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# Lung cancer and smoking: years lived with disability in Tuscany (Italy). An analysis from the ACAB study

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## Abstract

**Background** Lung cancer (LC) is among the most common neoplasms, mostly caused by smoking. This study, carried out within the ACAB project, aims to provide local, updated and systematic estimates of years lived with disability (YLD) from LC due to smoking in the Tuscany region, Italy.

**Methods** We estimated YLD for the year 2022 for the whole region and at subregional level by local health unit (LHU) using data from the Tuscany Cancer Registry and local surveys. YLD were calculated by applying the severity-specific LC prevalence, estimated with an incidence-based disease model, to the corresponding disability weight. The burden from smoking was computed by: modelling the prevalence of smokers with a Bayesian Dirichlet-Multinomial regression model; estimating the distribution of smokers by pack-years simulating individual smoking histories; collecting relative risks from the literature.

**Results** In 2022 in Tuscany, LC caused 7.79 (95% uncertainty interval [UI] = 2.26, 17.27) and 25.50 (95% UI = 7.30, 52.68) YLDs per 100,000 females and males, respectively, with slight variations by LHU, and 53% and 66% of the YLDs were caused by smoking.

**Conclusion** The updated estimates of the burden of LC attributable to smoking for the Tuscany region as a whole and for each LHU provide indications to inform strategic prevention plans and set public health priorities. The impact of smoking on YLDs from LC is not negligible and heterogeneous by LHU, thus requiring local interventions.

**Keywords** Lung cancer, Years lived with disability, Smoking, Burden of disease

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## Background

In Italy in 2023, lung cancer (LC) was the second most common neoplasm in terms of incidence in men and the third in women, with 30,000 and 14,000 estimated new cases, respectively, causing, in 2022, 23,600 and 12,100 deaths [1]. Focusing on Tuscany, according to data from the Cancer Registry of Tuscany Region, each year between 2008 and 2010 in the provinces of Florence and Prato (population ≈ 1.2 million) about 1,830 and 760 new cases of LC were diagnosed respectively in men and women [2].

In addition to the number of new cases, the burden of disease due to LC can be quantified in terms of years of ill health or Years Lived with Disability (YLD). Such measure, together with the number of years of life lost (YLL) due to premature death and their sum, i.e., disability adjusted life years (DALYs), are quantities increasingly used in public health planning to compare the relative importance of different causes of premature deaths and disability within a given population, to set priorities of intervention, and to compare premature mortality and disability between populations and sub-populations [3].

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) systematically and comprehensively quantifies health loss from hundreds of diseases, injuries, and risk factors across countries, time, age, and sex [4]. After gathering health data from a large number of sources, such as hospitals, governments, surveys, cancer registries and other databases around the world, data is standardized and modelled through sophisticated tools to generate estimates.

The number of YLDs from LC estimated for 2019 in Italy was 6,880 (95% uncertainty interval [UI] = 4,659, 9,760) in males and 3,189 (UI = 2,151, 4,419) in females and, respectively, 74.2% (UI = 71.8%, 76.6%) and 59.3% (UI = 56.2%,62.6%) of them were due to smoking [5].

Strategies to reduce LC burden should focus on prevention activities aimed at reducing exposure to modifiable risk factors based on accurate estimates of their impact. To circumvent the tobacco epidemic, in 2003 the World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC) was adopted to implement effective policies to reduce tobacco consumption [6] and, in order to help in the country-level implementation of these policies, the WHO introduced in 2008 the MPOWER package which consists of a set of six key and most effective strategies to reduce the tobacco epidemic [7]. Nevertheless, the impact and burden of LC attributed to smoking on global healthcare systems is likely to persist for decades. In 2013, the WHO set the target of a 30% smoking prevalence reduction by 2025 in all 178 countries that signed the FCTC. Italy ratified the WHO FCTC in 2008, and since then implemented many recommended tobacco control policies [8] that have contributed to the reduction in smoking prevalence in Italy from 29.8% in 2008 to 24.5% in 2023, and in Tuscany from 30.0% in 2008 to 22.5% in 2023 (https://www.epicentro.iss.it/passi/dati/fumo). However, further tax increases, well designed anti-tobacco mass media campaigns, promoting smoking cessation through the empowerment of the national quitline and the development of web-based quitting interventions have not yet been implemented in Italy. Moreover, from the 2020 COVID-19 pandemic, many smoking cessation services (SCSs) implemented in Italy since 2000 to support smokers willing to quit, have been closed because many SCS health workers were moved to carry out COVID-19 related tasks and other SCS health workers retired without being replaced. In fact, SCSs in 2008 were 362 in the whole of Italy and 36 in the Tuscany Region, whereas in 2023, these numbers were reduced almost by half to 197 and 20, respectively (https://smettodifumare.iss.it/it/centri-antifumo/) [9].

In order to define targeted and effective strategies to further reduce smoking exposure and tobacco-related health inequalities, local updated estimates are particularly important. In our knowledge, there are no estimates at the local/regional level for Italy on the burden of disease due to smoking, and there are no studies that directly use cancer registry data for the estimation of YLD and its attribution to smoking in Italy. Some in-depth analyses were made using GBD data for Italy [10] and, recently, Italian cancer cases attributable to smoking were estimated using data from some Italian cancer registries [11].

## Methods

The aim of this study is to estimate the burden of LC and its attribution to smoking in terms of YLDs for the Tuscany region and at the sub-regional level in 2022 using local and updated data and taking into account all the possible sources of uncertainty. This analysis was carried out within the "Attributable CAncer Burden in Tuscany: smoking, environmental and occupational risk factors and evaluation of prevention strategies" (ACAB) study funded by the Tuscany Region.

### Estimation of YLD

The sex, area and age-specific YLD is given by the sum over cancer phases (*s*) of the products of the person-time spent in each severity-specific cancer phase ($PY_s$) and the corresponding disability weight ($W_s$):

$$YLD = \sum_s PY_s \cdot W_s$$

We considered the following cancer phases: diagnosis and primary therapy; controlled phase; metastasis;

terminal phase. We considered surviving cases as those who survived for over 10 years after diagnosis and for them we assumed only the first two phases.

We derived the disability weights for the cancer phases from the GBD Study [12] (see S1 in Supplementary material). We used an incidence-based disease model (IBDM) which allows for estimation of the total person-months spent in the different cancer phases [12]. On the basis of LC incidence and survival (or 10 years for surviving cases), we assumed a duration for each phase. In accordance with the literature, we assumed the duration of 1 month for the terminal phase [12]. We used the duration of diagnosis and primary therapy estimated respectively from the UK 2001–2002 "General Practice Research Database" and the UK "National Survey of NHS Patients: Cancer" by adding two months in order to include the duration of treatment [12, 13]. We used the duration of the metastatic phase estimated in the Surveillance, Epidemiology and End Results (SEER) program, considering patients diagnosed between 2000 and 2017 [14]. Finally, we estimated the duration of the controlled phase as the remainder of total survival (or the remainder of 10 years for surviving cases).

We used sex, age, time and province-specific data on LC incidence and survival from the Tuscany Cancer Registry (ages ≥ 15, years 2004–2016 for Florence and Prato, 2013–2016 for the other eight Tuscan provinces -Arezzo, Grosseto, Livorno, Lucca, Massa-Carrara, Pisa, Pistoia and Siena) followed up to 2022. By implementing different strategies based on an incidence and a survival estimation procedure, we were able to estimate YLDs for all Tuscan provinces for each year in 2013–2022 (see S2 in Supplementary Materials). Finally, we obtained YLDs by local health unit (LHU) by reproportioning the province-specific YLD according to the population size when needed. This was done in order to align YLD results with the smoking ones that are estimated by LHUs, which are geographical areas smaller that the provinces and for which cancer data were not available.

#### Estimation of the burden attributable to smoking

We estimated YLDs from LC attributable to smoking using the Comparative Risk Assessment approach, which estimates the contribution of a risk factor to a disease as a proportion of the whole burden by means of the population attributable fraction (PAF), which represents the proportion of the disease that would be reduced if exposure to the risk factor was reduced to an ideal scenario [15, 16]. The burden of disease attributable to the risk factor is computed by multiplying the PAF by the burden estimated in terms of YLD.

The sex, age and LHU-specific PAF for smoking in a given year, assuming the ideal scenario of complete absence of exposure, is based on the following equation:

$$PAF = \frac{P(n) + P(c)\int_x P(x)\ RR(x)\,dx + P(f)\int_y P(y)\ RR(y)\,dy - 1}{P(n) + P(c)\int_x P(x)\ RR(x)\,dx + P(f)\int_y P(y)\ RR(y)\,dy}$$

where P(n), P(c), and P(f) are respectively the prevalence of never, current and former smokers in the given year, P(x) and P(y) are the prevalence distributions respectively by pack-years among current smokers and by years since quitting among former smokers in the given year, and RR(x) and RR(y) are the corresponding relative risks. We selected dose-response risk curves RR(x) and RR(y) from the literature by applying a transformation for RR(y) (see S3 in Supplementary Material) [17]. In the PAF estimation, by taking into account pack-years in current smokers, which is a cumulative measure of exposure, and time since quitting in former smokers, we are able to consider the time period between smoking exposure and LC occurrence.

We obtained a sample from the posterior distribution of the sex, age, year and LHU-specific prevalence of current, former and never smokers by implementing a Bayesian Dirichlet-Multinomial regression model to data from the surveillance systems carried out on people aged ≥ 15 years by the Italian National Institute of Health since 2008 "Progress by local health units towards a healthier Italy" (PASSI) and "PASSI d'Argento" [18, 19] (see S4 in Supplementary material).

We generated age and sex-specific distributions of current smokers by pack-years for the whole Tuscany region through a model that simulates individual smoking histories grounding on GBD methodology [20]. The model is based on the distribution of age of smoking initiation from the National Institute of Statistics (ISTAT) "Health conditions and use of health services" (1994,1999,2004,2013) multipurpose survey (https://www.istat.it/it/archivio/5471) and on the amount smoked estimated from the ISTAT "Aspects of daily life" (1993–2019) multipurpose survey (https://www.istat.it/en/archivio/186845) adjusted for data on annual total sales (see S5 in Supplementary Material).

We estimated age and sex-specific distributions of former smokers by time since quitting for the whole Tuscany region from the ISTAT "Health conditions and use of health services" (1994,1999,2004,2013) surveys (not reported).

Finally, we computed the PAF by applying the formula and estimated the number of YLDs from LC due to smoking for each sex and LHU, by applying the sex and age-specific PAF to the corresponding YLD for each LHU and summing over ages.

We present results as rough counts and age-standardized rates per 100,000 with the European 2013 population as standard.

### Uncertainty propagation

We sampled each uncertain quantity from an appropriate distribution 1,000 times in a Monte Carlo framework. We then generated point estimates and 95% UIs by taking the mean and the 2.5 and 97.5 percentiles of the simulated values. The distributions for uncertainty propagation in YLD and PAF estimation are reported in section S6 in Supplementary Material.

### Ethical considerations

This study received ethics committee approval from Comitato Etico Regionale per la Sperimentazione Clinica della Regione Toscana and consent to participate was not necessary since only anonymized and pooled data were used. This study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) and a completed GATHER checklist is provided in Supplementary material S7. All statistical analyses were performed using R software version 4.2.2 (R Development Core Team, 2022). The R packages "splines", "flexsurv" and "mixdist" were used to implement the models for cancer incidence and survival, and the to model probabilistic distributions in uncertainty propagation, respectively.

## Results

### YLD from lung cancer

We estimated that in Tuscany in 2022, LC accounted for 194.4 (95% UI=125.7, 314.2) and 541.4 (95% UI=319.0, 878.0) YLDs in females and males, respectively, with an age-standardized rate of 7.8 (95% UI=2.3, 17.3) and 25.5 (95% UI=7.3, 52.7) per 100,000, respectively (Table 1, Supplementary Fig. 1). In both females and males, the number of YLDs increased by age reaching the maximum around 70–74 years of age and decreasing thereafter (Table 1).

Analyzing the spatial distribution of YLD rates, we observed slight variations with the highest rates estimated in the Florence LHU (10.7, 95% UI=1.9,26.4 per 100,000 females and 29.8, 95% UI=3.9,76.4 per 100,000 males) and the lowest in the Arezzo LHU (5.7, 95%

**Table 1** Years lived with disability (YLDs) counts (N) and age-standardized rates per 100,000 in 2022 by Local Health Unit (LHU), age and sex. UI: uncertainty interval

| LHU/Age | *N* (95%UI) | | | | | | Rate per 100,000 (95% CI) |
|---|---|---|---|---|---|---|---|
| | 18–34 | 35–49 | 50–69 | 70–74 | 75+ | all ages | |
| ***Males*** | | | | | | | |
| Arezzo | 0.3 (0.0,1.5) | 1.9 (0.5,4.4) | 20.0 (9.1,36.5) | 8.5 (2.7,19.5) | 10.6 (5.7,19.3) | 41.4 (22.7,69.5) | 21.1 (6.1, 49.8) |
| Empoli | 0.1 (0.0,0.2) | 1.6 (0.7,3.4) | 15.3 (7.8,30.9) | 5.9 (1.2,15.0) | 11.1 (3.4,23.4) | 33.9 (17.7,67.1) | 28.4 (5.2, 68.0) |
| Florence | 0.5 (0.2,1.1) | 6.1 (2.6,13.8) | 58.4 (28.0,129.9) | 24.5 (3.6,66.8) | 48.8 (10.2,108.9) | 138.2 (64.6,289.0) | 29.8 (3.9, 76.4) |
| Grosseto | 0.2 (0.0,1.2) | 0.7 (0.1,2.0) | 14.5 (6.5,28.2) | 6.6 (2.2,16.1) | 9.8 (4.9,18.6) | 31.9 (17.4,55.5) | 23.6 (7.0, 56.6) |
| Livorno | 0.0 (0.0,0.2) | 1.7 (0.4,3.9) | 23.7 (11,44.2) | 7.8 (2.5,19.0) | 16.1 (8.4,29.7) | 49.4 (27.6,85.1) | 24.7 (7.4, 58.0) |
| Lucca | 0.0 (0.0,0.0) | 1.2 (0.4,2.8) | 15.7 (7.1,29.6) | 5.5 (1.8,12.5) | 9.3 (4.9,17.4) | 31.7 (17.4,53.4) | 24.3 (7.1, 56.6) |
| Massa Carrara | 0.4 (0.0,1.8) | 1.8 (0.5,3.9) | 12.0 (5.3,22.5) | 4.3 (1.4,9.8) | 9.1 (4.8,17.3) | 27.5 (15.2,45.6) | 23.8 (6.7, 58.0) |
| Pisa | 0.0 (0.0,0.0) | 1.6 (0.4,3.9) | 24.7 (11.2,46.6) | 7.3 (2.3,17.0) | 14.5 (7.5,27.5) | 48.2 (26.8,82.9) | 22.8 (6.9, 52.6) |
| Prato | 0.1 (0.1,0.3) | 2.1 (0.9,4.7) | 17.8 (8.5,39.9) | 7.0 (1.0,19.2) | 12.9 (2.6,28.9) | 40.0 (19.3,84.2) | 29.7 (3.9, 76.2) |
| Pistoia | 0.0 (0.0,0.0) | 2.3 (0.6,5.1) | 22.0 (10.3,40.6) | 6.6 (2.1,16.1) | 12.8 (6.7,23.8) | 43.7 (24.4,73.8) | 26.0 (7.7, 60.7) |
| Siena | 0.2 (0.0,1.2) | 2.4 (0.7,5.1) | 14.4 (6.4,28.1) | 5.5 (1.7,13.3) | 9.7 (5.2,17.7) | 32.2 (17.9,55.8) | 21.5 (6.0, 52.6) |
| Viareggio | 0.0 (0.0,0.0) | 0.8 (0.3,1.9) | 12.0 (5.5,22.7) | 3.9 (1.3,8.8) | 6.6 (3.5,12.3) | 23.3 (12.7,39.8) | 24.3 (7.1, 56.6) |
| Tuscany | 1.9 (0.6,4.5) | 24.2 (10.4,44.1) | 250.5 (131.4,444.8) | 93.4 (27.1,195.4) | 171.4 (82.6,310.1) | 541.4 (319.0,878.0) | 25.5 (7.3, 52.7) |
| ***Females*** | | | | | | | |
| Arezzo | 0.0 (0.0,0.1) | 0.6 (0.1,1.4) | 6.3 (2.9,12.7) | 1.7 (0.6,4.0) | 4.1 (2.4,7.1) | 12.6 (7.7,19.3) | 5.7 (1.7, 16.1) |
| Empoli | 0.0 (0.0,0.1) | 0.5 (0.3,1.2) | 5.5 (2.9,11.6) | 2.4 (0.5,5.7) | 5.3 (1.9,11.1) | 13.8 (7.9,26.6) | 9.9 (2.0, 23.1) |
| Florence | 0.1 (0.1,0.3) | 2.2 (1.5,2.0) | 22.9 (11.3,52.0) | 10.5 (1.9,26.5) | 25.1 (7.8,55.2) | 60.9 (32.8,124.6) | 10.7 (1.9, 26.4) |
| Grosseto | 0.0 (0.0,0.0) | 0.7 (0.1,1.8) | 4.7 (2.1,9.2) | 1.0 (0.4,2.7) | 2.6 (1.5,4.6) | 9.0 (5.5,14.5) | 6.1 (1.6, 17.8) |
| Livorno | 0.0 (0.0,0.0) | 1.1 (0.2,2.5) | 5.8 (2.7,12.1) | 2.4 (0.9,6.2) | 5.4 (3.2,9.2) | 14.7 (9.2,23.1) | 6.4 (1.9, 17.8) |
| Lucca | 0.0 (0.0,0.0) | 0.6 (0.1,1.5) | 4.4 (2.1,8.8) | 1.6 (0.6,4.1) | 4.2 (2.5,7.4) | 10.9 (6.7,16.8) | 7.3 (2.4, 20.2) |
| Massa Carrara | 0.0 (0.0,0.1) | 0.4 (0.0,1.1) | 3.5 (1.6,7.3) | 1.2 (0.4,2.9) | 2.6 (1.5,4.6) | 7.7 (4.6,12.2) | 5.7 (1.6, 16.5) |
| Pisa | 0.1 (0.0,0.1) | 0.4 (0.1,1.2) | 7.3 (3.3,14.7) | 2.2 (0.8,5.5) | 4.9 (2.8,8.4) | 14.9 (9.0,23.6) | 6.1 (1.9, 17.1) |
| Prato | 0.0 (0.0,0.1) | 0.7 (0.3,1.6) | 6.8 (3.4,15.3) | 2.9 (0.5,7.4) | 6.5 (2.1,14.2) | 17.0 (9.2,34.7) | 10.6 (1.9, 26.0) |
| Pistoia | 0.0 (0.0,0.1) | 0.7 (0.1,1.7) | 6.0 (2.7,12.3) | 1.8 (0.7,4.4) | 5.0 (3.0,8.7) | 13.5 (8.1,21.4) | 6.9 (2.1, 19.1) |
| Siena | 0.1 (0.0,0.2) | 0.7 (0.1,2.0) | 5.9 (2.7,11.9) | 1.5 (0.5,3.6) | 3.0 (1.7,5.3) | 11.1 (6.7,17.8) | 6.5 (1.9, 18.7) |
| Viareggio | 0.0 (0.0,0.0) | 0.4 (0.1,1.1) | 3.5 (1.6,7.0) | 1.2 (0.5,3.1) | 3.3 (1.9,5.8) | 8.4 (5.2,13.0) | 7.3 (2.4, 20.2) |
| Tuscany | 0.4 (0.1,0.8) | 9.0 (3.4,17.3) | 82.7 (44.4,141.1) | 30.3 (9.0,62.5) | 72.0 (35.7,128.4) | 194.4 (125.7,314.2) | 7.8 (2.3, 17.3) |

UI=1.7, 16.1 per 100,000 females and 21.1, 95% UI=6.1, 49.8 per 100,000 males) (Table 1).

### Smoking prevalence and PAF

By visual inspection of traceplots, we checked that the results of the Bayesian prevalence model produced stationary Markov chains and all chains reached the equilibrium distribution.

In 2022, 17.1% (95% UI=1.11%, 20.1%) of females and 19.5% (95% UI=16.2%, 23.7%) of males were current smokers in Tuscany, with a higher prevalence in middle-aged females (24.3%, 95% UI=18.1%, 30.6%, in age class 35–49) and in young males (28.6%, 95% UI=21.2%, 35.2%, in age class 18–34). Former smokers were 16.9% (95% UI=13.7%,19.8%) in females and 29.9% (95% UI=24.7%, 33.3%) in males, with a higher proportion in women aged 70–74 years (26.3%, 95% UI=22.4%, 30.3%) and men over 75 years (40.3%, 95% UI=33.9%, 47.6%) (Supplementary Fig. 2).

Analyzing the spatial distribution, slight variations were estimated, with the highest prevalence of current smokers in both females and males in the LHU of Siena (19.4%, 95% UI=15.1%, 23.5% in females; 23.7%, 95% UI=19.9%, 27.2% in males). Among females, the highest prevalence of former smokers was registered in the LHU of Florence (20.2%, 95% UI=15.9%, 24.7%), whereas in males in Lucca LHU (34.2%, 95% UI=30.6%, 37.2%) (Supplementary Figs. 3, 4).

Table 2 reports the PAF estimated for females and males for 2022 by age and LHU: in females, the PAF in the whole Tuscany region showed values ranging from 41.3% (95% UI=40.6%,42.0%) to 60.8% (95% UI=60.5%,61.2%) in persons aged respectively over 75 years and 50–69 years. On the contrary, in males, the lowest fraction (40.2%, 95%UI=39.3%,41.2%) was estimated in young men, whereas the highest (69.7%, 95%UI=69.0%,70.3%) was in those aged 70–74 years (Table 2).

We estimated that in Tuscany in 2022, smoking caused 102.5 (95% UI=66.1,168.1) and 358.73 (95% UI=211.9,579.3) YLDs in females and males, respectively, with an age-standardized rate of 4.2 (95% UI=2.7,7.0) and 16.9 (95% UI=10.0,27.5) per 100,000. Slight variations by LHU were estimated (Fig. 1) with higher YLD rates in the LHU of Florence for both females and males (8.8, 95% UI=4.3,18.0, and 23.5, 95% UI=10.8,49.4 per

**Table 2** Smoking population attributable fraction (PAF) in 2022 by Local Health Unit (LHU), age class and sex. UI: uncertainty interval

| LHU/Age | PAF (95%UI) | | | | | |
|---|---|---|---|---|---|---|
| | 18–34 | 35–49 | 50–69 | 70–74 | 75+ | All ages |
| **Males** | | | | | | |
| Arezzo | 36.1 (35.0,37.1) | 67.9 (67.6,68.2) | 66.7 (66.4,67.0) | 81.6 (81.3,81.9) | 73.3 (72.9,73.7) | 65.1 (64.9,65.4) |
| Empoli | 33.4 (32.1,34.6) | 67.5 (67.1,67.8) | 68.1 (67.8,68.4) | 77.4 (77.0,77.9) | 63.5 (62.9,64.1) | 62.0 (61.7,62.3) |
| Florence | 53.7 (53.2,54.2) | 68.5 (68.2,68.7) | 71.9 (71.7,72.1) | 73.1 (72.8,73.5) | 63.1 (62.7,63.5) | 66.1 (65.9,66.2) |
| Grosseto | 42.3 (41.0,43.5) | 61.4 (60.9,61.9) | 64.0 (63.6,64.3) | 82.3 (81.9,82.7) | 72.5 (72.1,73.0) | 64.5 (64.2,64.8) |
| Livorno | 18.0 (16.9,19.2) | 66.7 (66.4,67.0) | 67.3 (67.0,67.6) | 86.6 (86.3,86.8) | 69.1 (68.7,69.5) | 61.5 (61.3,61.8) |
| Lucca | 30.5 (29.1,31.8) | 64.1 (63.7,64.5) | 69.5 (69.2,69.8) | 78.2 (77.8,78.6) | 76.2 (75.8,76.6) | 63.7 (63.4,64.0) |
| Massa Carrara | 24.9 (23.4,26.5) | 65.4 (65.0,65.9) | 67.7 (67.3,68.0) | 74.3 (73.6,75.0) | 69.9 (69.3,70.6) | 60.5 (60.1,60.8) |
| Pisa | 47.5 (46.7,48.4) | 68.1 (67.7,68.3) | 68.5 (68.2,68.8) | 73.0 (72.5,73.5) | 81.8 (81.5,82.1) | 67.8 (67.5,68.0) |
| Prato | 48.0 (47.0,48.9) | 67.9 (67.6,68.2) | 71.2 (70.9,71.5) | 76.8 (76.1,77.5) | 54.9 (54.4,55.5) | 63.7 (63.5,64.0) |
| Pistoia | 31.8 (30.6,32.9) | 64.3 (63.9,64.7) | 71.9 (71.6,72.1) | 70.4 (69.6,71.1) | 63.5 (62.7,64.2) | 60.4 (60.0,60.7) |
| Siena | 31.1 (29.9,32.3) | 66.0 (65.7,66.4) | 68.8 (68.5,69.2) | 72.9 (72.2,73.5) | 70.8 (70.3,71.4) | 61.9 (61.6,62.3) |
| Viareggio | 24.6 (23.0,26.3) | 60.5 (60.0,61.1) | 68.5 (68.1,68.9) | 83.5 (83.0,83.9) | 82.9 (82.5,83.3) | 64.0 (63.6,64.4) |
| Tuscany | 40.2 (39.3,41.2) | 67.3 (67.0,67.6) | 68.1 (67.8,68.4) | 69.7 (69.0,70.3) | 61.8 (61.2,62.5) | 61.4 (61.2,61.7) |
| ***Females*** | | | | | | |
| Arezzo | 50.0 (49.2,50.9) | 61.0 (60.5,61.4) | 59.4 (59.0,59.7) | 63.3 (62.0.6,64) | 48.4 (47.8,49.0) | 56.4 (56.1,56.7) |
| Empoli | 44.1 (42.9,45.2) | 54.2 (53.6,54.8) | 48.9 (48.4,49.5) | 65.9 (65.2,66.5) | 61.4 (60.8,61.9) | 54.9 (54.6,55.2) |
| Florence | 49.9 (49.4,50.5) | 63.1 (62.8,63.4) | 62.3 (62.0,62.5) | 63.8 (63.4,64.2) | 57.5 (57.1,57.8) | 59.3 (59.1,59.5) |
| Grosseto | 56.2 (55.3,57.1) | 54.9 (54.2,55.4) | 63.2 (62.8,63.6) | 47.0 (45.6,48.4) | 45.1 (44.2,45.9) | 53.3 (52.9,53.7) |
| Livorno | 39.0 (38.0,40.1) | 52.3 (51.8,52.8) | 61.6 (61.2,62.0) | 65.2 (64.7,65.6) | 69.1 (68.7,69.4) | 57.4 (57.1,57.7) |
| Lucca | 49.8 (48.7,50.8) | 57.1 (56.5,57.6) | 56.4 (55.9,56.9) | 69.9 (69.2,70.5) | 39.0 (38.2,39.8) | 54.4 (54.1,54.8) |
| Massa Carrara | 41.2 (39.8,42.5) | 56.3 (55.7,56.9) | 60.4 (59.9,60.8) | 61.2 (60.3,62.1) | 51.3 (50.6,52.0) | 54.1 (53.7,54.5) |
| Pisa | 34.7 (33.6,35.8) | 57.5 (57.0,57.9) | 56.1 (55.7,56.5) | 77.7 (77.3,78.0) | 71.3 (71.0,71.6) | 59.4 (59.2,59.7) |
| Prato | 52.7 (51.8,53.6) | 61.0 (60.6,61.5) | 61.8 (61.4,62.1) | 59.8 (58.7,60.8) | 46.5 (45.9,47.2) | 56.4 (56.0,56.7) |
| Pistoia | 31.9 (30.7,33.1) | 47.3 (46.7,48.0) | 51.7 (51.3,52.2) | 45.8 (44.9,46.7) | 43.1 (42.4,43.8) | 44.0 (43.6,44.3) |
| Siena | 51.8 (50.9,52.7) | 57.5 (56.9,58.0) | 66.9 (66.6,67.2) | 67.0 (66.2,67.6) | 42.8 (42.0,43.5) | 57.2 (56.9,57.5) |
| Viareggio | 43.4 (42.0,44.9) | 45.6 (44.8,46.4) | 54.9 (54.3,55.4) | 69.0 (68.1,69.7) | 68.0 (67.6,68.4) | 56.2 (55.8,56.6) |
| Tuscany | 47.4 (46.5,48.2) | 57.1 (56.7,57.6) | 60.8 (60.5,61.2) | 56.2 (55.5,57.0) | 41.3 (40.6,42.0) | 52.6 (52.3,52.9) |

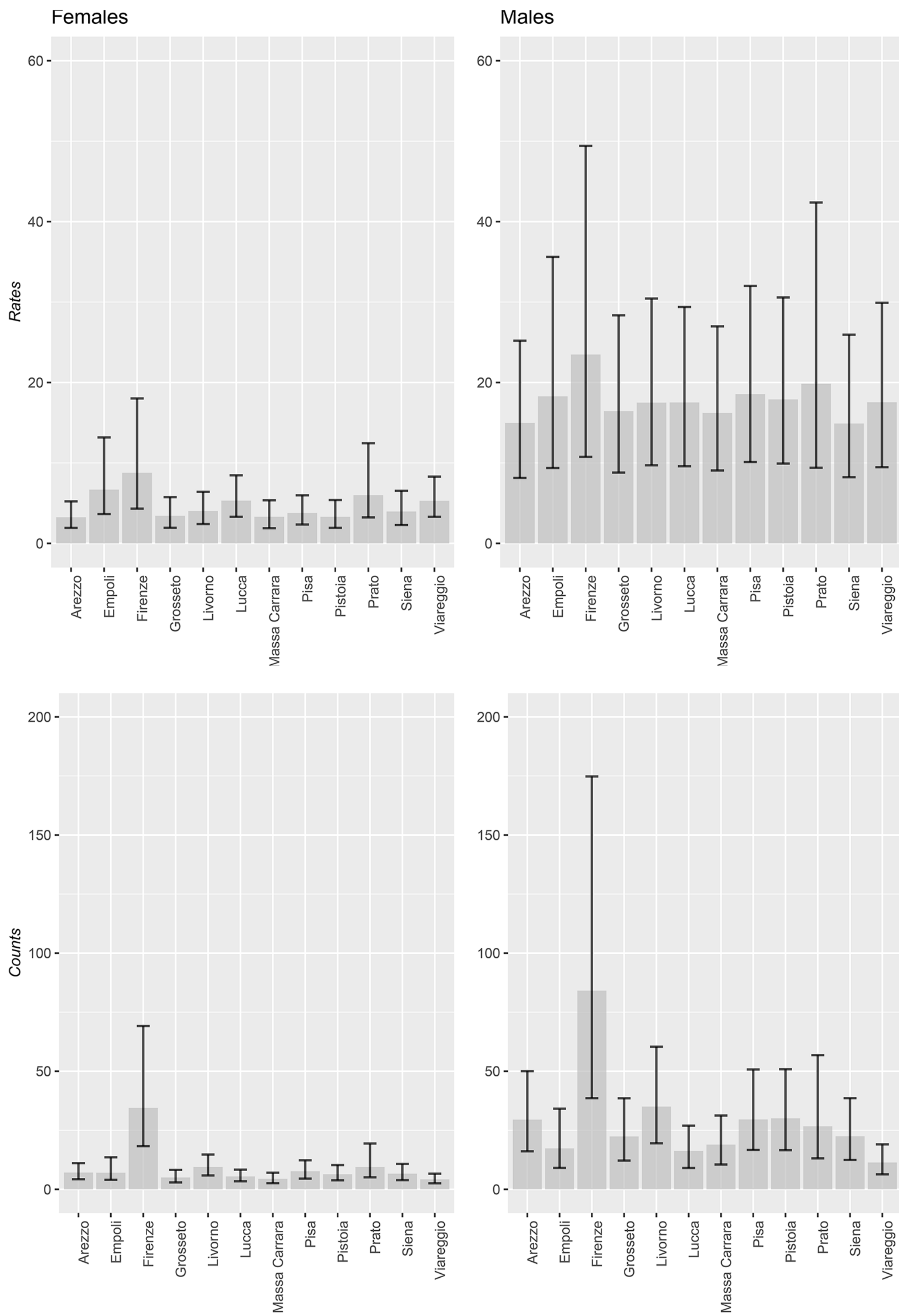


**Fig. 1** Years lived with disability (YLD) from lung cancer attributable to smoking (age-standardized rate per 100,000 and counts) by sex and Local Health Unit (LHU), 2022: point estimates and 95% uncertainty intervals

100,000, respectively) and lower in Arezzo (3.3, 95% UI=1.9,5.2 and 15.0, 95% UI=8.1, 25.2 per 100,000).

## Discussion

We estimated that in 2022 in Tuscany LC caused 7.8 (95% UI=2.3,17.3) and 25.5 (95% UI=7.3,52.7) years of ill health per 100,000 females and males, respectively, out of which 53% and 66% were caused by smoking (YLD per 100,000: 4.2, 95% UI=2.7,7.0 in females; 16.9, 95% UI=10.0,27.5 in males).

Lung cancer incidence in the last decades had a decreasing trend among males, whereas it is still increasing among females [21, 22]. Although both the YLDs from LC and the burden attributable to smoking are lower in women compared to men, it should be highlighted that women are experiencing a delay in the smoking epidemic, as well known from the literature [23] and as can also be deduced from the delay in the distribution by age of both the smoking prevalence and the PAF in women compared to men. This suggests that a further increase in the burden due to smoking is expected in the next years in females, as already evident from the growing trend in LC incidence. However, in the last years, survival from LC increased, especially in women, for non-small-cell LC (NSCLC), which is the LC histological subtype mainly associated with smoking, presumably due to NSCLC diagnostic and treatment innovation that has positively and powerfully impacted the survival length [21, 22].

Both YLD and smoking habits showed slight variations by LHU, resulting in a variable burden from smoking with higher YLD in 2022 in the LHU of Florence for both females and males, and lower in Arezzo LHU. The modeling procedure, which was based on incidence and survival data from Prato and Florence only, may have smoothed out any further differences by LHU. Previous studies carried out in the Tuscany region found that, for cohorts born between 1905 and 1940, risks of mortality for LC were higher in all industrial areas moving from the North-Western part of the region, the historically developed part, to the rural South-East part, e.g. Arezzo and Siena LHU [24, 25], associated to socio-demographic factors [26]. Our findings confirm a geographic transition in time as hypothesized in a study on LC mortality at the national level [27], suggesting a shift to higher risks in more urbanized areas. These results suggest that, albeit in a small geographical area, the differences in LC burden and risk factor exposure are not negligible and need special attention from decision-makers.

Our results based on the Cancer Registry of Tuscany and local surveys are in line with those estimated for Italy from the GBD study which used different sources of information (2019 YLD rate per 100,000: 10.3, 95% UI=7.0,14.3 in females and 23.5, 95% UI=15.9,33.3 in males; YLD rate due to smoking per 100,000: 6.1, 95% UI=4.1, 8.5 in females, 17.4, 95% UI=11.7,24.8 in males) [5]. As evidenced by our UIs, our results appear more uncertain than the GBD ones, because they allow for multiple and diverse sources of uncertainty. This larger variability around the estimates should not be seen as a flaw but rather as a strength of our study, since it follows from a correct procedure of error propagation and reflects actual sampling and epistemic uncertainties.

This study has some limitations. First, in the estimation procedure, we did not take into account the COVID-19 pandemic which may have reduced the LC incidence for 2020 and 2021 due to delays in diagnosis and, in part, to the increased deaths for COVID-19 [28] (LC incidence should have returned to previous values in 2022). Moreover, the effect of the COVID-19 pandemic, with the associated stay-at-home measures, resulted in a decrease in smoking prevalence especially among youths, albeit with an increase in smoking intensity [29]. However, the disease burden due to smoking should not have undergone substantial changes due to the lagged effect of smoking on cancer [30].

Secondly, the dose-risk curves come from a synthesis which includes studies conducted in countries with lifestyles and habits different from those of the context covered by this study [17]. Asian countries, for example, have smoking habits and concurrent causes of LC different from Tuscan ones due to lower smoking prevalence among women or higher ambient air pollution. However, meta-analytical risk estimates should not be highly affected by such differences due to the large strength of association between smoking and LC.

In addition, the parameters used for the duration of cancer phases and for disability weights come from populations other than those under study (different countries and time frame). The parameter used for the duration of diagnosis and primary therapy cancer phase was estimated in the UK more than a decade before the study period. Health care, health access and cancer treatments and protocols produce waiting times that vary considerably over time and place [31]. However, by carrying out a sensitivity analysis we found that the variability of such estimates does not affect our results (Supplementary material S1). Moreover, the duration of the metastatic LC phase is based on estimates from the SEER US population which is slightly younger that the Tuscany one. However, accounting for uncertainty on parameters protects us from obtaining results that are dependent only on the distribution's mean. Nonetheless, further efforts are needed to improve these estimates by using local data.

Finally, our modeling strategy is carried out in a frequentist framework, except for the smoking prevalence model for which a Bayesian model was used due to its hierarchical complexity.

One of the strengths of this study is the use of local data from the Tuscany Cancer Registry which draws upon multiple sources of information, such as hospital discharge records, death certificates, pathology reports and other sources. Moreover, we used data from the PASSI survey at the local level, allowing us to produce detailed estimates of the burden of disease from LC and its attribution to smoking. Moreover, most sources of uncertainty were taken into account and propagated in the modeling procedure, producing timely updated estimates with a measure of uncertainty.

## Conclusions

In conclusion, the methodology described in our study, in part grounded in the GBD study, together with the use of local estimates on both disease incidence and exposure prevalence could be applied to different diseases and risk factors, and to explore disparities related to socio-economic level. Finally, the detailed and timely updated estimates produced in our study can help policymakers and practitioners to set priorities and allocate resources at the regional level and practitioners to improve communication with patients.

### Abbreviations

| | |
|---|---|
| ACAB | Attributable Cancer burden in tuscany |
| DALY | Disability adjusted life year |
| FCTC | Framework convention on tobacco control |
| GATHER | Guidelines for accurate and transparent health estimates reporting |
| GBD | Global burden of diseases |
| IBDM | Incidence-based disease model |
| ISTAT | Italian national institute of statistics |
| LC | Lung cancer |
| LHU | Local health unit |
| NSCLC | Non-small-cell lung cancer |
| PAF | Population attributable fraction |
| PASSI | Progress by local health units towards a healthier Italy |
| SCS | Smoking cessation services |
| SEER | Surveillance, epidemiology and end results |
| UI | Uncertainty interval |
| UK | United kingdom |
| WHO | World health organization |
| YLD | Years lived with disability |
| YLL | Years of life lost |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-024-20109-4.

Supplementary Material 1

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Not applicable.

### Author contributions

MCM performed the statistical analyses; MB contributed to statistical analyses and wrote the final version of the manuscript; AC, GGa, GMan, FP contributed in data acquisition; GGo, ML, GMas, LM contributed to data interpretation; GC conceived the work, contributed to statistical analyses and wrote the final version of the manuscript; all authors read and approved the final manuscript.

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### Data availability

Most of the data that support the findings of the present study cannot be shared for ethical or legal reasons. Informations could be obtained from the corresponding author. Other data and materials are available from the corresponding author upon reasonable request.

## Declarations

### Ethics approval and consent to participate

The study received ethics committee approval from Comitato Etico Regionale per la Sperimentazione Clinica della Regione Toscana, Sezione: AREA VASTA CENTRO10/05/2022 (22207_oss). Consent to participate was not necessary since only anonymized and pooled data were used.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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### References

1. Associazione Italiana Oncologia Medica (AIOM). - Associazione Italiana Registro Tumori (AIRTUM). I numeri del cancro in Italia 2023. Brescia: Intermedia Editore; 2023.[online] https://www.aiom.it/wp-content/uploads/2023/12/2023_AIOM_NDC-web.pdf (Accessed 05/02/2024).
2. Bray F, Colombet M, Mery L et al. Cancer Incidence in Five Continents, Vol. XI. IARC Scientific Publication No. 166. Lyon: International Agency for Research on Cancer [online]. 2021. https://publications.iarc.fr/597. (Accessed 05/02/2024).
3. Murray CJL, Salomon JA, Mathers CD. A critical examination of summary measures of population health. In: Murray CJL, Salomon JA, Mathers CD, Lopez AD. Summary measures of population health: concepts, ethics, measurement, and applications. Geneva: World Health Organization. 2002:13–40.
4. Murray CJL. The global burden of Disease Study at 30 years. Nat Med. 2022;28:2019–26.
5. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019. (GBD 2019) Results. Seattle, United States: Institute for Health Metrics and Evaluation (IHME) [online]. 2020. https://vizhub.healthdata.org/gbd-results/ (Accessed 02/23/2024).
6. World Health Organization. WHO framework convention on tobacco control [online]. 2003. https://www.who.int/fctc/text_download/en (Accessed 05/02/2024).
7. World Health Organization. MPOWER measures [online]. 2008. https://www.emro.who.int/tfi/mpower/index.html (Accessed 05/02/2024).
8. Levy D, Gallus S, Blackman K, Carreras G, La Vecchia C, Gorini. Italy SimSmoke: the effect of tobacco control policies on smoking prevalence and smoking attributable deaths in Italy. BMC Public Health. 2012;12:709. https://doi.org/10.1186/1471-2458-12-709.
9. National Institute of Health. Guide for the Italian local health services for tobacco use cessation. Edited by the National Centre on Addiction and Doping 2021 (in Italian) [online] 2021. https://www.iss.it/documents/20126/0/21_S1+web.pdf/272d5cb6-e163-f47f-1168-f0d794e327c9?t=1622450825748 (Accessed 05/02/2024).
10. Bosetti C, Traini E, Alam T, Allen CA, Carreras G, Compton K, Fitzmaurice C, Force LM, Gallus S, Gorini G, Harvey JD, Kocarnik JM, La Vecchia C, Lugo A, Naghavi M, Pennini A, Piccinelli C, Ronfani L, Xu R, Monasta L. National burden of cancer in Italy, 1990–2017: a systematic analysis for the global burden of disease study 2017. Sci Rep. 2020;10:22099. https://doi.org/10.1038/s41598-020-79176-3.
11. Collatuzzo G, Malvezzi M, Mangiaterra S, Di Maso M, Turati F, Parazzini F, Pelucchi C, Alicandro G, Negri E, La Vecchia C, Boffetta P. Cancers attributable to

tobacco smoking in Italy in 2020. Cancer Epidemiol. 2024;92:102623. https://doi.org/10.1016/j.canep.2024.102623.
12. Global Burden of Disease 2019 Cancer Collaboration. Cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life years for 29 cancer groups from 2010 to 2019: a systematic analysis for the global burden of Disease Study 2019. JAMA Oncol. 2021. https://doi.org/10.1001/jamaoncol.2021.6987.
13. Allgar VL, Neal RD. Delays in the diagnosis of six cancers: analysis of data from the National Survey of NHS patients: Cancer. Br J Cancer. 2005;92:1959–70. https://doi.org/10.1038/sj.bjc.6602587.
14. Hu S, Zhang W, Guo Q, et al. Prognosis and survival analysis of 922,317 Lung Cancer patients from the US based on the most recent data from the SEER database (April 15, 2021). Int J Gen Med. 2021;14:9567–88. https://doi.org/10.2147/IJGM.S338250.
15. Ezzati M, Lopez AD, Rodgers A, et al. Selected major risk factors and global and regional burden of disease. Lancet. 2002;360:1347–60. https://doi.org/10.1016/S0140-6736(02)11403-6.
16. World Health Organization. In: Ezzati M, Lopez AD, Rodgers A, Murray CJL, editors. Comparative quantification of health risks. Geneva: World Health Organization; 2004.
17. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019. (GBD 2019). Relative Risks. Seattle, United States of America. Institute for health Metrics and Evaluation (IHME) [online]. 2020. https://doi.org/10.6069/GYVX-YR58 (Accessed 02/23/2024).
18. Baldissera S, Campostrini S, Binkin N et al. Features and initial assessment of the Italian Behavioral Risk Factor Surveillance System (PASSI), 2007–2008. Prev Chronic Dis. 2011; 8:A24. PMID: 21159236.
19. Contoli B, Carrieri P, Masocco M, et al. PASSI d'Argento (silver steps): the main features of the new nationwide surveillance system for the ageing Italian population, Italy 2013–2014. Ann Ist Super Sanita. 2016;52:536–42. https://doi.org/10.4415/ANN_16_04_13.
20. GBD 2019 Tobacco Collaborators. Spatial, temporal, and demographic patterns in prevalence of smoking tobacco use and attributable disease burden in 204 countries and territories, 1990–2019: a systematic analysis from the global burden of Disease Study 2019. Lancet. 2021;397(10292):2337–60. https://doi.org/10.1016/S0140-6736(21)01169-7.
21. Mangone L, Marinelli F, Bisceglia I, et al. Changes in the histology of Lung Cancer in Northern Italy: impact on incidence and mortality. Cancers (Basel). 2023;15:3187. https://doi.org/10.3390/cancers15123187.
22. Trama A, Boffi R, Contiero P, et al. Trends in lung cancer and smoking behavior in Italy: an alarm bell for women. Tumori. 2017;103:543–50. https://doi.org/10.5301/tj.5000684.
23. Gorini G, Carreras G, Allara E, Faggiano F. Decennial trends of social differences in smoking habits in Italy: a 30-year update. Cancer Causes Control. 2013;24(7):1385–91. https://doi.org/10.1007/s10552-013-0218-9.
24. Biggeri A, Catelan D, Dreassi E. The epidemic of lung cancer in Tuscany (Italy): a joint analysis of male and female mortality by birth cohort. Spat Spatiotemporal Epidemiol. 2009;1:31–40. https://doi.org/10.1016/j.sste.2009.07.006.
25. Gorini G, Chellini E, Martini A, et al. Lung cancer mortality trend by birth cohort in men, Tuscany, 1971–2006. Tumori. 2010;96:680–3. https://doi.org/10.1177/030089161009600506.
26. Dreassi E, Biggeri A, Catelan D. Space-time models with time-dependent covariates for the analysis of the temporal lag between socioeconomic factors and lung cancer mortality. Stat Med. 2005;24:1919–32. https://doi.org/10.1002/sim.2063.
27. Catelan D, Biggeri A, Bucchi L, et al. Epidemiologic transition of lung cancer mortality in Italy by sex, province of residence and birth cohort (1920-1929to1960-1969). Int J Cancer. 2023;153:1746–57. https://doi.org/10.1002/ijc.34657.
28. Ferrara G, De Vincentiis L, Ambrosini-Spaltro A, et al. Cancer Diagnostic Delay in Northern and Central Italy during the 2020 Lockdown due to the Coronavirus Disease 2019 Pandemic. Am J Clin Pathol. 2021;155:64–8. https://doi.org/10.1093/ajcp/aqaa177.
29. Carreras G, Lugo A, Stival C et al. Impact of COVID-19 lockdown on smoking consumption in a large representative sample of Italian adults. Tobacco Control 2021:tobaccocontrol-2020-056440. https://doi.org/10.1136/tobaccocontrol-2020-056440
30. Ockene JK, Kuller LH, Svendsen KH, et al. The relationship of smoking cessation to coronary heart disease and lung cancer in the multiple risk factor intervention trial (MRFIT). Am J Public Health. 1990;80:954–8. https://doi.org/10.2105/AJPH.80.8.954.
31. Jacobsen M, Silverstein SC, Quinn M, Waterston LB, Thomas CA, Benneyan JC, Han PK. Timeliness of Access to Lung Cancer diagnosis and treatment: a scoping literature review. Lung Cancer. 2017;112:156–64. https://doi.org/10.1016/j.lungcan.2017.08.011.

## Publisher's note