufficient or limited evidence in humans. Available: http://www.webcitation.org/6p6Q3eG4i, Accessed date: 20 March 2017.
Knutsson, A., 2004. Methodological aspects of shift-work research. Chronobiol. Int. 21, 1037–1047.
Lacourt, A., Gramond, C., Rolland, P., Ducamp, S., Audignon, S., Astoul, P., et al., 2014. Occupational and non-occupational attributable risk of asbestos exposure for malignant pleural mesothelioma. Thorax 69, 532–539.
Leveque-Morlais, N., Tual, S., Clin, B., Adjemian, A., Baldi, I., Lebailly, P., 2015. The agriculture and cancer (agrican) cohort study: enrollment and causes of death for the 2005-2009 period. Int. Arch. Occup. Environ. Health 88, 61–73.
Levin, M.L., 1953. The occurrence of lung cancer in man. Acta Unio Int. Contra Cancrum 9, 531–541.
Marant Micallef, C., Shield, K.D., Baldi, I., Charbotel, B., Fervers, B., Gilg Soit Ilg, A., et al., 2018. Occupational exposures and cancer: a review of agents and relative risk estimates. Occup. Environ. Med. 75 (8), 604–614.
National Research Council, 2006. Health Risks from Exposure to Low Levels of Ionizing Radiation: Beir Vii - Phase 2. Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation. National Academy of Sciences, Washington, DC, USA.
Nurminen, M., Karjalainen, A., 2001. Epidemiologic estimate of the proportion of fatalities related to occupational factors in Finland. Scand. J. Work. Environ. Health 27, 161–213.
Pearce, N., Blair, A., Vineis, P., Ahrens, W., Andersen, A., Anto, J.M., et al., 2015. Iarc monographs: 40 years of evaluating carcinogenic hazards to humans. Environ. Health Perspect. 123, 507–514.
Purdue, M.P., Hutchings, S.J., Rushton, L., Silverman, D.T., 2015. The proportion of cancer attributable to occupational exposures. Ann. Epidemiol. 25, 188–192.
Rushton, L., Hutchings, S., Brown, T.P., 2007. The burden of cancer at work: estimation as the first step to prevention. Occup. Environ. Med. 65 (12), 789–800.
Rushton, L., Bagga, S., Bevan, R., Brown, T.P., Cherrie, J.W., Holmes, P., et al., 2010. Occupation and cancer in britain. Br. J. Canc. 102, 1428–1437.
Santé Publique France, 2017. Surveillance épidémiologique des cancers. Saint-Maurice. Santé Publique France, France.
Shield, K.D., Parkin, D.M., Whiteman, D.C., Rehm, J., Viallon, V., Micallef, C.M., et al., 2016. Population attributable and preventable fractions: cancer risk factor surveillance, and cancer policy projection. Curr Epidemiol Rep 3, 201–211.
Siemiatycki, J., Richardson, L., Straif, K., Latreille, B., Lakhani, R., Campbell, S., et al., 2004. Listing occupational carcinogens. Environ. Health Perspect. 112, 1447–1459.
Soerjomataram, I., Lortet-Tieulent, J., Parkin, D.M., Ferlay, J., Mathers, C., Forman, D., et al., 2012. Global burden of cancer in 2008: a systematic analysis of disability-adjusted life-years in 12 world regions. Lancet 380, 1840–1850.
Steenland, K., Burnett, C., Lalich, N., Ward, E., Hurrell, J., 2003. Dying for work: the magnitude of us mortality from selected causes of death associated with occupation. Am. J. Ind. Med. 43, 461–482.
Travis, R.C., Balkwill, A., Fensom, G.K., Appleby, P.N., Reeves, G.K., Wang, X.S., et al., 2016. Night shift work and breast cancer incidence: three prospective studies and meta-analysis of published studies. J. Natl. Cancer Inst. 108.
Vincent, R., Kauppinen, T., Toikkanen, J., Pedersen, D., YOung, R., Kogevinas, M., 1999. Carex. International information system on occupational exposure to carcinogenic agents in europe. Occupational exposure to carcinogenic agents in France from 1990 to 1993. Cah. Notes Doc.Hyg.Sécurité Travail 176, 49–90.
Vinck, L., Memmi, S., 2015. Les expositions aux risques professionnels. Les produits chimiques. Enquête sumer 2010. (Synthèses Stat').Direction de l'animation de la recherche, des études et des statistiques.
Woodburn, A.T., 2000. Glyphosate: production, pricing and use worldwide. Pest Manag. Sci. 56, 309–312.
World Health Organization, 2013. Who Global Plan of Action on Workers' Health (2008-2017): Baseline for Implementation. World Health Organization, Geneva, Switzerland.