National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Work-related cancer in the European Union

Size, impact and options for further prevention

RIVM Letter report 2016-0010
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Werk-gerelateerde kanker in de Europese Unie

Ondanks vele beschermende maatregelen kunnen mensen tijdens hun werk worden blootgesteld aan kankerverwekkende stoffen. Aanvullende beleidsmaatregelen zijn nodig om het aantal gevallen van werkgerelateerde kanker en sterfte in de toekomst terug te dringen. Om de noodzaak hiervan te agenderen heeft het RIVM de omvang van de ziektelast en de maatschappelijke schade in kaart gebracht die hierdoor in de EU wordt veroorzaakt.

Geschat wordt dat jaarlijks bij 122.600 (met een marge van 91.500 - 150.500) mensen in de EU kanker vastgesteld wordt doordat zij in het verleden tijdens hun werk aan kankerverwekkende stoffen zijn blootgesteld. Daarnaast sterven hierdoor per jaar ongeveer 79.700 (marge 57.700 - 106.500) mensen in de EU. Als dit ‘vervroegde overlijden’ wordt omgezet naar verloren levensjaren zijn dat er bijna 1,2 (0,8 - 1,6) miljoen.

Kankerpatiënten ervaren een verminderde kwaliteit van leven, krijgen medische zorg en kunnen vaak niet of minder werken. Naast het (individuele) lijden ontstaan hierdoor kosten. Dit wordt gezamenlijk uitgedrukt in maatschappelijke schade. De kosten voor de gezondheidszorg en verminderde productiviteit op het werk door werkgerelateerde kanker in de EU worden op €4-7 miljard per jaar geschat. Als ook de immateriële schade van het ziek zijn en mogelijk vroegtijdig sterven wordt meegerekend, loopt de totale maatschappelijke schade op tot €334 (marge 242 – 440) miljard per jaar.

Kernwoorden: kanker, carcinogene stoffen, werk, ziektelast, maatschappelijke schade, grenswaarden.

Synopsis

Work-related cancer in the European Union

Despite many protective measures workers can be exposed to carcinogenic substances at work. Additional policy interventions are needed to reduce the future burden of work-related cancer in the EU. The RIVM addressed this issue by providing insight into the magnitude of work-related cancer, in terms of the number of cases, deaths and the societal costs, caused by exposure to carcinogenic substances in the EU.

We estimate that in de EU 122,600 (range 91,500 - 150,500) people were newly diagnosed with cancer, caused by past exposure to carcinogenic substances at work. The attributed cancer deaths are estimated to be 79,700 (range 57,700 - 106,500). In total almost 1.2 (0.8 - 1.6) million years of life were lost due to premature death caused by past exposure to carcinogenic substances at work in the EU-population.

The consequences of this work-related cancer, and its impact on society, extend further than mortality and morbidity figures. They also include the reduction in the quality of life, productivity losses and the provided health care. Next to the individual emotional suffering and pain associated with the disease, this leads to economic cost for society. Health care expenditure and productivity losses are estimated to cost between €4-7 billion annually for the EU. When welfare losses of premature deaths and diagnosis with cancer are added, the total annual economic representation of the societal impact is estimated to be in an order of magnitude of €334 (242 – 440) billion.

Keywords: cancer, carcinogenic substances, work, disease burden, societal costs, limit values

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Summary

The work environment constitutes a risk factor for developing cancer. One of the factors that may cause cancer within the work environment is exposure to carcinogenic substances. Many workers in the European Union (EU) have been, and often still are being, exposed to carcinogenic substances. This leads every year to new work-related cancer cases and work-related cancer deaths. Work-related cancer makes up the largest share of all work-related deaths, but an estimate of the number of work-related cancer cases and related cancer deaths that can be attributed to an exposure to carcinogenic substances is lacking for the EU. This report aims to provide a rough estimate of this work-related cancer burden in the EU-28, to introduce the existing legislative regime and explore further options to realize a reduction of this burden.

Exposure to carcinogens at work is regulated within the EU in the interplay of two important EU legal frameworks:

- Carcinogens & Mutagens Directive (CMD) concerning the protection of workers exposed to carcinogens;
- REACH/CLP legislation concerning the marketing and use of substances.

The CMD lays down the European Community rules for protecting workers from the risks related to exposure to carcinogens at work. One of the frameworks under the CMD allows setting of occupational exposure limits (OELs) for carcinogens. Genotoxic carcinogens are substances that cause an immediate change in DNA that may lead to cancer and therefore no threshold for effects can be defined. For such non-threshold carcinogens, an OEL always represents a residual risk. There are different views in the EU on the appropriateness of OELs as an instrument to control exposure in the workplace, the method for setting these OELs and the level of residual risk to be considered as tolerable/acceptable. The most relevant REACH provisions regarding carcinogens are authorization and restriction.

We estimate that in de EU-28 122,600 (91,500 - 150,500) people were newly diagnosed with cancer in 2012, caused by past exposure to carcinogenic substances at work. Lung cancer, prostate cancer, colorectum cancer and bladder cancer account for over 75% of the newly diagnosed cancer cases. An estimated 79,700 (57,700 - 106,500) cancer deaths were attributed to work-related exposure to carcinogenic substances in 2012. Lung cancer accounts for most of these deaths in both men and women in absolute numbers, followed by mesothelioma and colorectum cancer. Cancer types with the highest proportion of all deaths in the general population that can be attributed to work-related exposure to carcinogenic substances are lung (17%), lip-oral cavity-pharynx (9%), bladder (8%), prostate (6%), larynx (6%) and Hodgkin and lymphomas (5%). For mesothelioma-related deaths in the population, 85% of them are caused by work-related exposure to asbestos. In total almost 1.2 (0.8 - 1.6) million years of life were lost due to premature death caused by work-related exposure to

carcinogenic substances in the EU-population; 90% of the years of life lost were in men.

The consequences of work-related cancer, and its impact on society, extend further than just mortality and morbidity figures. They also include a reduction in the quality of life, productivity losses, informal care given by relatives and the health care costs of cancer. The annual economic representation of the societal impact of work-related cancer caused by carcinogenic substances is estimated to be at least in an order of magnitude of €334 (242 – 440) billion. Welfare loss associated with cancer morbidity and mortality represents by far the largest share (€329 billion). Health care expenditure and productivity losses are estimated to be approximately €4.4 (2.8 - 5.4) billion per year with a maximum of €7.5 (4.9 - 8.8).

If policy remains unchanged, the magnitude of work-related cancers caused by carcinogenic substances is expected to remain the same. Additional policy interventions are needed to reduce the future burden of work-related cancer in the EU. The existing regulatory framework covering risk management includes a large number of possible interventions. Intensification at all levels is required to realize a substantial reduction of work-related cancers.

1 Introduction

Cancer is one of the leading causes of illness and death worldwide, with around 14 million new cases and 8 million cancer-related deaths in 2012 (WHO 2015). In the European Union (EU-28), an estimated 1.3 million people die each year due to cancer, with lung cancer as most prevailing type. Cancer has a huge impact on society and there are numerous policy programmes aimed at the prevention and treatment of cancer. The societal impact of cancer extends much further than mortality figures suggest and includes the economic costs of illness and the reduction in the quality of life caused by cancer. Furthermore, cancer has a direct effect on productivity, causing productivity losses due to illness and death. The total economic burden of cancer across the EU was valued at € 126 billion in 2009 (Luengo-Fernandez et al. 2013) and included health care costs, informal care and productivity losses. The emotional and social impact of cancer, such as a loss in the quality of life, was not accounted for in this estimate. Recent work commissioned by the European Chemicals Agency (ECHA) valued the welfare loss associated with cancer-related mortality and morbidity at € 3.5 million and € 0.4 million per case respectively (ECHA 2015).

Tobacco use, alcohol use, unhealthy diet and physical inactivity are indicated worldwide as the main cancer risk factors. Besides these, the work environment is a risk factor as well. Within the work environment, factors that contribute to cancer development include exposure to chemicals, biological agents, physical agents (such as radiation) and work organization (such as shift work that disrupts the circadian cycle). The International Labour Organization (ILO) estimates that, globally, 666,000 deaths can be attributed to work-related cancer every year (Takala 2015). This estimate is based on population cancer mortality figures and attributing a proportion of this cancer mortality to chemical, biological and physical carcinogenic factors in the work environment, (Hamalainen 2010; Nenonen et al. 2014). In a report made for the 2014 Greek Presidency Conference on Occupational Safety and Health, the EU share of this was estimated to be 102,500 deaths. According to Takala (2014), work-related cancer is by far the largest cause (53%) of all work-related deaths.

Exposure to carcinogenic substances, next to the other carcinogenic factors (solar radiation) and an increased sensitivity (shift work disrupting the circadian cycle), is a major factor causing work-related cancer (Rushton et al. 2012b). In the EU, the carcinogenic substances to which the largest numbers of workers are currently exposed are benzo[a]pyrene, diesel engine exhaust emission, hardwood dust, hydrazine, mineral oils (such as used engine oil), 4.4'methylenedianiline, chrome VI, respirable crystalline silica, formaldehyde and asbestos (Cherrie et al. 2011; Puts and Ter Burg 2015). Often there is a substantial latency time between the start of exposure to carcinogenic substances and the development of cancer. In other words, (long-lasting) exposure does not lead to cancer immediately after the beginning of exposure.

In the EU, legislation aimed at worker protection against carcinogenic factors focuses mainly on exposure to chemical agents. The 2004/37/EC Carcinogens & Mutagens Directive (CMD) regulates the risks related to exposure to carcinogenic substances (classified as a category 1A or 1B carcinogen in Annex I to Regulation (EC) No 1272/2008). The CMD stipulates that employers have to (in descending order of feasibility) replace carcinogenic substances; ensure the carcinogenic substance is manufactured or used in a closed system; ensure that the workers' level of exposure is "reduced to the lowest level that is technically possible". In addition, the Directive provides for the establishment of work-related exposure limit values, known as Binding Occupational Exposure Limit Values (BOELV), that are legally binding for all Member States of the EU. So far, three BOELVs have been established under the CMD framework. Work-related cancer is not inevitable and can be avoided. Cutting exposure to carcinogens lessens cancers developing and spotting the signs of cancer early on means they can be treated and even cured in some cases (IOSH 2014).

Estimates of the work-related cancer burden in the EU that are related only to chemical factors, i.e. carcinogenic substances, are based on a limited selection of substances. The Global Burden of Disease (GBD) study incorporates 13 substances in their estimate of the burden of work-related cancer (Lim et al. 2012). In 2010, the estimated number of deaths attributed to work-related exposure to these carcinogenic substances was 58,190 (45,460 – 67,051) for the EU. In the recent update for 2013, this number increased to 59,748 (45,800 – 70,441) (IHME 2016a). The Institute for Occupational Medicine (IOM) looked at 25 work-related carcinogenic substances in the SHEcan project for the European Commission. In the EU in 2010, an estimated 12,791 deaths could be attributed to work-related exposure to these 25 carcinogenic substances, together with another 16,405 newly-diagnosed cases (Cherrie et al. 2011). These lower estimates, compared with the GBD study, can be explained by the fact that Cherrie and co-workers did not evaluate work-related cancer attributed to asbestos. In 2010, 53,717 deaths were related to asbestos exposure in the GBD estimate for the EU (IHME 2016a).

The above-mentioned studies estimated the number of work-related cancer deaths and/or newly diagnosed cancers for a selected number of carcinogenic substances. The burden of work-related cancers in the EU caused by exposure to all known carcinogenic substances is unknown. For this reason, the potential benefits for society of cutting exposure to carcinogenic substances at work remains uncertain.

1.1 Aim and scope

With this report, we aim to improve the understanding, and thereby contribute to a further reduction, of the burden of work-related related cancer caused by exposure to carcinogenic substances in the EU by:

1. Gaining insight into the magnitude of work-related cancer caused by exposure to carcinogenic substances in the EU-28, in terms of the number of cases, deaths and the societal costs.
2. Placing this insight into the context of the existing European legislative regime; its practical implementation and the

exploration of further options to realize a reduction in work-related cancer.

1.2 Structure of the report

In Chapter 2, the current European legislative regime for handling carcinogenic substances at work is briefly described. In Chapter 3, we provide a rough estimate of the number of cancer deaths, newly diagnosed cases and the years of life lost in 2012 that can be attributed to work-related exposure to carcinogenic substances. The societal impact of this work-related cancer burden is assessed by looking at health care costs, productivity and welfare losses. In Chapter 4, the views of various stakeholders on the improvements needed to further reduce work-related cancer are given. Chapter 5 summarizes the main findings and presents various options to further decrease work-related cancer caused by carcinogenic substances in the EU.

2 Introduction to the legislative frameworks

Exposure to carcinogens at work is regulated within the EU in the interplay of two important EU legal frameworks:

- 2004/37/EC Carcinogens & Mutagens Directive (CMD) concerning the protection of workers exposed to carcinogens;
- REACH/CLP legislation (Regulation) concerning the marketing and use of substances.

2.1 The CMD

The *CMD* lays down the European Community rules for protecting workers from the risks related to exposure to carcinogens at work. The CMD stipulates that the employer shall assess and manage the risk of exposure to carcinogens and mutagens, report relevant data (activities, quantities, exposures, number of exposed workers, preventive measures) to the authorities and inform the workers when exposure occurs that puts them at risk. When managing the risks, the employer must follow the principle of the hierarchy of protective measures, meaning that employers must, in the first place, replace carcinogens at their premises by a less hazardous substance if technically feasible. If replacement is not technically possible, the employer must ensure that the carcinogen is manufactured or used in a closed system. If, finally, using the chemical in closed systems is not possible, the employer must ensure that the level of the workers' exposure is "reduced to the lowest level that is technically possible", also referred to as the "minimization principle".

The CMD stipulates that the employer must assess the risks of the carcinogens that workers are likely to be exposed to and identify the protective measures to be taken - also referred to as the Risk Inventory and Evaluation (RI&E).

According to CMD, exposure at the workplace shall not exceed the limit value of a carcinogen set out in Annex III of that Directive. Annex III of the CMD currently includes limit values for three carcinogens: Benzene, Vinyl chloride monomer and Hardwood dusts. These are binding values, referred to as Binding Occupational Exposure Limit Values (BOELVs), as they are legally binding for all Member States in the sense that Member States must establish a corresponding national binding OEL value, which can be stricter, but cannot exceed the Community BOELV.

The CMD has been incorporated into national law in all Member States since 2004.There are, however, quite a few differences in the way Member States have implemented CMD in national law, the most notable of which is the way they address the risks related to carcinogens without a threshold (see 2.1.2).

2.1.1 OELs for carcinogens

An Occupational Exposure Limit (OEL) is the maximum permissible concentration of a chemical in the air in the workplace. OELs are used for controlling the risks from chemicals at work in general, not for

carcinogens in particular. OELs are considered by many as an important regulatory instrument (Terwoert et al. 2013):

- OELs increase the awareness of companies and workers with respect to the chemical risks present at their workplace;
- OELs are instrumental in specifying the exposure in the workplace and in evaluating effective prevention measures;
- If there is an OEL, companies can use it to prioritize the carcinogens that need to be addressed;
- Finally, OELs are easier to enforce. They are seen as clear-cut references that allow for straightforward enforcement.

Pronk (2014) provides a recent overview and comparison of the methodologies used by the Scientific Committee on Occupational Exposure Limits (SCOEL), ECHA and four Member States for the derivation of OELs for non-threshold carcinogens. It was found that there are many similarities, but also some differences. One of the similarities is that the methodologies are based on similar principles. All apply similar general criteria for quality and adequacy of the data selected to derive the limits. All also prefer the use of human data above the use of animal data, but recognize that in most cases these will not be available or will not form a sufficient basis on their own. Differences observed in OELs for non-threshold carcinogens are largely due to differences in cancer risk levels used. Other sources for the differences are the choice for the animal exposure levels which causes the adverse effect, and uncertainty factors applied in the extrapolation from animals to humans. When at a later stage other considerations such as socio-economic or technical feasibility are also taken into account, these may additionally lead to differences in the final occupational exposure limits.

The study of Cherrie et al. (2011) suggests that there are clear health benefits, in terms of avoided cancer cases, from introducing OELs for selected carcinogens. An important aspect in this respect is the fact that, in this study, only the health impacts of cancer were taken into consideration. The health benefits with respect to diseases other than cancer that may be caused by exposure to the studied substances may add to the argument in favour of introducing OELs for carcinogens.

2.1.2 Threshold vs. non-threshold carcinogens

In respect of adverse health effects for which a threshold can be defined, an OEL is intended to be the level below which a given substance can be present in the air at the workplace without harming the health of employees and their offspring, based on current scientific knowledge and for the employee's entire working life.

For effects without a threshold, as it is often the case with carcinogens (i.e., genotoxic carcinogens – substances that cause an immediate change in DNA, which may lead to cancer), an OEL for a non-threshold carcinogen always represents a residual risk. There are different views in the EU on the appropriateness of OELs as an instrument to control exposure in the workplace, the method for setting these risk-based OELs and the level of residual risk to be considered as tolerable/acceptable. Some Member States use no OELs for carcinogens. Their policies with regard to carcinogens in the workplace are aimed at reducing the exposure in the workplace at the lowest level that is "technically

possible", also referred to as the "minimization principle", an obligation that always applies. Other Member States set additional "pragmatic" OELs at levels that are "as low as is reasonably practicable", also referred to as the ALARP approach. Still others are developing OELs based on the underlying quantitative risk assessment (QRA) and the concept of tolerable/acceptable risk, usually in the range of 10^{-2} to 10^{-5} of extra risk for cancer due to work-related exposure during an entire working life of 40 years. These are often referred to as "risk-based". The setting of OELs for carcinogens, as a rule, involves an assessment of feasibility issues, ranging from technical feasibility to a broader socio-economic assessment. For this purpose, most Member States use a consultation of stakeholders in tripartite committees. Others also conduct a broader public consultation. In the United Kingdom, a systematic gathering and evaluation of data on the costs and benefits is conducted. It is important to realize that OELs for non-threshold carcinogens, whether pragmatic or based on a QRA, always represent a residual risk, the difference being that OELs based on a QRA allow the estimation of the actual risk in the workplace.

Many see the fact that risk-based OELs allow the maximization of health protection, in the light of insights into the costs associated with their realization, as their major advantage. Disadvantages in relation to risk-based OELs include the fact that the use of a numerical value for expressing the risk may jeopardize the obligation to minimize the exposure to carcinogens. Although this always applies, the mere existence of a limit value can work as a disincentive to minimization efforts. Another disadvantage is that setting risk-based OELs may be a costly and lengthy process that involves certain uncertainties, due to scientific issues related to the derivation of the exposure-risk relationship and, most notably, the uncertainties surrounding the assessment of socio-economic impacts. The monetary valuation of non-market impacts is especially recognized as a controversial area. So far, only a very limited number of BOELVs have been set under the CMD, but work is underway that is expected to result in BOELVs for a significant number of carcinogens at the workplace.

A number of Member States, but certainly not all, also launch national activities in the field of setting OELs. In a survey by the European Agency for Safety and Health at Work (EU-OSHA) among Member States on OELs for carcinogenic and mutagenic substances from 2008, nine out of 20 EU countries mentioned difficulties in the process of deriving OELs for carcinogenic and mutagenic substances, the most common problems being a lack of national exposure data in order to set priorities, a lack of toxicological data, as well as difficulty in reaching a consensus on the derivation method to be applied and the level of risk that is to be considered as "acceptable" (EU-OSHA 2009). Given the limited number of Member States actually deriving OELs for carcinogens, it is believed that developing OELs for carcinogens at the EU level will contribute to the overall protection of the workforce in the EU.

2.2 Registration, Evaluation, Authorization and Restriction of Chemicals (REACH)

The most relevant REACH provisions regarding carcinogens are authorization and restriction. Manufacturers and Downstream Users will have to get the European Commission's authorization for each proposed use of those carcinogenic substances included in Annex XIV of REACH (the authorization list) for a specific period and on a case-by-case basis. Carcinogens included in Annex XIV of REACH have a harmonized classification as carcinogens category 1A or 1B and normally have a wide dispersive[1] use or are high volume chemicals. To get authorization, applicants will have to show that the risks associated with the use of the chemical concerned are "adequately controlled" or that the risks are outweighed by socio-economic benefits and there are no suitable alternative substances or technologies. Theoretically, is it possible that all category 1A and 1B carcinogens, mutagenic or reprotoxic (CMR) substances end up in the authorization process. In practice, a prioritizing system is applied, depending on several factors such as hazard classification, annual volume and usage. Note that, under the authorization procedure used under REACH, carcinogens may be authorized for use for a certain period, even though a safer alternative might exist, depending on the technical and economic feasibility of such alternative. This contradicts the CMD principle of substitution when it is simply technically feasible. That said, one should also keep in mind that authorization is finally aimed at substitution of the substance of concern (such as carcinogens) and hence it is an instrument to enforce the CMD principle of substitution at the European Community level.

Restrictions within REACH prohibit the marketing or use of substances under specific conditions. Since the adoption of REACH, one carcinogenic substance (1,4-dichlorobenzene) is restricted due to the risk present for workers.

[1] Wide-dispersive uses are characterised by use(s) of a substance on its own, in a preparation or in an article at many places (sites) that may result in not insignificant releases and exposure to a considerable part of the population (workers, consumers, general public) and/or the environment..

3 The burden of work-related cancer caused by carcinogenic substances in the EU

3.1 Cancer mortality; morbidity and life years lost due to work-related exposure to carcinogenic substances in the EU

The aim of this analysis is to provide the order of magnitude, rather than a precise figure, of work-related cancer caused by carcinogenic substances in the EU. The estimates in this report are based on general mortality and incidence figures for cancer in the total population and previous estimates of attributable fractions related to carcinogenic agents in the working population. The years lost due to premature death can be expressed as 'years of life lost' (YLL).

3.1.1 General methodology

In this chapter, we estimate the number of newly diagnosed cancer cases, deaths and associated years of life lost (YLL) for 2012 that can be attributed to exposure to carcinogenic substances at work in the past for the EU-28. For this, we used attributable fraction. In short, attributable fractions are applied to cancer mortality (=deaths) and incidence (=newly diagnosed cases) figures for the EU-28 population in 2012 to obtain a rough estimate attributed to work-related exposure to carcinogenic substances. YLL are calculated from the number of deaths multiplied by the life expectancy at the age at which death occurs. If somebody dies at an early age, it will create more YLL than when somebody dies at a higher age. In this way, not only the number of deaths is accounted for but the impact of early death as well. The methodology is briefly described below and in greater detail in the Annex: Methodology (Size of the problem: data and methods).

One approach to calculating the cancer burden attributed to work-related exposure (Cherrie et al. 2011; Lim et al. 2012; IHME 2016b) is: the number of workers exposed to a certain carcinogenic substance and the associated level and duration of exposure are determined. Based on risk estimates (dose-response curves or relative risks estimates), the number of excess cancer cases or deaths in the exposed worker population, compared with a non-exposed worker population, is calculated and attributed to the work-related exposure. This is repeated for each carcinogenic substance of interest and summed to come to a total burden estimate. Using the number of excess cancer cases or deaths, one can estimate the fraction of each cancer type occurring in the general population that can be attributed to work-related exposure. This is called the population attributable fraction (AF).

In the EU, AFs were estimated for Finland in 1996 (Nurminen and Karjalainen 2001) and for the United Kingdom in 2005 (Rushton et al. 2012b). In both studies, the AFs for all the relevant carcinogenic agents and occupational circumstances were combined into a single AF estimate for each separate cancer. The AFs from both studies are used as the basis in our study. Industrial conditions vary within Europe and, by using both studies; we try to include as much data as is available. We

adapted some AFs in order to reflect only the contribution of carcinogenic substances. In general, we used the average of both studies as a central estimate and determined lower and upper ranges (Annex: Methodology – Attributable fractions; Tables A2 and A3). In total, 42 carcinogenic substances or substance groups and 16 occupational circumstances have been taken into account (see Tables A4 and A5 in the Annex). Age-dependent cancer mortality and incidence numbers for each separate cancer in the EU-28 population in 2012 are obtained from Eurostat and GLOBOCAN, respectively (see Table A1).

This approach should be interpreted as a means to generate rough estimates. There are substantial uncertainties such as data uncertainty, availability and representativeness for the EU-28. Furthermore, we used country-specific industry type, exposures and the general population characteristics of Great Britain and Finland and extrapolated them to the whole EU-28, as information on occupational exposure to carcinogens in the EU is, in general, outdated and incomplete, as was illustrated by the European Agency for Safety and Health at Work (EU-OSHA) (Lißner et al. 2014).

3.1.2 Incidence

In the EU-28 for 2012, it is estimated that each year 122,600 (91,500 – 150,500) people get cancer due to exposure to carcinogenic substances at work. Lung cancer, prostate cancer, colorectum cancer (only men) and bladder cancer account for more than 75% of the cancer incidence due to work-related exposure in the past. See Figure 3.1 and Table 3.1 for the cancer types and associated incidence numbers due to exposure to carcinogenic substances at work. Some cancer types are gender specific (prostate, cervix uteri and ovary). For colorectum cancer and Hodgkin lymphoma the AF for women was zero; for breast cancer the AF for men was zero.

More than 40% of the people that get cancer due to exposure to carcinogenic substances at work are diagnosed with lung cancer. Survival rates for lung cancer are low. In the EU, on average only 10% of all newly diagnosed patients are alive 5 years after being diagnosed with lung cancer (Rossi et al. 2015). Five-year survival rates for colorectum; bladder and prostate cancer are around 50%; 66% and 72% respectively. The lowest 5-year survival rates are associated with pancreas (4%), mesothelioma (4%), liver (9%), oesophagus (9%) and gallbladder (14%) cancers (Rossi et al. 2015).

Table 3.1: Total absolute incidence estimates of cancer in the EU-28 countries in 2012, as a result of past exposure to carcinogenic substances at work

Cancer type	**Lower range[1]**	**Central estimate[1]**	**Upper range[1]**
C33-34 - Lung	44,400	52,900	58,700
C61 – Prostate[3]	20,700	20,700	20,700
C18-21 – Colorectum[3]	10,800	10,800	10,800
C67 - Bladder	4,700	10,700	14,900
C45 – Mesothelioma[2]	6,500	7,200	8,200
C82-85, C96 - Non-Hodgkin lymphoma	40	4,000	6,700
C25 - Pancreas	0	3,000	6,700
C16 - Stomach	790	1,600	2,700
C32 - Larynx	370	1,600	2,500
C64-66 - Kidney	0	1,400	2,800
C70-72 - Brain, nervous system	20	1,400	2,600
C15 - Oesophagus	420	1,300	2,200
C53 - Cervix uteri	0	1,100	2,000
C43 - Melanoma of skin[3]	1,100	1,100	1,100
C22 -Liver	50	930	1,800
C56 - Ovary	0	580	930
C09-10, C12-14 - Other pharynx[3]	460	460	460
C00-08 - Lip, oral cavity[3]	400	400	400
C50 – Breast[3]	360	360	360
C91-95 - Leukaemia	90	360	2,300
C11 - Nasopharynx	60	280	1,200
C81 - Hodgkin lymphoma	250	250	250
C88+C90 - Multiple myeloma	0	90	230
C23-24 – Gallbladder[3]	80	80	80
Total	**91,500**	**122,600**	**150,500**

1 Rounded numbers (<1000 to the nearest ten; >1000 to the nearest 100)

2 Mortality taken as proxy for incidence

3 Only point estimate available

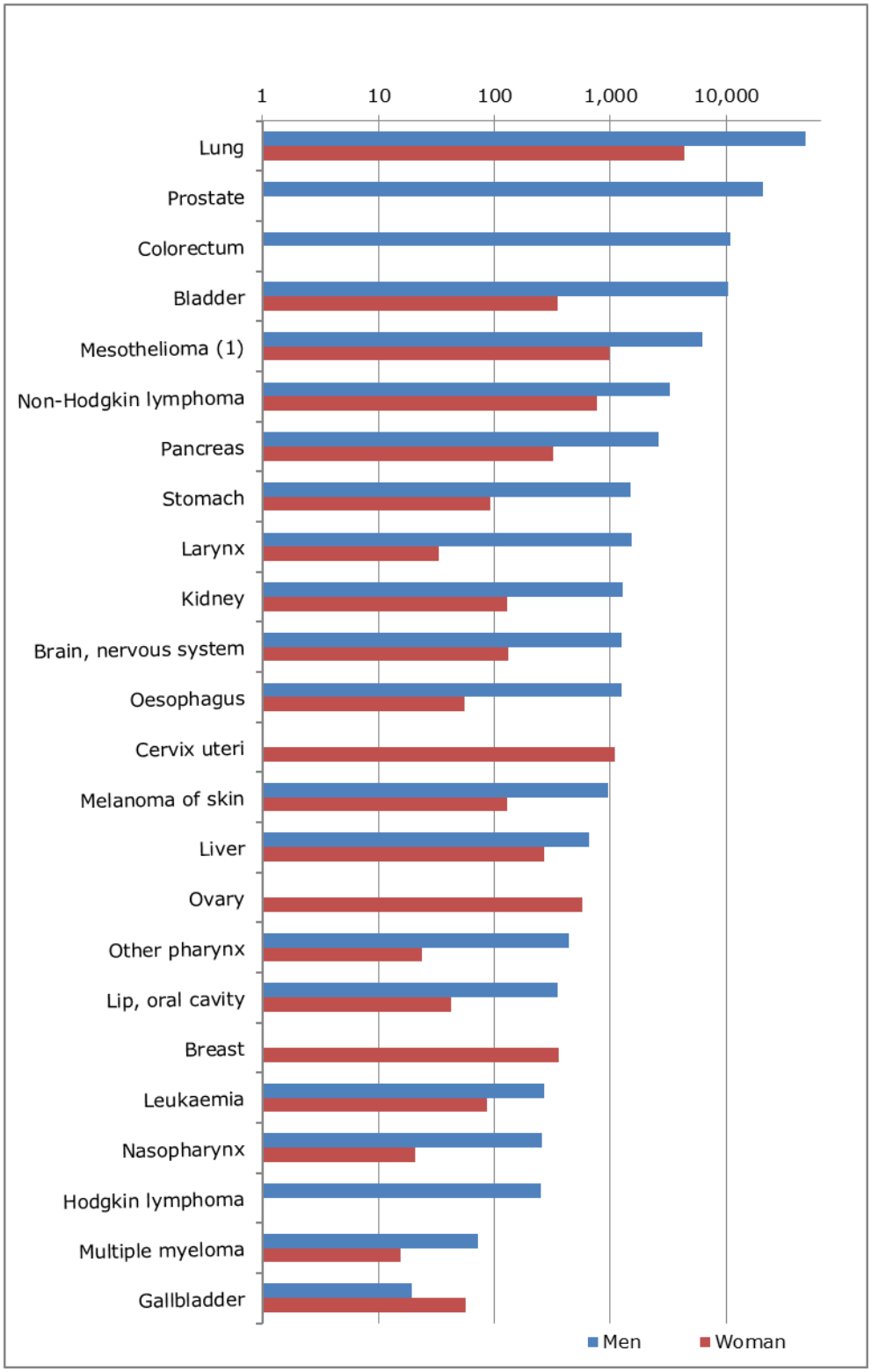

Figure 3.1. Absolute incidence of cancer in EU-28 for 2012 as a result of past exposure to carcinogenic substances at work, for men (blue coloured bars) and women (red coloured bars). In descending order of magnitude (total of men and women), central estimate presented.

1 Mortality taken as proxy for incidence.

3.1.3 *Mortality*

For 2012, we estimate that 79,700 (57,700 - 106,500) cancer deaths in the EU can be attributed to work-related exposure to carcinogenic substances. Lung cancer and mesothelioma account for most deaths in both men and women, followed by colorectum cancer in men. See Figure 3.2 and Table 3.2 for the cancer types and the associated mortality numbers due to exposure to carcinogenic substances at work.

Most mesothelioma-related deaths (85%) in the population are attributed to work-related exposure to asbestos. Other cancer types with a high proportion of deaths in the general population that are attributed to work-related exposure to carcinogenic substances are lung (17%), lip-oral cavity-pharynx (9%), bladder (8%), prostate (6%), larynx (6%) and Hodgkin and lymphomas (5%) (see Table A2 in the Annex).

Table 3.2: Total absolute mortality due to cancer in the EU-28 countries in 2012, as a result of exposure to carcinogenic substances at work

Cancer type	**Lower range[1]**	**Central estimate[1]**	**Upper range[1]**
C33_C34 - Trachea, bronchus and lung	38,500	45,900	50,900
C45 - Mesothelioma	6,500	7,200	8,200
C18-C21 Colon, rectosigmoid junction, rectum, anus and anal canal[2]	4,700	4,700	4,700
C61 - Prostate[2]	4,300	4,340	4,300
C67 - Bladder	1,500	3,500	4,900
C25 - Pancreas	0	3,000	6,800
C00-C14 - Lip, oral cavity, pharynx	560	2,600	11,300
C81-C85 - Hodgkin disease and lymphomas	10	1,500	2,500
C15 - Oesophagus	370	1,200	1,900
C16 - Stomach	570	1,200	2,000
C70-C72 - Brain and central nervous system	20	1,100	2,200
C22 - Liver and intrahepatic bile ducts	50	920	1,700
C32 - Larynx	160	680	1,100
C64 - Kidney, except renal pelvis	0	480	950
C56 - Ovary	0	390	620
C53 - Cervix uteri	0	360	650
C43 - Skin[2]	240	240	240
C91-C95 - Leukaemia	50	210	1,300
C50 - Breast[2]	90	90	90
C88_C90_C96 - Lymphoid, haematopoietic and related tissue	0	50	130
Total	**57,700**	**79,700**	**106,500**

1 Rounded numbers (<1000 to the nearest ten; >1000 to the nearest 100)

2 Only point estimate available

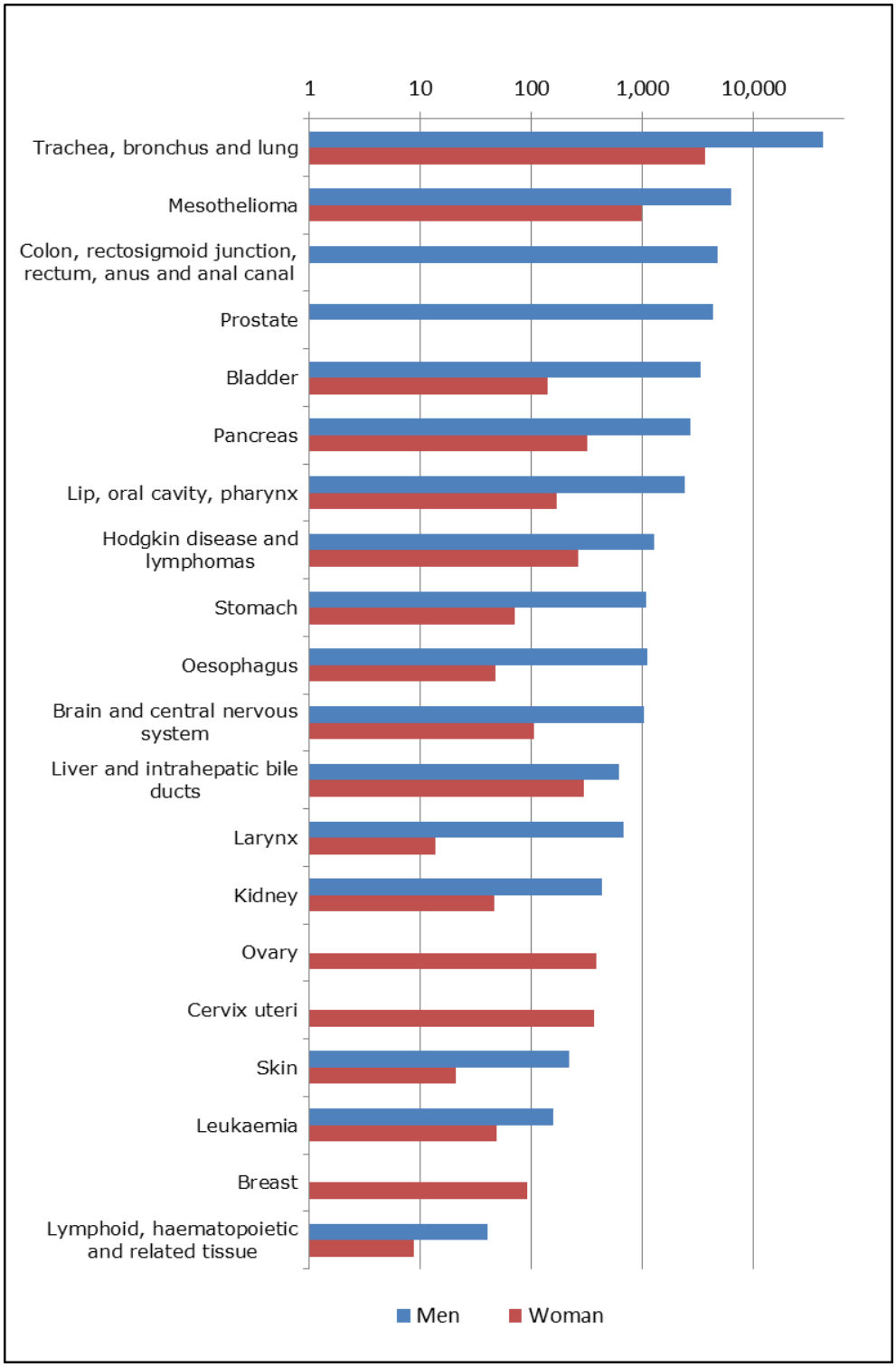

Figure 3.2: Absolute cancer mortality in the EU-28 countries in 2012, as a result of past exposure to carcinogenic substances at work, for men (blue coloured bars) and women (red coloured bars). In descending order of magnitude (total of man and women), central estimate presented. For the category of colon, rectosigmoid junction, rectum, anus and anal canal cancers the AF for women was zero. For breast cancer the AF for men was zero.

3.1.4 *Life years lost*

In total almost 1.2 (0.8 - 1.6) million years were lost due to work-related exposure to carcinogenic substances in the EU-population; 90% of the YLL were in men. The major share (59%) of the YLL was due to lung cancer, followed by mesothelioma (8%), colorectum (5%), lip, oral cavity, pharynx (4%), pancreas (4%) and prostate cancer (4%) (see Figure 3.3).

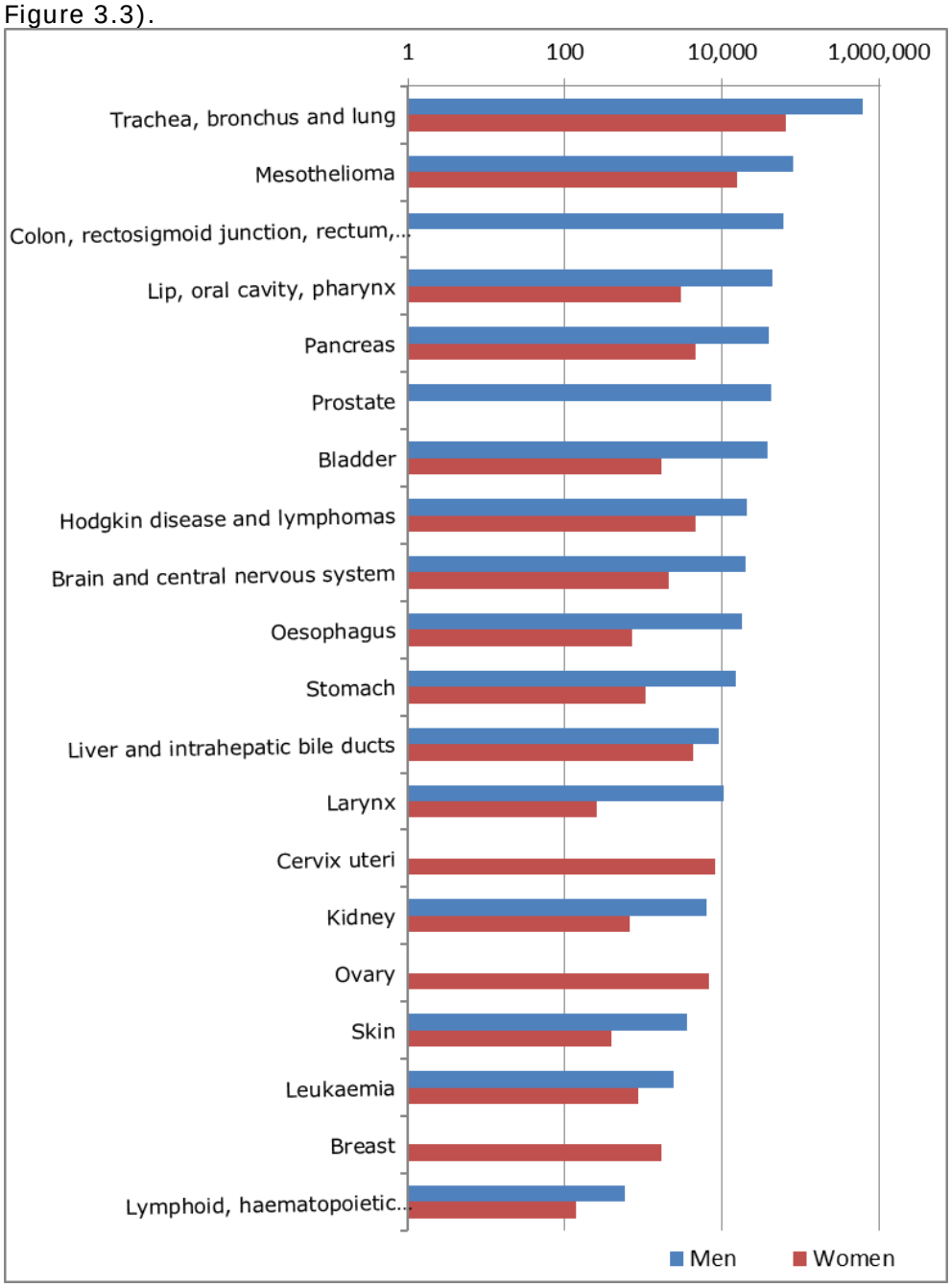

Figure 3.3: Years of life lost (YLL) in the EU-28 countries in 2012 as a result of past exposure to carcinogenic substances at work, for men (blue coloured bars) and women (red coloured bars). In descending order of magnitude, central estimate presented. For the category of colon, rectosigmoid junction, rectum, anus and anal canal cancers the AF for women was zero. For breast cancer the AF for men was zero.

3.1.5 *Age distribution*

Often there is a substantial latency time between the start of exposure to carcinogenic substances and the development of cancer. In other words, (long-lasting) exposure does not lead to cancer immediately after the exposure starts. The time between exposure and occurrence of cancer takes on average 10 to 35 years (IOSH 2014). Figure 3.4 describes the distribution of the mortality, incidence and YLL attributed to work-related exposure to carcinogenic substances between the different age classes. The mortality, incidence and YLL are described on a relative scale as percentage (%) of their total for each age class. In this way all three can be displayed in the same figure.

Most of the total mortality (71%) and total incidence (65%) occur after the age of 65. In contrast, almost half (47%) of the total YLL attributed to work-related exposure to carcinogenic substances occur before the age of 65. The average age of retirement in the EU in 2012 was 63 year (OECD). This means that the diagnosis of cancer and subsequent death often take place after the retirement age.

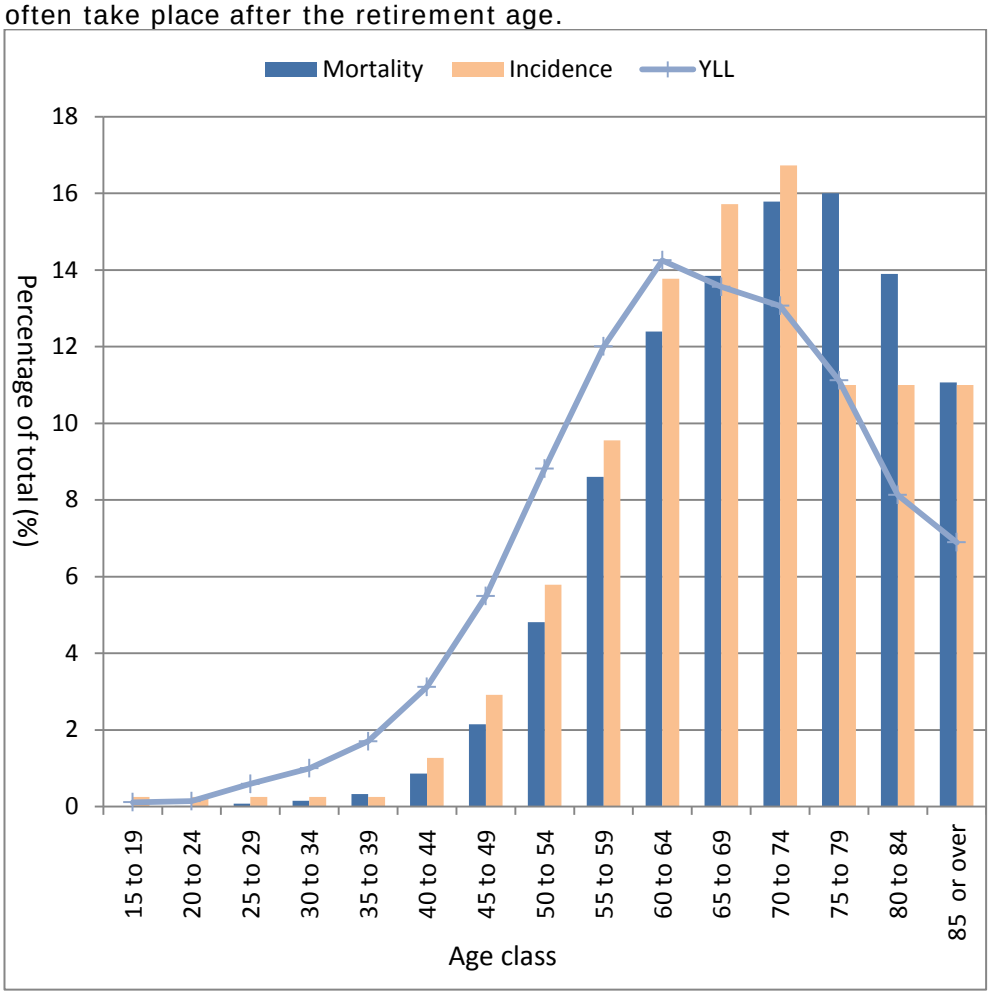

Figure 3.4: The distribution of the mortality, incidence and YLL attributed to work-related exposure to carcinogenic substances between the different age classes. For incidence, only the 75+ age class is available. This fraction is equally divided between the "75 to 79"; "80 to 84" and "85 or over" classes.

3.2 Societal impact of work-related cancer caused by carcinogenic substances in the EU

Cancer caused by exposure of workers to carcinogenic substances exacts a substantial cost from the European society. The aim of this analysis is to provide the order of magnitude, rather than a precise figure, for the societal costs of work-related cancer caused by carcinogenic substances in The EU. The cost estimates used in this report are based on existing cost-of-illness studies for cancer in general. Using the population attributable fractions (see table A3 in the Annex), the societal costs of work-related cancer caused by carcinogenic substances are estimated.

Previously, the total economic burden of cancer in the total population across the EU-27 was valued at € 126 billion in 2009 (Luengo-Fernandez et al. 2013) and included health care costs, informal care and productivity losses. We use this study and the newly diagnosed cancer cases estimated in the previous paragraph to calculate the economic burden of cancer attributed to work-related exposure to carcinogenic substances. Estimates are corrected for inflation and extrapolated to the EU-28. Productivity losses are assessed using the friction cost approach (FCA) and human capital approach (HCA). The FCA takes into account the replacement of involuntary unemployment assuming that ill individuals will be replaced over time. The HCA assesses the time between involuntary unemployment and expected retirement age to estimate the potential production loss.

In addition to the abovementioned economic burden, welfare losses associated with being diagnosed with cancer and cancer-related deaths are valued. The recently derived cancer-specific Value of Statistical Life (VSL) and Value of Cancer Morbidity (VCM) by ECHA (2015), based on the survey of Alberini and Ščasný (2014), are used to value the welfare losses.

3.2.1 Cost elements

There are various ways to calculate the societal cost of cancer and different cost elements can be included in such an assessment. In general, three different cost components can be distinguished. The first cost element relates to the actual money spent by society for the diagnosis and treatment of cancer and costs borne directly by the patient (direct cost elements). The second cost element concerns more indirect losses to society; these costs involve opportunity costs of unpaid care given by relatives and friends of severely diseased cancer patients, lost working days of cancer patients at times of illness and productivity losses due to early death caused by cancer (indirect cost elements). The third cost level tries to capture the suffering and pain of associated with cancer; the subsequent lower quality of life and the impact on relatives and close friends. It represents the important emotional and social aspect of the disease (intangible cost elements). In all estimates of cost elements, a societal perspective is taken.

Not all of the cost elements can be quantified when calculating societal costs and this depends on data availability. The cost elements that can be quantified are expressed in euros (€) and all components are added

together to estimate the total societal cost. It is important to realize that, although these various societal cost elements are expressed in euros, the outcome is not a cost figure comparable to the money that is actually spent by society. It is merely an economic representation of the societal impact of cancer caused by work-related exposure to carcinogenic substances. Table 3.3 describes the various cost elements used in our calculation. In the Annex, the methodology used, the assumptions and the justification of our calculation are described in greater detail.

Table 3.3: Overview of included cost elements to estimate the societal cost of cancer

Cost element	Explanation	Source
Direct costs		
Primary care	Visit to or from General Practitioner (GP) and practice nurse	Luengo-Fernandez et al. (2013)
Emergency care	Hospital emergency visits	
Outpatient care	Specialists consultations and treatment in outpatient wards, clinics or patients' homes	
Hospital inpatient care	Days in hospital and day cases	
Drug	Retail and hospital sales of antineoplastic drugs and endocrine treatment	
Indirect costs		
Informal care	Opportunity costs of unpaid care provided by relatives and friends in working or leisure time, or both. Estimated hours spent for patients severely limited in daily activities or terminally ill, multiplied by the mean hourly wage (employed carer) or minimum wage (unemployed carer)	Luengo-Fernandez et al. (2013)
Productivity loss due to morbidity	Includes both temporal and permanent absence (human capital approach (HCA)) or with a maximum of 90 days as employer is assumed to replace the worker after longer time of absence (friction cost approach (FCA))	
Productivity loss due to mortality	Includes both temporal and permanent absence (human capital approach (HCA)) or with a maximum of 90 days as employer is assumed to replace the worker after longer time of absence (friction cost approach (FCA))	Luengo-Fernandez et al. (2013) and own calculation based on Luengo-Fernandez et al. (2013)
Intangible costs		
Welfare loss of getting cancer	Individual stated willingness to pay for reducing the chance of getting cancer (Value of Cancer Morbidity (VCM))	Alberini and Ščasný (2014) and recalculations by ECHA (2015) adjusting for the interaction between the two WTP estimates.
Welfare loss of dying from cancer	Individual stated willingness to pay for reducing the chance of dying as a result of getting cancer (Value of a statistical life for cancer (VSL))	

3.2.2 *Rough estimate of the societal cost of work-related cancer caused by carcinogenic substances in the EU*

In 2012, the annual societal cost of work-related cancer caused by carcinogenic substances in the EU-28 was estimated to be at least in an order of magnitude of €334 (242 – 440) billion. Depending on the preferred methodology used to assess productivity losses, this cost estimate could increase up to €337 (244 – 444) billion. A central estimate and range is calculated based on the ranges provided in the AFs and estimates of newly diagnosed cases and cancer deaths caused by work-related exposure to carcinogenic substances. In Table 3.4 the estimated range and central estimate per cost element is stated.

Table 3.4: Estimated magnitude of societal costs per cost element for the EU-28 countries in 2012 attributed to work-related exposure to carcinogenic substances (in millions of euros).

Cost element	**Range[1]**	**Central estimate[1]**
Direct costs		
Primary care	80-180	**140**
Emergency care	20-40	**30**
Outpatient care	160-330	**270**
Hospital inpatient care	850-1,700	**1,400**
Drug	340-650	**560**
Subtotal	1,500-2,900	**2,400**
Indirect costs		
Informal care	900-1,600	**1,400**
Productivity loss due to morbidity		
Using FCA approach	310-600	**460**
Using HCA approach	460-950	**710**
Productivity loss due to mortality		
Using FCA approach	120-230	**170**
Using HCA approach	2,100-3,900	**3,000**
Subtotal	1,300-2,400 (FCA) 3,500-6,500 (HCA)	**2,000 (FCA)** **5,000 (HCA)**
Intangible costs		
Welfare loss of getting cancer	37,500-61,700	**50,300**
Welfare loss of dying from cancer	201,900-372,600	**279,000**
Subtotal	239,400-434,400	**329,300**
Total costs	242,200-439,700 (FCA) 244,400-443,800 (HCA)	***333,700 (FCA)*** ***336,800 (HCA)***

1 Rounded numbers (<1000 to the nearest ten; >1000 to the nearest 100)

The welfare loss associated with cancer mortality is by far the biggest social cost element, with an estimated share of 84% (83-85%). Welfare loss associated with cancer morbidity is the second biggest social cost element, ranging between 14 and 15%. Together, these cost figures

represent the willingness to pay in society to eliminate work-related cancer caused by exposure to carcinogenic substances.

Health care expenditure due to work-related cancer is estimated to be €1.5-2.9 billion every year in the EU-28. The impact from indirect costs due to the productivity losses and opportunity costs of informal care is estimated to be at least €2.0 (1.3 – 2.4) billion, with a maximum of €5.0 (3.5 – 6.4) billion each year. The direct and indirect societal costs together are estimated to be at least €4.4(2.8 - 5.4) billion, with a maximum of €7.5 (4.9 – 8.8) billion.

Due to large uncertainties in the calculation of the number of cancer cases attributed to work-related exposure to carcinogenic substances and in the calculation of societal burden, the figures presented here should be seen as rough estimates of the potential societal cost due to cancer at the work place.

Furthermore, there are large differences in health care costs between EU countries, as well as for various types of cancers. Here we present total cost figures for the EU, as the aim of this cost assessment is to provide a broad impression of the order of magnitude of societal cancer costs due to worker exposure to carcinogenic substances in the EU. More specific figures for direct and indirect costs per country and type of cancer can, however, be found in the study of Luengo-Fernandez et al. 2013.

4 View of stakeholders and experts involved in the policy on carcinogens at the EU level

In this report, we estimated the size of work-related cancer caused by carcinogenic substances and introduced the legislative frameworks for handling carcinogens at work. We present here an analysis of how to improve the protection of workers from carcinogens, with a special interest in the improvement of the process of BOELVs development as one of the possible preventive instruments in a broader strategy. For this reason, we have interviewed a number of stakeholders and experts involved in the policy field of carcinogens at the EU level and summarized this information below. Interviewed stakeholders are among others policy makers and experts at national and EU level; representatives of employers and trade unions. The expressed views are made under a personal title.

4.1 Understanding which carcinogens have the highest priority for deriving BOELVs requires agreement on selection criteria and good-quality data on the risks

The process of derivation of new BOELVs starts with the services of the European Commission with responsibility for EU policy on occupational safety and health - DG Employment (DG EMPL). DG EMPL establishes a list of priority substances for a BOELV after consulting with the tripartite Advisory Committee on Safety and Health and other relevant stakeholders.

To come to a meaningful prioritization of substances and to understand the impact of setting BOELVs, we need good-quality data on the actual exposure, which is not always available. To enable the development of BOELVs, it is therefore important to have a much better understanding of the number of people exposed to occupational carcinogens and the levels of exposure in different jobs and industries. This could be achieved by maintaining exposure databases and conducing periodic surveys to document the exposure prevalence and intensity of those agents contributing most to the cancer burden. It is important to note in this context is that our current knowledge on exposure is very limited.

To have a more detailed and up-to-date overview of actual exposure would require additional efforts to be made in order to better understand the priorities that stem from both industrial and service sectors. In connection with this, there is some interesting work underway which is at an early developmental stage. This concerns the HazChem@Work study funded by DG EMPL (www.hazchematwork.eu).

Moreover, future work on carcinogens will benefit from a transparent and systematic approach that is shared by all Member States and the social partners. To this end, it is felt by some that an agreement on formal selection criteria for relevant carcinogens is highly recommended.

4.2 Scientific consensus on the method for deriving OELs

For non-threshold carcinogens, as is the case for most carcinogens, the SCOEL estimates the risk of adverse health effects at specified levels of exposure. When doing this, SCOEL follows a QRA approach. The SCOEL methodology for non-threshold carcinogens shares the same principles as the methodologies applied by these Member States when deriving OELs based on the underlying QRA, the so-called risk-based OELs (see 2.1.1 and 2.1.2).

However, despite the methodological similarities, different values have been observed between the risk-based OELs of different Member States (Pronk 2014). Those differences are largely due to differences in the cancer risk levels considered as acceptable / tolerable and feasibility issues which are of a political nature and not the domain of scientific committees such as SCOEL. Still, some other sources for the differences lie in the scientific domain: the choice of the animal exposure levels that cause the adverse effect, and uncertainty factors applied in the extrapolation from animals to humans. Given the limited number of Member States that apply QRA for OELs and the observed differences in the scientific approach, some stakeholders believe that the process of setting OELs for carcinogens can benefit from efforts aimed at increasing the alignment of views among experts in all Member States on the most appropriate methodology.

4.3 Involvement of national scientific committees

Already SCOEL work is benefiting from the work undertaken by national scientific committees. Because the scientific work of SCOEL is a complex and therefore very resourceful activity, some are calling for more extensive and formal cooperation. More specifically, some are proposing that national scientific committees actually conduct the QRA for selected carcinogens and SCOEL be given a role in adopting a final recommendation for the further legislative process.

4.4 Simplified impact assessment for carcinogens for which broad consensus exists among stakeholders

The proposal for a BOELV is also based on considerations concerning socio-economic, health and environmental impacts (this is often called an “impact assessment”). This impact assessment (IA) is a very challenging process, both in terms of the applied methodology and in terms of the necessary data. Currently, this is done according to the European Commission Impact Assessment Guidelines. Many people involved in the process of BOELVs derivation argue that it should be possible to develop a standardized methodology that fits the purpose with the appropriate level of detail; one that reflects a balance between understanding the impacts of BOELVs and actually having them officially adopted. More specifically, some argue that it should be possible to differentiate between substances for which a broad consensus exists in the tripartite Advisory Committee on Safety and Health at Work and the more controversial ones. For the first group of substances, the required IA can have a limited scope and be of a more qualitative nature and that the IA should require extended analysis and quantification of the costs and benefits for only the most controversial ones.

4.5 More efficient legislation

Carcinogenic chemicals fall within the scope of the CMD. The formal legislative procedure for developing limit values for these chemicals follows the Ordinary legislative procedure. In this procedure, the Commission submits a legislative proposal to the Parliament and Council for approval. The approval by these bodies is concluded in two readings. An argument can be made that this process could be simplified if the setting of BOELVs could be viewed as "non-legislative acts of general application to supplement or amend certain non-essential elements" of the CMD. Article 290 of the Treaty allows the Parliament and the Council, in this case, to delegate to the Commission the power to adopt amendments to CMD by "delegated acts". Delegation can be seen as a tool for better law-making, the aim of which is to ensure that legislation can remain simple and be supplemented and updated without needing to resort to the repeated adoption of legislation. One way forward could be to set priority carcinogens by means of the Ordinary legislative procedure and to allow the further setting of BOELVs to be realized by delegated acts.

Another aspect of the current legislative procedure where there may be room for improvement is that of the IA (see 4.4). The IA is very challenging, both in terms of the applied methodology and the necessary data. Currently, this is done without a predefined and well-developed methodology. It should be possible to develop a methodology that fits the purpose with the appropriate level of detail, one that reflects a balance between understanding the impacts of BOELVs and actually having them officially adopted.

4.6 Understanding and utilizing REACH as a framework to manage carcinogens in the workplace

There is an ongoing discussion about the contribution of REACH to the management of risks related to carcinogens at the workplace. There is a broad view that REACH can improve the information on safe use in the supply chain mainly through the registration process. Additionally, REACH provides two additional instruments for regulating carcinogens in the workplace, namely restriction and authorization. A common understanding among authorities and social partners with respect to concerns related to carcinogens in the workplace, where the REACH regulatory instruments can be of added value, increases the possibilities for managing their risks.

4.7 (B)OEL(V)s are a means not an end. Working on the prevention of exposure by the implementation of good hygienic practices and substitution is the key to reducing the risks from carcinogenic substances at work.

(B)OELVs for carcinogenic substances are only an instrument used to prevent cancer at work. (B)OEL(V)s are standards that help to specify the preventive measures that need to be taken in the workplace. For non-threshold carcinogenic substances this means that they represent a residual risk. They should therefore be seen as a part of a broader strategy aimed at preventing exposure by establishing good practices,

with substitution by less harmful substances as the ultimate goal. Additionally, arguments for such a broader strategy are:

1. deriving (B)OEL(V)s and maintaining them is a very resourceful activity that cannot possibly be undertaken for all relevant carcinogens within a reasonable time frame;
2. a lack of data may frustrate the setting of meaningful (B)OEL(V)s, while the necessity to reduce exposure is still a must;
3. many employers, especially the ones in small enterprises, may not have the capacity to measure whether the exposures in their workplace complies with the relevant (B)OEL(V)s. For such companies, easy-to-apply, good hygienic practices are deemed to be a more appropriate instrument.

But in the latter case, knowledge of the risk levels associated with different hygienic practices is necessary to decide on their appropriateness. Hence the establishment of (B)OEL(V)s is still necessary, even if they are not used as an enforcement instrument.

5 Discussion

In this report, we have briefly introduced the current legislative frameworks for handling carcinogenic substances at work to describe the efforts undertaken to prevent work-related cancer caused by carcinogenic substances. We also estimated the magnitude of work-related cancer caused by past exposure to carcinogenic substances at work. Therefore, we used previously estimated attributable fractions for work-related cancer in Great Britain and Finland and adapted these in our analysis. Our analysis has shown that an estimated 122,600 (91,500 - 150,500) newly diagnosed cases and an estimated 79,700 (57,700 - 106,500) cancer deaths can be attributed to work-related exposure to carcinogenic substances. This results in a loss of 1.2 (0.8 - 1.6) million life years and an estimated total societal cost of €334 (242 - 440) billion each year.

Our figures should be interpreted with caution because the attributable fractions are based on two country-specific studies in Great Britain and Finland. Industry characteristics and exposure conditions vary widely within the EU. Extrapolation to the EU-28 creates substantial uncertainties in the estimated figures because of data uncertainty, availability and representativeness. For this reason, no Member State or substance-specific figures have been generated.

Rushton et al. (2012) showed that, in Great Britain, exposure to asbestos, mineral oils, crystalline silica, diesel engine exhaust, polycyclic aromatic hydrocarbons, dioxins and second-hand tobacco smoke (non-smokers), as well as working as a painter or a welder count as the most adverse working conditions with respect to work-related cancer caused by exposure to carcinogenic substances. Of these, exposure to silica, diesel engine exhaust and working as a painter or a welder are projected to become the main causes of occupational cancers in the future in Great Britain (HSE 2014). In our analysis, asbestos is an important work-related carcinogen. Mesothelioma alone already accounts for approximately 15% of all work-related cancer deaths and some 10% of the new work-related cancer cases. Trends in mesothelioma deaths suggest the burden of asbestos-related cancer caused by past work-related exposure is continuing to increase.

Because cancer can have a long latency period, there is not much we can do to prevent the current cancer cases caused by past exposure. Yet we can prevent future cancer cases due to exposure at work. Based on the estimated attributable fractions, cancer mortality is expected to keep on rising EU-wide in an absolute sense. This is mainly based on increased life expectancy, since cancer is more prevalent in older people and these people are a growing part of the population. Corrected for changes in the age distribution of the EU population, relative cancer mortality is expected to decrease gradually.

The level of work-related exposure to carcinogens and other hazardous substances is reported to be decreasing. Numbers of up to 32% decrease yearly have been reported in the United Kingdom for trends in

the past (Creely et al. 2007). This has been the trend for the last thirty years and this development is likely to continue, with predicted declines of exposure levels between 5% and 15% per year (Cherrie et al. 2011). Factors commonly cited as being responsible for exposure reductions include legal obligations and the introduction of new standards such as OELs and enforcement. It is, however, not as straightforward to attribute these improvements to the current legislative and policy framework alone. At the company level, an important instrument to prevent exposure is the assessment of risks and the identification of measures - also referred as Risk Inventory and Evaluation (RI&E) - by the employer. A recent Dutch study (Terwoert et al. 2013) shows that there is a low level of awareness among (Dutch) companies regarding their legal obligations relating to the RI&E. Besides, much of the potential effect of the current legal provisions in place depends on enforcement at the level of the Member State and societal awareness regarding the risks of work-related cancers.

Improvements in exposure levels can be also understood as an autonomous process and the result of improved technology. This includes the development of safer alternatives and innovations in work organization, as well as outsourcing activities outside the EU, a development that may increase the numbers of workers being exposed globally and at higher levels.

One could argue that, as a result of current lower exposure levels, the future cancer burden will be overestimated. Yet, even with a decline in overall exposure, forecast impacts will probably not be lower than those of 2012, as previously exposed people will reach the age at which their cancer will appear. In addition, for some substances, population cancer risk might even increase due to the increased prevalence of exposure (e.g. diesel exhaust particles). In some work environments, such as painting, a decreasing trend in exposure levels has not been observed over the years (Cherrie et al. 2007; Cherrie 2009). In an estimate of work-related cancer in Great Britain, Hutchings et al. showed that, with unchanged policy, the number of newly diagnosed cancer cases will remain in the same order of magnitude in 2060 as in 2010 (Hutchings et al. 2012). This forecast included adjustments for declining exposure levels. Also, no new cases due to second-hand tobacco smoke were expected in 2060 due to indoor smoking bans.

EU-OSHA also recently expressed their concerns about young workers because some national sources, such as the French SUMER survey, give indications that young workers and maintenance workers may be more exposed and exposed to several carcinogens at a time. According to EU-OSHA research, young workers are also the group with the highest proportion of temporary contracts and they frequently work on a part-time basis and at irregular hours, which limits their access to preventive services (Lißner et al. 2014). This will make it more difficult to accurately assess the exposure to carcinogenic substances for this group of workers and whether this work-related exposure contributes to the development of cancer. There is little knowledge about the impact of new forms of working (e.g. subcontracting and more fragmented working careers). Most of the safety instructions are written in the language of the country in which the company is located. We anticipate

that the increase in flexibility in the labour market throughout the EU will put safety training and proper implementation of risk management measures under pressure and will likely have a negative impact on exposure levels.

In cases of unchanged policy, the magnitude of work-related cancer due to carcinogenic substances is expected to remain at a similar order of magnitude. Therefore, additional policy interventions are needed to reduce the future burden of work-related cancer in the EU. The existing regulatory frameworks covering risk management includes a large number of possible interventions. These include:

- Identification and monitoring of most relevant carcinogens, based on exposure data, whereby the latest findings have to be used;
- Substitution of carcinogenic agents/factors with harmless or less harmful ones;
- Prohibition of exposure to carcinogens at work as a general rule;
- Medical supervision of the workforce exposed to carcinogenic factors.

There is a broad consensus that intensification at all levels is required to realize a substantial reduction of work-related cancers.

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Annex: Methodology

Literature review

For this study, literature on the relationship between work-related exposure to carcinogens or substance and work-related cancer in The EU was searched by several routes. Information on specific substances and groups of substances was searched, as well as information on different types of cancer and total cancer. Furthermore, literature on incidence, prevalence, mortality and costs related to cancer were searched.
Both papers from peer-reviewed international journals (MEDLINE) and reports have been searched, published between 2000 and 2015. The search was supported by a library specialist. Key words that were used: neoplasms, work-related, exposure, chemically induced, risk, incidence, epidemiology, aetiology, mortality, costs, economics, and The EU. Both MeSH terms and free text words were used.

MEDLINE Search string:

1. exp Neoplasms/ci [Chemically Induced] (57697)
2. exp Risk/ (889547)
3. exp Incidence/ (187466)
4. exp Europe/ (1143860)
5. exp "Costs and Cost Analysis"/ (188884)
6. (*Work-related Diseases/ or exp *Work-related Exposure/) and exp *Neoplasms/ci (2119)
7. exp Global Health/ (32132)
8. exp Neoplasms/ec, ep, et, mo [Economics, Epidemiology, Aetiology, Mortality] (399090)
9. exp Work-related Diseases/ci, ec, ep, mo, pc [Chemically Induced, Economics, Epidemiology, Mortality, Prevention & Control] (53911)
10. exp Work-related Exposure/ae, ec, pc [Adverse Effects, Economics, Prevention & Control] (20246)
11. exp *Neoplasms/ci or exp *Neoplasms/ec, ep, et, mo (197901)
12. exp *Work-related Diseases/ci, ec, ep, mo, pc or exp *Work-related Exposure/ae, ec, pc (48306)

Furthermore, various stakeholders, i.e. from the personal network of the authors of this work, as well as EU-funded projects were consulted for potentially additions.

Studies were selected if these were published between 2000 and 2015 and were focused on all the following:

- the working population,
- exposure to carcinogens,
- work-related cancer,
- prevalence or incidence or mortality or costs,
- Europe or other western countries (USA, Australia, Canada).

Size of the problem: data and methods

To show the size of the problem we estimated the morbidity and mortality in the EU-population in 2012, as well as premature mortality or the years of life lost (YLL) due to occupational exposure to carcinogenic agents. Therefore, for each EU-country (EU-28), we estimated the morbidity, mortality and YLL of a set of cancers in the population as a result of exposure to work. We estimated which part of the disease burden could be attributed to exposure to carcinogenic substances at the workplace. To estimate the number of cancer cases and deaths that can be attributed to work-related exposure to carcinogenic substances, we used attributable fractions (AF). The AF relates to the proportion of cases that would not have occurred in the case of absence of the exposure factors.

Data and data sources
All cancers (ICD-10 C00-C99) that are caused by occupational carcinogenic agents were considered in the analyses. Only chemical substances at the workplace were examined, therefore, only cancers that were likely to be caused by chemical substances at the workplace were considered.
To estimate the current burden of occupational cancers in the EU-population, we collected the following information:

- Incidence of the studied cancers by age and sex, by EU-country, 2012,
- Cancer mortality by age and sex, by EU-country, 2012,
- Size of the population by age and sex, by EU-country, 2012,
- Life expectancy by age and sex, by EU-country, 2012,
- Attributable fractions.

For all cancers, data on mortality (2012) by sex and five year age categories (0-85+) per EU-country were obtained from Eurostat, data on the incidence of cancer (2012) by sex and age categories (15-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74 and 75+) per EU-country came from the GLOBOCAN-website. Age and sex specific life expectancy for each EU-28-country (2012) were also obtained from Eurostat. Mesothelioma is not included in Eurostat or GLOBOCAN websites. Therefore, we collected the sex and age (0-95+) specific mortality of mesothelioma from the WHO mortality statistics, with the exception of Greece, as these data were not present in this database. Since mesothelioma is usually rapidly fatal following diagnosis (Health Council of the Netherlands: Committee on Asbestos protocols 1999) and the incidence is not registered for the EU, we used the mortality data as an indication for the mesothelioma incidence.

Table A1: The cancers for which mortality and incidence data was available.

Mortality		**Incidence**	
Malignant neoplasm of	ICD-10	Cancer	ICD-10
Malignant neoplasms, total	C00-C97	All cancers excl. non-melanoma skin cancer	C00-97/C44
Lip, oral cavity, pharynx	C00-C14	Lip, oral cavity	C00-08
		Nasopharynx	C11
		Other pharynx	C09-10,C12-14
Oesophagus	C15	Oesophagus	C15
Stomach	C16	Stomach	C16
Colon, rectosigmoid junction, rectum, anus and anal canal	C18-C21	Colorectum	C18-21
Liver and intrahepatic bile ducts	C22	Liver	C22
		Gallbladder	C23-24
Pancreas	C25	Pancreas	C25
Larynx	C32	Larynx	C32
Trachea, bronchus and lung	C33-34	Lung	C33-34
Melanoma of skin	C43	Melanoma of skin	C43
		Kaposi sarcoma	C46
Breast	C50	Breast	C50
Cervix uteri	C53	Cervix uteri	C53
Other parts of uterus	C54-55	Corpus uteri	C54
Ovary	C56	Ovary	C56
Prostate	C61	Prostate	C61
		Testis	C62
Kidney, except renal pelvis	C64	Kidney	C64-66
Bladder	C67	Bladder	C67
Brain and central nervous system	C70-72	Brain, nervous system	C70-72
Thyroid gland	C73	Thyroid	C73
Hodgkin disease and lymphomas	C81-C85	Hodgkin lymphoma	C81
Other malignant neoplasm of lymphoid, haematopoietic and related tissue	C88-C90-C96	Non-Hodgkin lymphoma	C82-85,C96
		Multiple myeloma	C88+C90
Leukaemia	C91-C95	Leukaemia	C91-95
Mesothelioma	C45	Mesothelioma	C45

Methods

There are no reliable and comparable occupational cancer statistics available at the EU-level. Therefore, we collected 'overall' data (data for the whole population, 0+ years) on cancer mortality and morbidity, we converted these to the 15+ or 25+ population (depending on the type of cancer, see *Latency period*) and used the AF to compensate for this lack. The AF can be seen as the proportion of cases that would not have

occurred in the absence of exposure. The AF method is widely used to assess work-relatedness of a broad range of diseases and disorders. We used the AF's calculated in the international studies of Nurminen and Karjalainen (2001) and Rushton and colleagues (Rushton et al. 2012b).

Latency period
As all cancers have a period of time between the beginning of exposure and occurrence of cancer (latency period), we defined a latency exposure, in line with Rushton and co-workers (Rushton et al. 2010; Rushton et al. 2012b). The latency period relates to the period during which a person is exposed to an occupational carcinogen and the cancer is diagnosed. As there are very little data available on cancer latency and this latency differs per person, we defined –according to Rushton and co-workers two latency periods. For the solid tumours, we assumed a latency period between 10 to 50 years, and for haematopoietic tumours (ICD-10 C81-C96), we assumed a latency period between 0 and 20 years (Rushton et al. 2010; Rushton et al. 2012b).

Population
We obtained data for all EU-28 countries, if available: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom. Data for the EU-28 was counted as the sum of the data of the individual countries.

To estimate the mortality in the working population, we related the estimates of the total population in five-year age categories and sex to the latency periods being considered. This means that for solid tumours diagnosed in 2012, only cancers in ages 25+ were counted as these could have been initiated 10 to 50 years before (during the exposure periods). For haematopoietic cancers, ages 15-85 were included, as due to the assumed latency period for these cancers no morbidity or mortality due to work-related exposure occurs beyond the age of 85. For the incidence, however, the smallest age categories were: 15-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75+. Therefore, we did not convert these data taking into account the latency periods.

Attributable fractions
We combined the AFs published in the studies of Rushton and co-workers (Rushton et al. 2010) and Nurminen and Karjalainen (Nurminen and Karjalainen 2001) to use as much data available. In short, above studies obtained data on the risk of the disease due to the exposure of interest, taking into account confounding factors and overlapping exposures and the proportion of the target population exposed over the period in which relevant exposure occurred. In both studies, for each causal relationship between cancer and carcinogenic factor, the most appropriate relative estimate was obtained from epidemiological studies. Furthermore, an estimate of the proportion of the population exposed was taken from national employment data or from a job-exposure matrix. The results of a pooled analysis of (usually population-based) case control studies are used for an estimate of relative risk, with internal estimates of the proportion of the population exposed (Pr(E)) or the proportion of cases exposed (Pr(E|D)) obtained from the distribution

of exposures amongst the controls or cases. The overall attributable fraction was calculated on a ‘cancer by cancer’ basis. The attributable fraction (AF) can be calculated as: AF = Pr(E|D) * (RR – 1) / RR where Pr(E|D) = proportion of cases exposed (Rushton et al. 2012a) .
The estimations in both studies were carried out for carcinogenic agents or exposure circumstances classified by the International Agency for Research on Cancer (IARC) as definite (Group 1) or probable (Group 2A) human carcinogens. The study by Nurminen and Karjalainen looked at 74 chemical, physical and microbiological agents and the study by Rushton et al. evaluated a total of 41 carcinogenic agents and occupational circumstances. In both studies, the AFs for all the relevant carcinogenic agents and occupational circumstances were combined into a single AF estimate for each separate cancer.

We only used the AFs for carcinogenic substances and altered the AFs if necessary (e.g. left out shift work in the AF for breast cancer and recalculated the AF). As there are differences in exposure at the workplace between men and women, there are AFs available for men, for women and for both. We first determined gender specific AFs. If for a type of cancer, there was an AF available in both studies, we calculated an overall AF as the average of both estimates. Furthermore, we calculated a range around the AF-estimate by taking the confidence interval of the AF-estimate in the study of Rushton and co-workers. However, if the overall combined estimate was outside this confidence interval, we used the AF-estimate of Nurminen & Karjalainen as the upper or lower limit. Furthermore, if no confidence interval was available (which was the case if we only had an estimate from the study of Nurminen & Karjalainen), we took the AF-estimate as both lower and upper limit. The AFs are supposed to be the same for specific mortality and incidence. For each cancer type the gender specific cases or deaths were summed and divided by the total number of cases or deaths for that cancer type in the 15+ working and retired population to calculate the cancer specific overall AF. The overall AF for the total sum of the specified cancer types was calculated in the same way.

Table A2: Combined attributable fractions used for mortality (adapted from Nurminen and Karjalainen 2001; Rushton et al. 2012a)

ICD-10 code	**Malignant neoplasm of**	**Attributable fraction (%)**		
		Total[1] *(low-high)*	*Men (low-high)*	*Women (low-high)*
C00-C14	Lip, oral cavity, pharynx	8.8 (1.9 - 38.1)	10.8 (2.3 - 47.9)	2.4 (0.6 – 6.8)
C15	Oesophagus	3.8 (1.2 - 6.4)	4.9 (1.5 – 7.5)	0.7 (0.3 – 2.8)
C16	Stomach	1.9 (0.9 - 3.3)	3.0 (1.5 – 5.1)	0.3 (0.1 – 0.5)
C18-21	Colon, rectosigmoid junction, rectum, anus and anal canal[2]	3.1	5.6	0.0
C22	Liver and intrahepatic bile ducts	1.8 (0.1 - 3.4)	1.9 (0.1 – 3.5)	1.7 (0.1 – 3.3)
C25	Pancreas	3.8 (0.0 - 8.5)	6.7 (0.0 - 13.4)	0.8 (0.0 – 3.5)
C32	Larynx	5.6 (1.3 - 8.7)	6.1 (1.4 – 9.3)	1.1 (0.6 – 3.5)
C33-34	Trachea, bronchus and lung	17.1 (14.3 -19.0)	22.7 (19.0-24.5)	4.5 (3.8 – 6.4)
C43	Skin[2]	1.5	2.4	0.3
C50	Breast[2]	0.1	0.0	0.1
C45	Mesothelioma	84.9 (76.0- 96.2)	93.5 (90.0- 98.0)	53.8 (25.0-90.0)
C53	Cervix uteri	3.3 (0.0 – 5.9)	-	3.3 (0.0 – 5.9)
C56	Ovary	1.3 (0.0 -2.1)	-	1.3 (0.0 -2.1)
C61	Prostate[2]	6.0	6.0	-
C64	kidney, except renal pelvis	1.6 (0.0 -3.2)	2.4 (0.0 – 4.7)	0.4 (0.0 -0.8)
C67	Bladder	8.3 (3.6 - 11.6)	10.7 (4.6 - 14.2)	1.3 (0.7 – 3.9)
C70-72	brain and central nervous system	3.4 (0.1 - 6.4)	5.6 (0.1 - 10.6)	0.7 (0.0 -1.3)
C81-85	Hodgkin disease and lymphomas	5.3 (0.0 - 8.9)	7.8 (0.0 - 13.5)	2.1 (0.1 -2.9)
C88, C90, C96	lymphoid, haematopoietic and related tissue	0.3 (0.0 - 0.7)	0.4 (0.0 -1.0)	0.1 (0.0 – 0.3)
C91-95	leukaemia	0.6 (0.2 - 3.9)	0.8 (0.0 – 3.5)	0.4 (0.1 -4.5)
Overall attributable fraction for mortality[1]		*6.3 (4.5 - 8.4)*	*8.7 (6.2 - 11.5)*	*1.2 (0.6 -2.2)*

1 Calculated attributable fraction based on the sum of the attributable deaths for men and women in 2012 and total deaths in the population for 2012.

2 Only point estimate available

Table A3: Combined attributable fractions used for incidence (adapted from Nurminen and Karjalainen 2001; Rushton et al. 2012a)

ICD-10 code	**Malignant neoplasm of**	**Attributable fraction (%)**		
		Total (low-high)*	*Men (low-high)*	*Women (low-high)*
C00-C08	Lip, oral cavity[2]	0.9	1.2	0.3
C11	Nasopharynx	8.5 (1.8 - 36.9)	10.8 (2.3 - 47.9)	2.4 (0.6 - 6.8)
C09-10, C12-14	Other pharynx[2]	1.7	2.0	0.5
C15	Oesophagus	3.8 (1.2 - 6.3)	4.9 (1.5 - 7.5)	0.7 (0.3 - 2.8)
C16	Stomach	2.0 (1.0 - 3.3)	3.0 (1.5 - 5.1)	0.3 (0.1 - 0.5)
C18-21	Colorectum[2]	3.1	5.6	0.0
C22	Liver	1.8 (0.1 - 3.4)	1.9 (0.1 - 3.5)	1.7 (0.1 - 3.3)
C23-24	Gallbladder[2]	0.3	0.2	0.4
C25	Pancreas	3.7 (0.0 -8.4)	6.7 (0.0 - 13.4)	0.8 (0.0 - 3.5)
C32	Larynx	5.5 (1.3 - 8.7)	6.1 (1.4 - 9.3)	1.1 (0.6 - 3.5)
C33-34	Lung	16.9 (14.2- 18.8)	22.7 (19.0- 24.5)	4.5 (3.8 - 6.4)
C43	Melanoma of skin[2]	1.3	2.4	0.3
C45	Mesothelioma	85.0 (76.0- 96.3)	93.5 (90.0- 98.0)	53.8 (25.0- 90.0)
C50	Breast[2]	0.1	0.0	0.1
C53	cervix uteri	3.3 (0.0 - 5.9)	-	3.3 (0.0 - 5.9)
C56	Ovary	1.3 (0.0 - 2.1)	-	1.3 (0.0 - 2.1)
C61	Prostate[2]	6.0	6.0	-
C64-66	Kidney	1.7 (0.0 - 3.3)	2.4 (0.0 - 4.7)	0.4 (0.0 - 0.8)
C67	Bladder	8.6 (3.8 - 12.0)	10.7 (4.6 - 14.2)	1.3 (0.7 - 3.9)
C70-72	Brain, nervous system	3.3 (0.1 - 6.3)	5.6 (0.1 - 10.6)	0.7 (0.0 - 1.3)
C81	Hodgkin lymphoma[2]	3.9	3.9	0.0
C82-85, C96	non-Hodgkin lymphoma	5.1 (0.0 - 8.6)	7.8 (0.0 -13.5)	2.1 (0.1 - 2.9)
C88, C90	Multiple myeloma	0.3 (0.0 - 0.7)	0.4 (0.0 - 1.0)	0.1 (0.0 - 0.3)
C91-95	Leukaemia	0.6 (0.2 - 3.9)	0.8 (0.2 - 3.5)	0.4 (0.1 - 4.5)
*Overall attributable fraction for incidence**		*5,0* (3,7 -6,1)	*8.4* (6.4 - 9.9)	*0.9* (0.5 - 1.6)

1 Calculated attributable fraction based on the sum of the attributable new cancer cases for men and women in 2012 and total new cancer cases in the population for 2012.

2 Only point estimate available

Table A4: Considered carcinogens and relation with cancer type (adapted from Nurminen and Karjalainen 2001; Rushton et al. 2012b).

Exposure to substance	**Cancer type**
Acrylamide	Pancreas
Aromatic amines	Urinary bladder
Aromatic hydrocarbon solvents	Brain, Cervix uteri, Ovary
Arsenic	Bronchus and lung
Asbestos	Bronchus and lung, Colon, Larynx, Mesothelioma, Ovary, Rectum, Stomach
Aviation gasoline	Kidney (renal cell carcinoma)
Benzene	Leukemia
Beryllium	Bronchus and lung
Cadmium	Bronchus and lung, Kidney (renal cell carcinoma), Prostate
Chlorinated hydrocarbon solvents	Liver and intrahepatic bile ducts, Urinary bladder
Chromium VI	Bronchus and lung, Nose and nasal sinuses (sinonasal)
Cobalt	Bronchus and lung
Crystalline silica (quartz dust)	Bronchus and lung, Liver and intrahepatic bile ducts, Pancreas
Diesel engine exhaust	Bronchus and lung, Ovary, Urinary bladder
Dry-cleaning solvents	Kidney (renal cell carcinoma)
Ethylene oxide	Leukemia
Second-hand tobacco smoke	Bronchus and lung
Formaldehyde	Leukemia, Nasopharynx, Nose and nasal sinuses (sinonasal)
Fungicides	Non-Hodgkin's lymphoma
Gasoline and other petroleum products	Kidney (renal cell carcinoma)
Herbicides	Prostate, Non-Hodgkin's lymphoma
Hydrocarbon solvents	Esophagus, Gallbladder, Kidney (renal cell carcinoma), Oral cavity, Pharynx
(inorganic) Lead	Brain, Bronchus and lung, Kidney (renal cell carcinoma), Stomach, Urinary bladder
Leather dust	Nose and nasal sinuses (sinonasal), Ovary
Mineral oils	Bronchus and lung, Nose and nasal sinuses (sinonasal), Skin non-melanoma, Urinary bladder
Nickel	Bronchus and lung, Nose and nasal sinuses (sinonasal), Pancreas
Nickel sulfate	Bronchus and lung
Non-arsenical insecticides	Brain, Leukemia, Multiple melanoma, Non-Hodgkin's lymphoma
Other agents: arsenic, aflatoxin, PCB's	Liver and intrahepatic bile ducts
Organic solvents (including aliphatic and aromatic hydrocarbons)	Pancreas

Exposure to substance	Cancer type
Pesticides (herbicides and insecticides)	Pancreas
Polycyclic aromatic hydrocarbons	Bronchus and Lung, Esophagus, Oral cavity, Pancreas, Skin non-melanoma, Urinary bladder
Rubber chemicals including acrylonitrile	Larynx, Pancreas, Stomach
Solvents	Kidney (renal cell carcinoma)
Strong inorganic acid mists	Bronchus and Lung, Larynx
Styrene	Rectum
TCDD (Dioxins)	Bronchus and Lung, Non-Hodgkin's lymphoma, Soft Tissue Sarcoma (STS), Urinary bladder
Tetrachloroethylene	Cervix uteri, Non-Hodgkin's lymphoma
Textile dyes, paints, and pigments (2-naphthylamine)	Urinary bladder
Tricholoroethylene	Kidney (renal cell carcinoma), Liver and intrahepatic bile ducts, Non-Hodgkin's lymphoma
Vinyl chloride monomers	Liver and intrahepatic bile ducts
Wood dust	Nasopharynx, Nose and nasal sinuses (sinonasal)

Table A5: Considered occupations and relation with cancer type (adapted from Nurminen and Karjalainen 2001; Rushton et al. 2012b)

Work conditions	Cancer type
Farmers	Hodgkin's disease
Gardener	Pancreas
Hairdressers and barbers	Bronchus and lung, Esophagus, Female breast, Non-Hodgkin's lymphoma, Ovary, Urinary bladder
Industries: chemical and oil processing, production of pottery and glass, engine, engine and vehicle construction, paper, wood, printing, cleaning services, hairdressing, housekeeping, waste disposal metal production, processing workers, transportation workers and freight handlers, rubber and plastics industry, engine and vehicle construction, installation	Bronchus and lung
Industries: iron and steel	Kidney (renal cell carcinoma)
Industries: leather and rubber	Urinary bladder

Work conditions	Cancer type
Occupations: assemblers, metal workers (soldering fumes containing cadmium and lead), stock clerks, etc (diesel engine exhaust), restaurant and hotel service workers, waitresses (environmental tobacco smokers), ceramic and pottery workers (arsenic, asbestos, lead, silica), laundry workers and dry cleaners (chlorinated solvents and other industrial solvents) metal production and processing worker (polycyclic aromatic hydrocarbons, chromates, arsenic	Bronchus and lung
Oil refinery workers (petroleum refining, constituents of gasoline: benzene, etc)	Kidney (renal cell carcinoma)
Painter	Bronchus and Lung, Stomach
Precision metal workers, including machinists, tool and die makers, and sheet metal workers (metal dusts and fumes, lubricating oils, and solvents)	Brain
Printers, printing industry, printing press operators used gasoline as a cleaning agent	Kidney (renal cell carcinoma)
Tin mining (men only)	Bronchus and Lung
Transport inspectors and supervisors (polycyclic aromatic hydrocarbons in engine exhaust)	Pancreas
Warehouse clerks (indoor work, diesel engine exhaust)	Skin melanoma
Warehousemen (polycyclic aromatic hydrocarbons)	Pancreas
Welding and soldering fumes and gases (polycyclic aromatic hydrocarbons and other combustion products metal dust, irritant gases; mild steel welding; hexavalent chromium, nickel)	Bronchus and lung, Esophagus, Larynx, Nose and nasal sinuses, Pharynx

Size of the problem: Analyses

Occupational incidence, mortality and years of life lost
For each cancer type and every EU-28-country, we estimated the incidence and mortality of the occupational cancers using the data of the whole population taking into account the defined latency periods and the AFs. For each EU-country, the cancer specific incidence and mortality figures in 5-year age categories for men and women were available. We used sex-specific mortality figures of the 15-85 population for the haemopoietic cancers and of the 25+ population for the solid cancers. For the incidence, this was not possible (see above). We then calculated the incidence and mortality by multiplying the sex-specific AFs by sex-specific incidences and deaths from the cause with the matching ICD-code.

We also estimated the years of life lost of occupational cancers for each cancer and each EU-country. For a death at a certain age, the number of years of life lost equals the remaining life expectancy at that age. The number of years of life lost due to a certain disease (cancer) is the sum of the years of life lost of all the deaths due to that disease (cancer). In other words: the years of life lost (YLL) is the product of the number of deaths for all health outcomes of a disease in a certain population and period (N) and remaining life expectancy (LE) at the age of death (per age category): YLL = N x LE. Again, we restricted the YLL's for the haemopoietic cancers to the ages 15-85 and for the solid cancers to the ages 25+ and calculated the YLL's by multiplying the sex-specific AFs by sex-specific YLL's from the cause with the matching ICD-code.

Size of the problem: Limitations/uncertainties of the approach

Data
First of all, we estimated the burden of occupational cancer in 28 EU-countries, thus the data had to be available for all 28 countries in the same way and national data were not useful. Hence, we sometimes had to make concessions. Furthermore, the data had to be age- and sex-specific. Therefore, we used data from Eurostat, WHO Mortality statistics (for mesothelioma) and GLOBOCAN. We did not use mortality data from EUCAN or GLOBOCAN as these are based on model calculations, whereas the Eurostat mortality statistics are based on registered data. Furthermore, we used GLOBOCAN-data for the incidence, as EUCAN does not have age-specific data. Eurostat does not present incidence or prevalence data.

Analyses
We estimated the burden of occupational cancer in the EU. The estimates are based upon many data that are not always available or available for all EU-28-countries with a 100% certainty. Some of the uncertainty is being caused by the variance and uncertainty in the incidence and mortality of the cancer, the number of people in the workforce, the number of people exposed and the risk of cancer when exposed. We used the confidence intervals around the AFs to get an idea of the degree of uncertainty and variance.

As there are very little data available on cancer latency and this latency differs per person, we defined –according to Rushton and co-workers (Rushton et al. 2010; Rushton et al. 2012b) only two latency periods. For the solid tumours, we assumed a latency period between 10 to 50 years, and for haematopoietic tumours (ICD-10 C81-C96), we assumed a latency period between 0 and 20 years. To compensate for the lack of comparable occupational cancer statistics at the EU-level, we used the attributable fractions. The AF method is widely used to assess work-relatedness of a broad range of diseases and disorders. However, we could not calculate AFs for every EU-country or even calculate AFs for current exposure. Therefore, we had to use the best AFs available at this moment: AFs estimated by the Health and Safety Executive in Great Britain (Rushton et al. 2012a) and by Nurminen and Karjalainen in Finland (Nurminen and Karjalainen 2001). As there were no AFs present for all occupational cancers, we used two studies. However, the AFs that were present from both studies were sometimes very different. That is

why we combined the AFs in both studies and calculated a range. In addition, the AFs are corrected to represent only carcinogenic substances therefore excluding shift work, solar radiation, ionising radiation, sedentary work and low-frequency electromagnetic fields as risk factors.

Social cost: data and methods

There are various ways to calculate the societal costs of an illness and different elements can be included in such a cost assessment. For practical reasons, it was decided to base the cost estimates in this report on existing studies. The study of Luengo-Fernandez et al. (2013) was selected as the basis for the estimation of direct and indirect costs as this was the only previously published study that gives cancer cost estimates on the European level (EU-27). This study uses as much country-specific data that is available therefore minimising uncertain extrapolation of costs in one EU country to the whole EU. If no country-specific data was available, extrapolation based on a similar country was used. An annual timeframe is used, including all costs for 2009, irrespective of the onset of disease. Besides the direct and indirect costs that society actually faces due to cancer illness caused by worker exposure to carcinogens, cancer illness also causes intangible costs or damages to people that are confronted with cancer. These intangible costs or damages involve suffering and pain of patients following from the disease and/or early death resulting in lower quality of life of the patient and its relatives and close friends.

ECHA's Willingness To Pay (WTP) study on avoidance of cancer risk was selected as the basis for quantification of intangible burden related to patients' suffering following from the disease and the life years lost due to early deaths (Alberini and Ščasný 2014). This study was selected as this was the only study found that looked at intangible burden of cancer and besides that, specifically looked at cancer risk due to exposure to carcinogenic substances. The critical review and re-estimations of the Alberini and Ščasný (2014) study by ECHA are taken into account (ECHA 2015).

Direct and indirect costs
The analysis by Luengo-Fernandez et al. (2013) calculates cancer costs related to all cancers and specifically for colorectum, lung, breast and prostate cancer (see Table A6). These four cancers together contribute to 44% of the overall cancer costs. The previously estimated incidence in the working and retired population due to carcinogenic substances is divided by the incidence in the general population to obtain a correction factors for the direct cost and informal care estimates. This is done for colorectum, lung, breast, prostate cancer and the category other cancers.

Table A6: Summary of the cost of cancer (€ million) in the EU-27 in 2009 per specified cancer type (Luengo-Fernandez et al. 2013)

Cost element	**Cancer type**				**Total EU**
	Lung	*Colo-rectum*	*Breast*	*Prostate*	
Primary care	242	298	325	181	2,954
Emergency care	544	593	626	332	5,419
Outpatient care	51	70	65	38	659
Hospital inpatient care	2,874	4,040	2641	1,762	28,357
Drug	515	565	3,068	3,119	13,604
Productivity loss due to mortality	9,922	3,769	3,254	732	42,565
Productivity loss due to morbidity *(no friction period)*	813 (*1,396)*	921 (*1,582)*	1,788 *(3,071)*	391 (671)	9,431 (*16,196)*
Informal care	3,817	2,837	3,204	1,875	23,216
Total	*18,778*	*13,093*	*14,971*	*8,430*	*126,205*

The productivity loss estimates are already corrected for labour participation and the abovementioned correction is not necessary.
This section will briefly describe the general methodology used by Luengo-Fernandez et al. (2013) and the justification if deviated from this methodology. More detailed information on the approach and used data sources can be found in the published article itself and its annexes. For the direct costs borne by the patient itself (out of pocket expenses) no reliable data across the EU was available. The authors combined, where possible, publicly (insured) and privately (out of pocket) funded resource use for each country or made adjustments if the data source only reported publicly funded resource usage. By doing so, the co-payments by the patient themselves are captured to some extent but it is not possible to disaggregate this from the total cost figures. In the absence of specific data on cancer-specific co-payments of patients, the direct cost estimates are therefore underestimated but the size of this underestimation is unknown.

Table A7: The methodology used to estimate the various cost elements of the societal costs of cancer.

Cost element	**Explanation of method by Luengo-Fernandez (summarized)**	**Deviated from method**
Direct costs		
Primary care	Country-specific overall visits to primary care due to all conditions were obtained and the proportion of primary care that was attributed to cancer was applied. Depending on the country-specific data the proportion attributed to cancer was derived using: number of consultation per cancer patient.	No
Emergency care	Country-specific overall visits to accident and emergency care were obtained for 20 countries. National all-cause attendance figures were not available in 7 countries and accident and emergency care rates were derived from similar countries and applied to them. The proportion of accident and emergency care that was attributed to cancer was applied.	No
Outpatient care	Country-specific overall visits to outpatient care due to all conditions were obtained and the proportion of outpatient care that was attributed to cancer was applied.	No
Hospital inpatient care	National data on cancer (including cancer type)-related days in hospital and day-cases in all countries, except Estonia (estimated from Latvia data)	No
Drug	Medical expenditure of the sum of retail and hospital sales of antineoplastic agents and endocrine therapy by country. For 4 countries only retail data were available, hospital sales were derived by applying the ration of hospital to retail sales from similar countries. Proportion of cancer-related medicine expenditure on the different types of cancers was based on an average of two countries and applied to the remaining countries.	No
Indirect costs		

Cost element	Explanation of method by Luengo-Fernandez (summarized)	Deviated from method
Informal care	Hours of informal care for severely limited cancer patients and for terminally ill cancer patients were estimated by specific logistic and ordered logistic regression analyses using data from the SHARE (Survey of Health, Aging and Retirement in Europe) survey. For the 14 countries not in SHARE, the data was pooled per region and applied to the remaining countries by using regression analyses. Mean net hourly wage rates were applied for those carers in working age and who were economically active and in employment. For those carers in retirement, unemployment or economically inactive, the national hourly minimal wage was applied.	No
Productivity loss due to morbidity	For temporary absence from work due to sickness, country-specific overall annual days of sickness leave due to all conditions were obtained from all countries. The proportion of sickness leave attributed to cancer was applied. For countries where no attributable proportion was available, proportions from other countries were applied. For permanent absence from work due to incapacity or disability, country-specific information on the numbers of working-age individuals receiving incapacity or disability benefits and not be able to work due to all conditions were obtained. The proportion of sickness leave attributed to cancer was applied. For countries where no attributable proportion was available, proportions from other countries were applied. The mean annual earnings were converted to mean daily earnings. The number of working days lost was multiplied with the mean daily earnings, after adjustment of the friction period of 90 days. In the sensitivity analysis an estimate is provide for productivity loss without the friction period.	No

Cost element	Explanation of method by Luengo-Fernandez (summarized)	Deviated from method
Productivity loss due to mortality	Age and gender specific deaths due to cancer were obtained for all countries. The number potential working years lost was estimated as the difference between the age of death and maximum age of retirement (79 years). The working years lost were corrected for economic activity by using age and gender specific unemployment and activity rates for each country. The total number of working years lost was multiplied by gender-specific average annual earnings. Because the productivity loss would be incurred in the future, lost earnings were discounted to Net Present Value with a 3.5% annual rate.	Yes

Luengo-Fernandez et al. (2013) use the human capital approach (HCA) to estimate the productivity loss due to mortality and the friction cost approach (FCA) to estimate productivity loss due to morbidity. The HCA calculates the potential welfare loss due to premature death. It is questionable whether this approach is the most realistic in assessing the economic impact of an illness. The HCA does not take into account the replacement of the involuntary unemployment. Alternatively, the friction cost approach (FCA), as used by Luengo-Fernandez et al. (2013) to estimate the productivity loss due to morbidity, is based on the assumption that an ill individual can eventually be replaced. Productivity losses estimated using the HCA are usually higher than those calculated using the FCA, especially in the case of long term absence. The academic debate on which approach is more favourable is based on normative judgements and different schools of thought leading to fundamental differences on how to measure and value productivity loss (Krol and Brouwer 2014). In this report, we choose to use the FCA to estimate the productivity loss due to mortality for two reasons. First, in our opinion the FCA is a more realistic estimate for the economic costs due to productivity losses and reflects the labour market better in times of low economic growth. Secondly, it is more consistent with the methodology used by Luengo-Fernandez et al. (2013) to estimate the economic costs of permanent absence from work due to incapacity or disability due to morbidity.

In the FCA estimation of the productivity loss of mortality, we use the maximum retirement age of 79 and use a friction cost period of 90 days to be consistent with the analyses of Luengo-Fernandez et al. (2013). Age, country and gender-specific mortality numbers are obtained from Eurostat and corrected with age, country and gender-specific unemployment rates for 2009. These adjusted mortality numbers are multiplied by country and gender specific average annual income earnings adjusted for the friction period. All figures are obtained for EU-27 and 2009.

Productivity loss of mortality and morbidity is also estimated using the HCA method for comparison and to provide the potential economic

losses. The overall HCA estimate for morbidity is provided by Luengo-Fernandez et al. (2013) in their sensitivity analysis. The breakdown into the various types of cancer is not shown. We used the overall increase in production loss between the FCA and when the HCA is used (1,717) as a constant factor. The cancer type specific morbidity production loss estimated using the FCA is multiplied by this factor. This assumes no difference in treatment duration and absence from work between the various cancer types. Although such assumption is not justified, no data was available to correct for this.

Intangible costs

Alberini and Ščasný (2014) performed a stated preference study among four EU member states to estimate the Willingness to pay (WTP) for reducing the chance of getting cancer due to exposure to carcinogens and subsequently increasing the change of survival if diagnosed with cancer. The countries surveyed were the United Kingdom, the Czech Republic, Italy and the Netherlands. In short, the study used binary discrete choice questions (contingent valuation questions) with one of the options being the status quo and a total of seven questions were asked per respondent. Table A8 shows the attribute levels and their values used in the study. The status quo, or baseline, chances of getting cancer and of survival that was determined based on annual age-specific incidence rates for the EU for both sexes (25 per 1.000) and 5-year survival rates (60%) subsequently.

Table A8: Characteristics and their levels in the discrete choice experiment (Alberini and Ščasný 2014)

Characteristics	**Possible values**		
Chance of getting cancer within the next 5 years	Reduce the baseline by 0, 2, 3, 5 in 1.000 over 5 years		
Chance of survival at 5 years from the diagnosis (if you get cancer)	Increase the baseline by 0%, 5%, 10%, 20%		
Effects on everyday activities (if you get cancer)	Fully active No heavy physical work Unable to work Confined to bed half of the time		
Pain (if you get cancer)	Mild pain Moderate pain		
Cost per year for each of the next 5 years	IT & NL	UK	CZ
	€ 110 € 225 € 370 € 540	£ 100 £ 210 £ 340 £ 500	CZK 2.000 CZK 4.000 CZK 6.600 CZK 9.600

In total, 3.888 respondents were interviewed providing 3.407 valid interviews. All of the respondents were between 45 and 60 years of age. The analysis excluded speeders and respondents who failed to correctly answer a screening question on probabilities. The description of cancer provided to the respondents was unspecified to avoid labelling and consequences of cancer are described in two attributes of pain and effects on everyday activities. In addition, before the valuation questions were administered, potential loss in quality of life is presented to the respondents. Although there is a wide variation in quality of life lost

among cancer patients, some example effects resulting in quality of life lost are presented:

- suffering of facing problems in daily activities due to the disease,
- pain caused by the illness in general or during treatment,
- potential anxiety and depression due to the illness,
- feeling of social isolation due to the illness,
- problems at work due to the illness,
- worry of coming back of illness after treatment, etc.

Alberini and Ščasný (2014) estimate the WTP for an EU average Value of a Statistical Case of Cancer (VSCC) of € 396.000 purchasing power standard (pps) for 2012. Besides that, the study provides an estimate of the value of statistical life (VSL) of € 5.000.000 pps for 2012. The ECHA used the data from Alberini and Ščasný (2014) for an alternative analyses and estimation of the WTP (ECHA 2015). This recalculation adjusts for a possible interaction between the valuation of an improved survival and the valuation of reductions in the incidence rate of cancer. This is important because the two rates are not independent of each other. An improvement in survival chances will devaluate a reduction in the incidence rate and the other way around. The VSCC and VSL estimates obtained from the additional analysis by ECHA are in the order of € 350.000 pps and € 3.500.000 pps, respectively for 2012. In addition, a value of cancer morbidity (VCM) of € 410.000 pps is derived. This VCM defines the value of cancer morbidity as the marginal value of a reduction in the incidence rate keeping the unconditional risk to die from cancer fixed.

We propose to use the WTP figures from ECHAs alternative analysis to provide a crude indication of the welfare losses in case of cancer, as these are the only figures available specifically for cancer risk caused by exposure to carcinogens. Such intangible damage is not presented to society as an actual cost figure; however, it does represent a very important emotional and social aspect of the disease.

Social cost: analyses

The direct societal costs
Cost estimates for direct costs are available for four specific cancer types and total cancer at EU-27 level in 2009 (Luengo-Fernandez et al. 2013). EU direct cost estimates available for a specific cancer type are multiplied by a cancer type specific incidence fraction (central estimate and range) based on previously estimated newly diagnosed cases attributed to work-related exposure to carcinogenic substances and the total incidence for the whole population (without adjusting for latency periods) of the specific cancer type. A new EU direct cost estimate for all remaining cancer types is computed by subtracting the cost estimates for the specific cancer types from the total EU direct cost estimate. A new incidence fraction (central estimate and range) for all remaining cancers is composed using the same approach as above and multiplied with the EU cost estimate for the remaining cancer types.

The indirect societal costs
Cost estimates for indirect costs are available for four specific cancer types and total cancer at EU-27 level in 2009 (Luengo-Fernandez et al.

2013). The same methodology as for the direct cost estimates is used, i.e. use cancer type specific indirect cost estimates multiplied by cancer specific incidence fractions. In case of productivity losses for mortality and morbidity, the cancer specific AFs estimates for mortality and incidence are used.

Productivity losses due to mortality are also estimated based on a simplified friction cost approach. Absolute country and sex specific mortality figures for prostate [C61], breast [C50], colon, [C18-21], lung [C33-34] and all remaining cancers [C00-99] in the working population (15-65) were obtained from Eurostat for 2009. Mortality figures are adjusted for 5-year sex specific unemployment rates. Attributable fractions per specific cancer type and for all remaining cancers are applied as described above. A default friction period of 3 months and no elasticity factor (Koopmanschap et al. 1995) was used as no country specific labour market specific information was at hand. Country specific mortality figures were multiplied with sex specific mean annual earnings from Luengo-Fernandez et al. (2013) adjusted for 3 months.

Adjustment of the direct and indirect cost estimates to EU-28 and 2012
The cost estimates obtained for the direct and indirect costs are based on EU-27 country specific data. Extrapolation to EU-28 is done by simple extrapolation based on the size of the total population. In 2009 the EU-27 consisted of almost 498 million inhabitants and the EU-28, including Croatia, of 502 million. Therefore, the direct and indirect cost estimates are multiplied by 1,0087. In addition, all direct and indirect cost estimates are inflation corrected by 8% to represent 2012 prices based on EU-28 inflation rates for 2009-2012.

This simple adjustment only accounts for differences in population size and inflation but does not take into account differences in healthcare expenditure or prevalence rates between 2009 and 2012.

The intangible societal costs
The intangible cost element is estimated using the EU-28 mortality and morbidity figures estimated in chapter three. Welfare losses associated with being diagnosed with or dying from cancer are based on the survey from Alberini and Ščasný (2014). The number of new cancer cases attributed to work-related exposure to carcinogenic substances are multiplied by the Value of Cancer Morbidity (VCM) as composed by ECHA (2015). Mortality due to work-related exposure to carcinogenic substances is multiplied by the Value of Statistical Life (VSL) based on the analysis of ECHA (2015).

Size of the problem: Limitations/uncertainties of the approach

The approach used in this report is based on existing cost studies and should be interpreted as a crude estimate of the order of magnitude of the societal costs of work-related cancer due to carcinogenic substances in the EU. Several flaws in the used approach are identified and discussed below:

- There is a large uncertainty in the used AFs for the various types of cancers.

- The use of a composed AF for all remaining cancers for the direct and indirect cost estimates introduces a large uncertainty on the accuracy of these estimates. More accurate estimates could be made be going back to the original data sources used by Luengo-Fernandez et al. (2013) and try to estimate the costs for each specific type of cancer. However, this would be a very labour intensive exercise and does not fall within the scope of our study
- Different time periods were used for the determination of direct and indirect costs versus intangible costs.
- Not all elements of the societal costs are captured in our approach, for instance the emotional and social impact on relatives of a cancer patients is not assessed.
- It is debatable which methodology to assess productivity loss should be used. In our approach, we estimated the productivity losses using both approaches. If the human capital approach would is used the estimate for productivity loss due to mortality is substantial higher.
- The figures are based on EU-27 data and extrapolated to EU-28.

Despite the number of uncertainties in our approach, we believe our estimate provides a useful order of magnitude of the societal costs associated with work-related cancer due to carcinogenic substances.

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