SHORT REPORT

uicc IJC
International Journal of Cancer

Burden of disease from breast cancer attributable to smoking and second-hand smoke exposure in Europe

Giulia Carreras[1] | Alessio Lachi[1] | Roberto Boffi[2] | Luke Clancy[3] |
Silvano Gallus[4] | Esteve Fernández[5,6,7,8] | Maria José López[9,10,11] |
Joan B. Soriano[8,12] | Ángel López Nicolás[13] | Sean Semple[14] |
Panagiotis Behrakis[15] | Giuseppe Gorini[1] | TackSHS Project Investigators[†]

[1]Oncologic Network, Prevention and Research Institute (ISPRO), Florence, Italy

[2]Fondazione IRCCS Istituto Nazionale dei Tumori (INT), Milan, Italy

[3]TobaccoFree Research Institute Ireland (TFRI), Dublin, Ireland

[4]Istituto di Ricerche Farmacologiche Mario Negri IRCCS (IRFMN), Milan, Italy

[5]Catalan Institute of Oncology (ICO), L'Hopitalet de Llobregat, Spain

[6]Bellvitge Biomedical Research Institute (IDIBELL), L'Hopitalet de Llobregat, Spain

[7]University of Barcelona, Barcelona, Spain

[8]Consortium for Biomedical Research in Respiratory Diseases (CIBER en Enfermedades Respiratorias, CIBERES), Madrid, Spain

[9]Public Health Agency of Barcelona (ASPB), Barcelona, Spain

[10]CIBER Epidemiologia y Salud Pública (CIBERESP), Barcelona, Spain

[11]IIB Sant Pau, Barcelona, Spain

[12]Hospital Universitario La Princesa (IISP), Madrid, Spain

[13]Polytechnic University of Cartagena (UPCT), Cartagena, Spain

[14]Faculty of Health Sciences and Sport, University of Stirling, Stirling, UK

[15]Hellenic Cancer Society - George D. Behrakis Research Lab (HCS), Athens, Greece

Correspondence
Giulia Carreras, Oncological Network, Prevention and Research Institute (ISPRO), Florence, Italy.
Email: g.carreras@ispro.toscana.it

Abstract

Smoking and second-hand smoke (SHS) exposure have been recently linked to a higher risk of breast cancer in women. The aim of this work is to estimate the number of deaths and disability-adjusted life years (DALYs) from breast cancer attributable to these two risk factors in the European Union (EU-28) in 2017. The comparative risk assessment method was used. Data on prevalence of smoking and SHS exposure were extracted from the Eurobarometer surveys, relative risks from a recent meta-analysis, and data on mortality and DALYs from breast cancer were estimated from the Global Burden of Disease, Injuries and Risk Factors Study. In 2017, 82 239 DALYs and 3354 deaths from breast cancer in the EU-28 could have been avoided by removing exposure to these two risk factors (smoking and SHS exposure). The proportion of DALYs from breast cancer lost respectively from smoking and SHS

exposure was 2.6% and 1.0%, although geographically distributed with significant heterogeneity. These results represent the first estimates of breast cancer burden in women attributable to smoking and SHS exposure for the EU-28. It is important to increase awareness among women, health professionals and wider society of the association between smoking, SHS exposure and breast cancer, a relationship that is not widely recognised or discussed.

KEYWORDS

breast cancer, burden of disease, population attributable fraction, second-hand smoke, smoking

1 | INTRODUCTION

Tobacco smoke is the most ubiquitous, preventable human carcinogen and breast cancer is the leading cause of cancer among women, accounting for nearly one in four of all new cancer diagnoses worldwide in 2018, and about 15% of female cancer deaths. Among European women, breast cancer accounted for 523 000 new cases (28% of total cancers) in 2018, being also the leading cause of cancer-related deaths (138 000 deaths, 16% of total female cancer deaths), with the exception of Northern European countries, where it is now preceded by lung cancer.[1]

Until 2004, reports published by expert groups, such as the International Agency for Research on Cancer (IARC), California Environmental Protection Agency (CalEPA) or the United States Surgeon General, did not report any association between smoking and breast cancer. The 1986 IARC monograph even indicated that smoking reduced breast cancer risk.[2]

The 2005 CalEPA Report for the first time concluded that there was a positive association between smoking and breast cancer risk,[3] followed a few years later by a report by a group of Canadian experts,[4] and then by the 2012 monograph of the IARC, which for the first time, mentioned a causal relationship.[5] Also, the 2014 US Surgeon General reported an increased risk of breast cancer in smokers, particularly in postmenopausal women.[6]

Regarding second-hand smoke (SHS) exposure, both the 2005 CalEPA Report and the Canadian study reported a relationship consistent with causality between SHS exposure and occurrence of breast cancer, particularly in women before menopause, whereas the 2014 US Surgeon General reported a possible association in nonsmoking premenopausal women.[3,4,6]

The 2015 meta-analysis of all published studies on this research topic reported significant 9% and 20% increases in breast cancer risk respectively in smoking women and among nonsmoking women exposed to SHS, surprisingly. However, high heterogeneity was observed among studies, and respectively a 10% and 7% risk increase was estimated if considering only prospective studies accounting for heterogeneity.[7]

Several theories have been put forward to explain why SHS exposure could have a similar or stronger effect on breast cancer than active smoking, and the debate is ongoing. According to one theory,

What's new?

Smoking and exposure to secondhand smoke are not considered a major risk factor for breast cancer risk in Europe. Here, the authors publish the first analysis estimating how many deaths and years of disability can be attributed to smoking. Using the comparable risk assessment method, they determined that eliminating smoking could have saved 60 733 years of life with disability and 2719 deaths from breast cancer. Given the burden of disease from breast cancer attributable to smoking, it is important to increase awareness among health professionals and public.

smoking has an association with breast cancer weaker than expected due to the role of being both an anti-estrogenic protective factor and a risk factor for breast cancer.[2] According to others, SHS exposure has a predominant effect in premenopausal cancers, a hypothesis strongly supported by a Japanese cohort study that found three times higher risk of developing breast cancer among SHS exposed women in premenopausal age, but not in postmenopausal age.[8]

Overall, smoking prevalence in European Union (EU-28) has shown a slight decrease in recent years, yet with heterogeneous trends among countries, and, since the widespread implementation of smoking bans, important reductions in SHS exposure in EU-28 have been observed.[9]

It is important to highlight the impact that both smoking and SHS exposure have on women's health and to quantify the number of deaths and disability-adjusted life years (DALYs) lost that could be avoided. The aim of this work, conducted within the TackSHS project,[10] is to estimate the number of deaths and DALYs from breast cancer attributable to smoking and SHS exposure in the EU-28 in 2017.

2 | MATERIALS AND METHODS

The burden from breast cancer attributable to smoking and SHS exposure was obtained using the comparative risk assessment

method.[11] Briefly, the smoking and SHS attributable fraction (AF) for each country and age-class was first estimated using Levin's formula

$$AF = \frac{p \cdot (RR - 1)}{p \cdot (RR - 1) + 1}$$

where RR is the relative risk for exposed to smoking or SHS compared to nonexposed.

In the estimation of the AF from smoking p is the smoking impact ratio (SIR)

$$SIR = \frac{C_{LC} - N_{LC}}{S^*_{LC} - N^*_{LC}} \cdot \frac{N^*_{LC}}{N_{LC}}$$

where C_{LC} and N_{LC} are the age-specific lung cancer mortality rate respectively for the overall country under study and for never smokers only, and S^*_{LC} and N^*_{LC} are lung cancer mortality rates for smokers and never-smokers, respectively, in a reference population. The SIR represents the accumulated risk from smoking, using lung cancer mortality excess as a biological marker for accumulated smoking hazards. Since the effect of smoking on breast cancer depends on the smoking exposure history, such as age of starting smoking and number of cigarettes smoked per day, the SIR is usually preferred to the smoking prevalence alone that is an insufficient indicator of accumulated risk from smoking.[12]

In the estimation of the AF from SHS, p is the 10-years lagged age and country-specific prevalence of SHS exposure. A 10-year lag between SHS exposure and breast cancer death/occurrence was assumed in computing the AF, due to an expected long latency, as for active smoking.[11]

The number of breast cancer deaths/DALYs attributable to smoking was then obtained by multiplying the age- and country-specific number of breast cancer deaths/DALYs by the corresponding AF, and the burden attributable to SHS exposure was estimated among nonsmoking women, because the impact of smoking could mask the effect due to SHS.[11]

The RR for smoking women compared to nonsmokers was 1.10 (95% confidence interval [95% CI]: 1.09-1.12), and the RR for women exposed to SHS compared to nonexposed was 1.07 (95% CI: 1.02-1.13).[7] The sources and the data used in the analysis are reported in Tables 1 and 2, respectively.

For each estimate of deaths and DALYs attributable to smoking and SHS exposure, an uncertainty interval (UI) was obtained with a Monte Carlo procedure.[11]

A sensitivity analysis was carried out by using RR estimated pooling all prospective and retrospective studies, even if highly heterogeneous (RR for smoking: 1.09 [95% CI: 1.06-1.12]; RR for SHS exposure 1.20 [95% CI: 1.07-1.33]). [7] Moreover, an analysis estimating the burden form smoking by using the 10 years lagged prevalence of smoking instead of the SIR in the AF estimation was also performed.

TABLE 1 Sources of data used for the analyses

Variable	Source
Country and age-specific prevalence of SHS exposure at home in nonsmoking women in 2006 for the estimation of attributable fractions (defined as being ever exposed in the home daily)	Eurobarometer survey[9]
Country and age-specific prevalence of smoking women in 2017 for the estimation of nonsmoking women	Eurobarometer survey[9]
Relative risk of breast cancer for exposed to SHS compared to not exposed and for smokers compared to nonsmokers	Meta-analysis[7]
Country and age-specific lung cancer mortality rate in 2017 (C_{LC}) for SIR estimation	Global Health Data Exchange of the Global Burden of Disease study[13]
Country and age-specific lung cancer mortality rate for never smokers only (N_{LC})	Pooled estimate among white lifelong never smokers of European Descent[14]
Lung cancer mortality rates for smokers and never-smokers in a reference population (S^*_{LC}, N^*_{LC})	Estimate from Cancer Prevention study 2[15]
Country-specific estimates of mortality and DALYs from breast cancer	Global Health Data Exchange of the Global Burden of Disease study[13]

Abbreviation: SHS, second-hand smoke.

3 | RESULTS

In the EU-28 in 2017, the number of DALYs from breast cancer attributable to smoking and SHS exposure was estimated as of 50 610 (UI: 42506-61 471) and 10 123 (UI: 6793-14 377) respectively, and the number of deaths was 2340 (UI: 1953-2886) and 379 (UI: 239-601). The proportion of breast cancer DALYs attributable to smoking and SHS exposure on the 2 254 992 total DALYs from breast cancer was 2.2% and 0.4%, respectively (Figure 1), whereas the proportion of deaths were 2.3% and 0.4%, respectively (101 935 total deaths from breast cancer).

In terms of both DALYs and deaths, the highest burden due to both risk factors (smoking and SHS exposure) was estimated in Denmark, Malta, Croatia, Hungary and in the United Kingdom, with a proportion on the total breast cancer DALYs and deaths higher than 4% and 5%, respectively. The lowest burden was estimated in Cyprus, Lithuania, Latvia, Italy and Estonia with a proportion less than 1.5%. The proportion of DALYs and deaths from breast cancer attributable to smoking was higher than that due to SHS exposure for all EU-28 countries (Figure 1).

In the sensitivity analysis using meta-analytical RR of breast cancer with a high heterogeneity, the rank of the countries by the burden

TABLE 2 Prevalence of household second-hand smoke exposure in 2006 (SHS), smoking prevalence in 2006 (smoking), Smoking Impact Ratios (SIR), disability-adjusted life years from breast cancer in 2017 (DALYs) and deaths from breast cancer in 2017 (deaths) for women aged 15 to 80+ years with 95% confidence intervals (CI) or uncertainty intervals (UI)

Country	SHS % (95% CI)	Smoking % (95% CI)	SIR % (95% UI)	DALYs % (95% UI)	Deaths % (95% UI)
Austria	10.3 (6.5, 14.1)	24.3 (19, 29.5)	22.7 (15.7, 43.6)	35 328 (41 237, 29 942)	1688 (1462, 1938)
Belgium	4.5 (2.2, 6.8)	21.9 (17.4, 26.5)	24.5 (16.8, 46.8)	52 913 (62 554, 44 121)	2450 (2088, 2831)
Bulgaria	15 (10.4, 19.5)	29.6 (23.9, 35.3)	11.2 (7.1, 28.2)	34 462 (41 761, 28 086)	1356 (1120, 1624)
Cyprus	9.3 (3, 15.6)	16.1 (10.9, 21.2)	5.9 (3.9, 19.2)	4645 (5972, 3504)	169 (129, 212)
Czech Republic	6.2 (3.2, 9.2)	23.1 (18.5, 27.8)	18.3 (12.9, 36.9)	37 669 (44 246, 31 704)	1708 (1465, 1974)
Germany	6.6 (4, 9.2)	25.3 (22.3, 28.3)	17.3 (11.8, 36)	431 661 (529 364, 347 861)	20 000 (16 469, 24 073)
Denmark	4.2 (2, 6.3)	28.8 (21.8, 35.9)	44.7 (31.9, 73.4)	27 614 (32 734, 23 135)	1294 (1106, 1505)
Estonia	3.5 (0.8, 6.1)	24 (9.9, 38.1)	9.6 (6.6, 24.4)	4996 (6370, 3831)	219 (172, 274)
Spain	10.8 (6.7, 14.8)	28.3 (25.9, 30.7)	13.1 (9.3, 29.3)	151 940 (178 790, 128 086)	6749 (5815, 7784)
Finland	2.4 (0.6, 4.1)	22.5 (16, 29)	20.7 (13.5, 42.3)	21 210 (25 316, 17 655)	917 (777, 1073)
France	7.9 (4.6, 11.2)	27 (24.8, 29.1)	24.8 (17, 47)	282 360 (334 740, 235 115)	13 321 (11 376, 15 442)
United Kingdom	4.2 (1.9, 6.5)	31.9 (28.4, 35.4)	34.4 (24.5, 59.1)	307 453 (324 528, 291 743)	13 757 (13 356, 14 190)
Greece	12.1 (7.8, 16.5)	36.7 (31.4, 42)	16.2 (10.8, 34.9)	48 772 (57 738, 40 731)	2286 (1953, 2652)
Croatia	11.4 (7.1, 15.6)	25.1 (17.9, 32.3)	44.2 (30.1, 68)	19 720 (23 238, 16 635)	951 (815, 1107)
Hungary	14.9 (9.9, 19.9)	29.3 (24.3, 34.3)	30.3 (21.6, 54.4)	45 970 (53 912, 38 886)	2045 (1757, 2365)
Ireland	8.6 (5.2, 11.9)	29.4 (21, 37.9)	13.8 (9.4, 30.9)	18 578 (22 549, 15 134)	746 (617, 892)
Italy	7.2 (3.4, 10.9)	23.8 (21.8, 25.7)	6.7 (4.4, 20.4)	271 655 (318 234, 228 855)	12 769 (10 970, 14 667)
Lithuania	4.6 (1.5, 7.8)	20.2 (12.6, 27.8)	5.7 (3.6, 19.1)	12 627 (15 128, 10 414)	524 (439, 620)
Luxembourg	2.6 (0, 5.5)	23.4 (0.8, 45.9)	24.4 (16.8, 46.7)	2415 (3046, 1862)	104 (82, 128)
Latvia	8.9 (4.8, 13)	21.3 (10.4, 32.2)	7.2 (4.8, 21.2)	9098 (11 498, 7104)	393 (312, 491)
Malta	3.2 (0, 6.9)	21.6 (−2.1, 45.4)	41.3 (28.9, 69.8)	2328 (2815, 1887)	100 (83, 120)
Netherlands	5.6 (2.9, 8.3)	27.5 (23.5, 31.5)	28.3 (19.8, 51.4)	88 115 (103 121, 74 613)	3859 (3342, 4430)
Poland	13.8 (9.4, 18.2)	29.8 (27.2, 32.4)	7.5 (4.6, 22.3)	148 977 (176 781, 123 973)	6189 (5224, 7244)
Portugal	4.5 (1.7, 7.4)	13.9 (10, 17.9)	13.3 (8.7, 30.6)	43 016 (51 561, 35 325)	1927 (1618, 2268)
Romania	11.1 (7.1, 15.1)	19.9 (16.9, 23)	12.2 (8.2, 28.6)	82 129 (95 804, 69 693)	3345 (2867, 3871)
Sweden	4 (2, 5.9)	21.8 (16.9, 26.8)	18.4 (12.5, 37.6)	39 547 (45 131, 34 523)	1787 (1590, 1999)
Slovenia	11.1 (7.5, 14.8)	21.2 (11.1, 31.3)	10.9 (6.8, 27.4)	8034 (9720, 6567)	384 (322, 455)
Slovakia	5.6 (2.7, 8.4)	18.8 (12.8, 24.9)	22 (15.9, 41.7)	21 760 (27 502, 16 189)	898 (651, 1118)
Europe Union	7.6 (4.3, 11.1)	26.4 (25.7, 27.1)	19.6 (13.5, 39)	2 254 992 (2 645 390, 1 907 172)	101 935 (87 977, 117 345)

from both smoking and SHS exposure was similar to the main results, but for some countries, that is, Cyprus, Lithuania, Italy, Romania, Slovenia, Spain and Bulgaria, the proportion of DALYs from breast cancer attributable to SHS exposure was higher than that due to smoking. Using the 10-year lagged smoking prevalence instead of the SIR in the AF estimation produced an estimate of 48 619 (UI: 40067-58 386) and 10 122 (UI: 6791-14 365) DALYs from breast cancer attributable respectively to smoking and SHS exposure, and 1752 (UI: 1387-2222) and 378 (UI: 239-603) deaths.

4 | DISCUSSION

In 2017, 50 610 (2340) and 10 123 (379) years of life lived with disability (deaths) could have been avoided by removing respectively smoking and SHS exposure in the home in the EU-28, and in all countries the burden from smoking was larger than from SHS exposure. The burden from these two risk factors varied considerable across EU-28 countries, with a geographic gradient. On the one hand, the North-Western countries showed the largest proportion of breast cancer DALYs attributable to smoking. In these countries, as well as in Austria, Czech Republic, Finland, Hungary, Ireland, The Netherlands, Poland, Slovenia and Sweden, lung cancer was the leading cause of cancer deaths among women, as a consequence of earlier widespread of tobacco consumption among women.[1] Moreover, in most of these countries, SHS exposure prevalence is lower with consequently a lower burden from SHS.

On the other hand, South-Eastern EU-28 countries showed comparatively greater exposure to SHS and thus larger proportions of breast cancer DALYs attributable to SHS exposure, with over 0.7% in
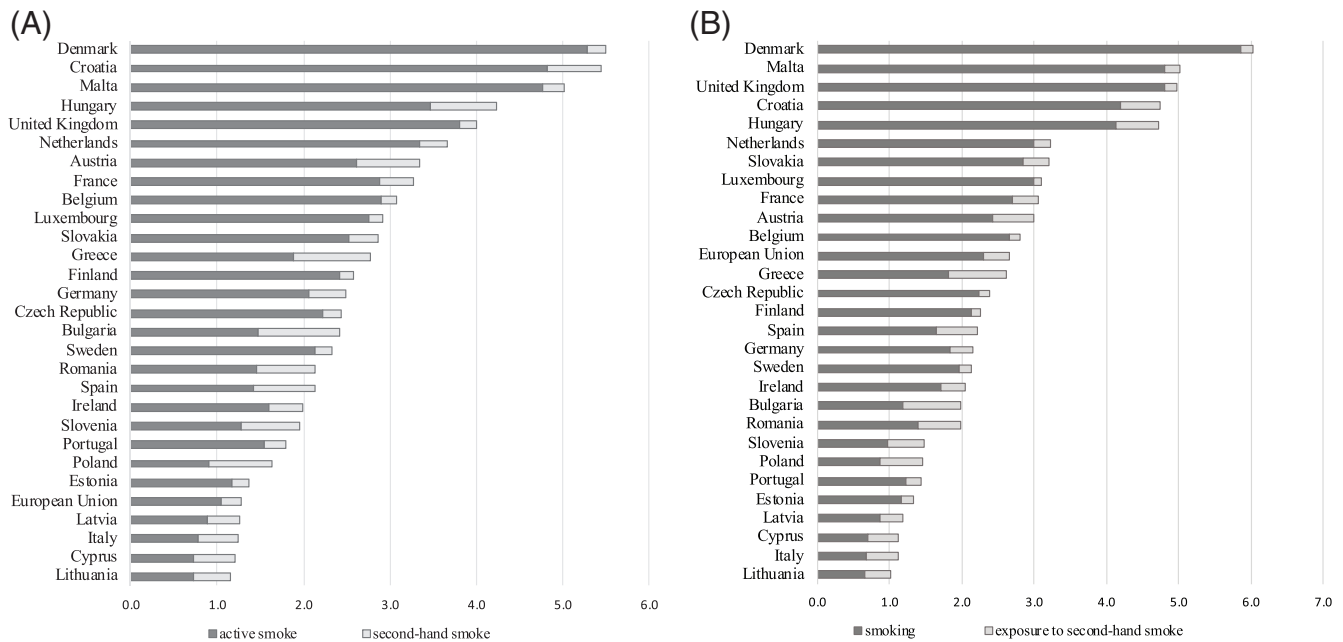
FIGURE 1 Proportion of, A, deaths and disability-adjusted life years (DALYs) and B, deaths from breast cancer attributable to smoking and second-hand smoke exposure in 2017 in the European Union countries

Greece, Bulgaria and Hungary. By considering a higher risk from SHS exposure, even if estimated with a large heterogeneity, the same countries showed proportions of breast cancer DALYs attributable to SHS exposure over 1.6%. In the South-Eastern countries, the burden from breast cancer due to smoking was lower than that due to SHS exposure as a consequence of the lower smoking prevalence than that recorded among women of North-Western countries.

Differently from other studies, the analyses on SHS exposure were carried out by considering household exposure only to explore the burden unrelated to the current legislation.

The SIR approach in the estimation of the burden attributable to smoking is usually the preferred method because it considers the accumulated risk from smoking, but also because it uses lung cancer mortality data, which are easily available for all countries.[16] Using a lagged prevalence of smoking to take into account for the time period between exposure and cancer occurrence, gives smaller attributable fractions than SIR-based estimates among females,[17] and this is confirmed in our sensitivity analysis.

The GBD framework, which provides a comprehensive assessment of risk factor exposure and attributable burden of disease, estimated for 2017 in EU-28 a PAF to smoking of 6.8% and 5.7% for DALYs and deaths, respectively.[13] Another study on the burden from smoking on cancers that analysed five European cohorts reported a proportion of attributable DALYs of 4.7%,[18] whereas a study carried out in Norway estimated a PAF to smoking of 11.9%.[19] Similar values were estimated in the present study for northern countries, such as Denmark (5.9%) and Great Britain (4.8%). Possible explanations of such differences could be in the distributions of risk factors and RR in the populations under study.

The association between SHS exposure and breast cancer needs further evidence. Within the last 10 years, only four groups investigated the burden from breast cancer due to SHS exposure. The results of these studies produced estimates of attributable fractions between 1.07% and 1.68% that are higher in comparison to our estimates.[20] The PAF to SHS exposure estimated from GBD for the EU-28 are 1.7% and 1.4% for DALYs and deaths, respectively, whereas the Norwegian study estimated a PAF of 3.2%.[13] The main differences in these results could be explained by the different definition for SHS exposure that in our case refers to household exposure only.

Our study has some limitations. In the SIR approach, we are using the lung cancer mortality as an indicator of smoking exposure history; however, the relationship of active smoking to breast cancer may depend also from other measures, such as years of smoking before first childbirth.[21] Moreover, in the SIR estimation, as lung cancer death rates in nonsmokers of the population under study we used, for all countries, a pooled estimate from never smokers of European Descent extracted from the Thun et al's study[14] since no rates specific for each Europe Union country was available.

We used an estimate of RR of breast cancer for overall SHS exposure, that were extracted from different studies exploring the effect of SHS exposure defined in several different ways, that is, spousal exposure, household exposure, workplace exposure. This could generate biased conservative estimates since the analyses are carried out by considering household exposure only. Moreover, we assumed the same RR for all ages since there were no robust meta-analytical RR estimates by age in the literature, even if there is evidence that premenopausal and postmenopausal breast cancer risks for active and SHS risks may differ.[8]

In conclusion, to the best of our knowledge, this is the first estimate on the burden from breast cancer attributable to smoking and SHS exposure in the EU-28. Although smoking (including SHS exposure) is not considered a major risk factor for breast cancer risk, the burden of disease from breast cancer attributable to smoking and SHS exposure is large in EU-28, and, given that awareness of both smoking and SHS exposure as risk factors for breast cancer remains low among the population, it is important to spread this link among the public and all stakeholders. Smoking and exposure to SHS are modifiable risk factors, and therefore important objects of primary prevention policies, in addition to the current population-based breast cancer early detection programmes across Europe.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

DATA ACCESSIBILITY

The data and the code that support the findings of our study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Specific need for ethics committee's approval was not necessary for this study since public aggregated data were used.

ORCID

Giulia Carreras https://orcid.org/0000-0002-1427-637X
Silvano Gallus https://orcid.org/0000-0002-8967-0400

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68:394-424.
2. International Agency for Research on Cancer. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Tobacco Smoking*. Vol 38. Lyon: International Agency for Research on Cancer; 1986.
3. California Environmental Protection Agency. *Proposed identification of environmental tobacco smoke as a toxic air contaminant*. San Francisco, CA: Center for Tobacco Control Research and Education, University of California at San Francisco; 2005.
4. Johnson KC, Miller AB, Collishaw NE, et al. Active smoking and secondhand smoke increase tobacco smoking and breast cancer: a life course approach 123 breast cancer risk: the report of the Canadian expert panel on tobacco smoke and breast cancer risk (2009). *Tob Control*. 2011;20(1):e2.
5. International Agency for Research on Cancer. *Some Chemicals in Industrial and Consumer Products, Food Contaminants and Flavourings and Water Chlorination by-Products: Volume 100E, Personal Habits and Indoor Combustions*. Lyon, France: International Agency for Research on Cancer; 2012.
6. U.S. Department of Health and Human Services. *The Health Consequences of Smoking-50 Years of Progress: a Report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.
7. Macacu A, Autier P, Boniol M, Boyle P. Active and passive smoking and risk of breast cancer: a meta-analysis. *Breast Cancer Res Treat*. 2015;154:213-224.
8. Hanaoka T, Yamamoto S, Sobue T, Sasaki S, Tsugane S. Japan public health center-based prospective study on cancer and cardiovascular disease study group. Active and passive smoking and breast cancer risk in middle aged Japanese women. *Int J Cancer*. 2005;114:317-322.
9. Research Data Centre "International Survey Programs". The European Commission's Eurobarometer Surveys. Available from: https://www.gesis.org/eurobarometer-data-service/home/. Accessed November 25, 2019.
10. Fernández E, López MJ, Gallus S, et al. Tackling second-hand exposure to tobacco smoke and aerosols of electronic cigarettes: the TackSHS project protocol. *Gac Sanit*. 2020;34:77-82.
11. Öberg M, Jaakkola MS, Prüss-Üstün A, Schweizer C, Woodward A. *Second-Hand Smoke: Assessing the Environmental Burden of Disease at National and Local Levels. WHO Environmental Burden of Disease Series, No. 18*. Geneva, Switzerland: World Health Organization; 2010.
12. Ezzati M, Lopez AD. Measuring the accumulated hazards of smoking: global and regional estimates for 2000. *Tob Control*. 2003; 12:79-85.
13. Global Burden of Disease Collaborative Network. *Global Burden of Disease Study 2017 (GBD 2017) Results*. Seattle, WA: Institute for Health Metrics and Evaluation (IHME); 2018 http://ghdx.healthdata.org/gbd-results-tool. Accessed November 25, 2019.
14. Thun MJ, Hannan LM, Adams-Campbell LL, et al. Lung cancer occurrence in never-smokers: an analysis of 13 cohorts and 22 cancer registry studies. *PLoS Med*. 2008;5:e185.
15. Thun MJ, Henley SJ, Burns D, Jemal A, Shanks TG, Calle EE. Lung cancer death rates in lifelong nonsmokers. *J Natl Cancer Inst*. 2006; 98:691-699.
16. Tachfouti N, Raherison C, Obtel M, Nejjari C. Mortality attributable to tobacco: review of different methods. *Arch Public Health*. 2014; 72:22.
17. Kong KA, Jung-Choi KH, Lim D, et al. Comparison of prevalence- and smoking impact ratio-based methods of estimating the smoking-attributable fractions of death. *J Epidemiol*. 2016;26:145-154.
18. Tsilidis KK, Papadimitriou N, Capothanassi D, et al. Burden of cancer in a large consortium of prospective cohorts in Europe. *J Natl Cancer Inst*. 2016;108(10):djw127.
19. Gram IT, Little MA, Lund EL, Braaten T. The fraction of breast cancer attributable to smoking: the Norwegian women and cancer study 1991–2012. *Br J Cancer*. 2016;115:616-623.
20. Carreras G, Lugo A, Gallus S, et al. Burden of disease attributable to second-hand smoke exposure: a systematic review. *Prev Med*. 2019; 129:105833.
21. Ha M, Mabucki K, Sigurdson AJ, et al. Smoking cigarettes before first childbirth and risk of breast cancer. *Am J Epidemiol*. 2007;166:55-61.

APPENDIX: The TackSHS Project Investigators

Catalan Institute of Oncology (ICO); Bellvitge Biomedical Research Institute (IDIBELL), Spain: Esteve Fernández, Yolanda Castellano, Marcela Fu, Montse Ballbè, Beladenta Amalia, Olena Tigova.

Public Health Agency of Barcelona (ASPB), Spain: Maria José López, Xavier Continente, Teresa Arechavala, Elisabet Henderson.

Istituto di Ricerche Farmacologiche Mario Negri IRCCS (IRFMN), Italy: Silvano Gallus, Alessandra Lugo, Xiaoqiu Liu, Cristina Bosetti, Enrico Davoli, Elisa Borroni; Istituto DOXA, Worldwide Independent Network/Gallup International Association, Italy: Paolo Colombo.

University of Stirling (UNISTIR), the UK: Sean Semple, Rachel O'Donnell, Ruaraidh Dobson

TobaccoFree Research Institute Ireland (TFRI), Ireland: Luke Clancy, Sheila Keogan.

Hellenic Cancer Society—George D. Behrakis Research Lab (HCS), Greece: Panagiotis Behrakis, Anna Tzortzi, Constantine Vardavas, Vergina Konstantina Vyzikidou, Gerasimos Bakelas, George Mattiampa.

Fondazione IRCCS Istituto Nazionale dei Tumori (INT), Italy: Roberto Boffi, Ario Ruprecht, Cinzia De Marco, Alessandro Borgini, Chiara Veronese, Martina Bertoldi, Andrea Tittarelli.

Istituto per lo Studio, la Prevenzione, e la Rete Oncologica (ISPRO), Italy: Giuseppe Gorini, Giulia Carreras, Barbara Cortini, Simona Verdi, Alessio Lachi, Elisabetta Chellini.

Polytechnic University of Cartagena (UPCT), Spain: Ángel López Nicolás, Marta Trapero-Bertran, Daniel Celdrán Guerrero.

European Network on Smoking and Tobacco Prevention (ENSP), Belgium: Cornel Radu-Loghin, Dominick Nguyen, Polina Starchenko.

Fundación para la Investigación Biomédica del Hospital Universitario La Princesa (IISP), Spain: Joan B. Soriano, Julio Ancochea, Tamara Alonso, María Teresa Pastor, Marta Erro, Ana Roca, Patricia Pérez, Elena García Castillo.

B-cell malignancies - A new knowledge hub on the latest research in therapeutic advances

EDUCATIONAL CONTENT AVAILABLE ON THE HUB:

- On-demand Webinars - earn CME credit
- Infographics
- Patient Case Studies
- Currated Research Articles
  ...and much more

VISIT KNOWLEDGE HUB TODAY

WILEY