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1 **Title:** Lung cancer risk assessment for workers exposed to polycyclic aromatic  
2 hydrocarbons in various industries

3

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14 ABSTRACT

15

16 *Background:* Millions of workers are exposed to carcinogenic polycyclic aromatic hydrocarbon (PAH) mixtures.  
17 The toxicity of PAH mixtures is variable and depends on the composition of the mixture, which is related to the  
18 emission sources. Although several indicators exist, the cancer risk estimation associated with occupational  
19 exposure to PAHs is poorly known.

20 *Objectives:* To assess the risk of lung cancer associated with PAHs in several industries using the atmospheric  
21 concentrations of benzo[a]pyrene (BaP) as a proxy.

22 *Methods:* A total of 93 exposure groups belonging to 9 industries were investigated. Eight indicators found in the  
23 literature were compared to assess risks. A consensual indicator was used to estimate lung cancer risks.

24 *Results:* Approximately 30% of the exposure groups were above the maximal risk level of the European Union  
25 ( $10^{-4}$ ). The risk probabilities were  $>10^{-3}$  for coke and silicon production;  $>10^{-4}$  for the manufacturing of carbon  
26 products and aluminum production;  $>10^{-5}$  for foundries and combustion processes;  $>10^{-6}$  for the use of  
27 lubricating oils and engine exhaust emissions; and  $>10^{-7}$  for bitumen. The risk probabilities were highly variable  
28 within industries (from 1 to 1,000 likelihood). A total of 27 (95% CI: 0.1-54) contemporary additional lung  
29 cancer cases could be expected per year in the French exposed population based on estimations using published  
30 data.

31 *Conclusion:* This study provides an overview of cancer risk estimation in many industries. Despite efforts and  
32 changes that had been made to decrease risks, PAHs remain a sanitary threat for people exposed to these  
33 pollutants in occupational environments.

34

35

36 *Keywords:* PAHs, human lung cancer risk assessment, risk probability, inhalation exposure, modeling

## 37 1. Introduction

38 Lung cancer is among the most encountered cancer in France, with 45,222 new cases (30,401 men and  
39 14,821 women) estimated for the year 2015 (INCa 2017a). Between 5 and 15% of these cases are  
40 believed to solely derive from occupational exposure to chemicals such as asbestos, polycyclic  
41 aromatic hydrocarbons (PAHs), fibers or dust (IARC 2018; INCa 2017b).

42 PAHs are a group of widespread persistent organic pollutants that are naturally found in the  
43 environment. PAHs form a family that includes more than 100 molecules composed of at least two  
44 fused benzene rings (Achten and Andersson 2015; Kim et al. 2013; Wickliffe et al. 2014). Although  
45 PAHs can be emitted by natural sources (e.g., forest fires, volcanic eruptions), anthropogenic activities  
46 contribute most to PAH emissions (Li et al. 2013). PAHs are always emitted in complex mixtures  
47 during the combustion process or the distillation of coal and oil (Kim et al. 2013). PAH mixtures are  
48 composed of a particulate (heavier compounds, potentially carcinogenic) and gaseous phases (lighter  
49 compounds, less toxic) (Park et al. 2002). The general population is mainly exposed to PAHs by  
50 inhalation of cigarette fumes for smokers (Ramirez et al. 2011) and ingestion of smoked food for non-  
51 smokers (Ravindra et al. 2008). Workers are mainly exposed to PAHs via inhalation and, to a less  
52 extent, cutaneous absorption (Ravindra et al. 2008).

53 PAHs are among the most toxic carcinogens currently known. The carcinogenicity of PAHs is mostly  
54 caused by their ability to attach DNA, thus generating several disorder effects that often lead to tumor  
55 initiation (Boström et al. 2002; Misaki et al. 2016; Zaccaria et al. 2013). Several epidemiological  
56 studies have incidentally shown an association between exposure to PAHs and an increased risk of  
57 developing lung, skin and bladder cancers (Armstrong et al. 2003; Boffetta et al. 1997; Bosetti et al.  
58 2007; Böstrom et al. 2002; Ifegwu and Anyakora 2015; Kim et al. 2016, Rota et al. 2014). More recent  
59 studies have suggested that PAHs are responsible for an increased risk of developing breast, kidney,  
60 prostate, larynx, blood (leukemia), brain and colorectal cancers (Clapp et al. 2008; Hamidi et al. 2016;  
61 Korsh et al. 2015; Pan et al. 2005; White et al. 2016).

62 PAHs are mainly encountered in occupational settings, where exposure can be high. The total airborne  
63 concentration levels and relative proportions of concentrations (profiles) of PAH congeners in  
64 mixtures are highly variable and depend on emission sources, which differ from industrial to other  
65 sectors (Maître et al. 2018, Manoli et al. 2004; Petit et al. 2017a). Occupational exposure varies over  
66 several orders of magnitude (Maître et al. 2018; Petit et al. 2017a). Because of the wide range of  
67 chemical compositions and concentrations in PAH mixtures, the toxicity of PAH mixtures is variable  
68 and depends on the emission sources.

69 Occupational exposure to PAHs is mainly associated with lung cancer. In the year 2000, it was  
70 estimated that 3% of lung cancer was attributable to occupational exposures in men exposed to PAHs  
71 in France (Boffetta et al. 2010), which is similar to results found in Italy (2.9%, 95% CI: 0.1%-5.9%)  
72 for the period from 2002-2005 (De Matteis et al. 2012). The attributable fraction of lung cancer among

73 this 3% of PAH exposed male workers was estimated to be equal to 27% (Boffetta et al. 2010). Thus,  
74 occupational exposure to PAHs was thought to be responsible for 188 lung cancer cases among  
75 exposed male workers in France in 2000 (Boffetta et al. 2010) and for 131 (95% CI: 5-266) in Italy in  
76 2005 (De Matteis et al. 2012). In 2015, the International Agency for Research on Cancer (IARC)  
77 estimated that occupational exposure to PAHs in France was responsible for 14 new lung cancer cases  
78 in men (IARC 2018). More accurately, using the previously mentioned attributable fractions and the  
79 incidence of the lung cancer, we estimated that between 12 to 37 lung cancer cases would be expected  
80 in France in 2015 among male occupationally exposed to PAHs<sup>1</sup>.

81 Millions of workers are exposed to PAHs in numerous industries, such as aluminum production,  
82 silicon production, electrode production or road paving (Burstyn et al. 2002, Marczynski et al. 2009).  
83 However, there is a lack of knowledge regarding the quantitative assessment of PAH carcinogenic  
84 risks.

85

86 The aim of this study was to assess the PAH occupational lung cancer risk in various industries and  
87 occupations. To achieve this goal, two issues must be considered: how such risk estimation can be  
88 performed, and which PAH congener or combination of PAH congeners should be used.

89 Regarding the how, the most commonly encountered approach is to use an indicator that quantitatively  
90 estimates exposure risk by calculating a probability corresponding to the chances of an additional  
91 human cancer over a certain period of time (usually a lifetime exposure). For example, a probability of  
92  $10^{-6}$  means that there is one chance in a million of observing an additional case of cancer for a lifetime  
93 exposure. Several indicators exist and are mainly used in environmental studies. The simplest  
94 indicator consists of multiplying the exposure concentrations (of a chosen PAH congener or  
95 equivalent) by a unit risk, such as the inhalation unit risk (IUR) for inhalation exposure (Callen et al.  
96 2014; Hsu et al. 2014; Jia et al. 2011). Other more elaborated indicators take into account different  
97 parameters of the exposure conditions and/or human characteristics to minimize the uncertainties of  
98 the risk estimation (Petit et al. 2018, in preparation). Probabilistic cancer risk assessments are valuable  
99 tools but can be problematic because approaches differ between countries and organizations and  
100 because they often result in uncertainty ranges that include the risk considered acceptable (Slob et al.  
101 2014). The provision of a range (e.g., 95% CI), however, is paramount because it demonstrates  
102 whether knowledge about cancer risk is poor and because it is preferable to single values that can be  
103 misleading and might lead to incorrect decisions (Slob et al. 2014; Du et al. 2014). To our knowledge,  
104 there is no guide, recommendation or gold standard concerning the best choice and condition for using  
105 these indicators. In addition, the indicators found in the literature provide risks that vary over several

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<sup>1</sup>lung cancer incidence for male in France for the year 2015 (30401) × attributable fraction of lung cancer associated to occupational exposure to chemicals (5% to 15%) × attributable fraction of lung cancer associated to occupational exposure in men exposed to PAHs in France (3%) × attributable fraction of lung cancer among the 3% of PAH exposed male workers (27%).

106 orders of magnitude, which is problematic because, depending on the indicator chosen, decisions will  
107 be completely different and could be misleading or incorrect (Petit et al. 2018, in preparation). In  
108 addition, it also limits the ability to provide consistency, to assess changes in risk, to compare risks, or  
109 to weigh the benefits of risk management options versus costs. Therefore, all indicators found in the  
110 literature were compared to confirm this result using our data, and a consensual indicator was used to  
111 perform the risk estimation.

112 Benzo[a]pyrene (BaP), the only PAH classified as a proven human carcinogen (IARC 2017) or in  
113 most cases, the benzo[a]pyrene toxic equivalent concentration (BaP<sub>eq</sub>), are used as proxy for the risk  
114 estimation (Cincinelli et al. 2007; Liu et al. 2013). The BaP<sub>eq</sub> approach is believed to take into  
115 account the total carcinogenic potency arising from exposures to a mixture of various PAH  
116 compounds with different toxicities. In this approach, the concentration of a given carcinogenic  
117 congener is expressed as a BaP equivalent concentration using a toxic equivalent factor (TEF) that  
118 utilizes BaP as a reference compound to adjust its original concentration depending on toxicity  
119 differences between both congeners (Boström et al. 2002). Ultimately, BaP<sub>eq</sub> corresponds to the sum  
120 of the BaP concentration and of all congener BaP equivalent concentrations. The TEFs and PAH  
121 congeners used for the BaP<sub>eq</sub> calculation vary between authors. Some, for instance, include all PAHs  
122 classified as carcinogens by the IARC while some include all 16 EPA (Environmental Protection  
123 Agency) PAHs. In addition, the use of TEF is a matter of debate, as their construction is not  
124 necessarily based on the inhalation route and as they could misestimate the actual risk when dealing  
125 with complex mixtures (Boström et al. 2002; Dreij et al. 2017). Indeed, BaP<sub>eq</sub> is based on the additive  
126 effect of each PAH congener toxicity within mixtures. However, predicting the effects of the whole  
127 PAH mixture on risk remains a challenge because both antagonistic and synergic effects/interactions  
128 have been observed during *in vitro* studies, even when dealing with simple binary mixtures (Genies et  
129 al. 2016; Jarvis et al. 2014; Tarantini et al. 2011). In addition, when calculating BaP<sub>eq</sub> concentrations,  
130 only a handful of PAH congeners among hundreds are taken into account, which could underrepresent  
131 the carcinogenic potency (Samburova et al. 2017). Finally, BaP<sub>eq</sub> may not be a better index of PAH  
132 mixtures than BaP, in particular because the TEFs assigned to each PAH congener are very low  
133 (Maître et al. 2018). Consequently, our analysis focused on BaP concentrations to estimate lung cancer  
134 risk. However, the results of the lung cancer risk estimation using BaP<sub>eq</sub> are also provided for  
135 comparative purposes in the main tables and in more detail in the Supplemental Material.

136

## 137 **2. Materials and Methods**

### 138 2.1 Data origin, selection and description

139 The data used in this study were from the Exporisq-HAP database (E-HAP), which includes  
140 measurements of atmospheric PAHs consistently performed with the same sampling strategy and  
141 analysis. A detailed description of the sampling procedure is presented in the Supplemental Material.

142 The creation and construction of the database is detailed in a previous work (Petit et al. 2017b). The E-  
143 HAP contained 1729 air samplings (personal and area) comprising the concentrations (in ng/m<sup>3</sup>) of 17  
144 PAHs over short-term sampling ( $\leq 2$  h) and long-term sampling ( $>2$  h) durations. The industrial  
145 landscape found in the E-HAP is organized into three imbricated hierarchical levels of increasing  
146 description. Each sampling was assigned a level 1 (L1G), level 2 (L2G) and level 3 (L3G) exposure  
147 group. L1Gs, which typically refer to product/raw material characteristics, were subdivided into L2Gs  
148 corresponding to the exposure source characteristics (locations and/or operations with different  
149 emission sources). In addition, L2Gs were split into L3Gs that typically referred to a task or a series of  
150 tasks that appeared to be the most homogeneous during the work study (Petit et al. 2017b). Levels 1, 2  
151 and 3 were the least, intermediate and most accurate levels, respectively, of the description of the  
152 occupational context. A detailed description and additional information (e.g., process description) for  
153 each exposure group are also available (Petit et al. 2017b).

154 Samplings were performed in nine L1Gs: aluminum production, silicon production, coke production,  
155 manufacturing of carbon products, foundries, combustion processes, use of lubricating oils, engine  
156 exhaust emissions, and bitumen (road paving). Each measurement was associated with additional  
157 information, such as the sampling time or protective equipment.

158 For the purpose of assessing the lung cancer risk, only personal samplings carried out for long-term  
159 durations were included in this study. Samplings with a missing measurement (or concentration) and  
160 samplings with no duration were excluded. Data below the limit of quantification (LOQ) were  
161 replaced by LOQ/2. Exposure groups (L1Gs, L2Gs, L3Gs) gathering at least six samplings were  
162 included. The exposure used to estimate the risk was representative because only long-term personal  
163 sampling were used and because these samplings were not worst-case samplings or regulatory  
164 samplings (Petit et al. 2017b). The BaP and BaP<sub>eq</sub> concentrations were used to assess human lung  
165 cancer. A detailed description of the calculation of the BaP<sub>eq</sub> concentrations are presented in the  
166 Supplemental Material. A comparison between risks calculated using the BaP and BaP<sub>eq</sub>  
167 concentrations was performed using Fleiss' Kappa (see Supplemental Material).

168 Although it is possible to estimate the cancer risk of each exposure group, the reliability of the  
169 estimation depends on the concentration dispersion (given by the geometric standard deviation for  
170 lognormal distributed concentrations), with a higher degree of reliability when the dispersion is low.  
171 The BaP concentrations were assumed to be log-normally distributed as exposure concentrations  
172 usually follow a lognormal distribution in industrial hygiene (Rappaport 1991). Therefore, the degree  
173 of confidence of the concentration can be expressed as a confidence interval (CI), as illustrated in  
174 Equation 1 with the 95% CI.

175

$$176 \quad 95\% \text{ CI } (C) = [GM/GSD^2; GM \times GSD^2] \quad [1]$$

177 where GM is the concentration geometric mean and GSD is the concentration geometric standard  
178 deviation.

179 The 95% CI was always provided to account for uncertainties associated to the exposure variability.  
180 The exposure groups with the lowest concentration dispersion possible are important for the greatest  
181 accuracy concerning the components of the worker exposures (Petit et al. 2017b) and thus the best risk  
182 estimation possible.

## 183 2.2 Comparison of risks assigned by each indicator found in the literature

184 The risk indicators found in the literature for inhalation exposure are listed in Table 1. The formulas  
185 shown in Table 1 slightly differ from those found in the mentioned references because they were  
186 modified such that each indicator (probability) had to range between 0 and 1 following the  
187 transformation:

188 “*Modified formula*” =  $1 - \text{exponential}(-\text{“formula found in the literature”})$

189 The former formulas were recovered in a low concentration limit. All of the risk indicators had a  
190 similar functional form (Equation 2) to the exposure concentration and differed in expression of the  
191 coefficient ( $\alpha$ ) multiplied by the concentration.

$$192 \quad R = 1 - e^{-\alpha \times C} \quad [2]$$

193 where  $R$  is a given risk indicator,  $C$  is the pollutant concentration and  $\alpha$  represents a falloff coefficient  
194 used to calculate the given risk indicator (Table 1, Supplemental Material), for example,  $\alpha =$   
195  $\frac{ET \times EF \times ED \times IUR}{AT}$  for the indicator RC and  $\alpha = IUR$  for the indicator LCR.

196 All of the parameters used for the calculations of the risk indicators are shown in Table S1. Following  
197 the convention that is typically used in France, we considered that workers weighed, on average, 70 kg  
198 and were exposed to a constant concentration  $C$  of PAHs over 8 hours per day, 5 days a week, 250  
199 days a year for 45 years, corresponding to an exposure duration  $T = 45$  years. For IUR and CSF, the  
200 values defined by the Office of Environmental Health Hazard Assessment (OEHHA) were used. Both  
201 the IUR and CSF values were defined assuming that an individual was continuously exposed on a  
202 daily basis with a lifetime inhalation exposure to an agent. Because we were investigating  
203 occupational exposures, the IUR and CSF values were rescaled to 45 years of exposure using a cross  
204 product, i.e.,  $IUR_{\text{occupation}} = IUR_{\text{lifetime}} \times 45/70$ . In occupational settings, people are not exposed  
205 24h a day and 365 days a year. This discontinuity in the exposure was taken into account in all  
206 indicators with the exception of LCR (Table 1). Thus, adapting LCR to account for the exposure  
207 discontinuity led to  $LCR = RC$ , so that only the RC indicator was kept in further analyses.

208 **Table 1.** Risk indicators found in the literature to estimate lung cancer risk due to PAH exposure

Indicator	Abbreviation	Expression as $1 - e^{-\alpha \times C}$	Reference
Modified lung cancer risk	LCR	$LCR = 1 - e^{-IUR \times C}$	Callen et al. 2014; Hsu et al. 2014; Jia et al. 2011; Lin et al. 2008; Liu et al. 2010; Ramirez et al. 2011; Wang et al. 2012
Modified cancer risk	RC	$RC = 1 - e^{-\left(\frac{ET \times EF \times ED \times IUR}{AT}\right) \times C}$	Irvine et al. 2014
Modified incremental lifetime cancer risk	ILCR	$ILCR_1 = 1 - e^{-\left(\frac{CSF \times \sqrt[3]{BW/70} \times EF \times ED \times IR}{BW \times AT \times PEF}\right) \times C}$	Huang et al. 2016; Soltani et al. 2015
		$ILCR_2 = 1 - e^{-\left(\frac{CSF \times \sqrt[3]{BW/70} \times EF \times ED \times IR \times cf}{BW \times AT}\right) \times C}$	Chen and Liao 2006; Hoseini et al. 2016; Singh et al. 2016; Wang et al. 2014
		$ILCR_3 = 1 - e^{-\left(\frac{CSF \times IR \times EF \times ED \times ET}{BW \times AT}\right) \times C}$	Hu et al. 2007; Li et al. 2013; Qu et al. 2015
		$ILCR_4 = 1 - e^{-\left(\frac{CSF \times IR \times EF \times ED \times A}{BW \times AT}\right) \times C}$	Li et al. 2014
		$ILCR_5 = 1 - e^{-\left(\frac{CSF \times IR \times EF \times ED \times cf}{BW \times AT}\right) \times C}$	Yu et al. 2015
Modified risk	RM	$RM = 1 - e^{-\left(\frac{IR_a \times EF \times ED \times ET}{BW \times AT \times IR_b}\right) \times (IUR \times BW \times cf)} \times C}$	Amarillo et al. 2014

209 Note: A: inhalation absorption factor, AT: averaging time, BW: body weight, C: given PAH  
 210 concentration, cf: conversion factor, CSF: inhalation cancer slope factor, ED: exposure duration, EF:  
 211 exposure frequency, IUR: inhalation unit risk, ET: exposure time, PEF: particles emission factor, IR:  
 212 inhalation rate, IR<sub>a</sub>: inhalation rate in m<sup>3</sup>/hour, IR<sub>b</sub>: inhalation rate in m<sup>3</sup>/day.

### 2.3 Risk assessment using a consensual risk indicator

As there is no guide or recommendations about the choice and condition for using these indicators, all of them were used in the first instance for all exposure groups constituting at least 6 long-term samplings (Table S2). The reliability of the agreement between all of the indicators was assessed using Fleiss' Kappa. If all of the indicators provided similar results (with at least substantial agreement, corresponding to Fleiss' Kappa > 0.6) for a given concentration, one was kept for further calculations. Otherwise, when the indicators provided dissimilar results, we constructed a consensual risk indicator (CRI) that combined the outputs of all of the indicators to perform the risk estimation. The purpose of the consensual risk indicator (CRI) was to aggregate the outputs of all indicators given in Table 1 to produce a single combined probability distribution for the risk estimation (Petit et al. 2018, in preparation).

The simplest strategy to construct a consensual indicator is to use a similar relation to Equation 2 (Petit et al. 2018, in preparation):

$$\text{Consensual risk indicator} = \text{CRI} = 1 - e^{-\beta C} \quad [3]$$

where  $C$  is the pollutant concentration and the coefficient  $\beta$ , which can be considered an effective IUR, is obtained from a linear combination of falloff coefficients of all indicators as follows:

$$\beta = \sum_{i=1}^n \omega_i \alpha_i \quad [4]$$

where  $n$  is the total number of indicators,  $\omega_i$  ( $0 \leq \omega_i \leq 1$  and such that all  $\omega_i$  sum to 1) is a weight attributed to the indicator  $R_i$  shown in Table 1 and  $\alpha_i$  is the falloff coefficient of  $R_i$  following the parameters shown in Table S1. Equation 3 with Equation 4 was derived from the linear approximation of the linear combination of  $R_i$  with weight  $\omega_i$ . Therefore, such a relationship remained valid for concentrations smaller than  $C_{max} = 2\beta/\text{variance}(\beta)$  above which the linear approximation broke down. The  $\omega_i$  were obtained using an optimization procedure, which consisted of attributing weights according to the inverse of the square Euclidean distance in the rank between each indicator and their rank barycenter, under the condition that all weights sum to one. As a result of this procedure, indicators closest to the barycenter were attributed the highest weights compared with those farthest from the barycenter.

As in most cases for  $\beta \times C < 1$ , the uncertainty on the overall consensual indicator can be obtained as,

245 
$$\frac{\Delta CRI}{CRI} = \frac{\Delta\beta}{\beta} + \frac{\Delta C}{C} \quad [5]$$

246 where  $\Delta\beta$  and  $\Delta C$  are the absolute error of  $\beta$  and  $C$ , respectively. In addition, the relative error for  $\beta$  is  
247 constant while the relative error of the concentration is variable, depending on the exposure group  
248 considered.

249 Uncertainties on the concentrations are provided in Equation 1. Regarding the uncertainty associated  
250 with the falloff factor  $\beta$ , we used the weighed standard deviation of  $\beta$ . However, to generate percentile  
251 values of the risk from which the 95% CI of the risks are derived, several simulations of the CRI  
252 presented in Equation 3 were run using a lognormal distribution for concentrations (as described in  
253 Section 2.1) and assuming for  $\beta$  a normal distribution with mean and standard deviation described  
254 above.

255

#### 256 2.4 Decision rule regarding the risk estimation/ranking

257 There are different thresholds provided by agencies and governments around the world to assign a  
258 risk. For instance, a probability  $> 10^{-6}$  is considered unacceptable by the US EPA, a probability of  $10^{-4}$   
259 is considered the maximal risk level in the European Union, while a probability  $> 10^{-3}$  is considered a  
260 high priority by the US EPA and a significant risk level by the US Supreme Court. The threshold  
261 considered acceptable for occupational exposure is always greater than the threshold for the general  
262 population. Based on the different existing thresholds that can be found in the literature, a decision  
263 rule was used to rank risks (Table 2). The decision rule was developed in such a way that a factor of  
264 10 (one order of magnitude) separated two consecutive classes (very low, low, moderate, high and  
265 very high) to allow an easy comparison with the existing risk threshold deemed relevant or applicable  
266 to a study/country. As each exposure group consisted of several samplings (at least 6), a distribution of  
267 risks/probabilities was subsequently generated. Therefore, the rule consisted of comparing the 90<sup>th</sup>  
268 percentile ( $P_{0.90}$ ) of the distribution of risks to different thresholds. In the Results and Discussion  
269 sections, the presented risk is always the 90<sup>th</sup> percentile of the distribution of risks.

270 **Table 2.** Decision rule for lung cancer risk estimation

Situation	Risk ranking	Interpretation
$P_{0.90} > 10^{-3}$	Very high risk	> 1/1000 chance of observing one additional lung cancer over a period of 45 years of work
$10^{-4} < P_{0.90} \leq 10^{-3}$	High risk	> 1/10000 chance of observing one additional lung cancer over a period of 45 years of work
$10^{-5} < P_{0.90} \leq 10^{-4}$	Moderate risk	> 1/100000 chance of observing one additional lung cancer over a period of 45 years of work
$10^{-6} < P_{0.90} \leq 10^{-5}$	Low risk	> 1/1000000 chance of observing one additional lung cancer over a period of 45 years of work
$P_{0.90} \leq 10^{-6}$	Very low risk	< 1/10000000 chance of observing one additional lung cancer over a period of 45 years of work

271 Note:  $P_{0.90}$  : 90<sup>th</sup> percentile of the risk probability distribution.

## 2.5 Expected number of additional lung cancer cases per year in France

Let  $P(\tau)$  denote the probability of the occurrence of lung cancer after an exposure of duration  $\tau$ , and  $N(\tau)$  be the number of individuals who were exposed to the pollutant of interest for a time period  $\tau$ , such that the total exposed population is  $N_{exp} = \sum_{\tau=0} N(\tau)$ . It follows that the expected number of additional lung cancers  $E(\tau)$  after an exposure of duration  $\tau$  can be obtained as,

$$E(\tau) = N(\tau) \times P(\tau) = N(\tau) \times [1 - \exp\{-\beta C_{\tau}(\tau/T)\}] \quad [6]$$

where  $C_{\tau}$  is the (constant) mean concentration of the pollutant that the population has been exposed to over the exposure of duration  $\tau$  and  $T = 45$  years is the maximal occupational exposure duration. For the sake of illustration, we consider three occupational exposure durations, 15 years, 30 years and 45 years, and aggregate the exposed population,  $N_{exp} = N_{\leq 15} + N_{15-30} + N_{>30}$ , into three subpopulations,  $N_{\leq 15}$ ,  $N_{15-30}$  and  $N_{>30}$  corresponding to the population in the exposure time intervals from 0 to 15 years, > 15 to 30 years, and > 30 years, respectively. For an occupational exposure of a given duration, we obtain the expected number of additional lung cancers as

$$\begin{cases} E_{15} = N_{\leq 15} \times \left[1 - \exp\left\{-\frac{\beta C_{15}}{3}\right\}\right] \\ E_{30} = N_{15-30} \times \left[1 - \exp\left\{-\frac{2\beta C_{30}}{3}\right\}\right] \\ E_{45} = N_{>30} \times [1 - \exp\{-\beta C_{45}\}] \\ E_e = N_{exp} \times [1 - \exp\{-\beta C_{45}\}] \end{cases} \quad [7]$$

where  $E_e$  is the expected number of additional lung cancers among the total exposed population after an exposure of duration 45 years,  $E_{45}$  is the expected number of additional lung cancers among the  $N_{>30}$  subpopulation after an exposure of 45 years,  $E_{30}$  is the expected number of additional lung cancers among the  $N_{15-30}$  subpopulation after an exposure of 30 years and  $E_{15}$  is the expected number of additional lung cancers among the  $N_{\leq 15}$  subpopulation after an exposure of 15 years.

This approach was used to estimate the expected contemporary number of additional lung cancer cases per year in France in each L1G. We mean that the estimation can be performed either retrospectively or prospectively depending on the time origin used for the exposure periods. In the retrospective scheme, the exposure had started 45 years prior, and the estimation then provides the number of additional lung cancers that would currently be expected; whereas in the prospective scheme, the first exposure occurred at the time of the measurements (between 2000 and 2014), and then the estimation reflected the number of additional lung cancers that would be expected in the next 30-45 years. If the number of people exposed and condition of exposure did not change over time, then this approach would provide the expected number of additional lung cancer cases per year in France in each L1G.

The French population of workers potentially exposed to PAHs was estimated in each L1G. The total L1G workforce was estimated through the national statistics, national studies and grey literature (AFA, 2016; DARES, 2014; FFF, 2014, 2016; FIM, 2016; FNTP, 2017; INSEE, 2017; Ministère du Travail, 2016; Pompiers, 2017; SCF, 2017). The exposed populations,  $N_{\leq 15}$ ,  $N_{15-30}$  and  $N_{>30}$ , were

304 determined from the E-HAP data, and we assumed that the BaP concentrations were identical for all  
305 exposure durations,  $C_{15} = C_{30} = C_{45}$ . The distribution of the BaP and BaP<sub>eq</sub> concentrations provided  
306 the distributions of the expected numbers of lung cancers, from which the summary statistics are  
307 reported.

308 No estimation of the expected number of additional lung cancer was performed for L2Gs and L3Gs  
309 because it is currently not possible to estimate the total number of workers for these groups. These  
310 groups are too accurate and specific to be found in national statistics, national studies or grey  
311 literature. Indeed, the available French national statistics and national studies only provide information  
312 regarding industries and sometimes jobs, which are too generic (not sufficiently descriptive) in  
313 comparison to L2Gs and L3Gs, which refer to locations/operations and tasks, respectively (Petit et al.  
314 2017b).

315

## 316 2.6 Software

317 Data analyses and all calculations were performed with R software 3.1.0® (R Core Team, Vienna,  
318 Austria) for Windows 7©.

319

## 320 3. Results

321 The measurement campaigns were carried out from 2000 to 2014. A total of 93 exposure groups were  
322 studied (Table S2). Among them, 9 were L1Gs, 35 L2Gs and 49 L3Gs.

323

### 324 3.1 Risk indicator comparison

325 Regardless of the exposure group considered, ILCR1 always assigned the same risk: very low risk of  
326 lung cancer (90<sup>th</sup> percentile of the risk probability distribution  $\leq 10^{-6}$ ) (Table S2). Among all  
327 indicators, ILCR4 always assigned the highest risk. This risk was 74.9, 124.7, 126.3, 224.4, 227.3 and  
328  $4.3 \times 10^{11}$  times higher than the one assigned by ILCR5, ILCR3, ILCR2, RM, RC and ILCR1,  
329 respectively. ILCR2 and RC provided almost the same results, with 91 similar risk assignments of 93  
330 possible. ILCR3 and RM provided almost the same results, with 92 similar risk assignments of 93  
331 possible. Regardless of the L1G considered, Fleiss' Kappa was very low (ranging from -0.01 for  
332 bitumen and aluminum production to 0.30 for silicon production). The overall Fleiss' Kappa was low  
333 (0.29), denoting only a fair agreement between all indicators (Table S2), which confirmed the  
334 usefulness of using CRI.

### 335 3.2 Estimation of lung cancer risk using CRI

336 Using all the indicators shown in Table 1 to construct CRI,  $\beta_{\text{BaP}} = 2.93 \times 10^{-4} \text{ m}^3/\mu\text{g} \pm 7.14 \times 10^{-5} \text{ m}^3/\mu\text{g}$   
337 was determined for the  $\beta$  value, which must be compared with  $\text{IUR} = 7.1 \times 10^{-4} \text{ m}^3/\mu\text{g}$  (see Table S1).  
338 We used this  $\beta$  in the CRI to perform the risk estimation as the highest BaP and BaP<sub>eq</sub> concentrations

339 in the E-HAP were  $65 \mu\text{g}/\text{m}^3$  and  $106 \mu\text{g}/\text{m}^3$ , respectively, which were lower than the maximum  
340 concentration allowed for using this approach ( $\text{BaP } C_{\text{max}} = 115 \text{ mg}/\text{m}^3$ ).

341 Among the existing indicators found in the literature, both ILCR3 and RM approaches were closest  
342 (factor 1.1) to the conclusions attained with CRI. The obtained results using  $\beta$  were 125 times lower  
343 than those that would have been obtained with ILCR4 and 1.1 to 1.7 times lower if ILCR3 or ILCR5  
344 had instead been used. By contrast, the use of this  $\beta$  provided results 1.1 to 1.8 times higher than if  
345 RM, ILCR2 or RC had been used and  $3.4 \times 10^9$  times higher than if ILCR1 had been chosen.

346 The estimated risks were 1.1 to 2.2 times higher (factor, on average, of 1.3) when BaP<sub>eq</sub> was used  
347 instead of BaP (Table S3). BaP and BaP<sub>eq</sub> provided similar results when assigning risk, with almost  
348 perfect agreement between them (Fleiss' Kappa of 0.92). Only 6 groups were assigned with different  
349 lung cancer risks when using the BaP and BaP<sub>eq</sub> concentrations (Tables 3 and S3). In these cases, the  
350 risk attributed to the BaP<sub>eq</sub> concentrations was always greater than the risk attributed with BaP  
351 concentrations, which was not surprising because the BaP<sub>eq</sub> concentrations were always higher than  
352 the BaP concentrations.

353 Table 3 synthesizes all the lung cancer risks estimated using CRI. The risk reliability of CRI mostly  
354 depended on measurement uncertainties and was usually highest for exposure groups with highest  
355 description accuracy. The relative error associated with  $\beta$  ( $\sigma/\beta$ ) was equal to 0.24. By contrast, the  
356 relative error associated with the concentration ( $\sigma/\mu_C$ , where  $\mu_C$  is the arithmetic mean concentration)  
357 was, on average, equal to 1.6 (min: 0.5, max: 8.3) for the BaP and 1.5 (min: 0.5, max: 8.2) for the  
358 BaP<sub>eq</sub>. The relative error associated with the concentration was highest for L1Gs: 3.1 on average  
359 (min: 1.4, max: 8.3) for the BaP and 3.1 on average (min: 1.4, max: 8.2) for the BaP<sub>eq</sub>. Regarding  
360 L2Gs, this relative error was, on average, equal to 1.6 (min: 0.5, max: 4.9) for both the BaP and  
361 BaP<sub>eq</sub>. The relative error associated with the concentration was lowest for L3Gs: 1.2 on average (min:  
362 0.5, max: 3.5) for BaP and 1.2 on average (min: 0.5, max: 3.4) for BaP<sub>eq</sub>. These observations are not  
363 surprising because the more detailed the level of description, the lower the dispersion of the BaP  
364 concentrations.

365 Based on the total of 93 exposure groups studied, 16% were estimated to have a very high risk (90<sup>th</sup>  
366 percentile  $> 10^{-3}$ ), 15% a high risk ( $10^{-4} < 90^{\text{th}} \text{ percentile} \leq 10^{-3}$ ), 27% a moderate risk ( $10^{-5} < 90^{\text{th}}$   
367 percentile  $\leq 10^{-4}$ ), 25% a low risk ( $10^{-6} < 90^{\text{th}} \text{ percentile} \leq 10^{-5}$ ) and 17% a very low human risk of lung  
368 cancer (90<sup>th</sup> percentile  $\leq 10^{-6}$ ) (Table 3).

369 Regarding L1Gs, French workers exposed to PAHs via products derived from coal (coke, aluminum,  
370 silicon production, manufacturing of carbon products and foundry) were the most at risk of developing  
371 a lung cancer. Coke production had the highest risk of lung cancer, with a chance of three in a  
372 thousand of an additional human lung cancer over 45 years of work. A very high risk of lung cancer  
373 was also estimated for silicon production ( $1.1 \times 10^{-3}$ ), which was almost four times higher than the risk  
374 of manufacturing carbon product ( $2.5 \times 10^{-4}$ ). There was an estimated risk of  $1.0 \times 10^{-4}$  for aluminum

375 production,  $1.8 \times 10^{-5}$  for foundries,  $1.5 \times 10^{-5}$  for combustion processes,  $1.9 \times 10^{-6}$  for engine exhaust  
376 emissions,  $1.7 \times 10^{-6}$  for the use of lubricating oils, and  $5.0 \times 10^{-7}$  for bitumen.

377 The risks were highly variable within L1Gs (up to 3 orders of magnitude in terms of likelihood).  
378 Regarding coke production, all exposure groups had either a very high (between  $2.0 \times 10^{-3}$  and  $6.7 \times 10^{-3}$ )  
379 or a high risk (from  $3.9 \times 10^{-4}$  to  $8.7 \times 10^{-4}$ ). For silicon production, lung cancer risks were most of the  
380 time greater (up to 6 likelihood) for tasks near the furnaces (maintenance activities and masonry) than  
381 near composite electrodes. The only exceptions were for the fluke damage and resistors dismantling  
382 activities. A high risk was found for all activities performed near Söderberg electrodes. Manufacture  
383 was the L2G with the lowest risk of lung cancer. In aluminum production, the risk of lung cancer was  
384 most of the time moderate ( $\leq 10^{-4}$ ), with the exception of the aluminum L1G itself, the maintenance of  
385 the paste tower and furnace L2G and its electricians L3G as well as the prebaked anode production –  
386 paste tower L2G, which demonstrated a high risk of lung cancer. With the exception of the cathode  
387 graphitization (moderate risk), all exposure groups in the manufacture of carbon products  
388 demonstrated a high risk ( $\leq 10^{-3}$ ) of lung cancer. For foundries, risks in steel foundries ( $2.4 \times 10^{-5}$ ) were  
389 24 times higher than in aluminum foundries. In the aluminum foundry, risks of lung cancer were either  
390 low ( $\leq 10^{-5}$ ) or very low ( $\leq 10^{-6}$ ). In addition, the driver and smelter had a risk of  $1.4 \times 10^{-6}$ , which was  
391 approximately twice as high as the risk of the caster ( $6.6 \times 10^{-7}$ ). For the steel foundry, the risk was  
392 always moderate.

393 With the exception of the firefighters and chimney sweepers from combustion processes, all exposure  
394 groups that used products derived from petroleum had either a low or a very low risk of lung cancers.  
395 All exposure groups with a low risk of lung cancer used only products derived from petroleum, with  
396 the exception of the aluminum foundries (Table 3). All exposure groups exposed to engine exhaust  
397 emissions had a probability that never exceeded  $4.6 \times 10^{-6}$  (for roadwork mechanics). Roadwork  
398 mechanics had a 2-3 times higher risk than heavy truck and agricultural mechanics. Workers using a  
399 hedge trimmer had a 3 times higher risk than workers using a brushwood clearer. Underground drivers  
400 had a ten times higher risk than open space drivers. With the exception of discharge mold and  
401 vehicles, all exposure groups using lubricating oils had a very low risk of lung cancer. All workers  
402 exposed to bitumen (road paving) had a very low risk of lung cancer, with the exception of workers  
403 applying hot bitumen in a tunnel using hot bitumen ( $1.2 \times 10^{-6}$ ). This activity had a three times higher  
404 risk when performed with hot bitumen rather than warm bitumen.

405 **Table 3.** Estimated risk of human lung cancer in nine L1Gs and all their L2Gs and L3Gs using the  
 406 BaP concentrations

Level groups	N	BaP level			Risk				BaPeq Ranking (Table S3)
		GM (ng/m <sup>3</sup> )	5 <sup>th</sup> p. (ng/m <sup>3</sup> )	95 <sup>th</sup> p. (ng/m <sup>3</sup> )	90 <sup>th</sup> p.	5 <sup>th</sup> p.	95 <sup>th</sup> p.	Ranking	
1. Aluminum production	138	55	8.0	464	1.0x10 <sup>-4</sup>	1.5x10 <sup>-6</sup>	1.7x10 <sup>-4</sup>	High	High
1.1 Prebaked anode production – paste tower	30	74	10	1156	2.2x10 <sup>-4</sup>	1.0x10 <sup>-6</sup>	4.1x10 <sup>-4</sup>	High	High
1.1.1 Manufacture operator	7	84	36	285	7.5x10 <sup>-5</sup>	5.4x10 <sup>-6</sup>	1.0x10 <sup>-4</sup>	Moderate	Moderate
1.1.2 Watchperson, heat attendant	18	43	7.7	486	8.7x10 <sup>-5</sup>	9.9x10 <sup>-7</sup>	1.5x10 <sup>-4</sup>	Moderate	High
1.2 Prebaked anode production – furnace	24	24	7.9	67	1.9x10 <sup>-5</sup>	1.8x10 <sup>-6</sup>	2.5x10 <sup>-5</sup>	Moderate	Moderate
1.2.1 Gas attendant, Overhead crane operator	16	24	7.4	73	1.9x10 <sup>-5</sup>	1.8x10 <sup>-6</sup>	2.5x10 <sup>-5</sup>	Moderate	Moderate
1.2.2 Heat attendant mason	8	25	8.9	54	1.9x10 <sup>-5</sup>	1.9x10 <sup>-6</sup>	2.5x10 <sup>-5</sup>	Moderate	Moderate
1.3 Maintenance of the paste tower and furnace	22	94	19	511	1.2x10 <sup>-4</sup>	3.8x10 <sup>-6</sup>	1.9x10 <sup>-4</sup>	High	High
1.3.1 Maintenance operator	6	73	29	345	7.6x10 <sup>-5</sup>	3.8x10 <sup>-6</sup>	1.1x10 <sup>-4</sup>	Moderate	Moderate
1.3.2 Mechanic	9	207	78	696	1.9x10 <sup>-4</sup>	1.2x10 <sup>-5</sup>	2.7x10 <sup>-4</sup>	High	High
1.3.3 Electrician	6	48	16	183	5.3x10 <sup>-5</sup>	2.3x10 <sup>-6</sup>	7.8x10 <sup>-5</sup>	Moderate	Moderate
1.4 Ramming: electrolysis construction and furnace restoration	57	48	7.8	201	6.6x10 <sup>-5</sup>	1.7x10 <sup>-6</sup>	1.0x10 <sup>-4</sup>	Moderate	Moderate
1.4.1 Tank construction: using small seals	14	23	4.0	148	3.8x10 <sup>-5</sup>	6.4x10 <sup>-7</sup>	6.3x10 <sup>-5</sup>	Moderate	Moderate
1.4.2 Tank construction: using large seals	13	33	7.6	151	4.4x10 <sup>-5</sup>	1.2x10 <sup>-6</sup>	6.9x10 <sup>-5</sup>	Moderate	Moderate
1.4.3 Tank construction: using both seals	30	78	13	249	7.9x10 <sup>-5</sup>	4.3x10 <sup>-6</sup>	1.1x10 <sup>-4</sup>	Moderate	Moderate
2. Silicon production	324	184	5.8	7167	1.1x10 <sup>-3</sup>	9.6x10 <sup>-7</sup>	2.5x10 <sup>-3</sup>	Very high	Very high
2.1 Composite electrodes	108	732	34	8535	1.9x10 <sup>-3</sup>	1.2x10 <sup>-5</sup>	3.7x10 <sup>-3</sup>	Very high	Very high
2.1.1 Paste loading in the electrode	37	1399	62	11899	3.9x10 <sup>-3</sup>	2.2x10 <sup>-5</sup>	7.4x10 <sup>-3</sup>	Very high	Very high
2.1.2 Casing welding of the electrode	55	914	80	5882	1.6x10 <sup>-3</sup>	2.4x10 <sup>-5</sup>	2.6x10 <sup>-3</sup>	Very high	Very high
2.2 Söderberg electrodes	13	131	20	1097	2.3x10 <sup>-4</sup>	3.6x10 <sup>-6</sup>	3.9x10 <sup>-4</sup>	High	High
2.2.1 Casing welding of the electrode	8	174	36	1188	2.7x10 <sup>-4</sup>	5.6x10 <sup>-6</sup>	4.2x10 <sup>-4</sup>	High	High
2.3 Manufacture	112	23	4.2	202	3.4x10 <sup>-5</sup>	7.8x10 <sup>-7</sup>	5.6x10 <sup>-5</sup>	Moderate	Moderate
2.3.1 Post's Chief	15	24	5.4	148	4.0x10 <sup>-5</sup>	6.6x10 <sup>-7</sup>	6.7x10 <sup>-5</sup>	Moderate	Moderate
2.3.2 Raw material loading	42	27	5.7	260	3.4x10 <sup>-5</sup>	1.1x10 <sup>-6</sup>	5.1x10 <sup>-5</sup>	Moderate	Moderate
2.3.3 Caster	54	20	3.5	179	3.2x10 <sup>-5</sup>	5.7x10 <sup>-7</sup>	5.3x10 <sup>-5</sup>	Moderate	Moderate
2.4 Heat attendant mason	25	868	4.2	23026	9.3x10 <sup>-3</sup>	2.4x10 <sup>-6</sup>	2.5x10 <sup>-2</sup>	Very high	Very high
2.4.1 Intervention in furnace	19	3448	441	26244	5.3x10 <sup>-3</sup>	1.1x10 <sup>-4</sup>	86x10 <sup>-3</sup>	Very high	Very high
2.5 Annual maintenance	62	497	35	16219	1.9x10 <sup>-3</sup>	5.6x10 <sup>-6</sup>	3.8x10 <sup>-3</sup>	Very high	Very high
2.5.1 Plate and/or ring dismantling	27	2480	298	25713	4.6x10 <sup>-3</sup>	6.5x10 <sup>-5</sup>	7.8x10 <sup>-3</sup>	Very high	Very high
2.5.2 Resistors dismantling	7	513	93	3731	1.0x10 <sup>-3</sup>	1.1x10 <sup>-5</sup>	1.9x10 <sup>-3</sup>	Very high	Very high
2.5.3 Fluke damage	22	101	35	449	8.9x10 <sup>-5</sup>	6.9x10 <sup>-6</sup>	1.2x10 <sup>-4</sup>	Moderate	High
3. Manufacturing of carbon products	107	67	1.7	921	2.5x10 <sup>-4</sup>	6.7x10 <sup>-7</sup>	5.5x10 <sup>-4</sup>	High	High
3.1 Cathodes production	107	67	1.7	921	2.5x10 <sup>-4</sup>	6.7x10 <sup>-7</sup>	5.4x10 <sup>-4</sup>	High	High
3.1.1 Raw cathode extruding	52	161	48	1006	2.2x10 <sup>-4</sup>	6.1x10 <sup>-6</sup>	3.4x10 <sup>-4</sup>	High	High
3.1.2 Cathode baking	18	47	0.77	1130	6.7x10 <sup>-4</sup>	9.8x10 <sup>-8</sup>	2.0x10 <sup>-3</sup>	High	Very high
3.1.3 Cathode graphitization	8	8.7	2.5	34	1.1x10 <sup>-5</sup>	4.2x10 <sup>-7</sup>	1.6x10 <sup>-5</sup>	Moderate	Moderate
3.1.4 Laboratory analysis	7	50	4.9	256	1.2x10 <sup>-4</sup>	9.3x10 <sup>-7</sup>	2.2x10 <sup>-4</sup>	High	High
4. Foundries	50	4.6	0.42	72	1.8x10 <sup>-5</sup>	4.6x10 <sup>-8</sup>	3.8x10 <sup>-5</sup>	Moderate	Moderate
4.1 Aluminum	15	0.58	0.03	2.6	9.9x10 <sup>-7</sup>	1.7x10 <sup>-8</sup>	1.7x10 <sup>-6</sup>	Very low	Low
4.1.1 Driver, smelter	8	0.72	0.19	2.9	1.4x10 <sup>-6</sup>	1.6x10 <sup>-8</sup>	2.5x10 <sup>-6</sup>	Low	Low
4.1.2 Caster	7	0.46	0.14	1.3	6.6x10 <sup>-7</sup>	1.6x10 <sup>-8</sup>	1.1x10 <sup>-6</sup>	Very low	Very low
4.2 Steel	35	11	1.1	121	2.4x10 <sup>-5</sup>	2.2x10 <sup>-7</sup>	4.3x10 <sup>-5</sup>	Moderate	Moderate
4.2.1 Fusion furnace operator	6	22	5.5	837	8.2x10 <sup>-5</sup>	2.4x10 <sup>-7</sup>	1.7x10 <sup>-4</sup>	Moderate	High
4.2.2 Crucible activity	6	19	3.6	61	2.8x10 <sup>-5</sup>	6.6x10 <sup>-7</sup>	4.4x10 <sup>-5</sup>	Moderate	Moderate
4.2.3 Heat attendant mason	21	6.7	1.0	43	1.2x10 <sup>-5</sup>	1.7x10 <sup>-7</sup>	2.2x10 <sup>-5</sup>	Moderate	Moderate
5. Use of lubricating oils	89	0.80	0.03	8.7	1.7x10 <sup>-6</sup>	1.9x10 <sup>-8</sup>	2.9x10 <sup>-6</sup>	Low	Low
5.1 Undercutting	14	0.65	0.28	1.7	5.0x10 <sup>-7</sup>	5.1x10 <sup>-8</sup>	6.5x10 <sup>-7</sup>	Very low	Very low
5.1.1 Undercutting, help-undercutting	7	0.71	0.29	1.7	5.6x10 <sup>-7</sup>	5.5x10 <sup>-8</sup>	7.5x10 <sup>-7</sup>	Very low	Very low
5.2 Turning	43	0.48	0.04	3.2	6.3x10 <sup>-7</sup>	1.9x10 <sup>-8</sup>	9.6x10 <sup>-7</sup>	Very low	Very low
5.2.1 Mechanic	30	0.27	0.03	0.62	2.4x10 <sup>-7</sup>	1.7x10 <sup>-8</sup>	3.3x10 <sup>-7</sup>	Very low	Very low
5.3 Discharge mold	13	4.9	1.6	18	4.8x10 <sup>-6</sup>	2.9x10 <sup>-7</sup>	7.0x10 <sup>-6</sup>	Low	Low
5.4 Vehicles	13	2.4	0.71	6.5	2.1x10 <sup>-6</sup>	1.6x10 <sup>-7</sup>	2.9x10 <sup>-6</sup>	Low	Low
5.4.1 Mechanic driver	9	1.7	0.66	4.5	1.4x10 <sup>-6</sup>	1.2x10 <sup>-7</sup>	1.9x10 <sup>-6</sup>	Low	Low
6. Engine exhaust emissions	263	0.70	0.03	8.4	1.9x10 <sup>-6</sup>	1.1x10 <sup>-8</sup>	3.5x10 <sup>-6</sup>	Low	Low
6.1 Highways	43	0.11	0.03	0.78	2.1x10 <sup>-7</sup>	3.1x10 <sup>-9</sup>	3.6x10 <sup>-7</sup>	Very low	Very low
6.1.1 Administration, Toll collector	23	0.09	0.03	0.66	1.3x10 <sup>-7</sup>	3.1x10 <sup>-9</sup>	2.1x10 <sup>-7</sup>	Very low	Very low
6.1.2 Highway services	15	0.18	0.03	1.2	3.4x10 <sup>-7</sup>	4.5x10 <sup>-9</sup>	5.6x10 <sup>-7</sup>	Very low	Very low
6.2 Heavy Truck (HT) garage + Roadwork + 2-Stroke engines	50	1.3	0.18	9.8	2.1x10 <sup>-6</sup>	3.6x10 <sup>-8</sup>	3.5x10 <sup>-6</sup>	Low	Low
6.2.1 HT mechanic	28	1.3	0.27	8.5	1.9x10 <sup>-6</sup>	4.4x10 <sup>-8</sup>	2.9x10 <sup>-6</sup>	Low	Low

6.2.2 Roadwork mechanic	9	0.96	0.15	36	4.6x10 <sup>-6</sup>	7.1x10 <sup>-9</sup>	1.0x10 <sup>-5</sup>	Low	Low
6.2.3 Agricultural mechanic	12	1.5	0.50	6.1	1.3x10 <sup>-6</sup>	9.9x10 <sup>-8</sup>	1.8x10 <sup>-6</sup>	Low	Low
6.3 Light Vehicles garage	70	1.0	0.21	6.6	1.2x10 <sup>-6</sup>	4.3x10 <sup>-8</sup>	1.9x10 <sup>-6</sup>	Low	Low
6.3.1 Mechanic (all engines)	56	0.97	0.21	6.8	1.1x10 <sup>-6</sup>	4.6x10 <sup>-8</sup>	1.7x10 <sup>-6</sup>	Low	Low
6.4 Driver: HT, delivery, roadwork, bus	15	0.54	0.21	1.5	3.7x10 <sup>-7</sup>	5.0x10 <sup>-8</sup>	4.8x10 <sup>-7</sup>	Very low	Very low
6.5 Downtown	11	2.1	0.98	4.0	1.3x10 <sup>-6</sup>	2.1x10 <sup>-7</sup>	1.7x10 <sup>-6</sup>	Low	Low
6.5.1 Sewage worker	6	1.9	0.86	4.0	1.4x10 <sup>-6</sup>	1.7x10 <sup>-7</sup>	1.8x10 <sup>-6</sup>	Low	Low
6.6 Use of 2-Stroke and 4-Stroke engines	30	2.5	0.83	11	2.3x10 <sup>-6</sup>	1.6x10 <sup>-7</sup>	3.2x10 <sup>-6</sup>	Low	Low
6.6.1 Brushwood clearer	7	1.6	0.81	4.4	1.2x10 <sup>-6</sup>	1.4x10 <sup>-7</sup>	1.6x10 <sup>-6</sup>	Low	Low
6.6.2 Hedge trimmer	8	3.1	0.97	15	3.5x10 <sup>-6</sup>	1.5x10 <sup>-7</sup>	5.2x10 <sup>-6</sup>	Low	Low
6.7 Generator	8	0.95	0.17	8.3	2.1x10 <sup>-6</sup>	2.1x10 <sup>-8</sup>	3.7x10 <sup>-6</sup>	Low	Low
6.8 Closed environment	35	0.33	0.03	18	2.7x10 <sup>-6</sup>	1.3x10 <sup>-9</sup>	7.5x10 <sup>-6</sup>	Low	Low
6.8.1 Underground – driver	9	2.4	0.23	8.2	4.3x10 <sup>-6</sup>	6.4x10 <sup>-8</sup>	7.3x10 <sup>-6</sup>	Low	Low
6.8.2 Work in tunnel	21	0.05	0.03	0.68	6.6x10 <sup>-8</sup>	2.3x10 <sup>-9</sup>	1.1x10 <sup>-7</sup>	Very low	Very low
7. Combustion processes	36	4.2	0.25	65	1.5x10 <sup>-5</sup>	5.0x10 <sup>-8</sup>	3.2x10 <sup>-5</sup>	Moderate	Moderate
7.1 Firefighter	7	28	7.3	77	3.0x10 <sup>-5</sup>	1.4x10 <sup>-6</sup>	4.4x10 <sup>-5</sup>	Moderate	Moderate
7.2 Chimney sweeper	10	12	2.8	51	1.3x10 <sup>-5</sup>	6.1x10 <sup>-7</sup>	1.8x10 <sup>-5</sup>	Moderate	Moderate
7.3 Household garbage incinerator	17	1.2	0.20	25	3.5x10 <sup>-6</sup>	1.5x10 <sup>-8</sup>	7.2x10 <sup>-6</sup>	Low	Low
7.3.1 Operating household garbage incinerator	13	1.2	0.19	10	2.8x10 <sup>-6</sup>	2.7x10 <sup>-8</sup>	5.2x10 <sup>-6</sup>	Low	Low
8. Bitumen/road paving	75	0.27	0.03	2.8	5.0x10 <sup>-7</sup>	6.5x10 <sup>-9</sup>	8.7x10 <sup>-7</sup>	Very low	Very low
8.1 Road paving: application of hot bitumen(>150°C)	61	0.28	0.03	3.0	5.4x10 <sup>-7</sup>	6.8x10 <sup>-9</sup>	9.7x10 <sup>-7</sup>	Very low	Very low
8.1.1 Tar application	27	0.18	0.03	2.5	4.5x10 <sup>-7</sup>	3.4x10 <sup>-9</sup>	8.5x10 <sup>-7</sup>	Very low	Very low
8.1.2 Coating application	11	0.14	0.03	0.25	1.1x10 <sup>-7</sup>	9.8x10 <sup>-9</sup>	1.5x10 <sup>-7</sup>	Very low	Very low
8.1.3 Work in tunnel	17	0.80	0.17	3.9	1.2x10 <sup>-6</sup>	2.7x10 <sup>-8</sup>	1.8x10 <sup>-6</sup>	Low	Low
8.2 Application of warm bitumen (≤150°C) in tunnel	8	0.18	0.03	1.8	4.2x10 <sup>-7</sup>	3.6x10 <sup>-9</sup>	7.7x10 <sup>-7</sup>	Very low	Very low
9. Coke production	84	932	90	11310	2.8x10 <sup>-3</sup>	1.3x10 <sup>-5</sup>	5.4x10 <sup>-3</sup>	Very high	Very high
9.1 Coke pusher	14	872	67	5945	6.7x10 <sup>-3</sup>	3.3x10 <sup>-6</sup>	1.8x10 <sup>-2</sup>	Very high	Very high
9.2 Furnace door settings	10	412	107	4184	8.7x10 <sup>-4</sup>	8.6x10 <sup>-6</sup>	1.5x10 <sup>-3</sup>	High	Very high
9.3 Coke withdrawn	8	531	244	1364	3.9x10 <sup>-4</sup>	4.2x10 <sup>-5</sup>	5.1x10 <sup>-4</sup>	High	High
9.4 Furnace battery cleaning-up	16	1035	99	4912	2.0x10 <sup>-3</sup>	2.7x10 <sup>-5</sup>	3.5x10 <sup>-3</sup>	Very high	Very high
9.5 Watchperson	12	499	9.2	16428	3.5x10 <sup>-3</sup>	2.5x10 <sup>-6</sup>	9.0x10 <sup>-3</sup>	Very high	Very high
9.6 Mason	18	1544	371	12317	2.3x10 <sup>-3</sup>	4.9x10 <sup>-5</sup>	3.6x10 <sup>-3</sup>	Very high	Very high
9.6.1 Furnace	12	822	318	2540	6.9x10 <sup>-4</sup>	5.9x10 <sup>-5</sup>	9.5x10 <sup>-4</sup>	High	High
9.6.2 Work in gallery	6	6112	1923	14029	5.7x10 <sup>-3</sup>	4.1x10 <sup>-4</sup>	7.9x10 <sup>-3</sup>	Very high	Very high

407 Note: 5<sup>th</sup> p.: 5<sup>th</sup> percentile, 90<sup>th</sup> p.: 90<sup>th</sup> percentile, 95<sup>th</sup> p.: 95<sup>th</sup> percentile, GM: geometric mean, N:  
408 number of samples. Groups with one number correspond to level 1 exposure groups (L1Gs), while  
409 L2Gs are preceded by two numbers and L3Gs by three numbers. Level 1 was related to product/raw  
410 material characteristics. Level 2 referred to exposure source characteristics (e.g., locations and/or  
411 operations with different emission sources). Level 3 corresponded to a task or a series of tasks. The  
412 sum of L2Gs is not necessarily equal to the total number of their L1G, as L2Gs with less than 6 long-  
413 term samplings are not shown here. The sum of L3Gs is usually not equal to the total number of their  
414 L2G, as L3Gs with less than 6 long-term samplings are not shown here. The 5<sup>th</sup> and 95<sup>th</sup> percentiles  
415 correspond to the lower and upper bounds of the 95% confidence interval, respectively. See Table 2  
416 for the risk ranking decision rule and interpretation.

417 3.4 Estimation of exposed workers and number of additional lung cancer cases per year in  
418 France

419 Fig. 1 displays the number of exposed workers ( $N(\tau)$ ) (on the left) and the expected number of  
420 additional lung cancer cases per year in France ( $E(\tau)$ ) (on the right) for each exposure duration  $\tau$ .

421 Table 4 reports  $N(\tau)$  and the associated  $E(\tau)$  calculated for the period from 2000-2014 for each L1G  
422 and  $\tau$  based on the BaP or BaPeq concentrations.

423 In the selected L1Gs, approximately 3.7 million French workers were potentially at risk of PAH  
424 exposure, most of whom (99%) were employed in L1G using products derived from petroleum (Fig. 1,  
425 Table 4). Among them, only 11% were exposed at the time of monitoring  $\leq 15$  years, while 41% were  
426 exposed  $>15-30$  years and 48%  $> 30$  years. More than 60% of the workers were exposed  $> 30$  years in  
427 aluminum, silicon production and manufacturing of carbon products. Regarding foundries, 74% of the  
428 workers were exposed  $>15-30$  years. For the remaining L1Gs, at least 40% of the workers were  
429 exposed  $>15-30$  years and at least 40%  $> 30$  years.

430 A total of 27 (95% CI: 0.14-54) cases of additional lung cancer ( $E_e$ ) could potentially be expected per  
431 year in France if all workers had been exposed for 45 years (Table 4). This estimation was higher  
432 when using BaPeq (37, 95% CI: 0.57-67), which is not surprising as BaPeq  $\geq$  BaP by definition (Table  
433 4). Both estimates can be compared to the number of lung cancer cases that would be expected in 2015  
434 in France among men occupationally exposed to PAHs. Using the incidence of the lung cancer and the  
435 attributable fractions mentioned in the Introduction section, between 12 and 37 cases would be  
436 expected.

437 The largest number of  $E_e$  was found in coke production and combustion processes, followed by engine  
438 exhaust emissions, silicon production, the use of lubricating oils, aluminum production, manufacturing  
439 of carbon products, foundries and bitumen. The largest number of expected additional lung cancer  
440 cases was not necessarily found for L1Gs that used products derived from coal, where exposure levels  
441 are highest. Although lung cancer risks were high or very high for L1Gs that used products derived  
442 from coal, the exposed population in these groups was far smaller (1,000 – 40,000 workers) than for  
443 L1Gs using products derived from petroleum (100,000 to 2 millions) where lung cancer risks are low  
444 or very low. Nevertheless, coke production was the L1G with the highest expected additional lung  
445 cancer cases despite the small population exposed (4,100 workers).

446 Regardless of the L1G, the number of additional lung cancer cases was highest for  $E_e$ , followed by  
447  $E_{45}$ ,  $E_{30}$ , and  $E_{15}$ . In addition, the sum of  $E_{45}$ ,  $E_{30}$  and  $E_{15}$  was always inferior to  $E_e$  because of the  
448 cumulative effect of the cancer risk.

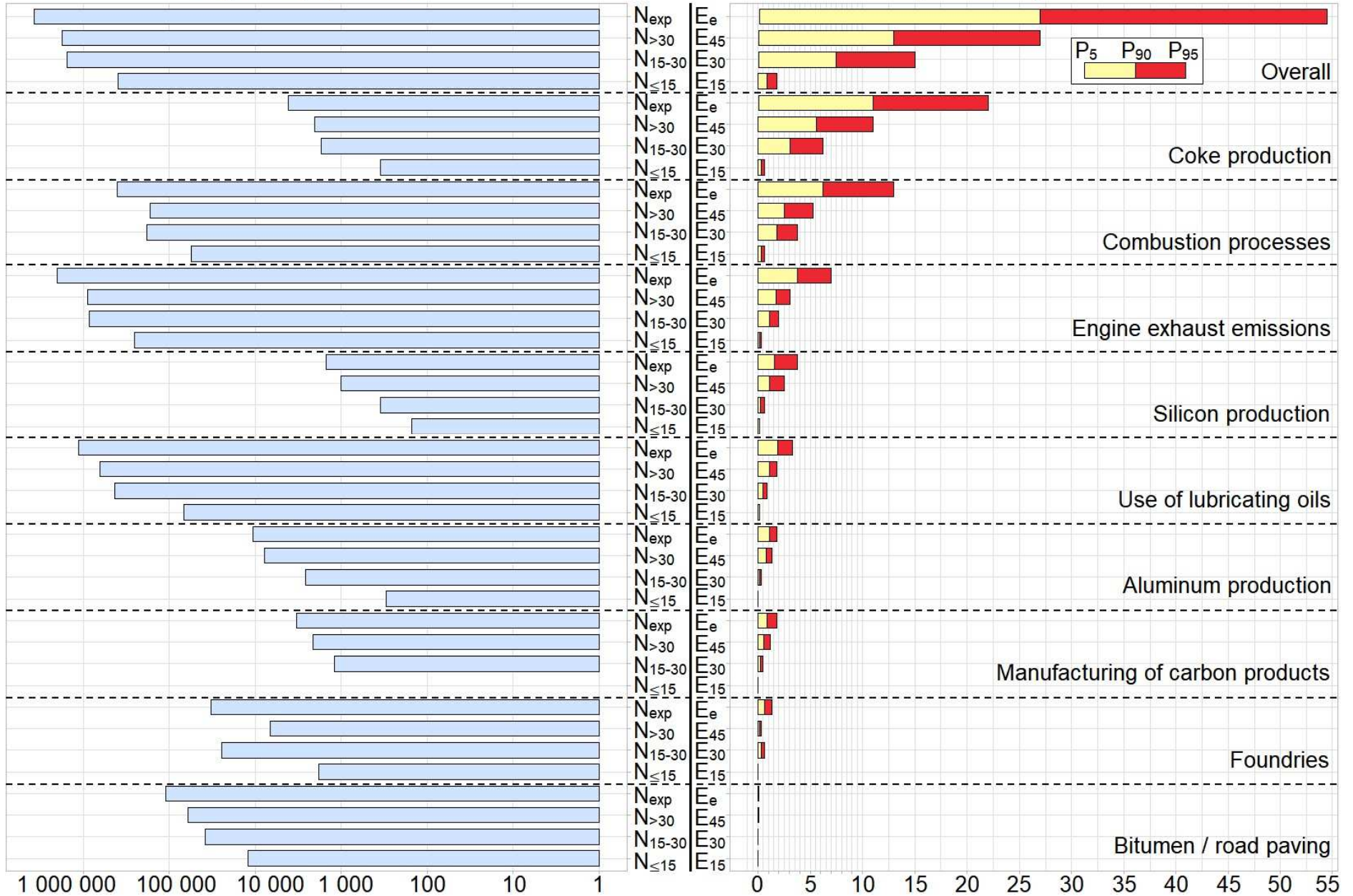
**Table 4.** Exposed population and number of additional lung cancer cases per year in France

L1G	$\tau$	$N(\tau)$	$E(\tau)$ _2000-2014 BaP: P <sub>90</sub> (95% CI)	$E(\tau)$ _2000-2014 BaPeq: P <sub>90</sub> (95% CI)
Coke production	45 years	4,100	11 (0.05, 22)	16 (0.26, 29)
	> 30 years	2,050	5.6 (0.03, 11)	8.2 (0.13, 14)
	15 – 30 years	1,700	3.1 (0.01, 6.2)	4.5 (0.07, 7.9)
	≤ 15 years	350	0.32 (0.002, 0.63)	0.46 (0.007, 0.81)
Silicon production	45 years	1,500	1.6 (0.001, 3.8)	2.7 (0.01, 5.6)
	> 30 years	1,000	1.1 (0.001, 2.5)	1.8 (0.006, 3.8)
	15 – 30 years	350	0.25 (2x10 <sup>-4</sup> , 0.59)	0.42 (0.001, 0.88)
	≤ 15 years	150	0.05 (5x10 <sup>-5</sup> , 0.13)	0.09 (3x10 <sup>-4</sup> , 0.19)
Aluminum production	45 years	10,700	1.1 (0.02, 1.8)	1.4 (0.05, 2.2)
	> 30 years	7,800	0.80 (0.01, 1.3)	1.0 (0.04, 1.6)
	15 – 30 years	2,600	0.18 (0.003, 0.29)	0.23 (0.008, 0.35)
	≤ 15 years	300	0.01 (2x10 <sup>-4</sup> , 0.02)	0.01 (5x10 <sup>-4</sup> , 0.02)
Manufacturing of carbon products	45 years	3,300	0.83 (0.002, 1.8)	1.2 (0.01, 2.3)
	> 30 years	2,100	0.53 (0.001, 1.2)	0.79 (0.008, 1.5)
	15 – 30 years	1,200	0.20 (5x10 <sup>-4</sup> , 0.44)	0.30 (0.003, 0.56)
	≤ 15 years	0	0 (0, 0)	0 (0, 0)
Foundries	45 years	32,830	0.60 (0.002, 1.3)	0.88 (0.008, 1.7)
	> 30 years	6,600	0.12 (3x10 <sup>-4</sup> , 0.25)	0.18 (0.002, 0.34)
	15 – 30 years	24,400	0.30 (7x10 <sup>-4</sup> , 0.62)	0.44 (0.004, 0.84)
	≤ 15 years	1,830	0.01 (3x10 <sup>-5</sup> , 0.02)	0.02 (2x10 <sup>-4</sup> , 0.03)
Combustion processes	45 years	400,000	6.2 (0.02, 13)	8.2 (0.08, 16)
	> 30 years	165,000	2.5 (0.008, 5.3)	3.4 (0.03, 6.4)
	15 – 30 years	180,000	1.8 (0.006, 3.8)	2.5 (0.02, 4.7)
	≤ 15 years	55,000	0.28 (9x10 <sup>-4</sup> , 0.59)	0.38 (0.004, 0.71)
Engine exhaust emissions	45 years	2,000,000	3.8 (0.02, 7.0)	4.4 (0.08, 7.6)
	> 30 years	890,000	1.7 (0.01, 3.1)	2.0 (0.03, 3.4)
	15 – 30 years	857,000	1.1 (0.006, 2.0)	1.3 (0.02, 2.2)
	≤ 15 years	253,000	0.16 (9x10 <sup>-4</sup> , 0.30)	0.19 (0.003, 0.32)
Use of lubricating oils	45 years	1,130,000	1.9 (0.02, 3.3)	2.1 (0.07, 3.4)
	> 30 years	632,000	1.1 (0.01, 1.8)	1.2 (0.04, 1.9)
	15 – 30 years	430,000	0.48 (0.006, 0.83)	0.53 (0.02, 0.87)
	≤ 15 years	68,000	0.04 (4x10 <sup>-4</sup> , 0.07)	0.04 (0.001, 0.07)
Bitumen/road paving	45 years	110,000	0.06 (7x10 <sup>-4</sup> , 0.10)	0.07 (0.002, 0.12)
	> 30 years	60,000	0.03 (4x10 <sup>-4</sup> , 0.05)	0.04 (0.001, 0.07)
	15 – 30 years	38,000	0.01 (2x10 <sup>-4</sup> , 0.02)	0.02 (5x10 <sup>-4</sup> , 0.03)
	≤ 15 years	12,000	0.002 (3x10 <sup>-5</sup> , 0.003)	0.003 (9x10 <sup>-5</sup> , 0.004)
Total	45 years	3,692,430	27 (0.14, 54)	37 (0.57, 67)
	> 30 years	1,766,550	13 (0.07, 27)	19 (0.29, 33)
	15 – 30 years	1,535,250	7.5 (0.04, 15)	10 (0.15, 18)
	≤ 15 years	390,630	0.88 (0.004, 1.8)	1.2 (0.02, 2.2)

450 Note: 95% CI: 95% confidence interval,  $\tau$ : exposure duration,  $N(\tau)$ : exposed population.  $N_{exp} =$   
451  $N_{\leq 15} + N_{15-30} + N_{>30}$ .  $N_{exp}$ : total exposed population,  $N_{\leq 15}$ : population exposed  $\leq 15$  years,  $N_{15-30}$ :  
452 population exposed 15-30 years,  $N_{>30}$ : population exposed  $> 30$  years.  $E(\tau)$ : expected number of  
453 additional lung cancers in France after an exposure of duration  $\tau$ ,  $E_e$ : expected number of additional  
454 lung cancers among the total French exposed population after an exposure of 45 years,  $E_{45}$ : expected  
455 number of additional lung cancers among the  $N_{>30}$  French subpopulation after an exposure of 45  
456 years,  $E_{30}$ : expected number of additional lung cancers among the  $N_{15-30}$  French subpopulation after  
457 an exposure of 30 years,  $E_{15}$ : expected number of additional lung cancers among the  $N_{\leq 15}$  French  
458 subpopulation after an exposure of 15 years. Beware  $E_e \neq E_{15} + E_{30} + E_{45}$  because of the cumulative  
459 effect of the cancer risk.

### Exposed population

### Expected lung cancer cases



462

463

**Figure 1.** Rough estimation of the expected number of additional lung cancer cases per year in France in each L1G using BaP concentrations

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$P_{0.05}$ : 5<sup>th</sup> percentile,  $P_{0.90}$ : 90<sup>th</sup> percentile,  $P_{0.95}$ : 95<sup>th</sup> percentile. Where there is only one bar colored in red, it means that  $P_{0.90} = 0$ .  $N_{exp} = N_{\leq 15} + N_{15-30} +$

465

$N_{>30}$ .  $N_{exp}$ : total exposed population,  $N_{\leq 15}$ : population exposed from 0 to 15 years,  $N_{15-30}$ : population exposed from 15 to 30 years,  $N_{>30}$ : population

466

exposed for more than 30 years.  $E(\tau)$ : expected number of additional lung cancers in France after an exposure of duration  $\tau$ ,  $E_e$ : expected number of

467

additional lung cancers among the total French exposed population after an exposure of 45 years,  $E_{45}$ : expected number of additional lung cancers among the

468

$N_{>30}$  French subpopulation after an exposure of 45 years,  $E_{30}$ : expected number of additional lung cancers among the  $N_{15-30}$  French subpopulation after an

469

exposure of 30 years,  $E_{15}$ : expected number of additional lung cancers among the  $N_{\leq 15}$  French subpopulation after an exposure of 15 years. Beware  $E_e \neq$

470

$E_{15} + E_{30} + E_{45}$  because of the cumulative effect of the cancer risk.

471

#### 4. Discussion

Risk indicators found in the literature provide extremely different risk probabilities for the same given concentration (Fleiss' Kappa: 0.29, Table S2). In addition to the fair agreement between existing indicators, there is, to our best knowledge, no guide, recommendation or gold standard concerning the best choice and condition for using these indicators. This information confirms the utility of using CRI.

The risk of lung cancer was found to be highly variable between and within exposure groups (up to 1,000 likelihood), showing that it was essential to focus on the most detailed level of description available (i.e., the L3G) because these groups had the lowest concentration dispersion and best risk reliability. A strategy to improve the risk reliability would be to lessen measurement uncertainties as they accounted for most of the uncertainties in the risk estimation. One strategy to diminish the concentration dispersion and improve the risk reliability would be to perform other measurements and/or to acquire a more detailed description of exposure groups that cannot currently be considered as having a low concentration dispersion (Petit et al. 2017b). Differences in the risk of lung cancer observed between and within groups may derive from several determinants of exposure, such as ventilation, raw material composition, distance from the emission source or process type and temperature, a topic that had been previously addressed (Maître et al. 2018). For instance, lung cancer risk among people working on Söderberg electrodes was 8 times lower than among those working near composite electrodes. This difference can be explained by the pouring of spherical pitch paste into electrodes during composite electrodes loading, which generates an important aerosol, in contrast to Söderberg electrodes, in which large paste cylinders are dropped into the electrode column semi-automatically with far less emissions.

Workers who were the most at risk of lung cancer were those exposed to PAH mixtures via products derived from coal, while the least at risk were those exposed to PAH mixtures via products derived from petroleum. Workers in coke production, where levels and risks were very high, necessitate a particular focus, regardless of the activity considered. In silicon production, a particular emphasis should be placed on maintenance work in the furnace, annual maintenance activities and paste loading of composite electrodes. In aluminum production, efforts should be focused towards maintenance tasks, the paste tower and ramming. In the manufacture of carbon products, raw cathode extrusion is of concern, and steel foundries should focus on the fusion furnace operator. Efforts are still needed to decrease exposures and therefore risks, especially in exposure groups using products derived from coal where the risk can exceed  $10^{-3}$ . A perspective to diminish the risk of human lung cancer would be to set/undertake/implement, when feasible and relevant, product modifications (raw materials, such as ramming paste, containing no PAH or containing less and less PAH, especially BaP), process modifications (decrease of the temperatures), collective protective equipment, and, as a last resort, personal protective equipment (PPE).

509 However, these results must be considered carefully because other routes of exposure (skin absorption  
510 in particular, which is known to lead to potentially high PAH exposure) were not taken into account.  
511 Taking into account several routes of exposure would require the use of additional formulas and/or  
512 new models (Park 2018). Estimated risks were most certainly overestimated because PPE were not  
513 taken into account. Although, on average, 65% of the workers were wearing gloves and 43% were  
514 wearing a respiratory mask, there was no information regarding the PPE efficiency. PPE efficiency is  
515 highly variable and depends mostly on how they are used, stored and replaced by the workers (Chen et  
516 al. 2012). Additionally, PPE varies from one company to another, and thus it is impossible to  
517 determine whether the worker has worn the PPE during the entire shift. For these reasons, correction  
518 for factors that take into account PPE was not used in the risk estimation. Biological monitoring is a  
519 good complementary approach to airborne monitoring to account for PPE, other routes of exposure  
520 and individual factors. As a result, biological monitoring was always performed simultaneously with  
521 airborne monitoring among workers included in the E-HAP (Barbeau et al. 2015; Lutier et al. 2016).  
522 Estimated risks are only valid for a given moment (when the campaigns of measurement were carried  
523 out) and a given exposure duration. Indeed, the exposure duration has a great influence on the  
524 estimated risk and number of potential additional lung cancer cases (Table 4, Fig. 1). In addition,  
525 exposure conditions do not necessarily remain the same over 45 years because levels can vary  
526 throughout time, processes can be improved and because the product composition can change (Creely  
527 et al. 2007; Peters et al. 2015). Additionally, it is becoming increasingly common that people perform  
528 different jobs, activities and tasks during their entire professional career, which must be taken into  
529 account when estimating risks (Kienzler et al., 2016). Although knowledge of the *cursus laboris* of  
530 each worker (Marchand 1956; Martin 1990; Martin and Robaux 1989) is paramount for a more  
531 accurate risk estimation, it can be rather complex if not impossible to establish (Lentz et al. 2015). In  
532 addition, a multitude of individual factors (e.g., genetic susceptibility, preexisting diseases) can have a  
533 great influence on the estimated risk and number of potential additional cancer cases; however many  
534 uncertainties persist regarding these factors (Abt et al. 2010; Gallagher et al. 2015; Setton et al. 2013;  
535 Shen et al. 2014).

536 It was found that additional lung cancer cases in France could be expected in all L1Gs (Fig. 1, Table  
537 4), for which epidemiological studies have demonstrated a significant positive association between  
538 exposure to PAHs and human lung cancer risk. There are, however, a few exceptions: silicon  
539 production, for which there is a paucity of studies, and combustion processes, in particular firefighters  
540 (approximately 280,000 workers exposed to PAHs (Pompier, 2017) with a risk of  $3.0 \times 10^{-5}$ ), for  
541 which studies are scarce because of the emergency context associated with such jobs. In addition,  
542 some epidemiological studies have shown a significant association between exposure to PAHs in  
543 public work, road paving and human lung cancer risk (Boffetta et al. 1997; Rota et al. 2014). Here,  
544 these occupations demonstrated low risks (from  $5.0 \times 10^{-7}$  for bitumen application to  $4.3 \times 10^{-6}$  for  
545 underground drivers), and no additional lung cancer cases would be expected in bitumen/road paving,

546 even if 10 times more people were exposed. These differences could be explained by the finding that  
547 epidemiological studies investigate retrospective exposures (tumorigenesis may span more than 20 to  
548 40 years) and that changes in the exposure conditions occurred and lowered exposure levels over these  
549 past decades. Indeed, for road paving, the product composition (use of products derived from  
550 petroleum instead of from coal) and the decrease in application temperature significantly lowered  
551 exposure levels (Burstyn et al. 2002; Spickenheuer et al. 2011) and therefore risks. These variations  
552 may derive from several determinants of exposure, such as ventilation, raw material composition or  
553 process temperature. These features most certainly explained the smaller number of additional lung  
554 cancer cases for exposures that occurred between 2000 and 2014 than prior to 2000 (Boffetta et al.  
555 2010; De Matteis et al. 2012).

556 Based on the lung cancer risks calculated in this study and on the estimated number of exposed  
557 workers in each L1G, a rough estimation of the expected contemporary number of additional lung  
558 cancer cases in each L1G was performed (Fig. 1). This value is a rough estimation because of all the  
559 mentioned uncertainties and because the precise number of exposed workers was not accurately  
560 known. For example, the number of people who used lubricating oils was overestimated because many  
561 workers who answered that they were using mineral oils were in fact using synthetic oils (Ministère du  
562 Travail, 2016). The incidence of lung cancer may be underestimated because the smoking prevalence  
563 was not taken into account (50% of workers in the E-HAP were smokers, with even a greater % before  
564 2000) (Shen et al. 2014).

565 The largest number of expected additional lung cancer cases was not necessarily found for L1Gs that  
566 used products derived from coal because the number of exposed workers was far smaller (1,000 –  
567 40,000) than in L1Gs using products derived from petroleum (100,000 to 2 millions). Overall, a total  
568 of 27 (95% CI: 0.14-54) additional lung cancer could be expected per year in France among the 3.7  
569 million workers estimated to be exposed to PAHs (37, 95% CI: 0.57-67) if the BaP<sub>eq</sub> was used instead  
570 of the BaP). These values only indicate the likelihood of lung cancer and not whether they will or will  
571 not occur. This number might be underestimated because workers exposed to PAHs from other  
572 industries (e.g., aerospace, use of creosote, recycling, tire production, naval industries) are not  
573 currently in the E-HAP. The contemporary number of additional lung cancer cases in France was  
574 found to be 7 and 5 times lower than the number of lung cancer cases estimated for the year 2000 in  
575 France (Boffetta et al. 2010) and 2005 in Italy (De Matteis et al. 2012), but it was within the range of  
576 12-37 cases that would be expected in 2015 using the attributable fractions and the incidence of the  
577 lung cancer mentioned in the Introduction section. In contrast, our estimation was 2 times higher than  
578 the estimation of the IARC (2018) for 2015. The estimation proposed by the IARC (2018) could,  
579 however, be an underestimation because the study (SUMER study) they used to estimate the number  
580 of exposed workers (approximately 1.5 million) to PAHs was incomplete. For example, workers  
581 exposed to combustion processes, such as firefighters, were not taken into account, and for engine

582 exhaust emissions, only people exposed to diesel exhaust were taken into account; other exhaust  
583 emissions were not considered to be exposed to PAHs in the SUMER study.

584

585 The risk estimation was not performed for all individual PAHs other than BaP because the BaP is the  
586 only PAH with an inhalation unit risk (IUR) for lung cancer. Other available IURs were either  
587 established for another toxic effect (e.g., nasal respiratory epithelial adenoma and nasal olfactory  
588 epithelial neuroblastoma for naphthalene) or derived using a potency equivalency factor (TEF)  
589 procedure, for which TEFs were not necessarily based on the inhalation route nor on the same animal  
590 models (OEHHA 2017). Assessment of the mixture toxicity is, however, paramount but very  
591 challenging because it requires the identification of a suitable/genuine proxy that is representative of  
592 the whole mixture toxicity. BaP might not be sufficient to fully estimate the cancer risk of the whole  
593 PAH mixture. BaP<sub>eq</sub> is often used as a proxy in this regard, but its use is highly discussed, as  
594 explained in the Introduction section. Currently, there is no clear agreement concerning which PAH  
595 congeners should be reported (Boström et al. 2002). The highest burden of hazardous effects of PAH  
596 mixtures is commonly represented by heavier PAHs (composed of at least 4 benzene rings, such as  
597 BaP) that can be absorbed onto particles (in contrast to the lighter PAHs that are predominantly in the  
598 gas phase). In addition, the absorption of some PAHs onto particles could also have an impact on the  
599 cancer potency of PAH mixtures. In fact, particles carry many other compounds (not just PAHs) with  
600 carcinogenic properties (Boström et al. 2002; Buonanno et al. 2015), and the effects of PAH exposure  
601 alone cannot be easily separated from those of particles (Guerreiro et al. 2016). The study of exposure  
602 functions (Petit et al. 2017a) is thus important to determine “typical source mixtures” (signature)  
603 because the PAH mixture composition and toxicity vary substantially due to the multitude of emission  
604 sources. The identification of suitable markers for assessing the mixture toxicity is needed but very  
605 challenging due to the interactions among the components of a mixture (cocktail effects) (Boström et  
606 al. 2002). Tools (e.g., exposure functions, correlation network analysis) and models (e.g.,  
607 physiologically-based pharmacokinetic) considering these interactions are needed and are being  
608 developed (Lentz et al. 2015; Petit et al. 2017a).

609 Despite efforts and changes that had been made in the past to decrease exposure levels and risks,  
610 PAHs remain a sanitary threat for people who are exposed to these pollutants in occupational  
611 environments. Further efforts, changes and appropriate safe PAH guidelines are still needed to better  
612 protect the populations exposed to PAHs and thus reduce the number of lung cancer cases.

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# Exposed population

# Expected lung cancer cases

