

**Smoking and mortality in Eastern Europe: results from the PrivMort retrospective
cohort study of 177,376 individuals**

Authors

Denes Stefler, PhD (corresponding author)

Department of Epidemiology and Public Health, University College London

1-19 Torrington Place, WC1E 6BT, London, UK

Email: denes.stefler.10@ucl.ac.uk

Tel.: +44 (0)20 7679 1680 / 53083

Michael Murphy, Professor

Department of Social Policy, London School of Economics

Houghton Street, WC2A 2AE, London, UK

Darja Irdam, MPhil

Department of Sociology, University of Cambridge

Free School Lane, CB2 3RQ, Cambridge, UK

Pia Horvat, PhD

Department of Epidemiology and Public Health, University College London

1-19 Torrington Place, WC1E 6BT, London, UK

Martin Jarvis, Professor

Department of Epidemiology and Public Health, University College London

1-19 Torrington Place, WC1E 6BT, London, UK

Lawrence King, Professor

Department of Sociology, University of Cambridge

Free School Lane, CB2 3RQ, Cambridge, UK

Martin McKee, Professor

Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine

15-17 Tavistock Place, WC1H 9SH, London, UK

Martin Bobak, Professor

Department of Epidemiology and Public Health, University College London

1-19 Torrington Place, WC1E 6BT, London, UK

Accepted Manuscript

ABSTRACT

Background. The estimated prevalence of smoking and proportion of deaths due to tobacco in Eastern European countries are among the highest in the world. Existing estimates of mortality attributable to smoking in the region are mostly indirect. The aim of this analysis was to calculate the proportion of tobacco-attributed deaths in three Eastern European countries using individual level cohort data.

Methods. The PrivMort project established a cohort of relatives of participants in population sample surveys in Russia, Belarus and Hungary. Survey participants provided data on smoking habits and vital statistics of their close relatives between 1982 and 2013. Population attributable risk fractions (PARF) in men (n=99,528) and women (n=77,848) aged 40-79 years were calculated from the prevalence rates of smoking and hazard ratios of mortality for smokers vs. non-smokers. Trends in PARF over four 8-year time periods (1982-1989, 1990-1997, 1998-2005 and 2006-2013) were examined.

Results. In men in the most recent period (2006-2013), the proportions of deaths attributable to tobacco were 23% in Russia, 22% in Belarus and 22% in Hungary. The respective estimates in women were lower (2%, 2% and 13%), possibly due to underestimation of smoking prevalence. PARF estimates have declined slightly since the early 1990s in men but increased in women.

Conclusions. Consistently with existing indirect estimates, our results based on individual level cohort data suggest that over one fifth of all deaths in men aged 40-79 years are attributable to tobacco. While these proportions are lower in women, the increasing trend is a major concern.

IMPLICATIONS

This is the first large scale, individual-level cohort study which estimated the mortality attributable to tobacco smoking directly in Eastern European population samples. The results confirm previous indirect

estimates and show that more than 20% of all deaths in Eastern European men can be attributed to tobacco. The study also confirms the increasing trend in smoking-related deaths among women. These findings emphasize the importance of targeted policy interventions in Eastern European countries.

Accepted Manuscript

INTRODUCTION

Tobacco smoking is one of the leading causes of mortality and morbidity worldwide. It has been estimated that tobacco smoke was responsible for 20% of all deaths and 14% of all Disability Adjusted Life Years globally in 2013. Among men, smoking causes higher disease burden than any other risk factor.^{1,2} Although there has been progress in slowing or reversing the tobacco epidemic in some high income countries, many low and middle income countries have witnessed no change or even increase in smoking prevalence.³⁻⁵

Smoking rates in Eastern Europe have historically been high. A survey in 1996 found prevalence rates over 60% among Russian men in all age groups between 18 and 54 years. Although only 5% of older women smoked, this figure was over 25% in the younger generation.⁶ In a 2000 survey in Belarus, it was reported that 53% of men and 9% of women were current smokers, with a similar pattern by age.⁷ More recent data show a small decline in male smoking in both countries since then, but increases among women.^{4,8} The situation in Hungary is rather different. Although male smoking rates are also high, at 31%, they are lower than in Russia and Belarus, while female rates are much higher, at 25%.⁹

The estimated proportion of deaths due to smoking is also higher in Eastern Europe than in other global regions.¹⁰⁻¹² In order to compare these proportions internationally, previous studies calculated population attributable risk fractions (PARF) by adopting an indirect method developed by Peto and colleagues,¹⁰ which had the advantage of data parsimony, using only (i) country specific lung cancer death rates and (ii) relative risks of mortality from the US based Cancer Prevention Studies (CPS). However, this approach makes a number of assumptions, including a constant relative risk associated with smoking across different populations and settings, and estimates smoking rates indirectly. A recent large systematic review has suggested that relative risks may vary between different parts of the world, although caution is required as the review was funded by the tobacco industry.¹³ Consequently, it has been recommended that, where data exist, direct estimates of PARF are preferable, using both country specific estimates of

the relative risk and prevalence rate of smoking.^{10,11} This may be especially important in Eastern Europe, given the particular circumstances and very high rates of lung cancer.¹⁴ However, as individual level data on the relationship between smoking and mortality in Eastern European populations remain sparse,¹⁵ no direct estimates of PARF in sufficiently large cohort studies in the region have been published.

The aim of these analyses was to estimate the proportions of mortality attributable to tobacco smoking in three Eastern European countries, the Russian Federation, Belarus and Hungary, and to examine how the proportions of tobacco-attributable deaths in these countries changed between 1982 and 2013, which is a period of large socio-political changes and, in parts of the region, unprecedented fluctuations in mortality rates.

METHODS

Study sample and data collection

The primary aim of the PrivMort Project is to examine the role of privatization and other societal and individual level factors in the mortality crisis of the mid-1990s in Eastern European countries. Details of the study design, sample selection and data collection process have been described previously.¹⁶ Briefly, individual level data were collected from random population samples in 30 Russian, 20 Belorussian and 52 Hungarian medium sized towns. All included towns had between 5,000 and 100,000 inhabitants, and were outside the catchment area of the capital cities. In Russia and Belarus settlements were matched based on a number of likely predictors of mortality, with deliberate variation in industrial structure (mono- versus multi-industrial towns) and the speed of privatization, while in Hungary a random sample of eligible towns was selected.

Data collection took place between January 2014 and December 2015. The selected settlements were first divided into street-centered clusters, which were then randomly distributed among the interviewers who carried out up to 25 interviews per cluster. A random walk procedure was used to identify households,

and one respondent was selected from each, even when more than one family shared the same house. If more than one person in the household matched the screening criteria (older than 42 years of age; relatives lived in the same settlement between 1980 and 2010), the person whose birthday was closer to the date of the survey was selected for the interview.¹⁶

Participants were asked to answer extensive questions about their socio-economic circumstances, employment history, health and lifestyle, including whether they were regular smokers, ex-smokers or never smokers. The full list of topics covered by the questionnaire is described elsewhere.¹⁶ Respondents provided information about themselves and their close relatives (mothers, fathers, siblings (two oldest in case of multiple sibships) and partners of female respondents). Vital status of relatives, including the year of birth and death (if not alive), were also collected. This indirect approach was originally developed by demographers (particularly William Brass) to assess child mortality in low income settings, and often referred to as “Brass techniques”.¹⁷ However, the method based on informants reporting their relatives’ mortality can also provide information that could not realistically be obtained otherwise. For example, the extension of this method was successfully used to study the relationship of education, smoking and alcohol intake with adult mortality in Russia.¹⁸⁻²⁰ Overall, 63,073 individuals took part in the study (overall response rate 54%) and they provided information on 205,607 relatives.

The present analyses used data on relatives only. To be comparable with previous estimations of tobacco attributable deaths,¹² the analyses were restricted to the experience of subjects between ages 40 and 79 years from 1982 to censoring/death. To do so, we excluded individuals who were older than 79 years in 1982 (beginning of the study period) or younger than 40 years in 2013 (end of the study period) or at the time of death. Subjects were further excluded if data on vital statistics, sex or smoking habits were not available, or if information on frequency of alcohol intake and education were missing. After these exclusions, 177,376 individuals (57,425 Russians, 49,434 Belarussians and 70,517 Hungarians) were included in the analysis.

Follow up time

Information was available on the vital status of all individuals (whether he/she was dead or alive) in every year between 1982 and 2013. In order to examine temporal changes, these 32 years were divided into four 8-year periods (1982-1989, 1990-1997, 1998-2005 and 2006-2013). The total follow-up time in each period was equal to the number of years spent between the beginning of the period and the year of death or the end of the period, whichever came first. For each period, only individuals who were younger than 80 years at the beginning and older than 39 years at the end of that interval were included in the analysis, and only life years within the specified age range counted towards the follow up time.

Statistical analysis

As the proportionality assumptions for the Cox proportional hazard models were not met, we used flexible parametric survival models to estimate the hazard ratios (HR) of death by smoking status.²¹ Age was included in the models as a time-dependent variable with three degrees of freedom. Individuals were censored (without reaching the endpoint) if they died from external causes (suicide, homicide or accident); this was also done in previous studies because smoking has no (or very limited) impact on risk of deaths from external causes.¹⁰⁻¹²

Kaplan-Meier survival curves in regular and never smokers were plotted for the entire observation period between 1982 and 2013. They were adjusted for age, type of relation to respondent (i.e. whether the individual was the mother, father, sibling or partner of the respondent), sex of respondent, highest level of education and frequency of alcohol intake. The median survival time was calculated as the smallest survival time for which the survivor function was less than 0.5.

HRs of mortality in regular vs. never smokers were calculated separately by sex, country and follow up period. In model 1, HRs were adjusted for age, type of relation to respondent and sex of respondent. The latter two variables were used to take into account the inaccuracy of reporting by survey participants and

the potential biases related to these characteristics. In model 2, the hazard ratios were further adjusted for education and frequency of alcohol intake. Additional analyses showed that further adjustment for material deprivation and binge drinking did not materially change the results, and these factors were therefore not included in the final models. PARFs were calculated from the prevalence rates of regular smokers and the respective HRs with the standard formula.²² All statistical analysis was carried out using the statistical software STATA 13.1 (StataCorp, Texas, US).

RESULTS

Characteristics of the analytical sample

Characteristics of the study sample regarding mortality, smoking and age, separately by sex, country and follow up period are shown in table 1.

Age standardized mortality rates (SMR) indicate that death rates in these study populations followed patterns similar to official figures:²³ In the 1980s Belarus had lower rates of mortality than the other two countries for both males and females. Hungary has shown a more or less consistent improvement in mortality rates over the last 30 years but mortality fluctuated sharply in Belarus and Russia during the 1990s and early 2000s, particularly in males, and sustained improvement in these two countries occurred only in the most recent decade.

The prevalence of smoking in men also agreed well with official figures in men; in women, the prevalence rates were lower than previous estimates.²³ Smoking was particularly common in Russian men, while Hungarian women smoked more than their Russian or Belorussian counterparts. The data also indicated that smoking prevalence declined slowly in men over the 32-year period but the opposite trends were seen in women, with prevalence rates increasing steadily in all three countries.

Association between smoking and mortality

Figure 1 in supplementary material shows the adjusted survival curves of regular smokers and non-smokers across the 32 years of observational period by country and sex. Compared to never smokers, the median survival of smokers was shorter by 7, 6 and 8 years in Russian, Belorussian and Hungarian men, respectively. Among women, the average difference between smokers and non-smokers in the three countries was about 9 years.

Hazard ratios for the mortality rates comparing regular and never smokers, together with the respective estimates of the population attributable risks fractions are shown in table 2. Multivariable adjusted hazard ratios remained relatively stable for Russian men, however, in the other subgroups substantial fluctuation over time can be seen, with increasing tendencies, especially for women.

In men, the highest PARF due to smoking was found in the Russian sample in the first follow up period, but over time it declined consistently in this country. In Hungarian and Belorussian men, the proportion of deaths attributable to smoking increased between the first and second periods (during the early/mid 1990s), before they leveled off or started to decline in the latest 8-year interval. In women, the proportion of deaths due to smoking was the highest in Hungary in all four time periods. Due to low prevalence rates and low HRs, PARFs were under 3% in Russia and Belorussia. However, the proportion of smoking related deaths increased over time in all three countries, with the steepest rise in Hungarian women.

In comparison with previously published indirect PARF estimates,¹² we found that in most time periods our figures were somewhat lower than those calculated using the Peto method (Supplementary table 1). The difference was particularly large for Hungarian men and Russian women.

The differences in hazard ratios between study periods, particularly among women, may be genuine (due to changing intensity of smoking) but they may also reflect inaccuracy in the retrospective recall and reporting of smoking. We have therefore, as a sensitivity analysis, recalculated PARFs using hazard ratios

in the last study interval (Supplementary table 2). These alternative estimates, in line with the changes in smoking prevalence rates and similarly to our main results, suggest slowly declining trends of tobacco attributable mortality over time among men but steep increase in women.

In addition, we also calculated the HRs of mortality between ever smokers (including ex- and regular smokers) and non-smokers (Supplementary table 3). As expected, the results of this sensitivity analysis indicated weaker relationship between smoking and mortality compared to our main findings when the exposed group was restricted to regular smokers, however the trends over time did not differ considerably.

Because the reported prevalence rates of smoking in the PrivMort study may be underestimated, particularly in females, we also calculated the PARF values by using prevalence data from the WHO in three recent time periods (1990-1997, 1998-2005 and 2006-2013) (Supplementary table 4). These PARFs did not differ considerably from our main findings in males. In females, however, WHO prevalence data produced much higher estimates of attributable mortality.

DISCUSSION

Main findings

In this retrospective cohort study with data collected from relatives of study participants in three Eastern European countries, trends in male mortality and smoking prevalence were similar to official figures between 1982 and 2013. Smoking prevalence in women was lower than expected, most likely due to under-reporting. In multivariable models, the proportion of deaths attributable to smoking ranged between 17% and 28% in males and between 0.2% and 13% in females during this 32-year period. PARF in the most recent time interval (between 2006 and 2013) was the highest in Russian men and Hungarian

women. While the proportion of deaths attributable to smoking have been declining since the early/mid 90s in men, the data indicated an increasing trend in women.

Strengths and limitations

This study is the first that estimated the proportion of deaths attributable to tobacco smoking in sufficiently large Eastern European population samples using country-specific individual level cohort data. In addition to the large sample size, further advantage is the retrospective cohort design which allowed us to estimate PARF due to smoking in the 1990s, in a period when massive social, political and economic changes had huge impacts on population health in the region.

On the other hand, our study also has important weaknesses. The limitations which are related to the study design and the indirect data collection process in general have been described in detail previously.¹⁶ Most importantly, the convenience cohort based on the Brass method is not directly representative of a defined population and the chance of inclusion is not uniform. For example, the probability of inclusion for unmarried men or childless individuals was smaller than for others. However, as we obtained information from a range of relatives, this effect was minimized. Secondly, the impact of measurement error and recall bias can be particularly large when data is collected from proxy informants (i.e. relatives). The consequent misclassification may lead to underestimation of the associations' strengths between risk factors and mortality, and can reduce the statistical power of the study.

In addition to these general considerations, several issues specific to this analysis need to be taken into account. First, measurement error related to smoking status, and the consequent misclassification of individuals in smoker and non-smoker groups, may affect our results. There are a number of reasons for this error to occur. (1) Previous validation study found that underreporting of smoking status is especially prevalent in Russian females.²⁴ Due to cultural stigma associated with smoking and drinking among women, it is likely that many participants did not know (or did not admit) that their mothers or sisters

were smokers. The comparison of our PARF estimates with those calculated indirectly and those estimated using WHO prevalence rates suggests that our method is reliable for males, but less so for females. (2) Underreporting of smoking is probably greater in the analysis related to the first two time periods (1980s and early/mid 90s) because it is more difficult for the respondents to remember the correct smoking habits of relatives who died 25-30 years ago than for those who are still alive or died just a few years before the interview. The information regarding the year of death can also be less precise in the 80s compared to the 2010s. It is likely that these measurement biases resulted in underestimation of HR/PARF in Russian and Belorussian females, and in the earlier periods.

Second, selection bias and the fact that our sample is not representative for the respective countries as a whole also need to be considered. For example, data from the Russian Longitudinal Monitoring Survey suggest that female smoking prevalence rates are more than twice as high in the largest cities compared to other urban or rural areas in Russia.²⁵ The fact that the PrivMort survey collected data only in middle-sized towns may have also contributed to underestimation of smoking prevalence among Russian females and the consequent low PARF in this group. On the other hand, mortality and male smoking prevalence rates in this study were similar to other more representative surveys,²³ which suggest that this sample was probably similar to the general population regarding these aspects.

Third, the role of residual confounding between smoking and mortality cannot be excluded entirely because potential confounding factors, such as BMI, diet or physical activity, were not measured and were not taken into account. However, reduction of HRs after adjustment for alcohol and education was similar to other studies where some of these additional factors were also adjusted for.¹¹

Finally, we had no specific information on the number of cigarettes an individual smoked per day, or the age when someone took up or gave up smoking. Although we excluded ex-smokers from the “exposed” group, the age of initiation and the intensity of smoking can affect the strength of the examined associations. In fact, these factors are likely to contribute to the increased HRs and PARFs in later

decades, particularly among women. Unfortunately, this information was not captured in the surveys and so cannot be confirmed using this dataset.

Interpretation

In women, particularly in Russia, the low PARF estimated by our study is probably due to the underreporting of smoking prevalence and the non-representativeness of our dataset. In Hungarian men, it is likely that our results reflect the actual values more closely than previous indirect estimates. PARF in this country was lower than in Russia and Belarus because of the lower smoking prevalence rates, and these rates were very similar to those reported by other surveys.²³ It is possible that the high PARF in Hungarian men reported by previous studies is due to high levels of lung-cancer mortality in non-smokers in this country. This speculation is supported by a previous study which found that the cumulative risk of lung cancer in never smokers was higher in Hungary than other CEE and FSU countries in both men and women.²⁶ Potential exposures to carcinogens, for example indoor or outdoor air pollution or, given the very high incidence of colorectal cancer in Hungary, misdiagnosis of secondary adenocarcinomas as primaries, may contribute to explaining these international differences within the region.

The tendency towards higher HRs in the more recent time periods may be partly due to the fact that individuals in the late 1990s and 2000s had a longer smoking career and spent longer time of their life smoking than those in the 1980s. In addition, there is known to be a cohort effect among men in the countries of the former USSR because of changing access to cigarettes, and thus smoking initiation among adolescents, in the 1940s and 1950s.²⁷ It is also possible that people in these later decades smoked more cigarettes per day or smoked in a different way (inhaled more deeply). For example, the number of cigarettes sold in Russia nearly doubled between 1990 and 2004, and sales during this period also increased in Belarus.²⁸ Higher relative risks in more recent generations, as the tobacco epidemic matures, have been described in several previous cohorts as well.²⁹⁻³¹ However, as noted before, it is likely that

misclassification of smokers and non-smokers was more common in individuals who died in the 1980s or early 1990s, and this also contributed to the low HRs in the earlier periods.

The reduction of HRs after adjustment for education and alcohol consumption was more substantial in recent years compared to earlier periods, especially in Russian men. This suggests a change in the characteristics of smokers over time. In fact, further analysis of the current data (not shown), as well as results of other studies,³² indicate that socio-economic inequalities in smoking increased as the smoking epidemic matures. Changes in the relationship between smoking and other lifestyle and socio-economic factors over time could be subject of further investigations.

Finally, our results mostly correspond well with data from the US which found approximately 10-year difference in life expectancy between smokers and non-smokers.³³

Conclusion

This large retrospective cohort study provided direct estimates which are largely consistent with previously reported indirect figures, particularly in men. These individual level data confirm that the proportion of deaths due to smoking in Eastern Europe is high. The increasing trend in smoking-related deaths among women, possibly linked to the post-communist transition, presents an important public health issue which need to be targeted by appropriate policy interventions.

FUNDING

The study was funded by European Research Council (a competitive externally peer reviewed Advanced Grant Scheme, grant agreement No. 269036).

COMPETING INTEREST

None declared.

Accepted Manuscript

REFERENCES

1. World Health Organization. WHO Global report: mortality attributable to tobacco. 2012; WHO Press, Geneva.
2. Global Burden of Disease Study 2013 Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2015;386:2287-2323.
3. World Health Organization. WHO report on the global tobacco epidemic, 2015. 2015; WHO Press, Geneva.
4. World Health Organization. WHO global report on trends in prevalence of tobacco smoking 2015. 2015; WHO Press, Geneva.
5. Islami F, Torre LA, Jemal A. Global trends of lung cancer mortality and smoking prevalence. *Transl Lung Cancer Res*. 2015;4:327-338.
6. McKee M, Bobak M, Rose R, Shkolnikov V, Chenet L, Leon D. Patterns of smoking in Russia. *Tob Control*. 1998;7:22-26.
7. Gilmore AB, McKee M, Rose R. Prevalence and determinants of smoking in Belarus: a national household survey, 2000. *Eur J Epidemiol*. 2001;17:245-253.
8. Roberts B, Gilmore A, Stickley A et al. Changes in smoking prevalence in 8 countries of the former Soviet Union between 2001 and 2010. *Am J Public Health*. 2012;102:1320-1328.
9. American Cancer Society, World Lung Foundation (2015). Tobacco Atlas. Available at <http://www.tobaccoatlas.org/> [Accessed: 24th February 2017].
10. Peto R, Lopez AD, Boreham J, Thun M, Heath C Jr. Mortality from tobacco in developed countries: indirect estimation from national vital statistics. *Lancet*. 1992;339:1268-1278.

11. Ezzati M, Lopez AD. Estimates of global mortality attributable to smoking in 2000. *Lancet*. 2003;362:847-852.
12. Renteria E, Jha P, Forman D, Soerjomataram I. The impact of cigarette smoking on life expectancy between 1980 and 2010: a global perspective. *Tob Control*. 2015 pii: tobaccocontrol-2015-052265 [Epub ahead of print].
13. Lee PN, Forey BA, Coombs KJ. Systematic review with meta-analysis of the epidemiological evidence in the 1900s relating smoking to lung cancer. *BMC Cancer*. 2012;12:385.
14. Primic-Zakelj M, Zadnik V, Zagar T. Is cancer epidemiology different in Western Europe to that in Eastern Europe? *Ann Oncol*. 2005;16 Suppl 2:ii27-29.
15. Pesch B, Kendzia B, Gustavsson P et al. Cigarette smoking and lung cancer--relative risk estimates for the major histological types from a pooled analysis of case-control studies. *Int J Cancer*. 2012;131:1210-1219.
16. Irdam D, Gugushvili A, Azarova A et al. Mortality in Transition: A Multilevel Convenience Cohort Study. Study protocol of the PrivMort Project. *BMC Public Health*. 2016;16:672.
17. Brass W, Coale AJ, Demeny P et al. The Demography of Tropical Africa. Princeton, NJ: Princeton University Press; 1968.
18. Hill K, Trussell J. Further developments in indirect mortality estimation. *Popul Stud*. 1977;31:313-334.
19. Bobak M, Murphy M, Rose R, Marmot M. Determinants of adult mortality in Russia: estimates from sibling data. *Epidemiology*. 2003;14:603-611.
20. Murphy M, Bobak M, Nicholson A, Rose R, Marmot M. The widening gap in mortality by educational level in the Russian Federation, 1980-2001. *Am J Public Health*. 2006;96:1293-1299.
21. Lambert PC, Royston P. Further development of flexible parametric models for survival analysis. *The Stata Journal*. 2009;9:265-290

22. Bhopal R. Presentation and interpretation of epidemiological data on risk. In: Bhopal R (ed.) *Concepts of Epidemiology*. 2nd edn. 2008. Oxford: Oxford University Press, pp. 235–284.
23. WHO Regional Office for Europe (2016). European Health for All Database. Available at: <http://data.euro.who.int/hfad/>
24. Laatikainen T, Vartiainen E, Puska P. Comparing smoking and smoking cessation process in the Republic of Karelia, Russia and North Karelia, Finland. *J Epidemiol Community Health*. 1999;53:528-534.
25. Perlman F, Bobak M, Gilmore A, McKee M. Trends in the prevalence of smoking in Russia during the transition to a market economy. *Tob Control*. 2007;16:299-305.
26. Brennan P, Crispo A, Zaridze D et al. High cumulative risk of lung cancer death among smokers and nonsmokers in Central and Eastern Europe. *Am J Epidemiol*. 2006;164:1233-1241.
27. Shkolnikov V, McKee M, Leon D, Chenet L. Why is the death rate from lung cancer falling in the Russian Federation? *Eur J Epidemiol* 1999;15:203-206.
28. Forey B, Hamling J, Hamling J, Thornton A, Lee P. International smoking statistics (web edition): a collection of worldwide historical data, USSR and successor countries. P N Lee Statistics and Computing Ltd. Available at: <http://www.pnlee.co.uk/ISS.htm> [Accessed: 11th July 2016].
29. Doll R, Peto R, Wheatley K, Gray R, Sutherland I. Mortality in relation to smoking: 40 years' observations on male British doctors. *BMJ*. 1994;309:901-911.
30. Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. *BMJ*. 2004;328:1519.
31. Chen Z, Peto R, Zhou M et al. Contrasting male and female trends in tobacco-attributed mortality in China: evidence from successive nationwide prospective cohort studies. *Lancet*. 2015;386:1447-1456.

32. Pärna K, Pürjer ML, Ringmets I, Tekkel M. Educational differences in cigarette smoking among adult population in Estonia, 1990-2010: does the trend fit the model of tobacco epidemic? *BMC Public Health*. 2014;14:709.
33. Jha P, Ramasundarahettige C, Landsman V et al. 21st-century hazards of smoking and benefits of cessation in the United States. *N Engl J Med*. 2013;368:341-350.

Accepted Manuscript

Table 1. Basic characteristics of the study sample regarding mortality, smoking and age in the four time periods

		1982-1989	1990-1997	1998-2005	2006-2013
MALES					
Russia	Number of all participants	20,537	23,453	23,322	19,742
	Number of deaths (per 1000 person-years)	2,586 (19.3)	3,760 (24.2)	4,965 (31.9)	4,165 (30.7)
	SMR (95% CI) ¹	0.98 (0.95-1.02)	1.08 (1.05-1.12)	1.21 (1.17-1.24)	1.01 (0.98-1.04)
	Number of regular smokers (%)	11,600 (56.5)	12,978 (55.3)	12,714 (54.5)	10,354 (52.4)
	Mean age at baseline (SD)	48.1 (10.3)	50.1 (11.0)	52.7 (11.5)	55.8 (11.3)
Belarus	Number of all participants	17,182	19,364	20,207	17,971
	Number of deaths (per 1000 person-years)	2,002 (17.4)	2,804 (21.7)	3,821 (28.4)	3,477 (28.2)
	SMR (95% CI) ¹	0.88 (0.84-0.92)	0.96 (0.92-0.99)	1.06 (1.03-1.10)	0.94 (0.91-0.97)
	Number of regular smokers (%)	8,646 (50.3)	9,744 (50.3)	10,130 (50.1)	8,849 (49.2)
	Mean age at baseline (SD)	48.6 (10.5)	50.5 (11.0)	52.6 (11.9)	55.1 (11.9)
Hungary	Number of all participants	27,742	28,973	27,479	23,538
	Number of deaths (per 1000 person-years)	4,225 (23.2)	4,604 (23.7)	5,087 (27.1)	4,367 (26.7)
	SMR (95% CI) ¹	1.08 (1.05-1.11)	1.02 (0.99-1.05)	0.96 (0.93-0.99)	0.80 (0.78-0.82)
	Number of regular smokers (%)	10,341 (37.3)	10,593 (36.6)	9,831 (35.8)	8,163 (34.7)
	Mean age at baseline (SD)	49.2 (11.1)	51.0 (11.1)	54.2 (11.4)	57.2 (11.4)
FEMALES					
Russia	Number of all participants	20,011	20,386	18,492	14,676
	Number of deaths (per 1000 person-years)	1,933 (13.9)	2,491 (17.4)	3,108 (24.0)	2,375 (23.4)
	SMR (95% CI) ¹	0.96 (0.92-1.01)	0.96 (0.92-1.00)	1.04 (1.01-1.08)	0.85 (0.82-0.88)
	Number of regular smokers (%)	351 (1.8)	512 (2.5)	616 (3.3)	627 (4.3)
	Mean age at baseline (SD)	51.9 (11.2)	54.8 (11.6)	58.1 (11.7)	61.1 (11.4)
Belarus	Number of all participants	15,906	16,758	16,298	13,755
	Number of deaths (per 1000 person-years)	1,303 (11.8)	1,742 (14.8)	2,219 (19.6)	1,853 (19.3)
	SMR (95% CI) ¹	0.86 (0.81-0.91)	0.88 (0.84-0.92)	0.90 (0.86-0.93)	0.76 (0.73-0.80)
	Number of regular smokers (%)	242 (1.5)	325 (1.9)	423 (2.6)	449 (3.3)
	Mean age at baseline (SD)	51.2 (11.2)	53.9 (11.7)	56.8 (12.2)	59.4 (12.0)
Hungary	Number of all participants	24,496	24,591	22,377	18,394
	Number of deaths (per 1000 person-years)	2,748 (16.4)	2,998 (17.4)	3,176 (20.2)	2,536 (19.8)
	SMR (95% CI) ¹	1.11 (1.07-1.16)	1.02 (0.98-1.05)	0.90 (0.87-0.93)	0.73 (0.70-0.76)
	Number of regular smokers (%)	1,935 (7.9)	2,609 (10.6)	2,865 (12.8)	2,733 (14.9)

Mean age at baseline (SD)	51.6 (11.5)	54.2 (11.7)	57.9 (11.6)	60.7 (11.3)
---------------------------	-------------	-------------	-------------	-------------

¹SMR (standardized mortality rate) is calculated using the pooled population in the first period (1982-1989) as the standard (separately for males and females)

Accepted Manuscript

Table 2. Hazard ratios of mortality and population attributable risk due to smoking in the four time periods

	1982-1989		1990-1997		1998-2005		2006-2013			
	HR (95% CI)	PARF (95% CI)	HR (95% CI)	PARF (95% CI)	HR (95% CI)	PARF (95% CI)	HR (95% CI)	PARF (95% CI)		
MALES										
Russia	model1	1.73 (1.56-1.92)	29.2 (24.0-34.2)	1.76 (1.61-1.91)	29.6 (25.2-33.5)	1.90 (1.76-2.04)	32.9 (29.3-36.2)	1.97 (1.82-2.13)	33.7 (30.1-37.2)	
	model2	1.69 (1.51-1.89)	28.0 (22.4-33.5)	1.64 (1.50-1.80)	26.1 (21.7-30.7)	1.61 (1.49-1.75)	25.0 (21.1-29.0)	1.58 (1.45-1.72)	23.3 (19.1-27.4)	
Belarus	model1	1.53 (1.38-1.70)	21.0 (16.0-26.0)	1.86 (1.70-2.04)	30.2 (26.0-34.5)	1.93 (1.79-2.09)	31.8 (28.4-35.3)	1.82 (1.68-1.96)	28.7 (25.1-32.1)	
	model2	1.46 (1.30-1.63)	18.8 (13.1-24.1)	1.75 (1.58-1.93)	27.4 (22.6-31.9)	1.77 (1.63-1.92)	27.8 (24.0-31.5)	1.57 (1.44-1.70)	21.9 (17.8-25.6)	
Hungary	model1	1.58 (1.47-1.70)	17.8 (14.9-20.7)	1.92 (1.79-2.06)	25.2 (22.4-28.0)	1.92 (1.80-2.05)	24.8 (22.3-27.3)	2.05 (1.91-2.20)	26.7 (24.0-29.4)	
	model2	1.55 (1.43-1.68)	17.0 (13.8-20.2)	1.79 (1.65-1.93)	22.4 (19.2-25.4)	1.72 (1.60-1.84)	20.5 (17.7-23.1)	1.82 (1.69-1.97)	22.2 (19.3-25.2)	
FEMALES										
Russia	model1	1.12 (0.76-1.67)	0.2 (-0.4-1.2)	1.40 (1.03-1.91)	1.0 (0.1-2.2)	1.77 (1.40-2.24)	2.5 (1.3-3.9)	1.71 (1.33-2.19)	3.0 (1.4-4.9)	
	model2	1.09 (0.71-1.60)	0.2 (-0.5-1.1)	1.20 (0.87-1.67)	0.5 (-0.3-1.6)	1.50 (1.17-1.92)	1.6 (0.6-2.9)	1.40 (1.07-1.82)	1.7 (0.3-3.4)	
Belarus	model1	1.36 (0.88-2.10)	0.5 (-0.2-1.6)	1.25 (0.85-1.82)	0.5 (-0.3-1.5)	1.86 (1.40-2.49)	2.2 (1.0-3.7)	1.64 (1.18-2.29)	2.1 (0.6-4.1)	
	model2	1.45 (0.93-2.25)	0.7 (-0.1-1.8)	1.12 (0.76-1.66)	0.2 (-0.5-1.2)	1.73 (1.28-2.32)	1.9 (0.7-3.3)	1.67 (1.19-2.33)	2.2 (0.6-4.2)	
Hungary	model1	1.68 (1.42-1.98)	5.1 (3.2-7.2)	2.00 (1.76-2.29)	9.6 (7.5-12.0)	1.94 (1.72-2.18)	10.7 (8.4-13.1)	2.15 (1.92-2.41)	14.6 (12.1-17.4)	
	model2	1.67 (1.41-1.97)	5.0 (3.1-7.1)	1.93 (1.69-2.21)	9.0 (6.8-11.4)	1.83 (1.63-2.07)	9.6 (7.5-12.0)	2.01 (1.79-2.26)	13.1 (10.5-15.8)	

model1: adjusted for age, relative status, respondent sex

model 2: adjusted for age, relative status, respondent sex, alcohol intake and education

PARF – Population attributable risk fraction (expressed as percentage of total mortality)

34.