The cost of occupational cancer in the EU-28

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Executive summary, November 2017
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Contents

1. Aims of the study

It is estimated that there are approximately 1.3 million cancer deaths in the European Union (EU) every year, and past research suggests that 2-12% of cancer deaths may relate to occupational exposure to carcinogens. In order to establish an effective and efficient strategy for tackling this problem, a better understanding is required of the burden of occupational cancer and the associated key carcinogenic agents. Reliable quantification of the occupational cancer burden in the EU-28 is required for these purposes.

The aim of this study was to estimate the economic burden of cancer incidence resulting from past occupational exposure to selected carcinogenic agents in the EU-28, so as to assist the trade unions in refining their strategy and actions to tackle occupational cancer. The work involved estimating the current incidence of occupational cancer for the EU-28 and each Member State, and assessing the associated economic costs to workers, employers and governments. A key element of the study was a comprehensive consideration of gender-relevant aspects of occupational cancer.

2. Study approach

The study was separated into two different tasks, with the first involving quantification of the occupational burden of cancer. This work involved the following steps:

— Step 1: Selection of priority carcinogens/occupations for assessment;
— Step 2: Estimation of occupationally exposed populations;
— Step 3: Identification of the relative risks for the relevant carcinogens/occupations;
— Step 4: Derivation of the attributable fractions (AFs);
— Step 5: Estimation of the attributable numbers (ANs); and
— Step 6: Comparison with published AFs (ANs).

Placing an economic value on the costs to workers, employers and governments comprised the second task in the study. This involved the development of a cost framework describing the various cost components (direct, indirect and intangible) and who would bear each of the costs.

In order to address the uncertainty surrounding some of the data required for the assessment (numbers of workers exposed, relative risk, etc.), six scenarios were assessed for each carcinogen (three central scenarios and three further scenarios). The central estimates reflect the study team's judgement of the most reliable numbers of exposed workers and the most appropriate risk estimates for the exposure patterns experienced. The Central-core scenario is complemented with two further estimates (Central-high and Central-low) which provide a range that incorporates uncertainty regarding the relative risks in published literature. The Central-core estimate (and the accompanying low-high range) thus represents the most realistic estimate of the current

cancer incidence due to past occupational exposure to the 25 agents considered in this study.

The central scenarios are complemented with a low scenario (lowest assumptions on incidence, exposed population and relative risk), a high scenario (highest assumptions on incidence, exposed population and relative risks), and a mid-point estimate (midpoints between the input data used for the high and the low scenarios).

3. Priority carcinogenic agents

It was not possible to look at all carcinogenic agents within the scope of this study. As a result, the agents to be considered had to be prioritised. In particular, the aim was to identify the top carcinogens in terms of their contribution to the overall incidence of occupational cancer, and their gender relevance (in particular their contribution to the occupational cancer incidence for women, although agents specifically relevant to men were also identified), to ensure that the study was not skewed towards one of the two genders.

The starting point for this prioritisation was a review of existing studies that have assessed occupational exposure across a number of carcinogens and occupations. The results of the key meta-analyses were reviewed and their findings scored for prioritisation purposes based on the following attributes: relative risk and number of workers exposed; age of the underlying data; specificity; geographic scope; gender aspects; and scope in terms of the breadth of the carcinogenic agents examined.

The outcome of this prioritisation process was the identification of the 25 carcinogenic agents to be examined in more detail in this study, as listed in Table 1. These included chemical agents, process-generated substances such as wood dust and diesel exhaust, and occupational agents such as shift work and work in the rubber industry.

Although it is possible that the 25 agents account for the majority of occupational cancer incidence, this is by no means certain, and it is highly likely that the inclusion of additional agents in the assessment would have increased the estimated attributable fractions (AFs) and attributable numbers (ANs). For example, although organic solvents were not included in the core assessment due to significant uncertainties associated with the input data, an additional assessment is provided to show that their inclusion would increase the estimated AFs.

Table 1 **Final selection of the 25 carcinogenic agents**

Diesel exhaust engine emissions (DEEE)	Solar radiation
Silica	Environmental tobacco smoke (ETS)
Asbestos	Epichlorohydrine
Formaldehyde	Tetrachloroethylene
Benzene	Shift work
Mineral oils	Dioxins
Cadmium (Cd) and Cd compounds	Inorganic acid mists containing sulphuric acid
Wood dust	Rubber manufacturing industry
Arsenic	Ionising radiation
Vinyl chloride	Chromium (VI) compounds
Ethylene oxide	Aromatic amines
Polycyclic Aromatic Hydrocarbons (PAHs) (from coal tars and pitches)	Cytostatic drugs
Occupation as a welder	

4. Occupationally exposed populations

The proportion of workers exposed to the relevant carcinogenic agents over the reference period for the analysis (1966-2005 for cancers with 10-50 year latency and 1996-2015 for cancers with 0-20 year latency) was estimated. Developing estimates for the EU-28 involved extrapolating from existing data sources (CAREX, SUMER, ASA, etc.) and combining these extrapolations with estimated long-term trends and staff turnover ratios. These estimates were derived for the low, high, mid-point and central[1] estimate scenarios, with a summary of the results presented below.

1. Please note that the exposed populations under the Central-core, Central-low, and Central-high scenarios are identical.

Table 2 **Exposed population (adjusted for natural mortality) as % of the current working population**

Carcinogen	Reference period	Low	High	Midpoint	Central
01 DEE	1966-2005	4.9%	8.9%	6.4%	6.7%
02 Silica	1966-2005	2.1%	6.3%	4.6%	4.1%
03 Asbestos	1966-2005	0.2%	2.0%	1.2%	1.7%
04 Formaldehyde	1966-2005	1.1%	4.1%	1.9%	1.6%
	1996-2015	0.8%	2.3%	1.4%	1.1%
05 Benzene	1996-2015	0.1%	2.2%	0.7%	0.3%
06 Mineral oils	1966-2005	4.4%	11.4%	7.8%	11.1%
07 Cd and Cd compounds	1966-2005	0.1%	0.4%	0.3%	0.4%
08 Wood dust	1966-2005	3.1%	5.6%	4.0%	4.5%
09 Arsenic	1966-2005	0.3%	0.3%	0.3%	0.3%
10 Vinyl chloride	1966-2005	0.01%	0.1%	0.1%	0.1%
11 Ethylene oxide	1996-2005	0.002%	0.04%	0.02%	0.04%
12 PAHs	1966-2005	0.005%	1.3%	0.7%	0.9%
	1996-2015	0.004%	1.1%	0.6%	1.1%
13 Occupation as a welder	1966-2005	0.4%	6.7%	3.2%	4.3%
14 Solar radiation	1966-2005	9.7%	12.8%	11.3%	12.8%
15 ETS	1966-2005	2.3%	14.5%	10%	14.5%
16 Epichlorohydrine	1966-2005	0.1%	0.1%	0.1%	0.1%
17 Tetrachloroethylene	1966-2005	0.1%	0.6%	0.4%	0.4%
	1996-2015	0.1%	0.4%	0.4%	0.2%
18 Shift work	1966-2005	6.6%	20%	13.2%	20%
19 Dioxins	1966-2005	0.1%	4.6%	2.3%	2.3%
20 Inorganic acid mists	1966-2005	0.4%	0.8%	0.6%	0.6%
21 Rubber manufacturing	1966-2005	0.1%	0.5%	0.3%	0.3%
	1996-2015	0.1%	0.3%	0.2%	0.2%
	1966-2005 / Women	0.01%	0.1%	0.05%	0.04%
	1966-2005 / Men	0.1%	1.0%	0.5%	0.5%
22 Ionising radiation	1966-2005	0.2%	2.0%	0.8%	0.5%
	1996-2015	0.1%	1.1%	0.6%	0.3%
	1966-2005 / Women	0.1%	0.5%	0.2%	0.1%
	1966-2005 / Men	0.3%	3.4%	1.5%	0.9%
23 Cr(VI) compounds	1966-2005	0.5%	1.7%	0.9%	0.8%
24 Aromatic amines	1966-2005	0.3%	0.9%	0.6%	0.5%
25 Cytostatic drugs	1966-2005 / Women	0.7%	3.1%	1.5%	0.8%
	1996-2015	0.3%	1.1%	0.6%	0.3%

5. Relative risk

Information was then taken from the published literature on the relative cancer risk for workers exposed to the various carcinogenic agents. These relative risk estimates were taken from both meta-analyses and individual cohort studies. To the extent possible, the cancer sites for which risk estimates have been identified were based on those listed in the International Agency for Research

on Cancer (IARC, 2016)[2]. For some of the carcinogenic agents, it was not possible to source occupational risk estimates for all of the cancer sites, leading to a gap in our analysis. In other cases, additional sites to those listed in IARC were taken into account, in particular where these sites were identified as being relevant when establishing harmonised classifications for the substances under Regulation (EC) 1272/2008 on classification, labelling and packaging of substances and mixtures (as the relevant EU legislation).

In total, estimates were developed for 23 cancer sites across the 25 carcinogenic agents (see Table 2-9 in the main report).

6. Attributable fractions (AFs) and attributable numbers (ANs)

The Attributable Fraction (AF) is the proportion of cancer cases that would not have occurred in the absence of occupational exposure; this was estimated for each of the 25 carcinogenic agents and sites based on relative risks and the estimates of the exposed population. Levin's equation was used for the calculation of the AFs:

$$AF = Pr(E)\,(RR - 1)/\,\{1 + Pr(E)\,(RR - 1)\}$$

where RR=relative risk and Pr(E)=proportion of the 'at risk' population with a history of occupational exposure to the carcinogen.

The detailed results are summarised in Section 2.5 of the report, with Table 3 below setting out the overall AFs calculated for the three central scenarios.

Table 3 **Incidence AFs for all cancer sites across the 25 carcinogenic agents (reference year: 2015)**

Scenario	Central-low	Central-core	Central-high
Overall AF – Both genders	6%	8%	12%
Overall AF – Women	3%	5%	7%
Overall AF - Men	6%	10%	15%

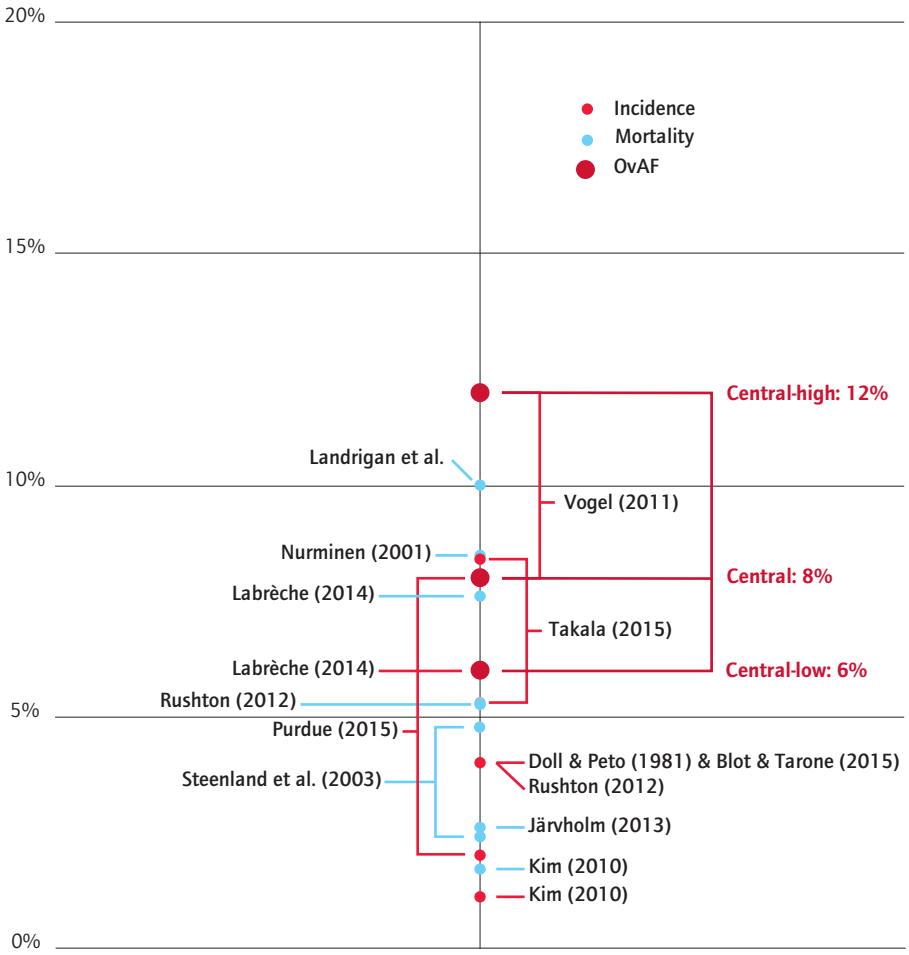
The AF derived under the CENTRAL scenario is 8%. When the 95% CI in the relative risk estimates is taken as a basis for the estimation, the central estimate is a range between 6% and 12%. These estimates are positioned closer to the higher estimates in the published literature and provide further support for studies that have estimated the overall AF for occupational cancer at 8% or above. It should be noted that the AFs estimated in this study are for cancer

2. IARC (2016): List of classifications by cancer sites with sufficient or limited evidence in humans, available at https://monographs.iarc.fr/ENG/Classification/Table4.pdf

incidence rather than mortality and that they relate to the 25 specific carcinogenic agents and do not capture cancer incidence resulting from all occupational carcinogens.

An important finding of this study is that, by including a specific gender focus on carcinogenic agents for women, this study found a higher AF for occupational exposure of female workers than previous studies. This is mainly due to the shift work, ionising radiation and cytostatic drugs examined within the scope of this study. The central estimates found by this study are compared with other published studies in Figure 1.

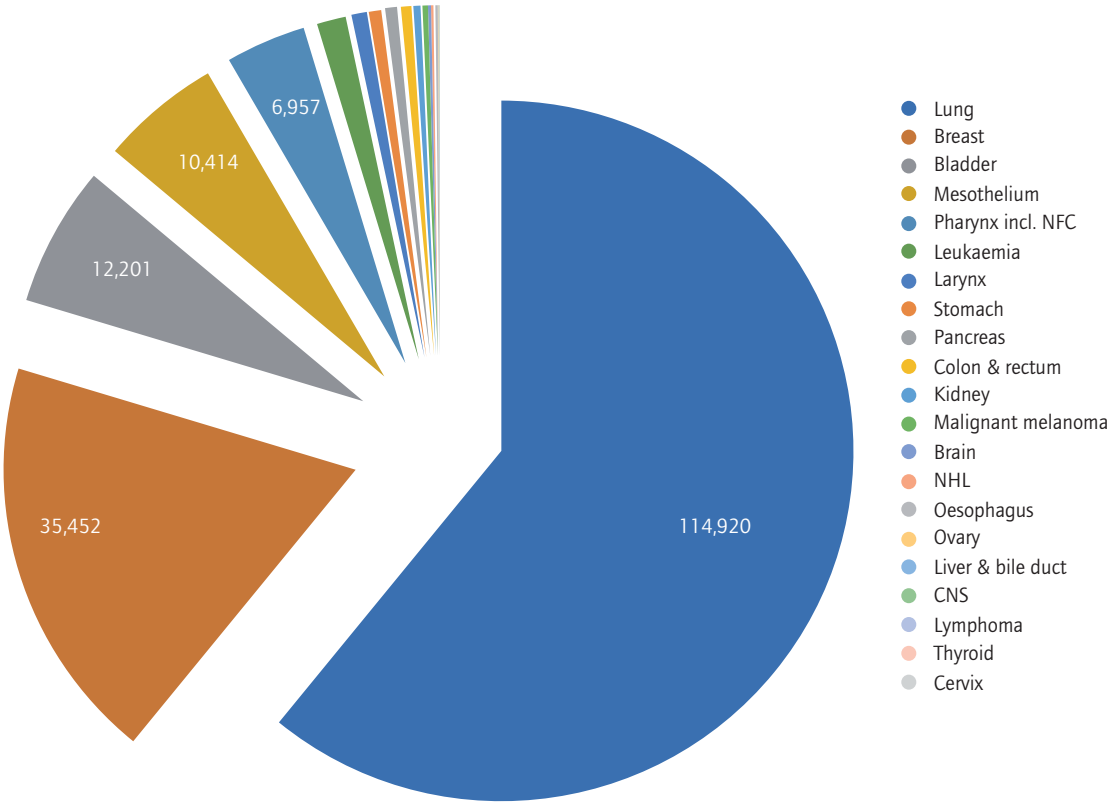
Figure 1 **Central scenarios - overall AFs compared with published estimates**



The calculated AFs were applied to national cancer incidence data from two Europe-wide cancer incidence registries (EUREG and EUCAN) and other sources to generate the numbers of occupational cancers in EU Member

States.[3] This provides estimates of the Attributable Numbers (ANs) of cancer registrations stemming from occupational exposures. Using data from EUCAN and other sources, it is estimated that each year around 190,000 cancer registrations are attributable to past occupational exposure to the 25 agents considered in this study (Central-low to Central-high: 125,000-275,000). A breakdown by cancer site is provided in Figure 2.

Figure 2 **Central-core scenario – contribution of cancer sites to the overall AN**



7. The economic burden of occupational cancer

The first step in estimating the annual economic burden of occupational cancer in the EU-28 was the development of a cost framework describing the different cost components (direct, indirect and intangible/human) and who would bear the costs. It is important to note that for the purposes of this study, this framework is constrained to the assessment of those costs that comprise true 'economic' or social costs, and excludes financial impacts that essentially reflect transfers between different groups in society.

3. In addition, lung cancer incidence attributable to asbestos exposure was estimated using mesothelioma incidence as a proxy.

From this perspective, the economic costs of cancer can be divided into:

— **Direct costs:** These are the medical costs associated with the treatment of cancer and the non-medical costs that arise directly as a result of cancer. Direct medical costs are those associated with the treatment and services patients receive, including the cost of hospitalisation, surgery, physician visits, radiation therapy and chemotherapy/ immunotherapy;
— **Indirect costs:** These are the monetary losses associated with the time spent receiving medical care, including productivity losses due to time spent away from work or other usual activities and lost productivity due to premature death;
— **Intangible or human costs:** These include the non-financial 'human' losses associated with cancer, e.g. reduced quality of life, pain, suffering, anxiety and grief.

The total costs for the different scenarios are summarised below, indicating that the total cost of cancer registrations recorded in a given year and caused by past occupational exposure to carcinogenic agents is between €270 and €610 billion when the full costs of both mortality and morbidity (as defined for this study) are taken into account. If the human costs associated with morbidity effects are removed from the assessment (i.e. the Willingness to Pay (WTP) value of €410,000), then the present value costs fall to between €250 and €570 billion. These ranges reflect the three central scenarios (Central-core, Central-high, Central-low) and whether cancer incidence data are built around the EUCAN or EUREG registry.

Both of these sets of estimates are primarily driven by valuation of the human costs. Excluding the Value of Statistical Life (VSL) (€4 million) and Value of Statistical Cancer Morbidity (VCM) estimates decreases the costs to between €4 and €10 billion, driven primarily by healthcare costs (both formal and informal).

Table 4 **Summary of the total present value costs of annual occupational cancer registrations**

Scenario	Source of data for calculation of AN	Total present value costs of 2015 cancer registrations (VSL and VCM) (€ billion)	Total present value costs of 2015 cancer registrations (VSL only) (€ billion)
Central-core	EUREG+GCO+UK	348	327
	EUCAN+UK	436	409
Central-low	EUREG+GCO+UK	267	253
	EUCAN+UK	295	279
Central-high	EUREG+GCO+UK	493	458
	EUCAN+UK	613	572

Note: These present value estimates represent the costs associated with cancer registrations recorded in a single year, with the associated costs possibly spread over a number of years.

These cost figures are significant, and equate to between roughly 1.8% and 4.1% of EU GDP (based on 2015 Eurostat data) for the estimates including both the VSL and VCM valuations of the human costs of cancer. Removing the figure for VCM from the estimates reduces this slightly to between 1.7% and 3.9% of EU GDP.

The costs in the table above are also of a similar order of magnitude to those estimated recently in RIVM (2016).[4] RIVM (2016) concluded that the total societal cost of work-related cancer is at least in the order of magnitude of €334 billion (range: €242-440 billion), the largest component of which is the welfare loss associated with cancer morbidity and mortality (€329 billion).

These figures compare to those produced by Luengo-Fernandez et al. (2013) on the per annum total costs of cancer in the EU, which they estimated at €126 billion for 2009, with healthcare accounting for €51.0 billion (40%). It is important to note that this figure covers occupational and non-occupational cancers. In addition, it reflects the costs associated with cancer in a given year, rather than the present value costs of the cancer registrations predicted for 2015, as developed by this study. Furthermore, the costs estimated by Luengo-Fernandez et al. do not include any allowance for intangible costs. Assuming that around 8% of the costs in Luengo-Fernandez et al. (2013) are caused by occupational cancer suggests that the costs of occupational cancer in 2009 were around €10 billion. This compares to around €14 billion calculated for the Central-core scenario in this study when all intangible costs are excluded from the analysis.

It should, however, be noted that a different methodology was used in RIVM (2016) and Luengo-Fernandez et al. (2013), with this study estimating the costs of annual cancer registrations incurred over several years rather than the costs incurred in a single year due to new registrations and the ongoing treatment of past registrations.

8. Distribution of the costs

In addition to their magnitude, the distribution of these costs to different groups within society is also of interest. Table 5 provides this information for the Central-core scenario and EUCAN estimates.

Because it was examining costs for a single country, HSE (2016) was able to develop estimates of the costs borne by employers.[5] For the UK, they estimated that around 3% of total costs to society was borne by employers, with this equating to a cost of roughly €17 per worker per annum. Multiplying it across

4. RIVM (2016): Work-related cancer in the European Union, available at http://rivm.nl/en/Documents_and_publications/Scientific/Reports/2016/mei/Work_related_cancer_in_the_European_Union_Size_impact_and_options_for_further_prevention

5. HSE (2016): Costs to Britain of Work-Related Cancer, Research Report 1074, available at: http://www.hse.gov.uk/research/rrhtm/rr1074.htm

the EU-28 worker population (aged 15 to 64) gives a total figure of €4.13 billion in costs to employers associated with the costs of production disturbance, sickness payments due to worker absence and legal obligations with regard to employers' liability insurance. This figure of course reflects requirements in the UK, which may be more or less onerous than those that apply in other Member States. However, it provides an indication of the significance of these costs.

Table 5 **Distribution of costs across different types (€ billion), Central-core/EUCAN+UK**

Type of cost	Group bearing the cost	Total present value costs	Share of total costs
Healthcare	Government/taxpayers	6	1.3%
Lost working days	Worker/family	0.4	0.1%
Informal care	Worker/family	1	0.3%
VSL	Worker/family	394	90.3%
VCM	Worker/family	35	8%
Total		**436**	

They are only a small percentage of the total costs, with this type of finding being attributed to the nature of cancer as an occupational disease. Many of the cancers considered here have latency periods of between 10 and 50 years. As a result, most individuals diagnosed with occupational exposure-related cancer (estimated at over 70%) will have left work by the time they are diagnosed, or may have changed jobs. The relevant employer during the period of exposure will not therefore bear the costs of disruption from sickness absence, paying sick pay, etc. As noted by the UK HSE, this estimate is also an under-estimate as it fails to capture some costs to employers that may be significant, such as those associated with the loss of expertise, and reductions in productivity of those returning to work after successful cancer treatment. Reputational damage (which can impact on sales and recruitment) is also not included.

9. Sensitivity analysis

Sensitivity analysis was undertaken to test key uncertain assumptions. This focused on testing assumptions regarding the intangible costs of cancer within the economic analysis.

As noted above, the total cost of cancer registrations recorded in a given year and caused by past occupational exposure to carcinogenic agents has been estimated to be between €270 and €610 billion, with this figure being driven by the assumed value of a statistical life. The VSL of €4 million is higher than the VSL which would apply to a non-cancer fatality. For example, ECHA's

guidance on Socio-Economic Analysis (SEA)[6] provides a central value of around €1.33 million when updated to 2015 prices. Adopting this figure significantly reduces the estimated total present value costs of cancer registrations, as can be seen from Table 6.

Table 6 **Summary of economic costs – sensitivity analysis on the VSL**

Scenario	Source of data for calculation of AN	Total cost of annual cancer registrations (€ billion) VSL: €4 million	Total cost of annual cancer registrations (€ billion) VSL: €1.33 million
Central-core	EUREG+GCO+UK	348	134
	EUCAN	436	167

10. Limitations of the analysis

Calculated attributable fractions (AFs), attributable cancer cases (ANs), associated costs and country- specific breakdown derived in this project are inevitably subject to considerable uncertainties, as are estimates of the costs associated with a cancer registration. The study has attempted to provide *ranges* for the estimates (High, Low, Central-core, Central-high, Central-low, Mid-point). However, these ranges reflect only part of the variability and uncertainty, while 'true' numbers may spread over an even larger range. As a result, the central estimate should only be regarded as a qualified *order of magnitude* figure instead of an exact number.

More generally, it is important that the limitations of the analysis presented here are recognised. Importantly, gender differences in cancer attributable to occupation could only partly be addressed. This analysis focused on the gender-specific exposure profiles, whereas the intrinsic different biological potency of the carcinogenic agents, leading to gender discrepancies, was not (or was only marginally) addressed.

There are some parameters which may *increase* the overall estimated AF:

— If selection were not restricted to 25 carcinogenic agents;
— If selection were not limited to only a few cancer sites and risk quantifications (as 'relative risk'), which were restricted to the most relevant ones according to IARC plus some additional - not necessarily representative - information sources;
— If many suspected carcinogens, 'possible' carcinogens and carcinogens found only to be carcinogenic in animal studies, were examined, including those with high production tonnages;
— Moreover, no extended and systematic supplemental assessment could be performed from different starting points apart from 'carcinogenic agents'. Starting from 'cancers attributed to occupations' and

6. Based on environmental pollution willingness to pay values.

'occupations and carcinogenic agents attributed to cancer sites' could have provided a more complete coverage of some carcinogenic impacts.

There are some parameters which may *decrease* the overall estimated AF:

— Relative risks (RRs) may often be quantified at elevated exposure levels, and risks at lower exposures may be associated with a significantly lower cancer risk. Because a realistic exposure concentration was not modelled and the exposure level associated with the RR was not explicitly taken into account, and because some non-genotoxic carcinogens (but even genotoxic carcinogens) may be associated with a sublinear exposure risk relationship or even a threshold type of carcinogenicity, these elements may contribute to an overestimation of the final overall AF; and
— Because some suspected carcinogens were included as if they were confirmed carcinogens (e.g. tetrachloroethylene or shift work), new data may disprove suspicion and lead to lower estimated carcinogenic impact.

There are some parameters leading to significant uncertainties, even though the direction (higher or lower estimate) could not be clearly determined:

— Not all of the carcinogenic agents are well-defined, which leads to significant uncertainties on all subsequent input figures (cancer sites, RR, AF, exposure, AN and costs), notably for mineral oils;
— Only epidemiological data were used for risk quantification. The large pool of 'additional risk' data from experimental animals may have been more appropriate for some substances and may lead to quantitative changes; and
— A more exhaustive search for epidemiological data including meta-analyses would have improved the reliability of the RRs finally adopted, but was not feasible within the framework of this project.

The overall result of cancer incidence attributed to occupation is not far away from other similar assessments. This provides some confidence in the overall result, although the above-mentioned uncertainties are acknowledged.

11. Conclusion

In order to estimate the current economic burden of cancer incidence resulting from past occupational exposure to carcinogens, this study first determined the carcinogenic agents thought to be accountable for the majority of occupational cancer incidence in the EU-28.

A selection of 25 carcinogenic agents were identified. They included chemical agents, environmental tobacco smoke, solar radiation, process-generated substances such as diesel exhaust and crystalline silica, and occupational agents such as shift work and work in the rubber industry.

It is estimated that each year around 190,000 new cases of cancer (between 125,000 and 275,000 cases) are attributable to past exposure to these 25 agents. Lung, breast and bladder cancer are the most frequent occupational cancer sites. The overall attributable fraction for all cancer sites across the 25 carcinogenic agents is 8% (6-12%) for both genders, 5% (3-7%) for women and 10% (6-15%) for men.

These estimates are positioned closer to the higher estimates in the published literature and provide further support for studies that have estimated the overall attributable fraction for occupational cancer at 8% or above. Another important finding of this study is that the attributable fraction for occupational exposure to female workers is higher compared to previous studies.

The current total cost of cancer incidence resulting from past occupational exposure to the 25 selected carcinogenic agents is estimated to be between €270 and €610 billion per year in the EU-28 (which corresponds to 1.8-4.1% of EU GDP). These costs include direct costs (medical treatment, transport, etc.), indirect costs (productivity losses due to the cessation of work, etc.) and intangible or human costs for the victims (impact on the quality of life of workers and their families). These estimates are primarily driven by valuation of the human costs with over 98% of total cost borne by workers and their families. When human costs are excluded, the direct and indirect costs are estimated to be between €4 and €10 billion per year.

In conclusion, occupational cancer is associated with a significant economic burden. It is therefore essential that these costs are reduced and additional efforts in terms of prevention policies should be viewed through the prism of the substantial costs that could be avoided.