



Smoking, alcohol and cancer mortality in Eastern European men: findings from the PrivMort retrospective cohort study

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PARF – Population attributable risk fraction; SMR – Standardized mortality rate; OR – Odds ratio

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Brief description of novelty and impact

This study used a novel methodology to estimate cancer mortality rates in adults by collecting data on the relatives of survey respondents. To our knowledge, this is the first time when this method, also known as “Brass techniques”, is used to calculate cause-specific mortality rates. In addition, the population attributable risk of cancer mortality due to smoking and alcohol was calculated in Eastern Europe, in a region where such data are scarcely available.

ABSTRACT

Eastern European men have among the highest cancer mortality rates globally. Prevalence of smoking and alcohol intake in this region is also high. The aim of this study was to calculate population attributable risk fraction (PARF) of cancer deaths from smoking and alcohol in Russia, Belarus and Hungary, and to examine the contribution of these lifestyle factors to differences in male cancer mortality in the three countries. Data was collected as part of the PrivMort retrospective cohort study. Randomly selected participants living in mid-size towns in Russia, Belarus and Hungary provided information on smoking habits, alcohol consumption, vital status and cause of death (if applicable) of male relatives (fathers, siblings and partners). PARF of cancer deaths (age 35 to 79) due to smoking, alcohol consumption and both combined was estimated between 2001 and 2013. Among 72,190 men, 4,702 died of cancer. Age standardized cancer mortality rates were similar to official data in all three countries. The estimated PARF (95% CI) associated with measures of smoking, alcohol consumption, both combined, and overall smoking or drinking were 25% (19-30), 2% (0-4), 29% (19-39) 43% (32-53) in Russia, 18% (8-28), 2% (-1-6), 28% (20-35), 38% (25-50) in Belarus, and 17% (13-20), 1% (0-3), 25% (20-30) 35% (28-42) in Hungary, respectively. These results suggest that in Eastern Europe, at least one third of cancer deaths in males may have been attributable to smoking and/or alcohol consumption in recent years. Health policies targeting these lifestyle factors can have a major impact on population health.

INTRODUCTION

Eastern European countries have among the highest cancer morbidity and mortality rates in the World. The GLOBOCAN estimates for 2012 suggest that, of the 20 global regions, male cancer mortality rates were the highest in Eastern Europe, while death rates in females and incidence in both genders were also higher here than in most other regions.¹

Some countries stand out even within Eastern Europe as having exceptionally high overall and site-specific cancer rates. Hungary, for example, experiences higher incidence and mortality than most neighboring countries for several types of cancer, including lung, colon/rectum, oral cavity/pharynx, larynx, pancreas and bladder.² In fact, over the last two decades, this country has ranked first in the whole of Europe for many cancers,^{2,3} and the proportion of avoidable cancer cases among Hungarian males was estimated as high as 77%.⁴ Incidence and mortality rates in Russia and Belarus are particularly high for stomach cancer, but otherwise the patterns seen in these two countries are broadly similar to Eastern European averages.²

The prevalence of smoking and alcohol consumption among Eastern European men has also been historically high, and the contribution of these lifestyles to the region's prominent cardiovascular disease burden has been investigated extensively.^{5,6} On the other hand, cancer incidence and mortality attributable to smoking and alcohol in Eastern European countries is less well explored, and direct estimates of population attributable risk fraction (PARF) from large-scale individual level datasets are rare.^{7,8} While smoking prevalence has declined in many Eastern European states over recent decades, particularly in men, and alcohol consumption remained mostly stable or increased,^{9,10} it is unclear whether differences in drinking and smoking patterns can explain the between-country variation in cancer mortality rates within the region.

Using individual level data from the PrivMort retrospective cohort study, the aim of our analysis was to estimate the PARF of cancer deaths due to smoking and alcohol consumption among Russian, Belarusian and Hungarian men. We also examined whether these lifestyle factors can explain the observed differences in cancer mortality rates between the three population samples.

METHODS

Study populations

PrivMort study is a multi-center retrospective cohort created to explore the impact of societal and individual-level factors on mortality in Eastern Europe during a period of extensive socio-political change. Sample selection and data collection procedures have been described in detail previously.¹¹ In brief, individual-level data were collected between January 2014 and December 2015 in Russia, Belarus and Hungary. In each country, participants were recruited randomly from medium-sized towns (populations between 5,000 and 100,000) outside the catchment area of the capital cities. Settlements in Russia and Belarus were chosen based on their industrial structure, while they were selected randomly in Hungary. Households within the specific towns were identified using street-centered clusters and a random walk procedure. One person per household, who was older than 42 years and had at least one relative who lived in the same settlement between 1980 and 2010, was invited to participate in the study. Overall response rate was 58%.

Measurements

Participants completed an extensive questionnaire about their own socio-economic circumstances, lifestyle habits, as well as their close relative's (mother, father, two oldest siblings, partners of female respondents). Amongst other questions, they were asked whether they, or their relatives, smoked (never; ex-smoker; current smoker) or drank alcohol regularly (never; quit drinking; few times a year/special occasions; 2-4 times a month; several times a week; daily). In addition to this, information on the vital statistics of relatives, including their year of birth, and if dead, the year and cause of death, was also collected. Regarding the cause of death, five major disease groups (heart attack, other heart disease, stroke, cancer, alcoholism) and three external death causes (accident, homicide, suicide) were listed in the questionnaire from which the respondents could choose the most appropriate one. If none of these categories were adequate, the respondents also had the option to indicate the specific cause of death with their own words. This data collection method, which gathers information not directly but through relatives, is often referred as the "Brass technique". It was used previously in Russia to study socio-economic and lifestyle factors and their relationship with all-cause mortality.¹² However, to our knowledge, this is the first time that it has been used to examine cause specific mortality and its determinants in the general adult population anywhere.

Analytical sample

Previous analysis indicated that the prevalence of smoking among females in the PrivMort sample was considerably underreported.¹³ Therefore, in the current analysis we used data on male relatives (fathers, male siblings and partners) only. Those family members were included who were younger than 80 in 2001 and at least 35 in 2013, and only those life years within this

specific age range (35-79 years) counted towards the follow-up. Persons with missing data on their year of birth, year and cause of death (even after taking into account the textual answers), smoking and alcohol intake were excluded from the analysis. After these exclusions, data on 72,190 individuals (23,459 Russian, 21,129 Belarusian and 27,602 Hungarian men) formed the analytical sample.

Statistical analysis

We carried out the analysis in three separate steps. First, in order to assess whether the available data regarding cancer mortality in the PrivMort sample is of acceptable quality, we calculated age-standardized cancer death rates (SMR) in each year between 2001 and 2013 and compared them with the respective national-level figures published in the WHO Health for All database.¹⁰ The standardization was carried out using the direct method and the European standard population was used as standard.

In the second step, we estimated PARFs of cancer mortality due to smoking and alcohol with a method that considers the potential interaction between the two variables.¹⁴ To do this, first we categorized the study sample into four groups: (1) never alcohol/never smoking – individuals who have never drank alcohol or drink less than 2-4 times a month, and, at the same time, never smoked; (2) never alcohol/ever smoking – those who have never drank alcohol or drink less than 2-4 times a month, but are ex- or regular smokers; (3) ever alcohol/never smoking – drinks at least 2-4 times a month or quit drinking, and never smoked; (4) ever alcohol/ever smoking – drinks at least 2-4 times a month or quit drinking, and ex- or regular smokers. Subsequently, odds ratios (ORs) of cancer deaths were calculated in each of these groups using discrete-time survival models¹⁵ and the never alcohol/never smoking category as the reference. ORs referred to

the time-period between 2001 and 2013 and were adjusted for the age of the relative and their relationship with the respondent (i.e.: whether they were fathers, siblings or partners). PARF was then estimated from the respective prevalence and OR values, and the overall PARF as recommended for multi-categorical variables.¹⁴

Finally, we compared cancer mortality rates between the Hungarian, Russian and Belarusian sample using Hungary as the reference. A discrete-time survival analysis method was applied and the results were calculated in two models. In model 1, the ORs were adjusted for the age of the relative and their relationship with the respondent. In model 2, the associations were further adjusted for alcohol consumption and smoking.

All statistical analysis was carried out in STATA 13 (*StataCorp, TX, USA*).

RESULTS

Figure 1 presents the age standardized mortality rates in the PrivMort sample between 2001 and 2013 using moving averages and compared to WHO data. (The actual death rates are shown in table S1 in Supplement). Except from a few specific years (i.e.: 2004-05 in Hungary and 2010 in Belarus), the figures indicate relatively good agreement between the PrivMort and WHO data. SMRs are higher in Hungary than in Russia and Belarus. As for temporal trends, apart from the annual fluctuation, cancer death rates decreased slightly in the Russian sample but remained steady in the other two PrivMort cohorts.

Table 1 shows the PARFs of cancer deaths in the four alcohol/smoking categories and overall in the Hungarian, Russian and Belarusian samples. The proportions of individuals in each category,

as well as the odds ratios of cancer death in relation to the never smoker/never drinker category, are also indicated. The prevalence of smoking was higher in Russia and Belarus compared to Hungary, with proportions of 74%, 67% and 59% respectively, but alcohol consumption was fairly similar across the three countries: 45%, 39% and 43% respectively. The odds ratios for cancer mortality were the highest among those who both smoke and drink alcohol, and PARFs were also higher in this group than in any other categories. The overall PARF was highest in Russia and lowest in Hungary, but even in the latter, its value was above 35%. This suggests that more than one third of adult male cancer deaths can be attributable to smoking and alcohol in these populations.

Table 2 shows the differences in cancer mortality rates between countries with (model 2) and without (model 1) adjustment for alcohol consumption and smoking. Cancer deaths were found to be significantly lower in Russia and Belarus than in Hungary in both models. In fact, the differences became larger when they were adjusted for alcohol and smoking. For example, the gap increased from 25% to 33% in Russia, and from 38% to 43% in Belarus. The results are broadly similar if the cross-country differences in education attainment were also taken into account (Table S2 in Supplement).

DISCUSSION

Main findings

An individual-level longitudinal analysis was carried within a retrospective cohort study, using data collected on family members of participants selected randomly in a selection of towns in

three Eastern European countries. In these cohorts, male age-standardized cancer mortality rates were found to be similar to official figures for the Hungarian, Russian and Belarusian populations between 2001 and 2013. The results indicated that more than one third of total cancer deaths could be attributable to smoking and alcohol consumption in the three countries, although we were not able to confirm whether these lifestyle factors were responsible for the large differences in between-country mortality rates within the region.

Interpretation

The estimate of the proportion of cancer deaths attributable to smoking and alcohol in this sample is consistent with results from previous studies and analyses. For example, in a prospective cohort in Lithuanian men, using a different method to calculate PARFs, total cancer incidence due to smoking and alcohol were found to be 23% and 13%, respectively.^{7,8} Although our results in the three countries here are somewhat lower than the WHO estimates for smoking attributable cancer mortality, the differences in methodology, particularly the fact that we used individual-level prevalence data as opposed to the smoking impact ratio, is likely to be responsible for the discrepancies.¹⁶

Even though site-specific cancer rates could not be assessed in this study, smoking and alcohol are major risk factors for many cancer types which are particularly common in Eastern Europe. In addition, previous evidence suggests that these risk factors may interact and enhance each other's harmful effect, especially in the development of upper aerodigestive tract cancers.^{17,18} This means that reducing smoking and alcohol intake in the region has a particular importance, and would probably lead to the greatest impact on these localizations of the disease.

The reasons for the distinctively high cancer rates in Hungary, compared to other Eastern or Western European countries, have long been recognized but little investigated. Previous hypotheses suggested that smoking, alcohol consumption, dietary habits, obesity, occupational exposure to carcinogens, or genetic composition may contribute to this pattern.¹⁹⁻²¹ However, very few of these hypotheses have actually been tested in epidemiological analyses. This study was not designed to test all these potential explanations, and could only assess, to some extent, the contribution of smoking and alcohol. Our results suggest that these two factors are not responsible for the between-country variation in mortality rates. If anything, the higher prevalence of smoking and alcohol intake in Russia and Belarus make the observed differences in male cancer mortality rates compared to Hungary smaller. Further studies, using individual-level data on both males and females, would be needed to explore the reasons for the international variation of cancer deaths within Eastern Europe.

Limitations and strengths

General limitations of the PrivMort project related to study design and other aspects of the data collection procedures have been described earlier.¹¹ However, there are several particular issues which need to be emphasized here too.

Firstly, it is important to note that the data are not representative of the entire Hungarian, Russian and Belarusian populations. Survey participants were recruited from selected settings, mid-size towns, because the primary purpose was to test hypotheses about the health effects of large scale changes related to the local economies. There was only a moderate response rate, and by design individuals who did not get married or had no children had lower probability to be included in the analytical sample, comprised of close relatives of survey respondents.¹¹ Nevertheless, age-

standardized cancer death rates, as well as the prevalence of male smoking and alcohol consumption was similar to previous studies which estimated these values on more representative samples.^{22,23}

Secondly, measurement bias could also affect our findings. In fact, we did not calculate ORs of mortality and PARFs in females because, despite the good agreement with WHO data regarding age-standardized cancer mortality rates (Figure S1 in Supplement), previous analyses showed that the prevalence of women's smoking was markedly underreported.¹³ The elevated age-standardized cancer mortality rates in 2004-05 (exactly ten years before data collection) and 2010 (round year) are also likely due to misreporting of relative's year of death. However, apart from these fluctuations, the overall mortality trends followed the official figures well, which suggests that our method may be a suitable alternative if cancer mortality rates are to be explored retrospectively for the purposes of longitudinal analyses.

Third, the comparability of the alcohol-related PARF across countries is likely to be sensitive to our relatively crude measurement of intake. For example, we did not assess binge drinking or other hazardous drinking habits (i.e. consumption of home-made spirits or non-beverage surrogate alcohols), both of which are common in Eastern Europe and may be related to cancer mortality.^{24,25} Moreover, while the trajectory of smoking habits tends to be similar for most people, with initiation in adolescence and a progressive reduction through quitting, alcohol consumption over the lifecourse is much more variable, and the effects of heavy drinking are likely to cause competing mortality, whereby individuals die from other causes before developing, or perhaps being diagnosed with, cancer.

On the other hand, one of the novelties of our study is how it showed that the “Brass technique” can provide estimates of cancer mortality rates that agree with official data when used retrospectively. Furthermore, this is one of the first studies to estimate the proportion of cancer deaths attributable to alcohol and smoking directly in Eastern European populations using large scale individual-level epidemiological data, while exploring potential explanations for the between-country variations in cancer mortality rates within this region.

CONCLUSION

One in three cancer deaths in the examined Eastern European countries could be prevented if smoking and alcohol intake was reduced. This adds to the existing body of evidence on the need to implement effective public health policies which target smoking and alcohol consumption in Eastern Europe.

ROLE OF THE FUNDING SOURCE

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CONFLICT OF INTEREST STATEMENT

None declared.

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Table 1. Population attributable risk fractions (PARFs) of cancer mortality due to alcohol, smoking, joint consumption and overall in Russian, Belarusian and Hungarian males

Country	Alcohol/smoking category	Prevalence (%)	OR [†]	(95% CI)	PARF (%)	(95% CI)
Hungary (n=27,602)	Never alcohol, never smoking	31.1	1.00	ref.		
	Never alcohol, EVER SMOKING	25.7	1.77	(1.56-2.00)	16.5	(12.6-20.4)
	EVER ALCOHOL, never smoking	10.2	1.13	(0.96-1.33)	1.3	(-0.4-3.3)
	EVER ALCOHOL and EVER SMOKING	33.0	2.00	(1.76-2.28)	24.8	(20.1-29.7)
	Overall:				35.1	(28.1-41.6)
Russia (n=23,459)	Never alcohol, never smoking	20.2	1.00	ref.		
	Never alcohol, EVER SMOKING	35.0	1.93	(1.66-2.25)	24.6	(18.8-30.4)
	EVER ALCOHOL, never smoking	6.1	1.29	(1.01-1.63)	1.7	(0.1-3.7)
	EVER ALCOHOL and EVER SMOKING	38.7	2.07	(1.61-2.65)	29.3	(19.1-39.0)
	Overall:				43.1	(31.9-52.7)
Belarus (n=21,129)	Never alcohol, never smoking	26.5	1.00	ref.		
	Never alcohol, EVER SMOKING	35.1	1.62	(1.26-2.08)	17.9	(8.4-27.5)
	EVER ALCOHOL, never smoking	6.9	1.27	(0.87-1.85)	1.8	(-0.9-5.5)
	EVER ALCOHOL and EVER SMOKING	31.5	2.22	(1.81-2.72)	27.8	(20.3-35.1)
	Overall:				38.3	(25.2-49.5)

[†]Discrete time-survival method was used with robust standard errors; time period: 2001-2013; adjusted for age and relationship with respondent.

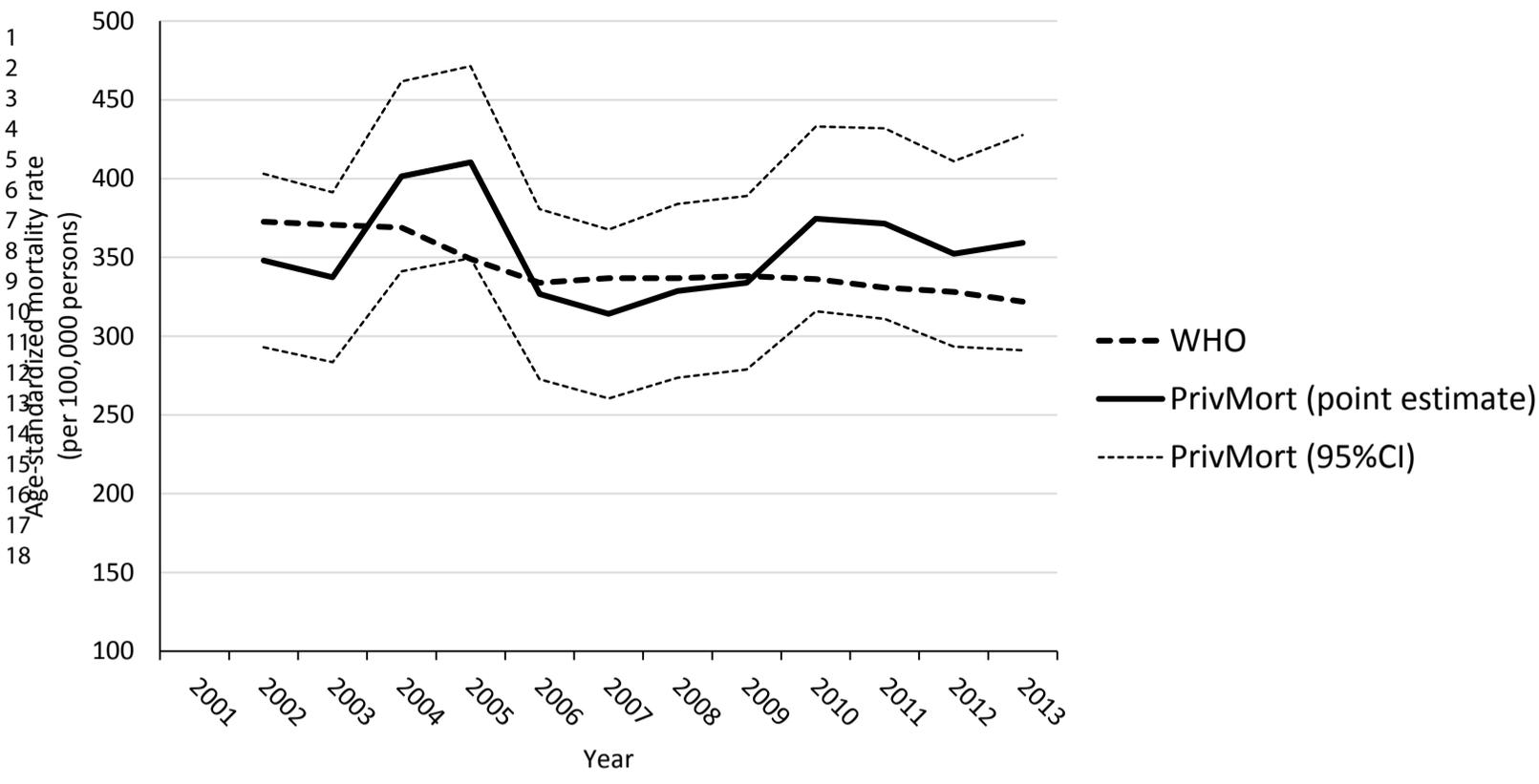
Table 2. Differences in cancer mortality rates between the three countries

	death/n	Model 1		Model 2	
		OR	(95% CI)	OR	(95% CI)
Hungary	2,335/27,602	1.00	(ref.)	1.00	(ref.)
Russia	1,361/23,459	0.74	(0.66-0.83)	0.67	(0.58-0.77)
Belarus	1,006/21,129	0.62	(0.54-0.71)	0.57	(0.50-0.65)

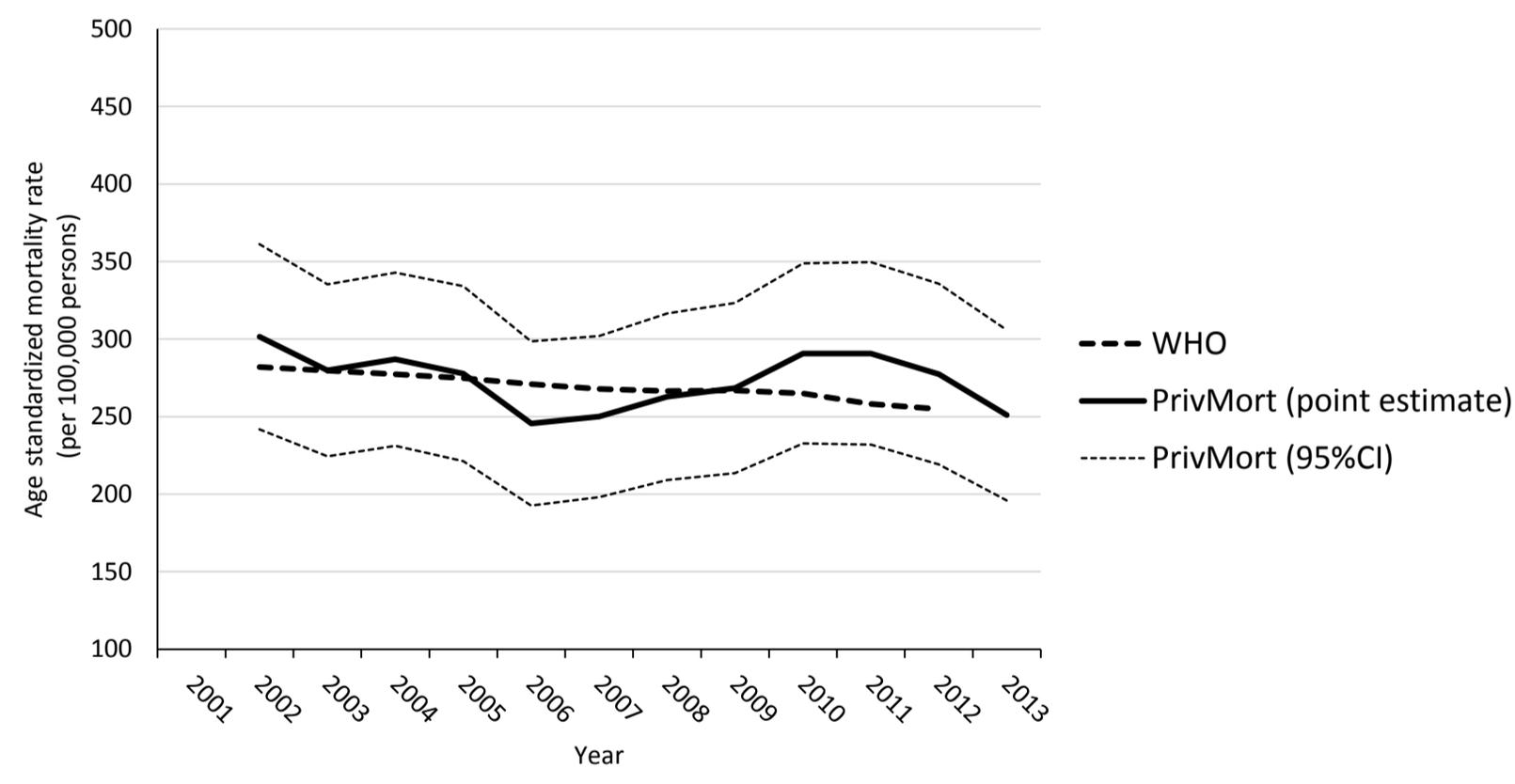
Model 1: adjusted for age and relationship with respondent

Model 2: adjusted for age, relationship with respondent, smoking and alcohol intake

HUNGARY



RUSSIA



BELARUS

