

Research Article

Can a National Lung Cancer Screening Program in Combination with Smoking Cessation Policies Cause an Early Decrease in Tobacco Deaths in Italy?

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Abstract

Objective is to predict smoking attributable deaths (SAD) for lung cancer and all causes in Italy, 2015 to 2040, assuming a yet unimplemented tobacco control policies (TCP) and a national, low-dose, lung cancer, computed tomography (CT) annual screening program (CT screen).

A dynamic model describing the evolution of smoking habits was developed to estimate quit rates, 1986 to 2009, and to predict SAD under different scenarios: keeping the status quo; raising cigarette taxes by 20%; implementing cessation treatment policies (funding treatment, setting up an active quitline, promoting counseling among health professionals); introducing a three-round annual CT screen for current and former heavy smokers aged 55 to 74, 70% compliance, 20% lung cancer mortality reduction; combining all the above-mentioned measures.

The CT screen brought a 3.0% constant annual reduction in lung cancer SAD and decreased or postponed all-cause SAD by 1.7% annually (a half due to respiratory diseases), relative to the status quo scenario. The effect was noticeable after few years from its introduction. TCP showed a steadily strengthening effect starting from 5 to 10 years after implementation. The lung cancer and all-cause SAD under cessation treatment policies, for instance, were reduced by 8.4% and 12.0% in 2030, respectively, and by 16.1% and 20.0% in 2040. TCP gave a greater effect than CT screen in reducing all-cause SAD because cessation brought about a reduction in smoking-related SAD other than lung cancer and respiratory diseases.

Combining TCP and CT screen could bring about an early decrease in lung cancer and respiratory disease SAD due to CT screen, followed by a more substantial drop in all-cause SAD in subsequent decades due to TCP. *Cancer Prev Res*; 5(6); 874–82. ©2012 AACR.

Introduction

Smoking is a major risk factor for many chronic diseases and tumors and reduces a person's length and quality of life (1). Among smoking attributable diseases, lung cancer remains the leading cause of cancer deaths in Italy and in other Western countries (2).

The implementation of tobacco control policies (TCP) recommended by the World Health Organization Framework Convention on Tobacco Control (WHO FCTC) is considered the leading primary prevention strategy to

reduce smoking prevalence and smoking attributable deaths (SAD) for lung cancer and for all causes at a population level (3). Western countries have already implemented many of these policies, although there is room for improvement (4). In Italy, for example, there could be measures to further increase cigarette taxes and to promote cessation strategies (funding of cessation treatments, setting up an active quitline for smokers, and promoting widespread use of cessation counseling among health professionals; refs. 5, 6).

On the other hand, observational studies have shown that screening with low-dose, helical, computed tomography (CT) can detect smaller sized and earlier stage lung cancers than can be detected symptomatically or with radiographic chest screening (7–9). A number of randomized trials to assess the efficacy of low-dose CT screening have been developed in the United States and Europe (10–13). Recently, the results of the U.S. National Lung Screening Trial showed that lung cancer mortality in the low-dose CT group was 20.0% lower than in the radiography group (14). On the basis of this result, the cost effectiveness of low-dose CT scan in the United States showed that annual screening of persons with at least 20 pack-years of smoking history costs \$126,000 to

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Note: Preliminary results of this work were presented at the Italian Consensus Meeting on Lung Cancer Screening, March 3, 2011, Pisa, Italy and at the 14th World Conference on Lung Cancer, July 3–7, 2011, Amsterdam, The Netherlands.

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doi: 10.1158/1940-6207.CAPR-12-0019

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169,000 per quality-adjusted life-years (QALY; ref. 15). If screen participation doubled background quit rates, the cost was more than halved (40,000–73,000/QALY; ref. 15). Thus, implementing an annual screening in a context in which cessation is strongly promoted to all smokers and specifically to screen participants through development of smoking cessation policies and tax measures may be a scenario to explore.

The main aim of this study is to evaluate the impact on all-cause and lung cancer SAD in Italy between 2015 and 2040 if certain primary and secondary strategies, either alone or in combination, were to have been implemented in 2015—such as cessation treatment policies, a tax policy, and a national low-dose CT screening program for current and former heavy smokers.

Materials and Methods

A mathematical model of smoking habits in the evolving Italian population between 1986 and 2009 was developed to estimate smoking quit rates, by selecting cessation rates that best reproduce observed smoking prevalence. Uncertainty in observed smoking prevalence was taken into account with a probabilistic sensitivity analysis. The model is already described elsewhere (5, 6). The model with the estimated quit rates was then used to estimate future smoking prevalence and SAD from the baseline year 2009 to 2040, and thus evaluate the effect of the primary and secondary prevention strategies from year 2015.

Model

In the model, the population is stratified into 3 mutually exclusive groups: never, current, and former smokers, the latter distinguished by time since smoking cessation (Appendix A). The model accounts for the population's evolution by allowing for births and deaths and, at the same time, for initiation, cessation, and relapse of smoking. A set of time continuous, differential equations describes the 1-year changes of the numbers of never, current, and former smokers, and of lung cancer and all-cause SAD, specified by gender and age (Appendix A). Because of the long and variable latency periods for different smoking-related diseases, the model applies a 10-year and 5-year lag of smoking rate in calculating lung cancer and all cause SAD, respectively (16, 17).

In comparison with the SimSmoke model developed for United States (18), this model is informed with Italian figures on population and smoking habits (prevalence, initiation rates, stratification of former smokers by time since quitting). Moreover, this model produced estimates of Italian quit rates (5, 6).

Data

Demographic data such as all-cause mortality rates and initial baseline population size (in 2009 30.9 millions of females and 29.1 millions of males; 6.4 millions of men and 7 millions of women aged 55–74 years) were available from the Italian Institute of Statistics (ISTAT; ref. 19). Initiation

rate data by gender and age group were available from ISTAT Multipurpose Surveys (19). The subdivision of former smokers by time since quitting was obtained from DOXA's 2001 to 2010 surveys on smoking habits for representative samples of the Italian population aged 15 years or more (DOXA is the Italian branch of the Gallup International Association; ref. 20). Sex and age-specific cessation probabilities were estimated for each year in the period 1986 to 2009 by selecting the set of parameters that best reproduced the age-specific observed smoking prevalence (5, 6).

Calibration

Because Italian data for smoker and former smoker death rates for all causes and for lung cancer were not available, a calibration procedure was carried out. First, Italian SAD according to the Peto method (21) for the period 1996 to 2009 were computed with the observed mortality data available from ISTAT (22). Then, a plausible range of values for sex and age-specific death rates for smokers and never-smokers, both for all causes and for lung cancer, was defined from published data (23). Finally, these rates were calibrated to match predicted SAD with those computed for Italy. According to Peto estimates (24), in 2000 in Italy, all-cause SADs were 24% and 5% of all-cause deaths for men and women aged 35 years or more, respectively.

Scenarios

Five scenarios were defined:

- 1) Status quo, that is, no implementation of further TCP or low-dose CT screening
- 2) 20% increase in cigarette taxes
- 3) Implementation of cessation treatment policies
- 4) Implementation of a national low-dose CT screening program
- 5) Combination of scenarios 2, 3, and 4.

Status quo scenario was implemented from 2009 to 2040, while the other scenarios were assumed to start from 2015. We used the SimSmoke model's tax module for the "20% tax increase" scenario (Levy and colleagues; submitted; ref. 18). In fact, price elasticity for Italy was comparable with that recorded in the United States (25, 26). So, we assumed a 6% reduction in initiation, a reduction in prevalence of 6% for smokers aged less than 25 years, 4% for smokers aged 25 to 34 years, and 2% for smokers of 35 years or more, and an increase in cessation of 4% for smokers aged 29 years or more, and of 2% for 30 years or more.

In the "cessation treatment policies" scenario, we assumed a combination of total reimbursement for cessation treatments, setting up of an active quitline, and promotion of widespread use of counseling among health professionals. The effect of this combination of measures, according to the SimSmoke model cessation treatment policy module adapted for Italy (Levy and colleagues; submitted; ref. 27), was a reduction of 4.75% in prevalence across all ages and sexes and an increase of 39.3% in cessation.

Three annual screenings were assumed in the "screening" scenario, as in the National Lung Screening Trial (NLST; ref. 14). We assumed a 20% decrease in lung cancer SAD 6 years after the program implementation with a linear increase from 2015 onward (14). Because in the NLST a reduction of deaths from respiratory diseases (about 40% of the all-cause mortality reduction) was also recorded after 6 years of follow-up, we assumed a similar reduction in deaths from respiratory diseases in the "screening" scenario (14).

We assumed only heavy smokers and former heavy smokers aged 55 to 74 years would be invited to be screened, and the compliance would be 70%, which is considered an acceptable goal for cancer screening programs in Italy (28). According to DOXA 2007 survey of a representative sample of the Italian population, for women and men, respectively, 31.3% and 34.5% of smokers smoked 15 or more cigarettes per day, had not attempted to quit, and had no future intention to quit (29). We used these proportions to estimate the number of both heavy and former heavy smokers: 5.3% and 10.2% of 55 to 74 aged women and men, respectively (about 377,000 women and 652,000 men in 2009). These estimates correspond to people with 28 or more pack-years of smoking (assuming they began smoking at 18 years of age), comparable with the eligibility criterion of 30 pack-years required in NLST.

Constant, proportional reductions were assumed for the "combination" scenario, implying that the relative effect of any one of the measures was independent of the other measures, but the absolute reduction in the smoking rate was smaller than in the single measure scenarios (Levy and colleagues; submitted; refs. 18, 27).

Sensitivity analysis

Given the uncertainty about some scenarios parameters, we evaluated the implications of alternative assumptions in a sensitivity analysis. Given that tax policy module was validated and already used in many studies worldwide (25), scenario 1 parameters were not varied. Scenario 3 (cessation treatment policies) is the combination of 3 measures that could be partly implemented, so its effect could be lower. About scenario 4, 70% compliance may be difficult to achieve, so we considered an optimistic scenario of perfect adherence in the screening program, as well as a scenario with 50% of compliance. Hence, we varied one parameter, holding all other parameters constant, to examine the robustness of our results with respect to: half effect of "cessation treatment policies" (scenario 3), screening compliance to 100% (scenario 4), and screening compliance to 50% (scenario 4).

Results

Predicted all-cause and lung cancer SAD under the best fitting set of death rate estimates were comparable with SAD computed with the Peto method, 1996 to 2009 (21), and consistent with the general shape of the death curves (Fig. 1).

In the "status quo" scenario, an increasing trend in all-cause SAD was estimated in women until 2033 with a peak at around 17,700 deaths. Lung cancer SAD in women showed an increasing trend until 2040 with 5,800 deaths. In contrast, a 12% and 20% decrease was estimated for men: from about 57,000 and 22,000 for all-cause and lung cancer SAD, respectively, in 2010, to 50,000 and 17,000 in 2040 (Tables 1 and 2; Figs. 2 and 3).

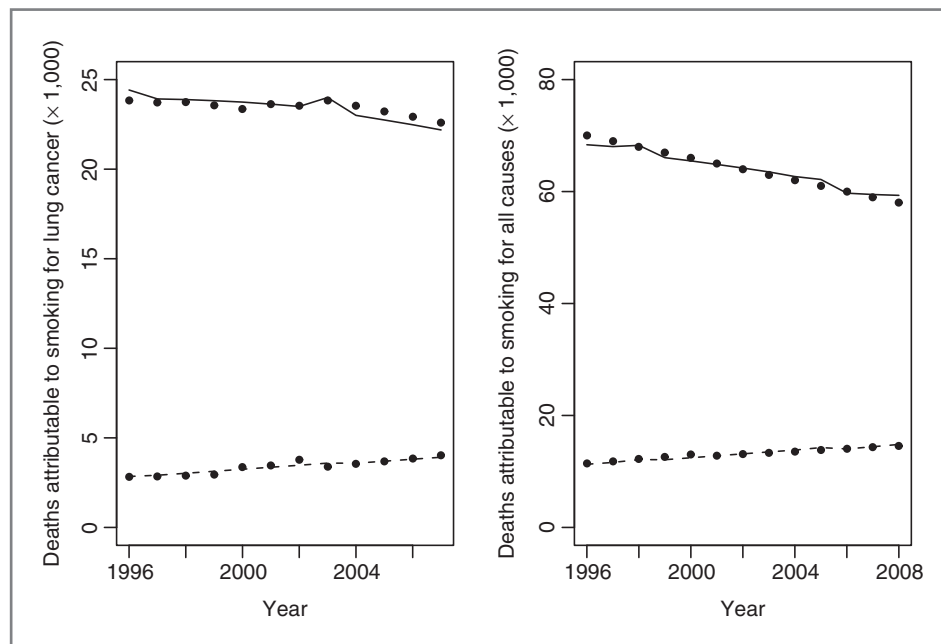


Figure 1. Scheme of the forecasting model used to compute the prevalence of smoking among Italians (≥ 14 years) over time.

Table 1. SADs for all causes in the status quo scenario, and number of lives saved under the four preventive scenarios, with the percentage decline with respect to the status quo

All causes				
Scenario/year	2015	2020	2030	2040
Women				
Status Quo	15,348	16,358	17,534	16,946
Tax policy	0	289 (1.8)	443 (2.6)	574 (3.5)
Cessation treatment policies	0	749 (4.8)	2,346 (15.4)	3,830 (29.2)
Low-dose CT scan screening, 70% compliance	0	224 (1.4)	257 (1.5)	374 (2.3)
2+3+4	0	1,245 (8.2)	2,930 (20.1)	4,526 (36.4)
Men				
Status Quo	54,671	53,169	52,920	50,229
Tax policy	0	893 (1.7)	1,317 (2.6)	1,674 (3.4)
Cessation treatment Policies	0	2,251 (4.4)	6,101 (13.0)	9,621 (23.7)
Low-dose CT scan screening, 70% compliance	0	945 (1.8)	855 (1.6)	941 (1.9)
2+3+4	0	4,040 (8.2)	7,948 (17.7)	11,594 (30.0)

Low-dose CT screening with a 70% compliance had a constant effect, relative to the status quo, in reducing all-cause and lung cancer SAD from the second year after the introduction of the screening program (Figs. 2 and 3). In fact, from 2020 to 2040 the annual reduction in lung cancer SAD remained around 2.8% (about 150 fewer deaths) and ranged from 3.1% to 3.4% (about 548 fewer deaths) for women and men, respectively (Table 2; Fig. 3). Considering only people aged 55 to 74 years, these reductions correspond to a 4.6% and a 5.1% decline in lung cancer SAD in women and men, respectively.

The impact of primary prevention strategies, however, did not become visible until 5 and 10 years after their implementation for all-cause and lung cancer SAD, respectively, and, thereafter, their effect was of a steady increase. In 2030,

cessation treatment policies recorded 1,463 fewer deaths (967 in the 55–74 age class) for male lung cancer SAD in comparison with the status quo scenario, while in 2040 there were 2,871 fewer deaths (1936 in the 55–74 age class). Similarly, tax policy recorded a 2.0% reduction for male lung cancer SAD in 2030, while in 2040 there were a 2.8% reduction (Table 2; Fig. 3).

Moreover, our estimation for TCP gave a greater effect than the screening scenario in reducing all-cause SAD both in women and men (Table 1; Fig. 2). In fact, in 2040 we estimated 1,674 fewer deaths (964 in the 55–74 age-class) in all-cause SAD for men in the "tax" scenario, while in the "cessation treatment policies" scenario, we estimated 9,621 fewer deaths (6,243 in the 55–74 age class), and for the low-dose CT screening program we estimated 941 fewer.

Table 2. SADs for lung cancer in the status quo scenario, and number of lives saved under the four preventive scenarios, with the percentage decline with respect to the status quo

Lung cancer				
Scenario/year	2015	2020	2030	2040
Women				
Status quo	4,533	4,929	5,573	5,849
Tax policy	0	0	109 (2.0)	157 (2.8)
Cessation treatment policies	0	0	436 (8.5)	883 (17.8)
Low-dose CT scan screening, 70% compliance	0	134 (2.8)	154 (2.8)	162 (2.8)
2+3+4	0	134 (2.8)	670 (13.7)	1,137 (24.1)
Men				
Status quo	20,337	18,923	17,169	17,410
Tax policy	0	0	339 (2.0)	481 (2.8)
Cessation treatment policies	0	0	1,463 (9.3)	2,871 (19.7)
Low-dose CT scan screening, 70% compliance	0	567 (3.1)	513 (3.1)	564 (3.4)
2+3+4	0	567 (3.1)	2,211 (14.8)	3,687 (26.9)

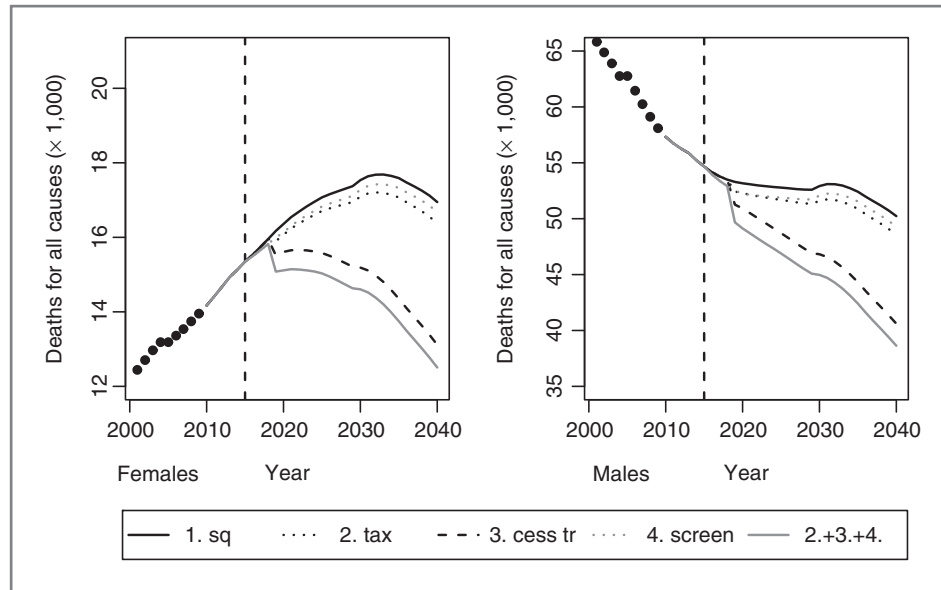


Figure 2. Observed SADs for all causes, Italy, 2000 to 2009, and future SADs for all causes, Italy, 2010 to 2040, in females (left), and males (right), according to the scenarios (see Methods): 1. sq: status quo, 2. tax: tax policy, 3. cess. tr: cessation treatment policy, 4. screen: low-dose CT screening, 5) combination. Vertical dotted line indicates 2015.

The greatest effect, as might be expected, was estimated for the "combination" scenario, with a reduction in all-cause SAD with respect to the status quo of 36.4% and 30.0% for women and men, respectively, in 2040, and a reduction in lung cancer SAD of 1,137 and 3,687 deaths for women and men, respectively (Tables 1 and 2).

Sensitivity analysis

Assuming a total screening adherence has obviously a stronger impact with respect to the 70% compliance scenario. Relative to the status quo in 2020 to 2040, the annual reduction in lung cancer SAD ranged from 5.4% to 5.8% and from 6.6% to 6.5% in women and men, respectively,

and in all-cause SAD it ranged from 2.7% to 3.3% and from 3.8% to 3.7%.

Assuming a 50% screening compliance in 2020 to 2040, the annual reduction in lung cancer SAD remained constant around 2.7% and 3.1% in women and men, respectively, and in all-cause SAD it ranged from 1.3% to 1.6% and from 1.8% to 1.9%.

Halving the effect of cessation treatments recorded a greater effect with respect to lung cancer screening about 10 and 20 years after their introduction for all cause and lung cancer SAD, respectively. Relative to the status quo, in 2030 to 2040, the annual reduction in lung cancer SAD ranged from 4.2% to 8.6% and from 4.6% to 9.6% in

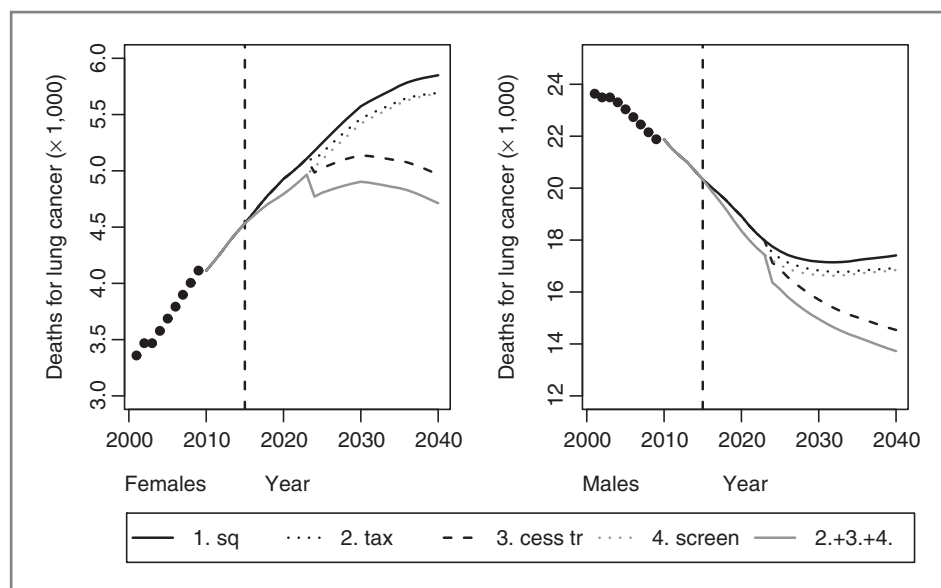


Figure 3. Observed SADs for lung cancer, Italy, 2000 to 2009, and future SADs for lung cancer, Italy, 2010 to 2040, in females (left), and males (right), according to the scenarios (see Methods): 1. sq: status quo, 2. Tax: tax policy, 3. cess. tr: cessation treatment policy, 4. screen: low-dose CT screening, 5) combination. Vertical dotted line indicates 2015.

women and men, respectively, and in all-cause SAD it ranged from 7.5% to 13.8% and from 6.4% to 11.4%.

Discussion

In the status quo from 2010 to 2040, there was a 20% and 40% increase for all-cause and lung cancer SAD, respectively, in women, and a 12% and 20% decrease in men. These results were consistent with findings that Italy is in the final stage of the tobacco epidemic (30). The introduction of a low-dose CT screening program in 2015 brought 6 years afterward a constant annual reduction in lung cancer SAD around 2.8% for women and 3.1% to 3.4% for men, relative to the status quo. In contrast, TCP showed their initial effect 5 and 10 years after their implementation in 2015, for all causes and lung cancer SAD, respectively, because of the model's time lag assumption, and thereafter their effect steadily rose. In fact, the reduction in all-cause SAD of tax policy doubled from 2020 to 2040 and for cessation treatment policies the 2040 decline was more than 5 times the 2020 decrease. However, we assumed that the effect of lung cancer screening was limited to 5 years, by considering only 3 annual rounds of CT scan. Studies on the impact of a longer lung cancer screening are not available.

Moreover, TCP gave a greater effect than screening in reducing all-cause SAD both in women and men because cessation brought about a reduction of lung cancer and other smoking-related diseases as well (cardiovascular and respiratory diseases, other tumors), while low-dose CT screening brought about a reduction in lung cancer and respiratory disease SAD only.

The strategies focusing mainly on cessation, such as cessation treatment policies and a tax policy, were chosen because they would give substantial mortality reductions over 2 to 3 decades, whereas choosing policies focusing mainly on smoking initiation in adolescents (e.g., school prevention programs, youth access restrictions, mass media campaigns) would give substantial mortality reductions only after 40 years (Levy and colleagues; submitted; refs. 5, 6, 15, 21, 27). Moreover, cessation treatment policies were chosen because methods to promote smoking cessation need to be enhanced in Italy.

Currently, the Italian National Health System (NHS) does not reimburse smokers for pharmacotherapy or behavioral cessation treatments and, in 2011, of those smokers who tried unsuccessfully to quit only 12% tried these methods and of former smokers only 5% tried them (31). Moreover, only about 30% to 40% of smokers reported having received advice to quit by their general practitioners (31, 32), and each of the almost 300 NHS smoking cessation services treat an average of only 70 to 77 smokers annually (33). Finally, the 2 national quitlines in Italy annually receive between 7,000 and 8,000 calls, thus reaching only 0.06% to 0.07% of Italian smokers (34, 35). In Italy, there is also room for improvement of tax measures. It is an interesting fact that the relative income price (RIP; proportion of per capita gross domestic product to buy 100 cigarette packages), and minutes of labor (MoL) needed to

buy the most affordable pack of cigarettes in 2006 in Italy were 1.4% and 28 minutes, respectively, with a price of \$3.8, whereas in the same year in the United Kingdom the price was \$8.6 and the RIP and MoL were 2.2% and 37 minutes, respectively (36).

TCPs obviously cost 10- to 100-fold less than an annual screening. In the World Health Organization—European Region A, where Italy is located, doubling the highest regional cigarette tax rate in 2000 cost \$13 per disability-adjusted life years (DALY), while a large-scale distribution of free nicotine replacement therapy (NRT) cost \$2,164/DALY (37). Moreover, offering 2-week supply of free NRT and telephone support through a national quitline in 2004 in Oregon cost \$500 per life-year saved (38), and a \$300 cessation therapy (bupropion and NRT for 30 days) with a 16% one-year abstinence rate offered every year to continuing smokers would cost about 2006\$ 15,000/QALY (15).

This study has some limitations. We applied the proportion of heavy smokers derived from national surveys to estimate the numbers of heavy and former heavy smokers because the proportions of former smokers who were heavy smokers in Italy were not available. This choice could have overestimated the effect of screening on lung cancer mortality, because former heavy smokers could be in a lower proportion, since heavy smokers experienced more difficulties in successfully quitting (39).

We did not take into account that participants in CT screening have higher cessation rates than nonparticipants (40). Thus, the introduction of a CT screening program could have a quantifiable and late effect on both lung cancer and all-cause mortality through a reduction in smoking prevalence.

The model specification has some limitations due to the simplifying assumptions or to the lack of data. Migration was not taken into account because of the inadequate data on smoking prevalence among migrants. However, because the resident population is large with respect to immigrants, it is unlikely that the difference would significantly influence results although smoking prevalence among immigrants may differ from that in the resident population.

Despite the dependence of smoking-related mortality on many factors, such as duration of smoking, smoking intensity, and time since quitting, the excess risks of death were simply modeled as the relative risks for current and former smokers, in order to decrease the complexity of the model.

In modeling, the relapse rates and the relative risks of former smokers through the 2 negative exponential curves, we used parameters estimated from cross-sectional surveys conducted in The Netherlands (41) because data for Italy were not available (Appendix A). Although relative risks for former smokers may be assumed to have similar patterns for The Netherlands and Italy, it is, however, uncertain whether or not the same assumptions could be made for the relapse rates.

Conclusions

A 3-round national low-dose CT screening program brought about a constant annual decrease of lung cancer

and respiratory disease SAD after few years from its implementation, and it showed a lesser impact than TCP in decreasing all-cause SAD.

A strategy combining cessation-focused TCP and a lung cancer screening program could result in an early decrease in lung cancer and respiratory disease mortality due to the screening program, and a more substantial drop in lung cancer and all-cause mortality in the following decades due to the implementation of TCP.

About lung screening program, a multiscreening approach integrating imaging technique and a biomolecular marker panel [allelic imbalance, free-circulating plasma DNA, K-Ras mutation (42); miRNA (43)], and/or a risk prediction model incorporating lung cancer risk factors to identify a high-risk group for low-dose CT screening (44), could be worth of further investigation to improve cost effectiveness, the impact on mortality, and to decrease the frequency of unnecessary treatments in lung cancer screening.

Appendix A

Model equations

For each gender, the total population Pop evolves with the following equation:

$$Pop_{a,y} = Pop_{a-1,y-1} \cdot (1 - q_a) \quad (A)$$

where a and y are the age and the year index, respectively. The term q_a is the age-dependent probability of death.

The population is divided into never-smokers, current smokers, and former smokers. The smoking groups for each gender evolve after the baseline year according to the equations below. The population is stratified at the baseline year according to observed prevalence data.

$$a = 18, \dots, 24 : s_{a,y} = s_{a-1,y-1} \cdot (1 - q_{a|s}) + ns_{a-1,y-1} \cdot (In) \cdot (1 - q_{a|ns}) \quad (B)$$

$$ns_{a,y} = ns_{a-1,y-1} \cdot (1 - In) \cdot (1 - q_{a|ns}) \quad (C)$$

$$a = 25, \dots : s_{a,y} = s_{a-1,y-1} \cdot (1 - \alpha_a) \cdot (1 - q_{a|s}) + \sum_{i=1}^{16} es_{a-1,y-1,i} \cdot (1 - q_{a,i|es}) \cdot rel_{a-1} \quad (D)$$

$$es_{a,y,1} = s_{a-1,y-1} \cdot (\alpha_a) \cdot (1 - q_{a|s}) \cdot (1 - rel_{a-1}) \quad (E)$$

$$es_{a,y,i} = es_{a-1,y-1,i-1} \cdot (1 - q_{a,i|es}) \cdot (1 - rel_{a-1}) \quad (F)$$

$$ns_{a,y} = Pop_{a,y} - (s_{a,y} + \sum_{i=1}^{16} es_{a,y,i}) \quad (G)$$

The terms $s_{a,y}$, $ns_{a,y}$, and $es_{a,y,i}$ are the number of smokers, never-smokers, and former smokers of age a in year y distinguished by gender. Former smokers are distinguished for time since quitting smoking $i = 1, \dots, 16$. The terms

α_a are the age class, year, and sex-dependent smoking cessation parameters previously estimated (6) and rel_a are the smoking relapse rates. In is the initiation rate. The terms $q_{a|s}$, $q_{a|ns}$, $q_{a,i|es}$ are the sex- and age-dependent death probability for smokers, never-smokers, and former smokers, respectively (the latter distinguished for time since quit smoking $i = 1, \dots, 16$).

Death probabilities are obtained by converting the corresponding death rates

$$Hq_{a|s} = 1 - \exp(-dr_{a|s}) \quad (H)$$

Relapse rates were assumed to follow a negative-exponential curve depending on time since quitting (42):

$$l_{\text{relapse}}(t) = \alpha \beta \exp(-\beta t) \quad (I)$$

The α and β parameters estimated from a series of cross-sectional population surveys on smoking behavior for The Netherlands were used since Italian figures were not available, and the relapse rates were converted to 1-year relapse probabilities (conditional on no relapse until that time; ref. 42).

Death rates for former smokers were computed from the corresponding relative risks. These were assumed to decrease according to a negative-exponential curve with a rate of convergence decreasing with age. The negative-exponential curve was parameterized according to parameter estimated from a series of cross-sectional population surveys on smoking behavior from The Netherlands since Italian figures were not available (42).

Smoking attributable deaths

The number of smoking attributable deaths (SAD) was estimated by smoking prevalence and age- and sex-specific relative risks of smokers and former smokers relative to nonsmokers (18). Specifically, the number of smokers at each age is multiplied by the difference between the death rates of smokers and never-smokers. The same for former smokers distinguishing for time since quitting smoking. All-cause and lung cancer SAD were estimated with the corresponding death rates. SADs were computed from the smoking prevalence of 10 years before—the aforementioned 10-year lag (16, 17).

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Development of methodology: G. Carreras, G. Gorini, E. Paci

Acquisition of data: G. Carreras, G. Gorini,

Analysis and interpretation of data: G. Carreras,

Writing, review, and/or revision of the manuscript: G. Carreras, G. Gorini, E. Paci

Study supervision: G. Gorini, E. Paci

Acknowledgments

The authors thank the following for their help and suggestions in preparing this article: Prof. David T. Levy, Pacific Institute for Research and Evaluation, Baltimore; and Dr. Silvano Gallus, Mario Negri Institute for Pharmacological Research, Milan, Italy.

Grant Support

This work was partly supported by the Centro Controllo Malattie (CCM), 2010 funding program (project no. 49), and by the Istituto Toscano Tumori (ITT; grant proposal 2008).

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Received January 16, 2012; revised April 16, 2012; accepted April 16, 2012; published OnlineFirst April 23, 2012.

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Cancer Prev Res 2012;5:874-882. Published OnlineFirst April 23, 2012.

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