European Code against Cancer, 4th Edition: Tobacco and cancer

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ABSTRACT

Tobacco use, and in particular cigarette smoking, is the single largest preventable cause of cancer in the European Union (EU). All tobacco products contain a wide range of carcinogens. The main cancer-causing agents in tobacco smoke are polycyclic aromatic hydrocarbons, tobacco-specific N-nitrosamines, aromatic amines, aldehydes, and certain volatile organic compounds. Tobacco consumers are also exposed to nicotine, leading to tobacco addiction in many users. Cigarette smoking causes cancer in multiple organs and is the main cause of lung cancer, responsible for approximately 82% of cases. In 2012, about 313,000 new cases of lung cancer and 268,000 lung cancer deaths were reported in the EU; 28% of adults in the EU smoked tobacco, and the overall prevalence of current use of smokeless tobacco products was almost 2%. Smokeless tobacco products, a heterogeneous category, are also carcinogenic but cause a lower burden of cancer deaths than tobacco smoking. One low-nitrosamine product, snus, is associated with much lower cancer risk than other smokeless tobacco products. Smoking generates second-hand smoke (SHS), an established cause of lung cancer, and inhalation of SHS by non-smokers is still common in indoor workplaces as well as indoor public places, and more so in the homes of smokers. Several interventions have proved effective for stopping smoking; the most effective intervention is the use of a combination of pharmacotherapy and behavioural support. Scientific evidence leads to the following two recommendations for individual action on tobacco in the 4th edition of the European Code Against Cancer: (1) “Do not smoke. Do not use any form of tobacco”; (2) “Make your home smoke-free. Support smoke-free policies in your workplace”.

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1. Tobacco use and exposure to second-hand smoke in Europe

1.1. Major form of tobacco use: cigarette smoking

Smoking is by far the most common way of using tobacco in Europe, and commercially manufactured cigarettes are the predominant product used by smokers. Recently, the overall crude prevalence of cigarette smoking in the European Union (EU) has decreased. In 2002, smoking prevalence in the 15 EU Member States was 39%, dropping to 28% in 2012 when the EU comprised 27 Member States (EU-27) [1,2]. However, smoking prevalence is still alarmingly high in some countries, and the potential for further reduction remains huge across the EU. In addition, smoking prevalence remains very high in low-income and disadvantaged groups across Europe, exacerbating smoking-induced health inequalities [3]. A 2010 population-based representative survey of tobacco use involving about 18,000 respondents aged ≥15 years in 18 European countries using the same questionnaire examined these differences (Table 1). The Pricing Policy and Control of Tobacco in Europe (PPACTE) survey revealed smoking prevalence estimates ranging between 15.7% and 44.3% in men (mean, 30.6%) and between 11.6% and 38.1% in women (mean, 24.1%) [4].
resulting in an overall European prevalence of 27.2%. Male-to-female smoking prevalence ratios showed countries where smoking was more common in men (e.g. ratio: 3.5 in Albania), similar in both sexes (ratio: 1.1 in England) or slightly higher in women (ratio: 0.85 in Spain). The highest smoking prevalence overall in the European countries covered was seen in the age group 25–44 years, in both men and women (39.8% and 32.0%, respectively). Overall, 16.3% and 9.0% of male and female current smokers, respectively, reported smoking tobacco daily and an equal proportion reported smoking cigars weekly. Percentages for pipe smoking were identical [2]. Results from the Eurobarometer survey in 2012 indicated that 16% of respondents had tried water-pipe smoking at least once, while only 1% used it regularly. Regular or occasional use was highest in the Baltic nations (Latvia, 12%; Lithuania, 9%; Estonia, 8%) [2]. However, there are reports in the literature about water-pipe tobacco smoking recently becoming a trendy way to smoke and spreading rapidly in Europe, especially among young people. In a survey of 2399 high-school students in north-western London in 2011–2012, involving mainly deprived and ethnic minority populations, the prevalence of current water-pipe smoking was more than twice that of cigarette smoking – 7.6% (95% confidence interval (95%CI): 6.6–8.7%) versus 3.4% (2.7–4.2%) – in students aged 12–18 years [9]. The proportion of students (24%; 22.3–25.7%) reporting ever having tried water-pipe smoking was higher than the proportion reporting ever having smoked cigarettes (15.8%; 14.4–17.3%). The tobacco typically used in water-pipe sessions is flavoured with different aromas, and this is believed to be in part responsible for the attractiveness of the product [10].

With the exception of Sweden, smokeless tobacco is rarely used in the EU Member States. The Eurobarometer survey [2] showed a wide range in the proportions of respondents reporting ever having tried smokeless tobacco (snus, chewing tobacco or nasal tobacco), ranging from 44% in Sweden to 17% in Austria, 15% in Denmark and Estonia, 2% in Romania, Hungary, Spain and Bulgaria and 1% in Greece [2]. The PPACTE survey found that 1.1% of the European population sampled (excluding Sweden) reported current use of smokeless tobacco, whereas in Sweden the proportion was 20.7% of men and 3.5% of women [5]. Use in Europe is clustered geographically and is product-specific, as in the case of Sweden and Norway where the predominant product used is snus (moist snuff). A 1989 EU tobacco directive (89/622/EEC) most recently ratified in 2014 reaffirmed the ban on exporting Swedish snus to other EU countries [11]. However, manufacturing and sale of other smokeless tobacco products not intended for mass marketing and including oral (dipping or chewing) and nasal tobacco are allowed within the EU. In certain countries chewing tobacco and other smokeless tobacco products are used by ethnic groups coming from parts of the world where these behaviours are prevalent: for instance, the use of betel quid with tobacco in the United Kingdom (UK) among migrant communities coming from Central, East, South and South-East Asia [12–15]. A comprehensive list of tobacco products used in Europe is given in Table 2.

1.2. Smoking products other than cigarettes and other forms of tobacco used in Europe

Smoking products other than manufactured cigarettes have recently become more popular in Europe. The use of hand-rolled cigarettes has become more common among smokers in some European countries, including England (27.3%), France (16.5%) and Finland (13.6%), with overall about 10.4% of current smokers using predominantly hand-rolled cigarettes in the 18 countries included in the PPACTE survey [6]. The General Household Survey of 2008 in Great Britain indicated that 28% of smokers used hand-rolled cigarettes, confirming the frequent use of this type of cigarette among smokers also in the period before the PPACTE survey [7]. The market segment corresponding to fine-cut tobacco for hand-rolled cigarettes, among all tobacco produced for consumption, increased in most EU countries between 2002 and 2010 but stayed under 10% in more than half of EU countries in 2010 [8], supporting a trend towards greater use of hand-rolled cigarettes while corroborating the dominance of manufactured cigarettes among smokers. This trend has been driven to a great extent by the lower excise tax rate traditionally applied to fine-cut tobacco for hand-rolled cigarettes, which has translated into lower product prices and an incentive towards product substitution after increases in the price of manufactured cigarettes.

Other forms of smoking – such as pipe smoking, smoking of small cigars or cigarillos, and water-pipe smoking – are also used in the EU. Cigar and pipe smoking are relatively uncommon in the EU compared with cigarette smoking. According to the Eurobarometer survey in 2012 1% of smokers reported smoking cigars daily and an equal proportion reported smoking cigars weekly. Percentages for pipe smoking were identical [2]. Results from the Eurobarometer survey in 2012 indicated that 16% of respondents had tried water-pipe smoking at least once, while only 1% used it regularly. Regular or occasional use was highest in the Baltic nations (Latvia, 12%; Lithuania, 9%; Estonia, 8%) [2]. However, there are reports in the literature about water-pipe tobacco smoking recently becoming a trendy way to smoke and spreading rapidly in Europe, especially among young people. In a survey of 2399 high-school students in north-western London in 2011–2012, involving mainly deprived and ethnic minority populations, the prevalence of current water-pipe smoking was more than twice that of cigarette smoking – 7.6% (95% confidence interval (95%CI): 6.6–8.7%) versus 3.4% (2.7–4.2%) – in students aged 12–18 years [9]. The proportion of students (24%; 22.3–25.7%) reporting ever having tried water-pipe smoking was higher than the proportion reporting ever having smoked cigarettes (15.8%; 14.4–17.3%). The tobacco typically used in water-pipe sessions is flavoured with different aromas, and this is believed to be in part responsible for the attractiveness of the product [10].

Table 1

<table>
<thead>
<tr>
<th>Country</th>
<th>N</th>
<th>Smoking prevalence (%)</th>
<th>M/F C/E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>18,056</td>
<td>27.2 30.6 24.1 1.27 1.70</td>
<td></td>
</tr>
<tr>
<td>Albania</td>
<td>1000</td>
<td>26.1 40.2 11.6 3.47 4.28</td>
<td></td>
</tr>
<tr>
<td>Austria</td>
<td>1001</td>
<td>30.4 37.6 23.9 1.57 1.97</td>
<td></td>
</tr>
<tr>
<td>Bulgaria</td>
<td>1027</td>
<td>40.9 44.3 37.7 1.18 2.66</td>
<td></td>
</tr>
<tr>
<td>Croatia</td>
<td>948</td>
<td>26.6 31.3 22.5 1.39 1.83</td>
<td></td>
</tr>
<tr>
<td>Czech Republic</td>
<td>1000</td>
<td>29.1 35.9 22.6 1.59 2.40</td>
<td></td>
</tr>
<tr>
<td>England</td>
<td>1030</td>
<td>24.9 26.5 23.3 1.14 1.03</td>
<td></td>
</tr>
<tr>
<td>Finland</td>
<td>962</td>
<td>26.3 33.9 18.8 1.80 0.96</td>
<td></td>
</tr>
<tr>
<td>France</td>
<td>1029</td>
<td>27.5 30.9 24.4 1.27 1.34</td>
<td></td>
</tr>
<tr>
<td>Greece</td>
<td>965</td>
<td>38.9 43.7 34.0 1.29 3.38</td>
<td></td>
</tr>
<tr>
<td>Hungary</td>
<td>1002</td>
<td>35.5 42.7 28.6 1.49 3.87</td>
<td></td>
</tr>
<tr>
<td>Ireland</td>
<td>1008</td>
<td>36.0 33.9 38.1 0.89 2.14</td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>1005</td>
<td>22.0 25.8 18.5 1.39 2.07</td>
<td></td>
</tr>
<tr>
<td>Latvia</td>
<td>1061</td>
<td>28.8 42.9 16.3 2.63 2.03</td>
<td></td>
</tr>
<tr>
<td>Poland</td>
<td>938</td>
<td>28.0 33.0 23.1 1.43 3.43</td>
<td></td>
</tr>
<tr>
<td>Portugal</td>
<td>1000</td>
<td>32.4 35.7 29.4 1.21 2.13</td>
<td></td>
</tr>
<tr>
<td>Romania</td>
<td>1080</td>
<td>26.1 34.9 17.7 1.97 2.18</td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td>1000</td>
<td>28.6 26.2 31.0 0.85 1.55</td>
<td></td>
</tr>
<tr>
<td>Sweden</td>
<td>1000</td>
<td>16.3 15.7 17.0 0.92 0.68</td>
<td></td>
</tr>
</tbody>
</table>

* Prevalence estimates for the overall population were computed weighting each country in proportion to the country-specific population aged 15 years or over.
### Table 2
List of tobacco products consumed in Europe.

<table>
<thead>
<tr>
<th>Smoked tobacco products</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarette</td>
<td>Any roll of tobacco wrapped in paper or other non-tobacco material; filter-tipped or untipped; also available flavoured; approximately 8 mm in diameter and 70–120 mm in length. Cigarettes usually contain blended tobaccos of different types. The type of tobacco used in these products influences the composition of the smoke produced. An individual cigarette contains approximately 1 g of tobacco and 1 mg of nicotine.</td>
</tr>
<tr>
<td>Roll-your-own cigarettes</td>
<td>Individually hand-rolled cigarettes made of fine-cut loose tobacco wrapped in cigarette paper, containing less tobacco than commercially manufactured types (approximately between 0.4 and 0.75 grams).</td>
</tr>
<tr>
<td>Cigar</td>
<td>Any roll of tobacco wrapped in leaf tobacco or in any other substance containing tobacco. There are different types: little cigars, small cigars (cigarillos), regular cigars, premium cigars. Some little cigars are filter-tipped and are shaped like cigarettes.</td>
</tr>
<tr>
<td>Pipe tobacco</td>
<td>A pipe is a device for smoking tobacco that consists of a chamber (the bowl) for the tobacco, connected to the mouthpiece (the bit) by a thin hollow stem (the shank). Pipes are often carefully treated, and loose tobacco for pipe smoking is blended to achieve flavour nuances not available in other tobacco products.</td>
</tr>
<tr>
<td>Hookah/water-pipe tobacco</td>
<td>A water-pipe is commonly used to smoke tobacco that is flavoured or fermented with molasses or other substances. The tobacco is heated by burning coal, and the smoke is cooled by passing through the water and into the hose and mouthpiece, where it is inhaled.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Smokeless tobacco products, by mode of use</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal</td>
<td>The tobacco is fire-cured, then fermented and processed into a dry, powdered form, referred to as dry snuff. Dry snuff is packaged and sold in small metal or glass containers. Used very rarely in Europe (used in the United Kingdom), it is inhaled into the nostrils. Powdered dry snuff can also be taken orally.</td>
</tr>
<tr>
<td>Oral</td>
<td>Oral use of smokeless tobacco in Europe consists of placing tobacco in the space between the lip or cheek and gum and either chewing or sucking it for a certain period of time. A chaw, which refers to a portion of tobacco the size of a golf ball, is generally chewed, whereas a quid is usually a much smaller portion and is held in the mouth rather than chewed. Newer smokeless tobacco products are used in Scandinavian countries, such as the Swedish snus or Swedish moist snuff, and consist of small pouches containing tobacco (portion-bag snuff). In Sweden, approximately 21% of men use smokeless oral tobacco. However, oral tobacco products are used by less than 2% of the European population overall.</td>
</tr>
<tr>
<td>Loose leaf</td>
<td>Consists of loose cigar tobacco leaves that are air-cured, stemmed, cut or granulated, and loosely packed to form small strips of shredded tobacco. Most brands are sweetened and flavoured with liquorice, and are typically sold in pouches. Loose-leaf tobacco is high in sugar content (approximately 35%). A pinch of tobacco is placed between the cheek and lower lip, typically towards the back of the mouth. It is either chewed or held in place. The saliva is spat out or swallowed.</td>
</tr>
</tbody>
</table>
extent of coverage varies [17]. Fig. 1 shows the scope of such legislation in the EU and other countries in Europe. A detailed description of smoke-free regulations in place in the EU is available at http://ec.europa.eu/health/tobacco/smoke-free_environments/index_en.htm [18] or in the latest WHO report on the global tobacco epidemic at http://www.who.int/tobacco/global_report/en/ [19].

According to a survey commissioned by the EU in 2012, of more than 12,000 people in the 27 Member States at the time, more than 25% reported being exposed to SHS at least occasionally at work. The overall proportion exposed in the EU-27 for more than 5 h/day was 3% (5% of smokers and 1% of non-smokers) [2]. The overall proportion reporting having seen smoking in restaurants and in bars in the 6 months prior to the survey was 14% and 28%, respectively. Country-specific estimates of exposure to SHS at these venues in 2009 and 2012 in the EU-27 are shown in Figs. 2 and 3. A trend towards decreased exposure to SHS is evident from 2009 to 2012, although certain countries still have high prevalence of exposure [17]. As there is wide variation in the prevalence of smoking and the extent to which smoking is banned in public and work settings among EU countries, the probability of exposure to SHS varies substantially [18]. Also, as smoking tends to be more prevalent in certain subgroups of the population, for instance the less educated, exposure to SHS represents a risk factor or, more commonly, spat out.

Swedish-type moist snuff (snus) consists of finely ground dry tobacco mixed with aromatic substances, salts (sodium chloride), water, humidifying agents, and chemical buffering agents (sodium carbonate). A pinch (called a dip) or a pouch is placed between the gum and upper lip. The average user keeps snuff in the mouth for 11–14 h per day. In Sweden, the portions come in two doses (regular and “mini-portions”) or loose. The European Commission bans the sales of snus in the European Union, with the exception of Sweden.

Betel quid is commonly used by minority groups residing in Europe, particularly in the United Kingdom among migrant communities arising from Central, East, South, and South-East Asia. Betel quid with tobacco, commonly known as paan or pan, consists of four main ingredients: (i) betel leaf, (ii) areca nut, (iii) slaked lime, and (iv) tobacco. Tobacco may be used in raw, sun-dried, or roasted form, then finely chopped or powdered and scented or boiled, made into a paste, and scented with rosewater or perfume. The final product (quid) is placed in the mouth and chewed.

Maras is a type of smokeless tobacco that is widely used in the south-eastern region of Turkey, especially in the cities of Kahramanmaras and Gaziantep. First, sun-dried tobacco leaves are powdered and mixed with the ash of wood, in particular oak, walnut, or grapevine. Then, water is sprinkled onto the mixture for humidification. A small amount of the mixture is placed between the lower labial mucosa and gingiva for 4–5 min. This procedure is repeated many times during the day; some people even sleep with the powder in their mouths.

1.3.2. SHS exposure at home

The home may be a place of frequent exposure if smokers smoke at home. In the Women in Europe against Lung Cancer and Smoking (WELAS) study, a population-based telephone survey of 4977 women in 2008, the proportion responding that no smoking was permitted inside the home was 59.5% in France, 61.3% in Italy, 63.5% in Ireland, 74.4% in the Czech Republic and 87.0% in Sweden [21]. In the PPACTE survey, conducted in 2010 and involving about 18,000 adults living in 18 European countries, 62.2% of respondents reported that smoking was not allowed inside the home (72.8% of non-smokers and 34% of current smokers) [22]. In the few European countries included in the 2011 edition of the Global Youth Tobacco Survey (GYTS), covering adolescents aged 13–15 years, the proportion responding that they lived in homes where others smoked in their presence was 66.9% in Croatia, 44.6% in Latvia, 43.0% in the Czech Republic, 41.3% in Slovenia and 22.2% in the Ukraine (Country Fact Sheets, GYTS, http://nccd.cdc.gov/GTSSData/Ancillary/DataReports.aspx?CAID=1) [23].

2. Tobacco use and cancer risk

Tobacco is the major cause of cancer, and tobacco-attributable cancer is entirely preventable. According to the WHO FCTC, “tobacco products” are wholly or partly made of leaf tobacco as the raw material and fabricated to be used for smoking, sucking, chewing or sniffing [24]. Tobacco use exposes consumers to a variety of carcinogens and other toxic agents while supplying nicotine, an addictive substance in cigarette smoke and smokeless tobacco products, which leads to long-term dependence on tobacco use, and cumulative exposure to these toxicants. Continued exposure, in turn, causes cancer and other chronic diseases.

2.1. Carcinogens in tobacco, tobacco smoke and SHS

All tobacco products contain carcinogens. Some carcinogens are constituents of the tobacco plant itself (i.e. tobacco-specific nitrosamines [TSNA] – including N-nitrosornicotinone [NNN] and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone [NNK]) – and most are formed when tobacco is burned (i.e. polycyclic aromatic hydrocarbons [PAHs], specifically benzo[a]pyrene [16,25]). Processing, curing, ageing or storing tobacco can also generate cancer-causing agents (i.e. volatile aldehydes, including formaldehyde and formic acid, and TSNA) [25,26]. Certain types of carcinogens are found across the whole range of tobacco products tested (i.e. TSNA), although their concentration varies
substantially across products, while other types are predominantly linked to how a product is used (i.e., benzene in tobacco smoke) [16,25,26]. More than 70 agents in tobacco smoke have been classified as carcinogenic to laboratory animals or to humans by the International Agency for Research on Cancer (IARC); 16 of these agents are considered carcinogenic to humans [25]. There are additional suspected carcinogens in tobacco smoke which have not been evaluated by the IARC. PAHs, TSNA, aromatic amines, aldehydes, and certain volatile organic compounds are the main agents through which tobacco smoke causes cancer [27].

Non-smokers breathing the smoke released into the air by smokers and by lighted cigarettes are exposed to and metabolise the same carcinogens that smokers inhale while puffing [16,28,29]. The concentrations of individual toxicants in SHS during a given time period can vary depending on the number of smokers emitting SHS, the size of the place where smoking occurs, the time elapsed since release into the air, and the environmental conditions of the place. Studies comparing people exposed and non-exposed to SHS indicate that the levels of metabolites of NNK (e.g., total NNAL or 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone), PAHs (e.g., hydroxypyrene) and nicotine are increased in the urine of exposed subjects [30–32].

2.2. Summary of tobacco smoking and cancer risk

Cigarette smoking is the most harmful form of tobacco use, causing the largest cancer burden. Based on an enormous body of published literature, the IARC Monographs Programme has classified tobacco smoking as a cause of cancers of the haematopoietic system (namely myeloid leukaemia), cervix, colorectum, kidney,
larynx, liver, lung, nasal cavity and paranasal sinus, oesophagus, oral cavity, ovary, pancreas, pharynx (naso-, oro-, and hypo-pharynx), stomach, ureter, and urinary bladder, as well as hepatoblastoma (in the children of smokers). Cigarette smoking is the major cause of lung cancer (see Section 2.8). There is also some evidence indicating that tobacco smoking may cause cancer of the breast and childhood leukaemia (in the children of smokers) [16,25,33].

2.3. Summary of smokeless tobacco use and cancer risk

The IARC Monographs Programme has identified smokeless tobacco as a cause of cancers of the oral cavity, oesophagus and pancreas [16,26,33], and has also identified betel quid with added tobacco as a cause of cancers of the oral cavity, oesophagus and pharynx [16,33–35]. Smokeless tobacco has also been identified as a cause of pre-malignant lesions in the oral cavity [26]. However, one type of smokeless tobacco, Swedish snus, is associated with a much lower risk of oral cancer. Studies from Sweden have not shown excess risk of oral cancer in association with snus use, while excess risk of oesophageal and pancreatic cancers have been reported in some studies [36].

2.4. Summary of SHS exposure and cancer risk

The IARC Monographs Programme has classified second-hand tobacco smoke as a cause of lung cancer and a possible cause of cancers of the larynx and pharynx [16,25,33]. Other cancer sites have been associated with SHS, although the evidence is less consistent. Parental smoking causes hepatoblastoma in children [16].

2.5. Major determinants of cancer risk due to tobacco smoking

In 2012, lung cancer ranked second and third among incident cancers in men and women, respectively, in the combined 27 EU Member States and Croatia, and contributed substantially to the overall burden of tobacco-attributable cancers [37]. Lung cancer is the most common cause of death from cancer in Europe [38]. Smoking is associated with an increased risk of squamous-cell carcinoma, adenocarcinoma, large-cell carcinoma and small-cell carcinoma of the lung [16]. The main factors that drive the remarkably high cancer risk associated with smoking are duration and intensity. Epidemiological studies conducted in the UK and the United States of America (USA) indicate that the number of years that a person smokes (self-reported) is more strongly associated with lung cancer risk than intensity of use, and that this association holds for men and women at different ages [16]. A comprehensive list of epidemiological studies conducted all over the world reporting on the effect of duration of smoking on lung cancer risk are available in the IARC Monographs Volumes 83 (2004) [25] and 100E (2012) [16]. Also, based on self-reporting in epidemiological studies, the risk of lung cancer increases with increasing daily dose (up to 15–20 cigarettes per day), but the effect levels off at very high intensities. This relationship has also been detected for cancers of the bladder, oral cavity, oesophagus and pancreas [16]. However, data from cohort studies examining risk of lung cancer associated with serum cotinine as a biomarker of exposure demonstrate a linear increase in lung cancer risk with rising concentration of cotinine [16], thereby not supporting the levelling-off effect at the higher doses of smoking reported above.
Cohort studies from Asia offer additional insight based on both urine cotinine and a metabolite of the TSNA carcinogen NNK; smokers with similar self-reported smoking histories differ substantially in lung cancer risk based on the concentrations of urine cotinine and NNAL [16,39].

2.6. Combined effect of smoking and alcohol consumption

Alcohol consumption increases the already high risk of cancers of the oral cavity, oropharynx, larynx and oesophagus associated with smoking. This effect appears to be synergistic in that the risk of cancer at these sites rises progressively with increasing alcohol consumption among smokers. Several mechanisms have been reported to contribute to these observed interactions, including: the increased permeability of tobacco-smoke carcinogens through the oral mucosa in the presence of alcohol; the increased solubility of tobacco-smoke carcinogens in ethanol; increased acetaldehyde production from alcohol oxidation by oral bacteria; alcohol-derived increased induction of CYP2E1 (an enzyme member of the cytochrome P450 oxidase system involved in the metabolism of xenobiotics in the body) in the liver, which can elevate the amount of toxic metabolites during the metabolism of carcinogens present in tobacco smoke (e.g. benzene); alcohol-induced increased generation of CYP3A4 and CYP1A2 (other members of the cytochrome P450 oxidase system), which can activate tobacco carcinogens such as NNK; and alcohol-induced inhibition of the family of CYP enzymes, which could result in locally increased accumulation of toxic agents by reduced metabolic activation [16,40].

2.7. Major determinants of smokeless-tobacco-associated cancer risk

Determinants of cancer risk are product-type-specific, and dose–response relationships have not been systematically documented in association with cancers of the oral cavity, oesophagus and pancreas in countries where dipping or chewing tobacco are traditionally used; hence the data are limited. In snuff users in the USA who did not report smoking or alcohol consumption, an increased risk of cancer of the gums and oral mucosa has been reported with increasing duration of use, in a dose–response manner. The dose–response relationship has not been observed for all head–and–neck subsites or in Swedish studies focusing on oral cancer. The risk of pre-cancerous lesions in the oral cavity has been reported to increase with duration and intensity of use of snuff or of chewing tobacco, while the dose–response relationship appears to be stronger with snuff use. An increase in the prevalence of lesions has been reported with increased number of hours of use per day, quantity of tobacco used, and duration of use. The severity of lesions is also correlated with duration of use [16,26]. Modest elevation of risk of oesophageal squamous-cell carcinoma with long duration of use has been reported in one Swedish study (odds ratio [OR] = 1.4, 95%CI = 0.9–2.3, for 25 or more years of use compared with never-users) [41]. One of the major challenges to improved characterisation of the determinants of cancer risk associated with smokeless tobacco is the relatively small number of studies compared with the large number of smokeless tobacco products available on the market, including commercially manufactured products as well as small-scale informal production; the constituents of these products – including carcinogens – vary substantially.

2.8. Cancer burden caused by smoking in Europe

Cigarette smoking causes cancer in multiple organ sites in humans and accounts for the premature death of more than half of long-term smokers [16,42–44]. The percentage of cancers caused by smoking is highest in the lung (82%) and the larynx (84%) [45]. These fractions indicate the proportions of cancers that could be prevented by eliminating smoking. In 2012, in the EU-27 and Croatia combined, the age-standardised (World standard) overall cancer rate was estimated to be 273.5 cases per 100,000 population, with 45.1 cases per 100,000 for lung cancer in men and 18.2 cases per 100,000 for lung cancer in women [37]. The risk of dying from lung cancer is 20–25 times as high in men and women who smoke as in their non-smoking counterparts [46]. Further, the overall risk of death in smokers is 2–3 times as high as that in never-smokers, with an average loss of 10 years of life expectancy [47].

In 2012 there were 312,645 cases of lung cancer in the pooled population of the EU-27 and Croatia [37]. For several countries in Europe there has been a progressive decline in the rate of lung cancer in men, mainly following a gradual decrease in smoking prevalence in men in the population. In 2013, for the first time in 80 years, the prevalence of smoking in England was recorded to be below 20% (19.3%, 95%CI = 18.8–19.8%) [48]. According to the 2012 Globocan estimates, the crude and age-standardised (world standard) lung cancer incidence rates in men in the EU-27 plus Croatia were highest for Hungary, with 124.7 per 100,000 and 76.8 per 100,000 respectively, and lowest for Sweden, with 40.7 per 100,000 and 19.4 per 100,000, respectively (Fig. 4) [37]. In women, the estimated crude and age-standardised lung cancer incidence rates were highest in Denmark (80.3 and 37.6 per 100,000) and lowest in Lithuania (15.9 and 7.2 per 100,000) (Fig. 4). The highest rates observed in European women are lower than the highest rates reported in men, and the lowest rates in women are considerably lower than the lowest rates in men. Overall, in the past, women in Europe have not smoked as long or as much as men have. But this trend is changing, regrettably, in several countries in Europe. In some, lung cancer rates have been similar in men and women in recent times (e.g. Iceland and Denmark) and are increasing. In several other countries, although lung cancer rates in women have been lower than those in men, they have been increasing since 1975, with projections for further rises (e.g. France, Italy, Spain, Switzerland, and The Netherlands) [49]. In Sweden, the rates in men and women are similar (see Fig. 4). Because there is a long lag time between the initiation of smoking and the appearance of overt lung cancer, current rates of lung cancer might not match current levels of smoking in the population in any given country.

Cancers at many organ sites, other than the lung, are also caused by smoking. Agudo et al. [45] calculated the attributable fraction of those other cancers due to smoking using data from a large European cohort study. They reported that these proportions were highest (above 80%) for cancer of the larynx, between 50% and 20% for cancers of the lower urinary tract and other respiratory and digestive cancers, and below 20% for all other cancers linked to smoking. Overall, they calculated that between 32% and 37% of those other cancers are caused by smoking [45]. This study highlights the amount of damage that smoking causes in the European population, but it similarly stresses how much disease can be prevented by quitting smoking.

Smoking also has a harmful effect on non-smokers, specifically individuals exposed to SHS. In the UK, breathing SHS is expected to cause 14–15% of lung cancers in non-smokers [50]. In countries with smoking prevalence higher than that in the UK, the fraction of lung cancers in non-smokers caused by SHS is expected to be higher, particularly in the presence of non-comprehensive or weak smoke-free policies. Using estimates of exposure from the 1990s, WHO estimated that in 2004 there were 3850 lung cancer deaths in Europe attributable to SHS exposure [51].
2.9. Cancer burden caused by smokeless tobacco use

A recent report from the United States National Cancer Institute and the Centers for Disease Control and Prevention has estimated that more than 300 million people in the world are smokeless tobacco users, stressing that South-East Asia has the majority of users and also has the highest rates of oral cancer in the world [52]. However, as stated above, smokeless tobacco products vary geographically and do not all entail the same cancer risk. Considering that snus is the predominant smokeless tobacco product used in Sweden, the EU country with the highest prevalence of smokeless tobacco use, only the cancer-related burden associated with snus in that country is provided here. The above-cited 2014 report [52] estimated that 13.5% of oesophageal cancers and 17.2% of pancreatic cancers in men in Sweden are due to snus use, while in women the estimates are 4.0% and 5.3%, respectively, although these estimates are based on only one review [36] and the report noted that there was some uncertainty associated with the values. Other types of smokeless tobacco products with higher toxicity are used by ethnic minorities from South-East Asia living in Europe [14].

2.10. Reduction in the risk of cancer and cancer death after smoking cessation

The risk of developing or dying from lung cancer is substantially lower in former smokers than in those who continue smoking. Within 5–9 years after cessation, the risk of lung cancer in former smokers decreases progressively with increasing time since quitting compared with the risk in continuing smokers [44]. This same pattern has been observed for the majority of the cancers associated with smoking, with variations in the length of time after cessation needed to observe a decrease in risk. Epidemiological data clearly support this for cancer of the larynx, pharynx and oral cavity, squamous-cell carcinoma of the oesophagus, stomach, pancreas, bladder and squamous-cell carcinoma of the cervix. The data are limited or inadequate for cancers of the liver, nasopharynx, sinonasal...
cancer and adenocarcinoma of the oesophagus, and for myeloid leukaemia [44].

2.10.1. Reduced cancer incidence and mortality risk with younger age at cessation

Studies comparing the risk of lung cancer, cancer death or total mortality in former and current smokers with the risk in never-smokers have shown the significantly lowered risk of any of these adverse health outcomes in those who have quit, with the risk diminishing progressively with decreasing age at smoking cessation, and approximating – although not reaching – the risk in never-smokers for those quitting at a very young age [44]. The benefits of quitting smoking in relation to reduced cancer or total mortality have been addressed in multiple epidemiological studies, with strong data in men documented in several countries, including the UK, Poland and the USA [42,45,46,53,54], and more recently in a large prospective study of women in the UK [55]. These studies are consistent in showing similar trends after smoking cessation. Compared with never-smokers, the relative risk of lung cancer death in women who quit smoking prior to 25 years of age, or at age 30, 40 or 50 years has been reported to be 1.56 (1.03–2.37), 1.84 (1.45–2.34), 3.34 (2.76–4.03) and 5.91 (5.01–6.97), respectively, with a risk substantially lower than that observed in women who continue to smoke, who show a 20-fold higher risk of lung cancer death than never-smokers. Women who stop smoking at the age of about 30 or 40 years avoid most of the excess risk observed in women who don’t quit, a decrease of 97% and 90% of the risk, respectively, according to Pirie et al. [55]. Smokers die prematurely, losing on average about 10 years of life expectancy. Fig. 5 shows the cumulative risk of death from lung cancer in men in the UK for continuing smokers and for former smokers according to the age when they quit, showing death rates in 1990 [56]. More recent studies continue to document the health benefits of quitting smoking, showing greater reductions in total mortality risk [54,55] or lung cancer mortality risk [55] with decreasing age at cessation in the USA and the UK.

3. Effective interventions to reduce the risk of cancer caused by smoking

The best option for individuals who want to take personal direct action to reduce their risk of cancer from tobacco is not to smoke and generally not to use any form of tobacco, as well as to avoid exposure to second-hand smoke by making their homes smoke-free and advocating for smoke-free laws for indoor workplaces and public places.

3.1. Quitting smoking

There are interventions available with demonstrated efficacy as smoking cessation aids; these include pharmacotherapy and behavioural support. The most frequently used effective pharmacotherapy includes medicinal nicotine or nicotine replacement therapy (NRT), antidepressant therapy using bupropion, and use of nicotine-receptor partial agonist medications, including varenicline and cytisine. Pharmacotherapy use can be associated with side-effects, but these are minor compared with the health effects caused by continued smoking.

Behavioural support commonly includes advice on strategies to plan a quit attempt, to manage nicotine cravings and withdrawal symptoms, to select pharmacotherapy and other information to help the smoker manage the stress related to smoking cessation. This advice can be dispensed in different modalities: individually or collectively, face-to-face, via the telephone or through electronic channels.

Scientific evidence indicates that the most effective intervention to help smokers quit is the use of a combination of pharmacotherapy and behavioural support. Providing behavioural support in addition to pharmacotherapy increases the proportion of successful attempts with at least a 6-month abstinence compared with pharmacotherapy with no, minimal or less intensive support for smokers (relative risk [RR] = 1.16, 95%CI = 1.09–1.24) [57].

3.1.1. Pharmacotherapy

NRT is available for different routes of administration (transdermal patch, nasal spray, chewing gum, oral spray and film strips, inhaler and sublingual tablets/lozenges and other forms) and dosages (16-h and 24-h transdermal patches; 2 or 4 mg chewing gum; 1, 1.5, 2 or 4 mg nicotine lozenges; 2 mg sublingual tablets and others). NRT is commonly available over the counter in Europe, but it can also be medically prescribed. All of the commercially available forms of NRT can help smokers increase their chances of successfully stopping smoking for at least 6 months. Recent systematic reviews have summarised the findings of multiple
randomised trials comparing NRT against placebo, in contrast with other types of pharmacotherapy, when using more than one formulation of NRT and in smokers who decide to quit abruptly or by progressively reducing the amount smoked daily. Results of the clinical trials evaluating these comparisons are available in the reviews by Stead et al. [57] and by Moore et al. [58].

In subjects intending to quit abruptly, all types of NRT have shown efficacy in maintaining abstinence for at least 6 months compared with no treatment (RR = 1.60, 95% CI = 1.53–1.68). Also, use of a combination of NRT products proved to be more effective than using a single formulation type (RR = 1.34, 95% CI = 1.18–1.51). NRT is also effective in aiding smokers who prefer to quit by gradually reducing the number of daily cigarettes until achieving sustained abstinence as opposed to quitting abruptly (6-month abstinence, RR = 2.06, 95% CI = 1.34–3.15). Studies comparing NRT with other medicinal cessation products showed that NRT seemed to be as effective as bupropion (RR = 1.01, 95% CI = 0.87–1.18), whereas the combination of NRT plus bupropion seems to confer additional benefit compared with bupropion alone (RR = 1.24, 95% CI = 1.06–1.45, based on four trials reported by Stead et al. [57]) and a substantial increased effect compared with placebo (a more than two fold increase in cessation: RR = 2.61, 95% CI = 1.65–4.12). Adverse effects reported in association with NRT are minimal and type-specific, such as skin irritation from patches and irritation in the oral cavity from use of gum or tablets.

Bupropion is an atypical antidepressant available by medical prescription in most European countries. A usual treatment regimen includes 300 mg/day for 7–8 weeks, beginning 1 week before the planned quit date. The original systematic review by Hughes [59] and its most recent update [60] summarise the findings of the trials assessing this type of cessation aid. The pooled estimates from these trials demonstrate that bupropion is effective in maintaining abstinence for 6 months (RR = 1.81, 95% CI = 1.51–2.16) or even longer (12 months, RR = 1.64, 95% CI = 1.46–1.84) compared with placebo. Also, bupropion appears to be as effective as NRT in the form of the transdermal patch (RR = 1.26, 95% CI = 0.73–2.18), but these results come from only three trials. Compared with varenicline, bupropion seems to be less effective, a conclusion based on very few trials (RR = 0.66, 95% CI = 0.53–0.82). The summary measure from six trials indicates that bupropion plus NRT is not more effective than NRT alone (RR = 1.26, 95% CI = 0.73–2.18). Other antidepressants compared in randomised trials have not shown efficacy in maintaining abstinence from smoking for 6 months. Adverse health effects have been reported in association with use of bupropion. There is a risk of seizures of about 1 in 1000 users, and there is suggestion of increased risk of suicide.

Varenicline is a nicotine-receptor partial agonist, which is available to smokers by medical prescription in most European countries. A typical treatment regimen consists of 11 weeks of administration starting 1 week before the planned date for quitting at a dose of 1 mg/day and subsequently at 2 mg/day until the end of treatment. Results attesting to the efficacy of this type of product have been abstracted from the systematic review by Cahill et al. [61]. Varenicline at the standard dose increases the chance of successful smoking abstinence for 6-month (RR = 2.27, 95% CI = 2.02–2.55) and 12-month (RR = 4.91, 95% CI = 2.56–9.42) intervals, an increase of between two- and almost five-fold compared with placebo. More participants quit successfully with varenicline than with bupropion (RR = 1.52, 95% CI = 1.22–1.88). Two open-label trials of varenicline versus NRT have suggested equivalence between the products (RR = 1.13, 95% CI = 0.94–1.35). The main adverse effect reported in association with use of varenicline is nausea (mostly mild to moderate, and usually subsiding over time). Lower dose regimens also confer benefits for cessation while reducing the incidence of collateral health effects.

Cytisine, another nicotine-receptor partial agonist, has been available in a few countries in central and eastern Europe for decades [62]. The treatment regimen usually lasts 4 weeks and starts 1 week before the planned quit date, with dosage decreasing progressively. Cytisine increases the chance of quitting smoking, although absolute quit rates have been modest in at least one earlier trial: 8.4% in the treatment arm versus 2.4% in the placebo arm at 12 months [63]. A recently reported randomised trial conducted in New Zealand has reported 1-month (40% versus 31%) and 6-month (22% versus 15%) quit rates significantly higher in the cytisine arm than in the NRT arm, with longer elapsed time from quit date to relapse in the cytisine arm (53 days versus 11 days) [64]. These quit rates are superior to those reported in earlier trials at 6 months, while the efficacy at 12 months was not reported in the recent trial. Self-reported adverse health effects were more frequent in the cytisine arm, with nausea, vomiting and sleep disorders being the most common complaints. In the earlier trial by West et al. [63], gastrointestinal complaints were more frequently reported in the cytisine arm of the trial.

An overview of 12 Cochrane reviews was published in 2013, including a network meta-analysis which allows for indirect comparisons between different treatments assessed in separate trials [65]. This synthesis concluded that NRT, bupropion and varenicline all improve the chance of quitting. Use of a combination of NRT is as effective as varenicline, and more effective than using a single type of NRT. Based on the evidence available at the time of that publication, the safety profiles of these treatment options were not discouraging, but nevertheless continued monitoring and research on the safety of varenicline was recommended, as well as the evaluation of the potential of cytisine as a safe, effective and affordable treatment option in smoking cessation [65]. Cytisine is more affordable than varenicline.

### 3.1.2 Behavioural support

This type of support can include advice by physicians and other health professionals, counselling, incentives, self-help and stage-based interventions and motivational interviews, among other possibilities. Based on the systematic review by Stead et al. [66] on physician advice, brief and simple advice given by physicians to their smoking patients consisting of verbal instructions with a “stop smoking” message is effective in helping people to stop smoking compared with the control group (RR = 1.76, 95% CI = 1.58–1.95). Interventions based on advice of different intensities have been compared, suggesting a probable benefit from the more intensive interventions compared with briefer advice, although subgroup analyses suggest that this might be small or non-existent in unselected smokers, but with a larger impact in high-risk groups.

Counselling, whether individual, group or telephone-based, has been evaluated as a smoking cessation intervention. Individual counselling is effective in helping people to stop smoking. For example, studies evaluating counselling consisting of more than 10 min of face-to-face contact versus minimal counselling have found increased success in abstinence for at least 6 months (RR = 1.39, 95% CI = 1.24–1.57). NRT plus individual counselling increases the chance of quitting smoking and maintaining abstinence for 6 months compared with NRT alone (RR = 1.27, 95% CI = 1.02–1.59) [67]. Group counselling includes discussion of motives for group members’ decisions and their emotional experiences, presentation of information and teaching of new skills to achieve and cope with cessation. Group programmes may be led by professional facilitators such as clinical psychologists, health educators, nurses or physicians, or occasionally by successful users of the programme. The implementation of smoking cessation programmes in groups has been a popular method of delivering behavioural interventions. These include
coping and social skills training, contingency management, self-control and cognitive-behavioural interventions. There may be a specific therapeutic benefit of the group format in giving people who smoke the opportunity to share problems and experiences with others attempting to quit. Group therapy is better than self-help (RR = 1.98, 95%CI = 1.60–2.46) [68].

Telephonic counselling may supplement face-to-face support, or substitute for face-to-face contact as an adjunct to self-help interventions or pharmacotherapy. Counselling may be helpful in planning a quit attempt, and helping to prevent relapse during the initial period of abstinence [69]. Telephonic counselling may be a way of providing individual counselling more cheaply. Telephonic contact can be timed to maximise the level of support around a planned quit date, and can be scheduled in response to the needs of the recipient. Telephonic counselling can be proactive or reactive. In a proactive approach, the counsellor initiates calls to provide support in making a quit attempt or avoiding relapse. This can be offered as part of an intervention, including face-to-face counselling, or provided as an adjunct to a mailed self-help programme or to pharmacotherapy. Reactive counselling, in contrast, is available on demand to people calling specific services, quitlines, helplines or hotlines. These telephone services may offer information, recorded messages, personal counselling or a mixture of components. In the systematic review by Stead et al. [70], those who had initiated contact with the quitline and who received multi-session proactive call-back counselling had a 40% increased likelihood of cessation and abstinence for at least 6 months compared with subjects who received only self-help materials or brief counselling during a single call (RR = 1.37, 95%CI = 1.26–1.50). There is evidence of a dose–response effect; one- or two-call protocols (RR = 1.07, 95%CI = 0.91–1.26) are less likely to provide a measurable benefit compared with donation of self-help materials or brief counselling at a single call. Three or more calls increase the odds of quitting compared with a minimal intervention such as providing standard self-help materials or brief advice, or compared with pharmacotherapy (RR = 1.34, 95%CI = 1.23–1.47). Telephonic quitlines provide important access to support for smokers, and call-back counselling enhances their usefulness [70,71]. More intensive behavioural support is likely to provide some additional benefit (four to eight contacts versus pharmacotherapy alone, RR = 1.25, 95%CI = 1.08–1.45).

3.2. Protecting against SHS at home

There is sufficient evidence that smoke-free policies at home diminish exposure of children to SHS [72]. In the households of smokers, adoption of a smoke-free home will reduce exposure to SHS in children, a vulnerable group whose exposure typically depends on parental smoking. These studies have measured exposure in different ways, some quantifying the number of hours of exposure and others biomarkers of exposure in saliva, urine, serum or hair (i.e. cotinine or nicotine). The study by Matt et al. [73] in the USA illustrates, consistently, the occurrence and level of exposure to SHS in children living in households with varying smoking exposure and SHS-restriction profiles. In this comparison, determinations in three different groups of families were made: those with no smoking adults, those with at least one adult smoker in the family but smoking only outside of the home or when the children were not present, and those with at least one adult smoker but no restrictions on smoking. Determinations of exposure included nicotine in household dust, in indoor air or on household surfaces, and in infant hair as well as cotinine levels in infant urine and hair. Infant urine cotinine concentrations were 0.32 ng/ml (95%CI = 0.19–0.47) in the families with no smokers, 2.88 ng/ml (95%CI = 1.22–5.79) in the families with smokers but smoking restrictions in the home, and 13.02 ng/ml (95%CI = 8.01–20.81) in the families with smokers and no restrictions. Similarly, infant hair cotinine and nicotine concentrations were 0.08 ng/mg (95%CI = 0.05–0.11) and 0.53 ng/mg (95%CI = 0.25–0.86), 0.52 ng/mg (95%CI = 0.20–0.92) and 2.65 ng/mg (95%CI = 1.10–5.34), and 1.05 ng/mg (95%CI = 0.55–1.72) and 5.95 ng/mg (95%CI = 3.25–10.37), respectively, in the three groups of families. Furthermore, no nicotine was detected on surfaces in the living room or the infant’s room in the families without smokers, while in the other two groups of families the following level of contamination was detected: the mean surface nicotine concentrations in the living room and in the infant’s room, respectively, were 10.08 µg/m² (95%CI = 0.01–21.10) and 8.19 µg/m² (95%CI = 2.69–14.98) in households with smokers but smoking restrictions and 51.33 µg/m² (95%CI = 19.17–32.16) and 41.85 µg/m² (95%CI = 24.71–59.09) in households of families with smokers and no smoking restrictions inside the home [72,73]. This study shows that the best protection from exposure to SHS is not to smoke, while adoption of smoking restrictions in the households of smokers can reduce exposure to SHS.

There is sufficient evidence that smoke-free policies at home lead to reductions in smoking among continuing smokers. Restricting smoking to outside the home imposes a barrier to smoking ad libitum and generates the inconvenience of having to leave the home in order to smoke. This mechanism can postpone the act of smoking, which generally leads to a reduction in the number of cigarettes smoked per day in adult smokers [72]. Seven longitudinal studies examining the effect of home smoking restrictions on smoking behaviour have found that smokers in smoke-free homes are more likely to quit or progress towards cessation and less likely to relapse [74–80]. Similarly, several of these studies also assessed the level of consumption among smokers in both types of households, finding a reduction in the number of cigarettes smoked that was larger in smokers living in smoke-free homes than in those living in homes without smoking rules [76–79]. Cross-sectional studies have also addressed smoking cessation and level of consumption in continuing smokers in homes according to the presence of smoking rules. Many of these studies found significantly lower consumption and more quit attempts in smokers living in homes with smoking restrictions than in those living in households without them [72]. In addition, evidence from cross-sectional studies suggests that adolescent offspring of non-smoking parents living in smoke-free homes are less likely to start smoking than similar adolescents living in households where there are no explicit rules against smoking inside the home [72].

Although there has been a time trend of increased adoption of smoke-free policies at home among smokers, non-smokers continue to be exposed to SHS at home in many parts of Europe, and thus there is room for a greater adoption of smoke-free homes. For instance, a greater proportion of children with smoking parents lived in smoke-free homes after the introduction of the 2007 ban on smoking in enclosed public places in England (48.1% in 2008) than before the ban (30.5% in 2006) [81]. Yet these figures indicate that further reductions in exposure could have been achieved at the time in the households of smokers, and particularly in deprived households, where exposure to SHS tends to be higher [82]. After the introduction of the smoke-free policy in England, there was an increase in the adoption of smoke-free homes, and the ban did not displace exposure to SHS to the home [81].

3.3. Protecting against SHS in indoor workplaces and public places

Article 8 of the WHO FCTC indicates that countries should adopt and implement effective legislation to protect citizens from exposure to tobacco smoke in indoor workplaces, in indoor
public places, in public transportation and when applicable in other public places. The article focuses on three principles: 100% smoke-free environments as opposed to implementing non-smoking rooms; universal protection from SHS reaching all people; and smoke-free laws, in contrast to voluntary interventions to reduce exposure to SHS [24]. The overwhelming majority of the evidence documents the substantial decline in exposure to SHS in indoor public settings after the introduction of smoke-free policies, with concomitant reductions in respiratory symptoms in workers, and quitting smoking or reductions in cigarette consumption among continuing smokers. Implementation of smoke-free legislation that bans smoking in all, or virtually all, indoor workplaces has shown reductions in SHS by 80–90% in venues where smoking was common indoors before the ban, such as bars and restaurants [72]. The drop in exposure to SHS in hospitality venues has been sustained over time in the majority of countries implementing comprehensive laws. In France, for instance, the percentage of bars where indoor smoking occurred went from 95.8% before the 2008 smoking ban to 3.7% a few months after the ban and to 6.6% 4 years later. In restaurants, similar determinations went from 64.7% before the ban to 2.3% and 1.4%, respectively [83]. In France, smoking in workplaces decreased from 42.6% before the ban to 19.3% immediately after the ban and to 12.8% in 2012 [83]. The decrease in exposure to SHS has been greater in workers in the hospitality industry than in the general population. The reduction in exposure to SHS after the implementation of comprehensive smoke-free laws is estimated to be about 80–90% in workplaces and 40% at the population level as revealed in a comprehensive study completed in Scotland [72].

Many studies have reported a significant decline in the rate of hospital admissions for cardiovascular events after the introduction of smoke-free laws [84–90]. The meta-analysis by Mackay et al. [91] reports a 10% decrease in the incidence of acute coronary events after the introduction of smoke-free laws (RR = 0.90; 95%CI = 0.86–0.94). Smoke-free legislation is expected to have a significant role in the reduction of lung cancer incidence in non-smokers in future decades; at present, it is too early to assess this effect as most smoke-free policies have been implemented recently [72].

4. Justification of recommendations

Smoking is a well-known major cause of cancer. Despite the known smoking-associated detrimental effects to health, almost 28% of adults in the EU smoke. Hence, the following recommendation was developed for the European Code Against Cancer: “Do not smoke”.

The overall European prevalence of current use of smokeless tobacco products is almost 2%, and is higher in some countries (see above). Although snus is associated with much lower risk of some forms of cancer compared with other types of smokeless tobacco, there is evidence that smokeless tobacco products overall cause cancer. Hence, the following recommendation was developed: “Do not use any form of tobacco”.

Smoking generates SHS, another well-known cause of cancer, and inhalation of SHS by non-smokers is still common in indoor workplaces and public places, and even more so in the homes of smokers. Hence, the recommendations for individual action to make homes smoke-free and to support smoke-free policies in the workplace were developed. The presence of smokers in a home increases the risk of smoking initiation, especially in adolescents, and reduces the likelihood of stopping smoking [72,92–94].

The impact of reduced prevalence of tobacco use, and in particular cigarette smoking, will be reflected not only in decreased cancer incidence and mortality but also in reduced morbidity and mortality due to chronic obstructive pulmonary disease (COPD), coronary heart disease, cerebrovascular disease and other health outcomes with more acute onset, such as the effects of smoking during pregnancy and the exacerbation of asthma, among other conditions [95]. Reduced smoking at the population level and comprehensive smoke-free laws will lead to decreased exposure to SHS in public places and workplaces as well as in the home, with concomitant protection of non-smokers from the harmful effects of SHS.

Furthermore, in an environment where the tobacco industry targets individuals to try its products and lobbies local or national governments to support its economic interests, the protection of the health of the individual from tobacco needs a comprehensive approach as mandated by the WHO FCTC, which defines tobacco control as a domain for government regulation for the protection of the individual and the overall population [24].

Overall, the tobacco-related recommendations for individual action in the 4th edition of the European Code Against Cancer, based on the available scientific evidence, are:

“Do not smoke. Do not use any form of tobacco.”

“Make your home smoke-free. Support smoke-free policies in your workplace.”

The last part of the second recommendation encourages individuals to require governmental action to protect them from tobacco smoke. Other individual actions people can follow to reduce their risk of cancer are listed in Box 1.

Conflict of interest

The authors declare no conflict of interest.

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**Box 1. European Code Against Cancer.**

**EUROPEAN CODE AGAINST CANCER**

**12 ways to reduce your cancer risk**

1. Do not smoke. Do not use any form of tobacco
2. Make your home smoke free. Support smoke-free policies in your workplace
3. Take action to be a healthy body weight
4. Be physically active in everyday life. Limit the time you spend sitting
5. Have a healthy diet:
   - Eat plenty of whole grains, pulses, vegetables and fruits
   - Limit high-calorie foods (foods high in sugar or fat) and avoid sugary drinks
   - Avoid processed meat; limit red meat and foods high in salt
6. If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention
7. Avoid too much sun, especially for children. Use sun protection. Do not use sunbeds
8. In the workplace, protect yourself against cancer-causing substances by following health and safety instructions
9. Find out if you are exposed to radiation from naturally high radon levels in your home; take action to reduce high radon levels
10. For women:
   - Breastfeeding reduces the mother’s cancer risk. If you can, breastfeed your baby
   - Hormone replacement therapy (HRT) increases the risk of certain cancers. Limit use of HRT
11. Ensure your children take part in vaccination programmes for:
   - Hepatitis B (for newborns)
   - Human papillomavirus (HPV) (for girls)
12. Take part in organised cancer screening programmes for:
   - Bowel cancer (men and women)
   - Breast cancer (women)
   - Cervical cancer (women)

The European Code Against Cancer focuses on actions that individual citizens can take to help prevent cancer. Successful cancer prevention requires these individual actions to be supported by governmental policies and actions.
Acknowledgements

The European Code Against Cancer project was co-funded by the European Union [grant agreement numbers: 2011 53 05; 2010 53 04 and 2007IARCo1] and the International Agency for Research on Cancer. The authors alone are responsible for the views expressed in this manuscript.

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