Alcohol and cause-specific mortality in Russia: a retrospective case–control study of 48 557 adult deaths

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Summary

Background Alcohol is an important determinant of the high and fluctuating adult mortality rates in Russia, but cause-specific detail is lacking. Our case–control study investigated the effects of alcohol consumption on male and female cause-specific mortality.

Methods In three Russian industrial cities with typical 1990s mortality patterns (Tomsk, Barnaul, Biysk), the addresses of 60 416 residents who had died at ages 15–74 years in 1990–2001 were visited in 2001–05. Family members were present for 50 066 decedents; for 48 557 (97%), the family gave proxy information on the decedents' past alcohol use and on potentially confounding factors. Cases (n=43 082) were those certified as dying from causes we judged beforehand might be substantially affected by alcohol or tobacco; controls were the other 5475 decedents. Case versus control relative risks (RRs; calculated as odds ratios by confounder-adjusted logistic regression) were calculated in ever-drinkers, defining the reference category by two criteria: usual weekly consumption always less than 0·5 half-litre bottles of vodka (or equivalent in total alcohol content) and maximum consumption of spirits in 1 day always less than 0·5 half-litre bottles. Other ever-drinkers were classified by usual weekly consumption into three categories: less than one, one to less than three, and three or more (mean 5·4 [SD 1·4]) bottles of vodka or equivalent.

Findings In men, the three causes accounting for the most alcohol-associated deaths were accidents and violence (RR 5·94, 95% CI 5·35–6·59, in the highest consumption category), alcohol poisoning (21·68, 17·94–26·20), and acute ischaemic heart disease other than myocardial infarction (3·04, 2·73–3·39), which includes some misclassified alcohol poisoning. There were significant excesses of upper aerodigestive tract cancer (3·48, 2·84–4·27) and liver cancer (2·11, 1·64–2·70). Another five disease groups had RRs of more than 3·00 in the highest alcohol category: tuberculosis (4·14, 3·44–4·98), pneumonia (3·29, 2·83–3·83), liver disease (6·21, 5·16–7·47), pancreatic disease (6·69, 4·98–9·00), and ill-specified conditions (7·74, 6·48–9·25). Although drinking was less common in women, the RRs associated with it were generally more extreme. After correction for reporting errors, alcohol-associated excesses accounted for 52% of all study deaths at ages 15–54 years (men 8182 [59%] of 13968, women 1565 [33%] of 4751) and 18% of those at 55–74 years (men 3944 [22%] of 17 536, women 1493 [12%] of 12 302). Allowance for under-representation of extreme drinkers would further increase alcohol-associated proportions. Large fluctuations in mortality from these ten strongly alcohol-associated causes were the main determinants of recent fluctuations in overall mortality in the study region and in Russia as a whole.

Interpretation Alcohol-attributable mortality varies by year; in several recent years, alcohol was a cause of more than half of all Russian deaths at ages 15–54 years. Alcohol accounts for most of the large fluctuations in Russian mortality, and alcohol and tobacco account for the large difference in adult mortality between Russia and western Europe.

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Introduction

The sharp fluctuations in Russian adult mortality rates since 1984 (figure 1 and panel 1) are unprecedented in a modern industrialised country. Although the largest relative changes were in the mortality attributed directly to alcohol poisoning, the largest absolute changes were in the mortality attributed to other external causes and to vascular disease.[4,5] Within vascular disease mortality, that from acute myocardial infarction was relatively low and stable; the greatest absolute fluctuations were in the mortality attributed on the death certificate to other forms of acute ischaemic heart disease, some of which represented misclassified alcohol poisoning.[6] The lowest overall mortality rates were in 1986–87, following the 1985 Soviet restrictions on alcohol production; previously, alcohol consumption had been increasing slowly for many years, but it decreased suddenly within a few months during 1985, was at a minimum during 1986–87 at about three-quarters of pre-1985 levels, increased (slowly then steeply) after 1987, and was at a maximum in 1994. The highest overall mortality rates also occurred in 1994, following the Soviet collapse in late 1991.[7,8] The relative changes in mortality were particularly extreme at ages 15–54 years. At these ages, both male and female Russian death rates approximately doubled between 1987 and 1994, then fluctuated but

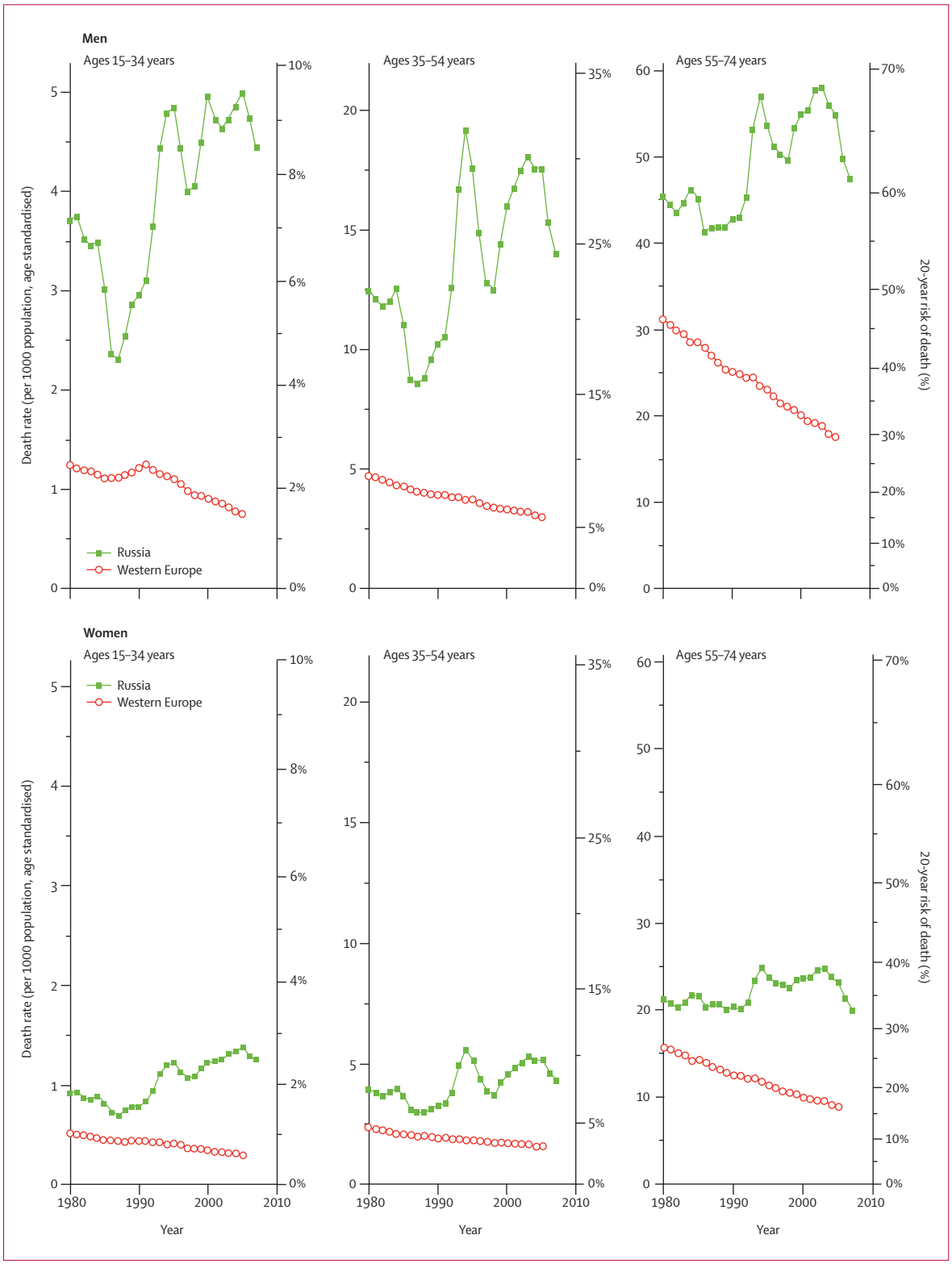

Figure 1: **All-cause mortality rates and 20-year risks of death in Russia and western Europe, 1980–2007**
Source: WHO death numbers and UN population estimates.[1-3] Western Europe=countries with mortality data available up to 2005 (Austria, Finland, France, Germany, Greece, Ireland, Luxembourg, Netherlands, Norway, Spain, Sweden, Switzerland, and UK). The death rate (*R* per 1000) in each 20-year age range is the mean of the rates in the four 5-year age ranges. The 20-year risk of death is then 1–exp(–20*R*/1000).

Panel 1: **Edge effects in 5-year age ranges**

There were sudden large decreases in Russian birth rates in 1932–34 and 1942–43 and large increases a few years later, so there are now sharp year-on-year irregularities (edge effects) in the age distribution of Russian adults. Hence, within a 5-year age range the mean age can differ by a few months from the midpoint, and standardisation by single years of age would, if possible, be preferable. Death rates were, however, available only in 5-year age ranges, within which fluctuations in mean age can cause appreciable artifactual fluctuations in mortality. For 1980–2007, the artifactual mortality fluctuations in particular 5-year age ranges for a reasonably stable cause of death (eg, female non-respiratory cancer) can be used to help quantify the expected artifactual effects for overall mortality. This suggests that such artifacts were negligible at ages 15–34 years and 55–74 years, and suggests that even at ages 35–54 years (where they slightly accentuated the decreases in 1984–88 and 1994–98 and the increases in 1988–94 and 1998–99 in overall mortality), any such artifacts were an order of magnitude smaller than the real changes in overall mortality.

remained high (figure 1). At the death rates of the year 2000,[7] the probability that a 15-year-old man would die before age 35 years was almost 10%, and the probability that a 35-year-old man would die before age 55 years was 27%; in western Europe these probabilities were only 2% and 6%, respectively.[1–3]

Evidence of a major effect of alcohol consumption on recent Russian mortality patterns comes from both cause-specific analyses of national mortality trends[4–10] and analytical studies of individuals.[11–14] These effects need to be measured reliably not only to assess the importance of alcohol, but also to help determine whether the main societal factors that underlie the Russian mortality fluctuations (eg, general economic uncertainty[15,16] or destabilising effects of rapid mass privatisation[17]) had any major effects on mortality other than through their effects on drinking patterns. A case–control study in Izhevsk based on proxy information from families of 1750 men who died in 2003–05 reported that 43% of male deaths at ages 25–54 years were caused by ethanol (either in vodka and other beverages intended for human consumption or in other products [non-beverage alcohol]).[14] To assess the effects of alcohol consumption on male and female mortality in a wider range of ages (15–74 years) and over a longer period (1990–2001) than in previous analytical studies, and to assess more reliably its role in specific causes of death, between 2001 and 2005 we obtained proxy information on alcohol consumption and other lifestyle factors from families of 48 557 Russian adults who had died in 1990–2001, and related this information to the certified cause of death.

Methods

Setting, participants, and procedures

This case–control study took place in three industrial cities of western Siberia with predominantly European Russian populations: Tomsk (2002 census population 0·5 million), Barnaul (0·7 million) and Biysk (0·2 million). Overall mortality rates (and the distribution of the main certified causes of death) were similar to those in the whole of Russia, and fluctuated in a similar way during the 1990s, with a sudden large increase in mortality during 1992–94.[5] Details, including name, address, age, and sex, of the 0·2 million registered residents who died at ages 15–74 years during 1990–2001 in these three cities were taken from local death registration records. Such records include virtually all urban deaths (but, until 2002, excluded deaths of migrants to the three cities). For each death record we ignored the local death coding,[5] and used the International Classification of Diseases and Related Health Problems 10th revision (ICD-10) to assign the underlying cause from the written death certificate.[18]

During 2001–05, teams of local physicians were trained in objective interview methods and worked (under supervision) mainly in those areas of town in which at least one had practised (although most were currently not doing so; this study was not identified with local health-care services). Working from lists that did not record causes of death, they visited, usually after 1800 h, 60 416 addresses of decedents; the adult family members found at these addresses were asked to participate in an interview, mainly about their own habits. Questions about decedents did not dominate the interview, since interviewers first completed standard questionnaires about smoking, drinking, and other factors for all adults present (for future prospective study). A fixed sequence was used to select a competent adult informant for the deceased individual; spouses were the first choice, then siblings, then parents, then adult children, then any other adult family member. Informants could be blood or in-law relatives living at the address. One in ten interviews about decedents was randomly chosen for repetition to monitor performance. Alcohol questions did not obtrude, because much other information was obtained, including ethnicity, marital status, education level, jobs held, job loss, income, recent changes in income, and smoking (usual daily amount, age started, age stopped). Smokers were defined as those who had smoked within 5 years of death or after age 55 years.

The questionnaire used in the interview asked about usual alcohol consumption patterns before the final year of life (usual weekly frequency of drinking spirits, beer, and wine, usual amounts of each per session, and maximum amount [just of spirits] per session). The main spirit used was vodka; other spirits are taken as equivalent in strength (ie, 40% alcohol). Beer was taken as 0·125 and wine as 0·25 times vodka in strength. Total weekly alcohol consumption (frequencies multiplied by usual amounts) was expressed in 500 mL bottles of vodka (or alcoholic

	Men		Women	
	15–54 years* (n=13 968)	55–74 years* (n=17 536)	15–54 years* (n=4751)	55–74 years* (n=12 302)
Year of death (with interview 2001–05)				
1990–91	1598 (11%)	1952 (11%)	545 (11%)	1473 (12%)
1992–93	2524 (18%)	2862 (16%)	811 (17%)	2039 (17%)
1994–95	3080 (22%)	3537 (20%)	1025 (22%)	2508 (20%)
1996–97	2734 (20%)	3432 (20%)	876 (18%)	2315 (19%)
1998–99	2186 (16%)	2967 (17%)	777 (16%)	2148 (17%)
2000–01	1846 (13%)	2786 (16%)	717 (15%)	1819 (15%)
Proxy interviewee				
Spouse/partner	4271 (31%)	6553 (37%)	840 (18%)	1265 (10%)
Sibling	1323 (9%)	572 (3%)	368 (8%)	413 (3%)
Parent	2049 (15%)	53 (0·3%)	563 (12%)	28 (0·2%)
Adult offspring	1341 (10%)	3906 (22%)	1005 (21%)	4309 (35%)
Other adult relative	4984 (36%)	6452 (37%)	1975 (42%)	6287 (51%)
Time intervals				
Years knew decedent	22 (11; 12–29)	30 (14; 20–40)	21 (11; 12–28)	30 (15; 17–41)
Years until interview	9 (3; 6–11)	8 (3; 5–11)	8 (3; 6–11)	8 (3; 6–11)
Quality of cooperation				
Good	11 724 (84%)	14 443 (82%)	3926 (83%)	9917 (81%)
Fair	1828 (13%)	2648 (15%)	673 (14%)	2058 (17%)
Poor	416 (3%)	445 (3%)	152 (3%)	327 (3%)
Certified cause of death				
Control diseases†	949 (7%)	1565 (9%)	959 (20%)	2002 (16%)
All other diseases	6503 (47%)	14 076 (80%)	2263 (48%)	9440 (77%)
Alcohol poisoning	1163 (8%)	458 (3%)	253 (5%)	174 (1%)
Accidents and violence	5353 (38%)	1437 (8%)	1276 (27%)	686 (6%)
Reported habits, for those who died of control diseases†				
Never smoked	210 (22%)	322 (21%)	816 (85%)	1855 (93%)
Smoker‡	694 (73%)	1102 (70%)	131 (14%)	131 (7%)
Never drank	114 (12%)	98 (6%)	300 (31%)	603 (30%)
Reference drinkers§	140 (15%)	223 (14%)	444 (46%)	1035 (52%)
Less than one bottle of vodka per week	290 (31%)	571 (36%)	119 (12%)	227 (11%)
One to less than three bottles of vodka per week	244 (26%)	458 (29%)	55 (6%)	94 (5%)
Three or more bottles of vodka per week	161 (17%)	215 (14%)	41 (4%)	43 (2%)

Data are n (%) or mean (SD; IQR). *Age at death. †Diseases that, in our prior judgment, are unlikely to be substantially affected by alcohol or tobacco, including some malignant neoplasms, all benign neoplasms, diabetes, diseases of the nervous system, non-alcoholic mental disorders, renal disease, and all infectious or parasitic diseases other than tuberculosis, pneumonia, or hepatitis. ‡Had smoked within 5 years of death or after age 55 years (almost all ever-smokers are smokers). §Most alcohol was consumed as vodka; weekly consumption of other alcohol is included as the equivalent amount of vodka (taking one bottle of vodka to contain 500 mL). Among ever-drinkers, the reference category is usual weekly consumption always less than 0·5 bottles of vodka or equivalent, and maximum consumption of spirits in 1 day always less than 0·5 bottles. Other ever-drinkers are classified only by usual weekly consumption (less than one bottle, one to less than three bottles, or three or more bottles of vodka or equivalent; in these groups the IQRs for maximum consumption in 1 day were 0·5–1·0 bottle, 1·0–1·0 bottle, and 1·0–2·0 bottles, respectively).

Table 1: **Characteristics of deceased men and women, and of interviewees**

equivalent). The same questions were asked about the final year of life, but the usual amounts reported for the two periods were similar, and only the greater of the two was used.

In ever-drinkers, the reference category was defined by two upper limits: usual weekly alcohol consumption always less than 0·5 bottles of vodka (or equivalent), and, to exclude binge drinkers, maximum consumption of spirits per session always less than 0·5 bottles. Other ever-drinkers were categorised only by weekly consumption (<one, one to <three, or ≥three bottles of vodka or equivalent), and relative risks and trend tests compare these three categories with the reference category. For decedents aged 15–39 years, interviewers also recorded regular drinking (yes/no) of non-beverage alcohol, but this information was not used in defining the alcohol categories.

Alcohol intake is difficult to assess reliably in proxy interviews several years after death. Moreover, if death was from a disease (or external cause) substantially affected by alcohol, families might tend to misreport amounts or even report no alcohol use, leading some drinkers to be misclassified as never-drinkers. Since real never-drinking is rare in Russia, at least in men, this could make the ratio of proxy-reported never-drinkers to ever-drinkers differ substantially between those who died from alcohol-affected diseases (or external causes) and other diseases. The main case–control analyses therefore ignore the small numbers reported as never-drinkers, compare the four categories of ever-drinkers, and make approximate correction for the effects of uncertainty in alcohol use. Sensitivity analyses include the never-drinkers.

Statistical methods

The case–control comparisons relate alcohol consumption category (reference or other) among ever-drinkers to underlying cause of death (case or control). Cases were those who had died from the causes that, in our prior judgment, could be substantially affected by alcohol or tobacco: alcohol poisoning (redefined to include the few deaths from alcoholic psychosis), other external causes, ill-defined causes, tuberculosis, respiratory disease, vascular disease, oesophagus, stomach, liver, or pancreas disease (apart from diabetes mellitus) and lung, upper aerodigestive tract, stomach, liver, pancreas, bladder, or breast cancer. Controls were those adults who had died from other diseases, including some malignant neoplasms, all benign neoplasms, diabetes, diseases of the nervous system, non-alcoholic mental disorders, renal disease, and all infectious or parasitic diseases other than tuberculosis, pneumonia, or hepatitis.

The main analyses are of ever-drinkers, and compare four alcohol categories. Case versus control odds ratios for the three higher alcohol categories (versus reference drinkers) were calculated simultaneously by logistic regression, stratified for age (in 5-year age-groups), city (three cities) and smoking (yes/no), and are described as relative risks (RRs, calculated as odds ratios by SAS version 9.1). For deaths in one alcohol category, the RR implies that the dose-related excess proportion is 1–1/RR. Sensitivity analyses involved cruder alcohol categories but more stratification. 95% CIs, trend tests, and two-sided p values are cited, making no allowance for multiple hypothesis testing.

Role of the funding source
The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Family members were found at 50 066 (83%) of the 60 416 addresses visited. 97% of interviews were completed, yielding information on 48 557 decedents (31 504 men, 17 053 women), of whom 43 082 were cases and 5475 were controls. Table 1 shows year of death, relationship of interviewee to deceased individual, certified causes of death, and, for controls (97% [5309/5475] of whom were ethnic Russian), their reported habits. Of 2514 male controls, 212 (8%) never drank alcohol, 363 (14%) were in the reference category, and 1939 (77%) were in the higher alcohol consumption categories. Of 2961 female controls, 903 (30%) never drank, 1479 (50%) were in the reference category, and only 579 (20%) were in the higher alcohol consumption categories. Within each category, however, male and female controls had similar consumption patterns. On average, those in the top category drank on 4·8 (SD 1·6) days a week, consuming 5·4 (1·4) half-litre bottles of vodka (or equivalent) a week, with maximum consumption of spirits in 1 day mostly reported as one bottle or two bottles (mean 1·4 [0·6] bottles). On average, those in the other three categories of ever-drinkers (ie, reference, <one bottle, or one to <three bottles) drank on 0·4 (0·6), 0·8 (0·8), or 2·2 (1·2) days a week, consuming 0·1 (0·1), 0·3 (0·3), or 1·5 (0·5) bottles of vodka (or equivalent) a week, with maximum spirits in 1 day 0·2 (0·1), 0·7 (0·3), or 1·0 (0·4) bottles.

Table 2 gives the main results for male mortality at ages 15–74 years in ever-drinkers, subdivided by cause and amount drunk. For neoplastic disease, the trend in risk across categories of ever-drinkers was significant only for upper aerodigestive tract cancer (RR 3·48, 95% CI 2·84–4·27, in the highest alcohol consumption category; trend p<0·0001) and liver cancer (2·11, 1·64–2·70; trend p<0·0001). The trends were not significant for lung cancer (p=0·18) or stomach cancer (p=0·46).

Six non-neoplastic disease groups were also strongly associated with alcohol in men, with RRs greater than 3·00 in the highest consumption category (all p<0·0001 for the trend in risk). These disease groups were tuberculosis (4·14, 3·44–4·98), pneumonia (3·29, 2·83–3·83), liver disease (6·21, 5·16–7·47), pancreatic disease (6·69, 4·98–9·00), acute ischaemic heart disease (IHD) other than myocardial infarction (3·04, 2·73–3·39), and death from an ill-specified disease (7·74, 6·48–9·25). The latter two groups include some misclassified deaths that were actually from alcohol poisoning.[6] Some other causes of death were significantly associated with alcohol, but the RRs were less extreme (eg, stroke [1·28, 1·15–1·43]). There was, however, no significant trend in mortality from acute myocardial infarction (p=0·62); in the heaviest drinkers (three or more bottles per week), acute myocardial infarction accounted for only 178 deaths, whereas acute IHD other than myocardial infarction accounted for 1044 deaths.

In the combined results for all causes of death strongly associated with alcohol in men (ie, liver cancer and anything with RR more than 3·00 in table 2) there was, of course, a definite and progressive dose-response relation (with RR 3·77, 3·44–4·12, for men in the highest alcohol category), whereas in the combined results for all other diseases the progressive association, although significant, was less strong (1·40, 1·29–1·52).

As expected, reported alcohol consumption was strongly associated with the mortality that was certified as caused by alcohol poisoning, but 41 (3%) of 1610 ever-drinkers who died from alcohol poisoning were in the lowest alcohol category (reference category), and a further 11 were reported as never-drinkers, indicating that proxy information sometimes missed life-threatening alcohol use. Moreover, another 188 (12%) deaths from alcohol poisoning were in men whose usual consumption was, perhaps inaccurately, reported to be less than one bottle per week. Reported alcohol consumption was also strongly associated with the other major groups of external causes of death, including transport accidents (4·20, 3·31–5·34), other accidents (6·07, 5·27–6·98), suicide (8·62, 6·99–10·62), and assault (9·47, 7·96–11·25; all p<0·0001 for the trend in risk).

Table 3 gives the corresponding results for women. For neoplastic disease, the RR in the highest drinking category appeared to be increased only for liver cancer and upper aerodigestive tract cancer, although no trend in cancer mortality was significantly positive (perhaps because of small numbers). For breast cancer, the trend was significantly negative (p=0·0002), and the relative risks in the two highest alcohol consumption categories were both substantially lower than 1·00.

The non-neoplastic disease groups that were most strongly associated with alcohol in men were even more strongly associated with alcohol in women, each with an RR of more than 3·00 not only in the heaviest drinkers but also in women drinking one to three bottles of vodka (or equivalent) per week (and each with p<0·0001 for trend). The same findings were seen for each main group of external causes, including transport accidents, other accidents, suicide, and assault. As in men, reported alcohol consumption in women was strongly associated with mortality from alcohol poisoning, but in the 424 female ever-drinkers certified as dying from alcohol poisoning, 51 (12%) were in the lowest alcohol category (reference category), and another 41 (10%) were reported to have usually consumed less than one bottle of vodka (or equivalent) per week. Again, the RR was substantially less extreme for acute myocardial infarction than for other acute IHD, and in the top two alcohol consumption categories,

	Reference drinkers*	Other drinkers, by usual weekly intake (half-litre bottles of vodka, or equivalent)						Four-group trend among drinkers†	
	Number of men	Less than one bottle		One to less than three bottles		Three or more bottles		*Z* score	p value
		n	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)		
Control diseases‡									
Neoplastic	230	544	..	448	..	217	..	..	..
Non-neoplastic	133	317	..	254	..	159	..	..	..
Total	363	861	1·0	702	1·0	376	1·0	..	..
Non-control diseases (ICD-10 codes)									
Upper aerodigestive tract cancer (C00–15, C32)	36	161	1·57 (1·29–1·92)	209	2·32 (1·90–2·82)	173	3·48 (2·84–4·27)	7·1	<0·0001
Liver cancer (C22)	27	73	1·01 (0·79–1·28)	75	1·28 (1·01–1·63)	63	2·11 (1·64–2·70)	4·3	<0·0001
Lung cancer (C33–34)	193	723	1·23 (1·10–1·38)	750	1·48 (1·32–1·65)	365	1·33 (1·17–1·50)	1·3	0·18
Stomach cancer (C16)	112	285	0·99 (0·86–1·12)	264	1·08 (0·94–1·24)	140	1·09 (0·93–1·26)	0·7	0·46
Pancreas cancer (C25)	36	74	0·78 (0·63–0·97)	84	1·04 (0·84–1·29)	52	1·22 (0·96–1·54)	1·8	0·06
Bladder cancer (C67)	17	63	1·46 (1·10–1·94)	52	1·37 (1·02–1·84)	19	1·05 (0·74–1·49)	–0·7	0·46
Cancer site unspecified (C76–80)	26	79	1·09 (0·86–1·40)	48	0·78 (0·60–1·01)	37	1·08 (0·82–1·42)	0·1	0·92
Tuberculosis (A15–19, B90)	52	139	1·01 (0·83–1·22)	235	1·97 (1·64–2·36)	283	4·14 (3·44–4·98)	11·4	<0·0001
COPD (I27, J40–47, J67)	90	290	1·22 (1·05–1·40)	271	1·40 (1·21–1·62)	179	1·79 (1·53–2·10)	3·8	0·0001
Pneumonia, etc (rest of J00–98)	78	187	0·95 (0·82–1·11)	332	1·92 (1·66–2·22)	327	3·29 (2·83–3·83)	11·2	<0·0001
Peritonitis (K65)	12	26	0·88 (0·61–1·27)	43	1·63 (1·16–2·30)	27	1·67 (1·15–2·41)	2·1	0·04
Liver disease (K70–77, B15–19)	45	93	0·92 (0·76–1·13)	144	1·77 (1·47–2·14)	298	6·21 (5·16–7·47)	16·1	<0·0001
Pancreatic disease (K85–86)	17	45	1·43 (1·04–1·95)	58	2·07 (1·53–2·80)	112	6·69 (4·98–9·00)	9·8	<0·0001
Gastro-oesophageal (K20–31, K92, I85)	20	62	1·25 (0·96–1·64)	73	1·67 (1·28–2·18)	47	2·05 (1·54–2·72)	2·8	0·005
Rheumatic heart disease (I00–09)	18	26	0·57 (0·41–0·78)	17	0·45 (0·31–0·64)	14	0·63 (0·43–0·92)	–0·4	0·68
Acute MI (I20–23)	120	388	1·23 (1·08–1·39)	323	1·18 (1·03–1·34)	178	1·20 (1·04–1·38)	0·5	0·62
Non-MI acute IHD (I24)	240	678	1·06 (0·96–1·18)	1027	1·79 (1·62–1·99)	1044	3·04 (2·73–3·39)	13·7	<0·0001
Chronic IHD (I25)	286	768	1·05 (0·95–1·17)	674	1·20 (1·08–1·33)	428	1·49 (1·33–1·68)	4·3	<0·0001
Stroke (I60–69)	374	967	1·06 (0·96–1·16)	866	1·14 (1·03–1·25)	491	1·28 (1·15–1·43)	2·5	0·01
Other vascular disease (rest of I00–99)	204	511	1·02 (0·91–1·14)	469	1·14 (1·02–1·28)	325	1·57 (1·39–1·78)	4·7	<0·0001
Ill-specified disease (R00–99)	48	152	1·29 (1·07–1·56)	274	2·84 (2·38–3·39)	432	7·74 (6·48–9·25)	17·3	<0·0001
Subtotals									
Diseases strongly associated with alcohol§	543	1528	1·11 (1·02–1·21)	2354	1·91 (1·76–2·08)	2732	3·77 (3·44–4·12)	18·5	<0·0001
Other non-control diseases	1508	4262	1·10 (1·02–1·18)	3934	1·22 (1·13–1·31)	2302	1·40 (1·29–1·52)	4·1	<0·0001
External causes, not disease (ICD-10 codes)									
Alcohol poisoning (X45, Y15, F10)	41	188	1·94 (1·59–2·36)	331	4·06 (3·35–4·91)	1050	21·68 (17·94–26·20)	27·1	<0·0001
Accidents and violence (rest of V00–Y99)	470	1410	1·44 (1·30–1·59)	1956	2·53 (2·29–2·79)	2438	5·94 (5·35–6·59)	20·4	<0·0001
Transport accidents (V00–99)	34	95	1·52 (1·20–1·93)	144	2·68 (2·13–3·38)	125	4·20 (3·31–5·34)	7·0	<0·0001
Other accidents (W00–X44, X46–59, Y37–99)	136	426	1·58 (1·38–1·82)	556	2·48 (2·16–2·84)	729	6·07 (5·27–6·98)	15·9	<0·0001
Suicide (X60–84)	41	99	1·21 (0·97–1·52)	238	3·47 (2·82–4·27)	378	8·62 (6·99–10·62)	14·9	<0·0001
Assault (X85–Y09, Y35–36)	75	243	1·75 (1·47–2·09)	404	3·67 (3·10–4·36)	619	9·47 (7·96–11·25)	16·4	<0·0001
Undetermined intent (remainder)	184	547	1·49 (1·30–1·71)	614	2·36 (2·06–2·71)	587	4·40 (3·81–5·08)	11·7	<0·0001

COPD=chronic obstructive pulmonary disease. ICD-10=International Classification of Diseases, 10th Revision (reference 18). IHD=ischaemic heart disease. MI=myocardial infarction. RR=relative risk, adjusted for age, city, and smoking. *Ever-drinkers with usual weekly consumption always less than 0·5 bottles of vodka or equivalent, and maximum consumption of spirits in 1 day always less than 0·5 bottles; excludes never-drinkers. †Test for trend (with respect to the weights 0·0, 0·1, 0·3, and 1·0) in log risk between four groups. If there were no real trend, *Z* would have an approximately standard normal distribution; hence, if $Z<1{\cdot}96$ then $p>0{\cdot}05$ (not significant). ‡Control diseases: all diseases not listed separately in this table. Neoplastic includes benign neoplastic (ICD-10 codes D00–49). The 863 deaths from non-neoplastic control diseases include 25 haematological (D50–99), 88 infective (other A or B ICD-10 codes), 86 endocrine (E), 10 non-alcoholic mental (other F codes), 209 nervous (G), 164 digestive (other K codes), 45 dermatological and musculoskeletal (L and M), 189 renal (N00–29), and 47 remaining (N30–Q99, H) diseases. §Liver disease, liver cancer, upper aerodigestive cancer, and other disease groups with RR more than 3·00 for men with usual consumption of three or more bottles of vodka per week (tuberculosis, pneumonia, non-MI acute IHD, non-neoplastic pancreatic disease, and ill-specified disease).

Table 2: **Male relative risk of death at ages 15–74 years, by proxy-reported alcohol intake (other drinkers *vs* reference drinkers, excluding never-drinkers) and certified cause (other causes *vs* control diseases)**

	Reference drinkers*	Other drinkers, by usual weekly intake (half-litre bottles of vodka, or equivalent)						Four-group trend among drinkers†	
	Number of women	Less than one bottle		One to less than three bottles		Three or more bottles		*Z* score	p value
		n	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)		
Control diseases‡									
Neoplastic	1025	232	..	92	..	38	..	..	..
Non-neoplastic	454	114	..	57	..	46	..	..	..
Total	1479	346	1·0	149	1·0	84	1·0	..	..
Non-control diseases (ICD-10 codes)									
Upper aerodigestive tract cancer (C00–15, C32)	43	14	1·27 (0·91–1·76)	8	0·99 (0·64–1·55)	8	2·21 (1·39–3·51)	1·6	0·11
Liver cancer (C22)	80	28	1·52 (1·20–1·92)	11	1·17 (0·82–1·68)	7	1·57 (1·01–2·43)	0·8	0·42
Lung cancer (C33–34)	169	48	1·08 (0·90–1·30)	30	0·92 (0·71–1·17)	16	0·97 (0·70–1·34)	0·0	0·99
Stomach cancer (C16)	287	86	1·38 (1·20–1·59)	31	1·05 (0·84–1·32)	10	0·66 (0·46–0·94)	–1·1	0·29
Pancreas cancer (C25)	82	21	1·17 (0·90–1·51)	13	1·68 (1·20–2·35)	4	1·08 (0·63–1·86)	0·6	0·56
Bladder cancer (C67)	16	2	..	0	..	0	..	–1·4	0·15
Breast cancer (C50)	390	94	0·99 (0·86–1·13)	28	0·54 (0·43–0·69)	7	0·26 (0·17–0·39)	–3·7	0·0002
Cancer site unspecified (C76–80)	67	15	0·93 (0·69–1·25)	9	0·97 (0·65–1·45)	2	0·33 (0·15–0·70)	–1·3	0·19
Tuberculosis (A15–19, B90)	38	12	0·93 (0·64–1·35)	31	4·06 (2·97–5·56)	22	5·32 (3·70–7·65)	5·0	<0·0001
COPD (I27, J40–47, J67)	150	33	0·96 (0·77–1·18)	27	1·45 (1·12–1·88)	13	1·60 (1·13–2·26)	1·4	0·15
Pneumonia, etc (rest of J00–98)	95	53	2·10 (1·74–2·54)	43	3·21 (2·56–4·02)	32	3·42 (2·64–4·44)	4·8	<0·0001
Peritonitis (K65)	17	16	2·97 (2·05–4·29)	9	1·98 (1·22–3·23)	1	0·42 (0·14–1·21)	–0·8	0·41
Liver disease (K70–77, B15–19)	100	58	2·50 (2·09–3·00)	80	7·07 (5·87–8·52)	80	12·08 (9·84–14·83)	12·6	<0·0001
Pancreatic disease (K85–86)	27	7	1·09 (0·70–1·70)	14	5·01 (3·45–7·29)	28	19·26 (13·64–27·21)	9·3	<0·0001
Gastro-oesophageal (K20–31, K92, I85)	29	12	1·84 (1·28–2·64)	7	1·69 (1·05–2·73)	4	2·09 (1·17–3·71)	1·2	0·25
Rheumatic heart disease (I00–09)	70	10	0·59 (0·41–0·84)	9	1·50 (1·00–2·25)	5	1·00 (0·59–1·68)	0·2	0·87
Acute MI (I20–23)	286	82	1·27 (1·10–1·47)	33	1·12 (0·90–1·39)	31	2·04 (1·59–2·61)	2·7	0·007
Non-MI acute IHD (I24)	348	167	1·79 (1·59–2·01)	216	4·61 (4·05–5·25)	247	9·25 (7·97–10·74)	17·1	<0·0001
Chronic IHD (I25)	805	211	1·39 (1·24–1·55)	88	1·42 (1·20–1·67)	59	2·58 (2·09–3·18)	4·9	<0·0001
Stroke (I60–69)	1369	411	1·38 (1·27–1·51)	189	1·36 (1·19–1·55)	101	1·62 (1·37–1·93)	3·1	0·002
Other vascular disease(rest of I00–99)	651	163	1·23 (1·10–1·37)	82	1·45 (1·24–1·70)	64	2·39 (1·97–2·90)	5·0	<0·0001
Ill-specified disease (R00–99)	99	46	2·11 (1·73–2·56)	68	7·16 (5·89–8·69)	79	14·89 (12·06–18·37)	14·1	<0·0001
Subtotals									
Diseases strongly associated with alcohol§	830	385	1·81 (1·66–1·98)	471	4·52 (4·05–5·03)	503	8·17 (7·17–9·32)	18·1	<0·0001
Other non-control diseases	4388	1204	1·25 (1·17–1·34)	555	1·26 (1·13–1·40)	317	1·43 (1·25–1·63)	3·0	0·003
External causes, not disease (ICD-10 codes)									
Alcohol poisoning (X45, Y15, F10)	51	41	3·11 (2·45–3·95)	105	18·03 (14·60–22·26)	227	75·23 (60·42–93·67)	23·8	<0·0001
Accidents and violence (rest of V00–Y99)	548	275	1·90 (1·71–2·11)	334	5·59 (4·94–6·32)	351	9·26 (8·02–10·69)	17·5	<0·0001
Transport accidents (V00–99)	50	27	1·98 (1·53–2·57)	28	4·48 (3·38–5·96)	14	3·17 (2·19–4·59)	3·5	0·0004
Other accidents (W00–X44, X46–59, Y37–99)	127	67	2·08 (1·75–2·48)	84	5·24 (4·35–6·30)	88	8·56 (7·01–10·45)	11·6	<0·0001
Suicide (X60–84)	28	21	2·82 (2·07–3·84)	38	8·22 (6·16–10·98)	38	14·75 (10·83–20·09)	8·6	<0·0001
Assault (X85–Y09, Y35–36)	64	63	3·55 (2·89–4·37)	94	10·23 (8·30–12·61)	105	19·11 (15·29–23·87)	13·5	<0·0001
Undetermined intent (remainder)	279	97	1·43 (1·23–1·66)	90	4·54 (3·80–5·41)	106	7·93 (6·53–9·64)	12·2	<0·0001

COPD=chronic obstructive pulmonary disease. ICD-10=International Classification of Diseases, 10th Revision (reference 18). IHD=ischaemic heart disease. MI=myocardial infarction. RR=relative risk, adjusted for age, city, and smoking. *Ever-drinkers with usual weekly consumption always less than 0·5 bottles of vodka or equivalent, and maximum consumption of spirits in 1 day always less than 0·5 bottles; excludes never-drinkers. †Test for trend (with respect to the weights 0·0, 0·1, 0·3, and 1·0) in log risk between four groups. If there were no real trend, *Z* would have an approximately standard normal distribution; hence, if $Z<1·96$ then $p>0·05$ (not significant). ‡Control diseases: all diseases not listed separately in this table. Neoplastic includes benign neoplastic (ICD-10 codes D00–49). The 671 deaths from non-neoplastic control diseases include 12 haematological (D50–99), 58 infective (other A or B ICD-10 codes), 143 endocrine (E), 10 non-alcoholic mental (other F codes), 98 nervous (G), 96 digestive (other K codes), 57 dermatological and musculoskeletal (L and M), 148 renal (N00–29), and 49 remaining (N30–Q99, H) diseases. §Liver disease, liver cancer, upper aerodigestive cancer, and other disease groups with RR more than 3·00 for men with usual consumption of three or more bottles of vodka per week (tuberculosis, pneumonia, non-MI acute IHD, non-neoplastic pancreatic disease, and ill-specified disease).

Table 3: **Female relative risk of death at ages 15–74 years, by proxy-reported alcohol intake (other drinkers *vs* reference drinkers, excluding never-drinkers) and certified cause (other causes *vs* control diseases)**

	Never-drinkers		Reference drinkers*	Other drinkers, by usual weekly intake (bottles of vodka, or equivalent)						Total deaths	Dose-related excess number of deaths (%)	
	Number of men	RR (95% CI)	Number of men	Less than one bottle per week		One to less than three bottles per week		Three or more bottles per week			Uncorrected†	Corrected‡
				n	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)			
Men aged 15–54 years												
Alcohol poisoning	8	0·3 (0·2–0·5)	32	131	1·9 (1·5–2·4)	230	3·8 (3·1–4·8)	762	19·7 (15·6–24·7)	1163	954 (82%)	1163 (100%)
Accidents and violence	428	1·40 (1·19–1·66)	383	1123	1·70 (1·49–1·94)	1538	3·08 (2·70–3·51)	1881	6·25 (5·43–7·19)	5353	3081 (58%)	3756 (70%)
Diseases strongly associated with alcohol§	295	1·77 (1·49–2·10)	226	655	1·32 (1·15–1·51)	1180	2·60 (2·27–2·97)	1431	4·46 (3·87–5·14)	3787	1995 (53%)	2432 (64%)
Other non-control diseases	190	1·25 (1·03–1·50)	242	804	1·29 (1·12–1·48)	864	1·48 (1·29–1·70)	616	1·56 (1·34–1·80)	2716	682 (19%¶)	831 (23%¶)
Control diseases (selected conditions)	114	1·0	140	290	1·0	244	1·0	161	1·0	949	0 (¶)	0 (¶)
Total (by addition)	1035	..	1023	3003	..	4056	..	4851	..	13 968	6712 (48%)	8182 (59%)
Men aged 55–74 years												
Alcohol poisoning	3	0·8 (0·4–1·5)	9	57	2·2 (1·5–3·2)	101	4·7 (3·3–6·8)	288	26·6 (18·6–38·0)	458	388 (85%)	458 (100%)
Accidents and violence	88	2·19 (1·78–2·68)	87	287	1·17 (1·01–1·36)	418	2·03 (1·75–2·36)	557	5·49 (4·71–6·41)	1437	710 (49%)	838 (58%)
Diseases strongly associated with alcohol§	371	2·27 (1·95–2·63)	317	873	1·01 (0·91–1·12)	1174	1·59 (1·43–1·77)	1301	3·43 (3·06–3·86)	4036	1367 (34%)	1614 (40%)
Other non-control diseases	560	1·15 (1·01–1·32)	1266	3458	1·03 (0·94–1·12)	3070	1·12 (1·03–1·23)	1686	1·36 (1·22–1·50)	10 040	876 (8%¶)	1034 (9%¶)
Control diseases (selected conditions)	98	1·0	223	571	1·0	458	1·0	215	1·0	1565	0 (¶)	0 (¶)
Total (by addition)	1120	..	1902	5246	..	5221	..	4047	..	17 536	3341 (19%)	3944 (22%)

RR=relative risk, adjusted for age, city, and smoking. *Ever-drinkers with usual weekly consumption always less than 0·5 bottles of vodka or equivalent, and maximum consumption of spirits in 1 day always less than 0·5 bottles; excludes never-drinkers. †Sum of (n–n/RR) for the three highest alcohol categories, expressed as a percentage of all deaths from the given certified cause in both ever-drinkers and never-drinkers. This is uncorrected for any misclassification of drinking habits (and ignores any excess risks in those reported to have been never-drinkers). ‡Uncorrected excesses multiplied by a common factor (1163/954 at ages 15–54 years, 458/388 at ages 55–74 years) chosen so that the dose-related excess is 100% for the alcohol poisoning deaths. §Liver disease, liver cancer, upper aerodigestive cancer, and other disease groups with RR more than 3·00 for men with usual consumption three or more bottles of vodka per week (tuberculosis, pneumonia, non-myocardial infarction acute ischaemic heart disease, non-neoplastic pancreatic disease, and ill-specified disease). Note that the strongly alcohol-related causes include not only these disease groups but also alcohol poisoning, accidents, and violence. ¶Percentages for other non-control diseases and control diseases (selected conditions) are combined.

Table 4: **Male dose-related excess mortality in ever-drinkers as a proportion of all mortality in male ever-drinkers and never-drinkers, by age and underlying cause of death**

only 64 women died from acute myocardial infarction compared with 463 from other acute IHD.

Table 4 subdivides the results for all men more narrowly by age (15–54 years and 55–74 years) and groups the causes as alcohol poisoning, accidents and violence, diseases strongly associated with alcohol in this study, other non-control diseases, and control diseases. (The strongly associated diseases were liver disease, liver cancer, upper aerodigestive cancer, and other disease groups with RR more than 3·00 for men with usual consumption three or more bottles of vodka per week [tuberculosis, pneumonia, acute IHD other than myocardial infarction, non-neoplastic pancreatic disease, and ill-specified disease].) The relative risks comparing never-drinkers with reference drinkers are consistent with families under-reporting moderate alcohol use more in men who had died from accidents, violence, and diseases strongly associated with alcohol than in men who had died from other diseases. This finding is particularly clear for men aged 55–74 years, in whom the ratio of reported never-drinkers to reference drinkers was 1·1 ([88+371]/[87+317]) for men who had died of accidents, violence, and diseases strongly associated with alcohol, compared with only 0·4 ([560+98]/[1266+223]) in men who had died of other diseases ($p<0·0001$ for difference in ratios).

Table 5 gives corresponding results for women. Discrepancies between never-drinkers and reference drinkers are less extreme than in men, but are still apparent, particularly at ages 55–74 years. The ratio of never-drinkers to reference drinkers at these ages was 0·9 (742/832) for female deaths from accidents, violence, and the diseases strongly associated with alcohol, and only 0·5 (2623/4868) for female deaths from other diseases, again consistent with variable under-reporting of moderate alcohol use.

The relative risks in ever-drinkers (which compare the three higher alcohol consumption categories with the reference category) might be more directly indicative of real associations. Even in ever-drinkers, however, substantial misclassification of real alcohol consumption patterns is inevitable. If some alcohol-associated deaths are included in the reference category, then uncorrected calculation of alcohol-dose-related excess mortality in the other three alcohol consumption categories will underestimate the real excess mortality.

	Never-drinkers		Reference drinkers*	Other drinkers, by usual weekly intake (bottles of vodka, or equivalent)						Total deaths	Dose-related excess number of deaths (%)	
	Number of women	RR (95% CI)	Number of women	Less than one bottle per week		One to less than three bottles per week		Three or more bottles per week			Uncorrected†	Corrected‡
				n	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)			
Women aged 15–54 years												
Alcohol poisoning	3	0·1 (0·0–0·2)	24	20	3·5 (2·4–4·9)	69	22·9 (16·9–31·1)	137	72·1 (52·4–99·2)	253	215 (85%)	253 (100%)
Accidents and violence	256	0·90 (0·79–1·03)	331	199	2·15 (1·85–2·50)	226	5·50 (4·59–6·59)	264	8·67 (7·12–10·55)	1276	525 (41%)	618 (48%)
Diseases strongly associated with alcohol§	167	1·12 (0·98–1·29)	215	161	2·60 (2·23–3·03)	204	5·80(4·84–6·96)	247	8·88(7·29–10·82)	994	487 (49%)	573 (58%)
Other non-control diseases	319	1·00 (0·89–1·12)	555	204	1·35 (1·18–1·55)	109	1·37 (1·13–1·67)	82	1·34 (1·08–1·67)	1269	103 (5%¶)	121 (5%¶)
Control diseases (selected conditions)	300	1·0	444	119	1·0	55	1·0	41	1·0	959	0 (¶)	0 (¶)
Total (by addition)	1045	..	1569	703	..	663	..	771	..	4751	1330 (28%)	1565 (33%)
Women aged 55–74 years												
Alcohol poisoning	0	0·0 (0·0–0·2)	27	21	2·8 (2·0–3·9)	36	14·0 (10·4–18·8)	90	78·9 (58·4–106·6)	174	136 (78%)	174 (100%)
Accidents and violence	198	1·60 (1·42–1·80)	217	76	1·64 (1·41–1·92)	108	5·71 (4·83–6·76)	87	9·96(8·06–12·30)	686	197 (29%)	252 (37%)
Diseases strongly associated with alcohol§	544	1·24 (1·14–1·35)	615	224	1·50 (1·34–1·67)	267	3·94 (3·44–4·51)	256	8·01 (6·70–9·57)	1906	498 (26%)	637 (33%)
Other non-control diseases	2020	0·93 (0·87–0·99)	3833	1000	1·22 (1·12–1·33)	446	1·21 (1·07–1·37)	235	1·51 (1·27–1·80)	7534	336 (4%¶)	430 (5%¶)
Control diseases (selected conditions)	603	1·0	1035	227	1·0	94	1·0	43	1·0	2002	0 (¶)	0 (¶)
Total (by addition)	3365	..	5727	1548	..	951	..	711	..	12302	1167 (9%)	1493 (12%)

RR=relative risk, adjusted for age, city, and smoking. *Ever-drinkers with usual weekly consumption always less than 0·5 bottles of vodka or equivalent, and maximum consumption of spirits in 1 day always less than 0·5 bottle; excludes never-drinkers. †Sum of (n–n/RR) for the three highest alcohol categories, expressed as a percentage of all deaths from the given certified cause in both ever-drinkers and never-drinkers. This is uncorrected for any misclassification of drinking habits (and ignores any excess risks in those reported to have been never-drinkers). ‡Uncorrected excesses multiplied by a common factor (253/215 at ages 15–54 years, 174/136 at ages 55–74 years) chosen so that the dose-related excess is 100% for the alcohol poisoning deaths. §Liver disease, liver cancer, upper aerodigestive cancer, and other disease groups with RR more than 3·00 for men with usual consumption three or more bottles of vodka per week (tuberculosis, pneumonia, non-myocardial infarction acute ischaemic heart disease, non-neoplastic pancreatic disease, and ill-specified disease). Note that the strongly alcohol-related causes include not only these disease groups but also alcohol poisoning, accidents, and violence. ¶Percentages for other non-control diseases and control diseases (selected conditions) are combined.

Table 5: **Female dose-related excess mortality in ever-drinkers as a proportion of all mortality in female ever-drinkers and never-drinkers, by age and underlying cause of death**

Exact correction for this is impossible, but approximate correction for it is made in tables 4 and 5 by multiplying the uncorrected excess mortality from each cause by a common factor, calculated within each age range to ensure that the corrected dose-related excess is 100% for the deaths from alcohol poisoning. At ages 15–54 years, the alcohol dose-related excess accounted for 6712 (48%) of 13 968 male deaths in the uncorrected calculations, and 8182 (59%) of 13 968 in the corrected calculations. Of the corrected excess, 90% ([1163+3756+2432]/8182 deaths) was from alcohol poisoning, accidents, violence, and the eight disease groups that are strongly related to alcohol; of the remaining 10% (831/8182 excess deaths in men at ages 15–54 years), much was from vascular disease. The corrected alcohol dose-related excess accounted for 3944 (22%) of 17 536 deaths in older men, 1565 (33%) of 4751 deaths in women aged 15–54 years and 1493 (12%) of 12 302 deaths in older women.

For sensitivity analyses, alcohol use was crudely split into lower (<one bottle per week, including never drinkers) and higher usual consumption categories, and the analyses of tables 4 and 5 were then repeated. With this crude split, the uncorrected dose-related excess for alcohol poisoning was only 72% (1466/2048), but correction (as in tables 4 and 5) automatically increased this to 100%, and made dose-related excess mortality at ages 15–54 years 50% (7045/13 968) for men and 27% (1305/4751) for women, and at ages 55–74 years made it 22% (3827/17 542) for men and 10% (1275/12 302) for women. These corrected percentages are similar to those shown in tables 4 and 5, and were not materially affected by finer stratification for potential confounders (amount smoked, year of death, years since death, marital status, relationship to informant, ethnicity, education, occupation, socioeconomic status, or recent change in socioeconomic status) or by inclusion in the controls of all cancers not strongly related to alcohol (data not shown).

Non-beverage alcohol use was strongly correlated with other alcohol use but, given vodka consumption, was no more common in those dying from strongly

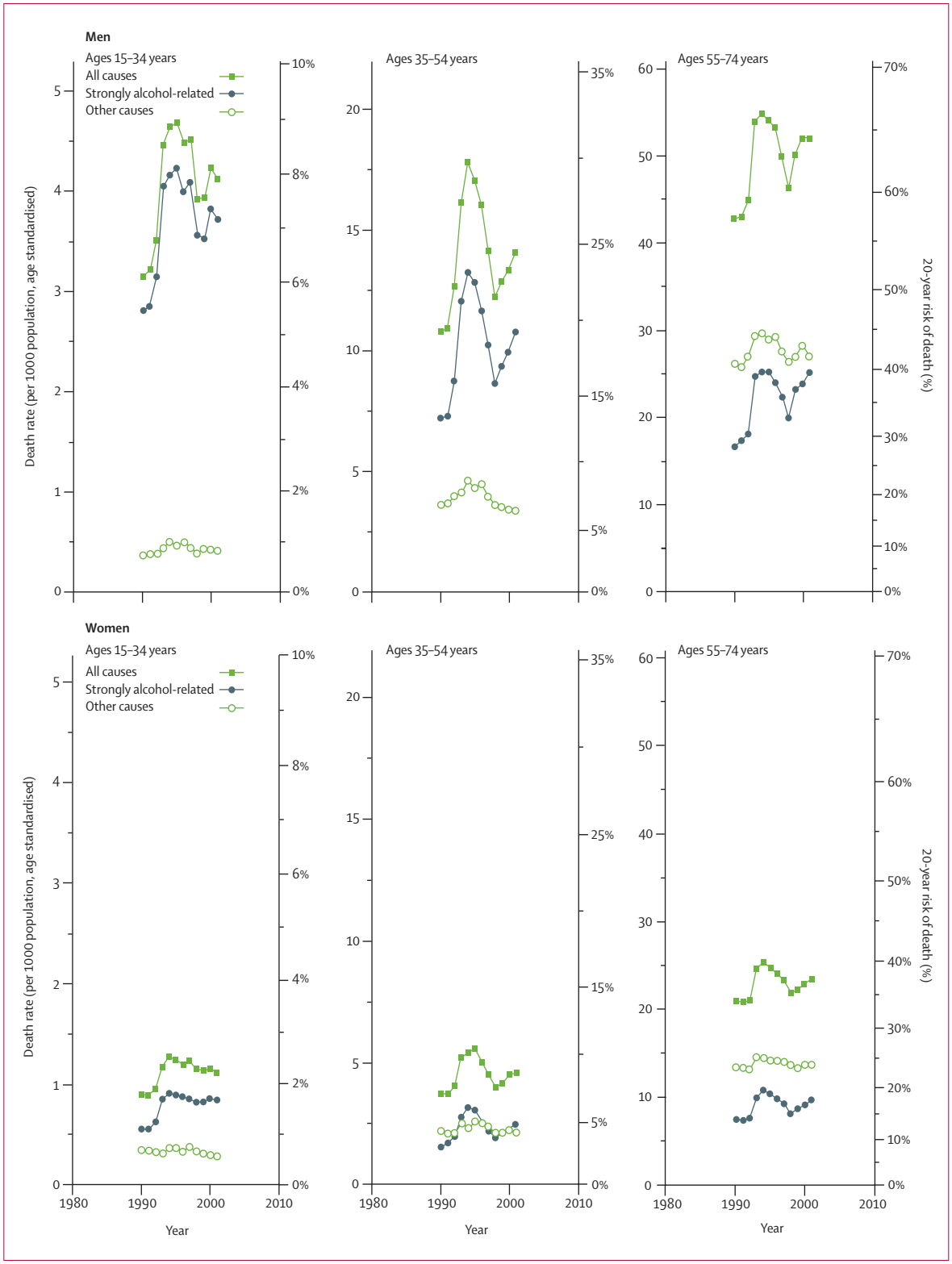

Figure 2: **Mortality from all causes, from causes strongly related to alcohol, and from other causes in the Altay and Tomsk regions of Russia, 1990–2001**
See panel 2 for definition of causes. These regions had total population 3·5 million in the 2002 census, and include the three study cities (total population 1·4 million, a third of which was covered). The death rate (*R* per 1000) in each 20-year age range is the mean of the annual rates in the four 5-year age ranges. The 20-year risk of death is then 1–exp(–20*R*/1000). Source: regional mortality and population estimates.

Panel 2: Russian cause of death coding

The strongly alcohol-related causes included in our analyses of regional time trends differ slightly from those used in all of our other analyses, because they had to be defined from Russian cause of death codes,[6] which changed in 1999 but still differed from the International Classification of Diseases, 10th revision.[18] The Russian codes included (for years 1990–98; then 1999–2001) were:
45–46 and 52; then 56–57 and 65 (upper aerodigestive tract cancer [liver cancer was unavailable])
9–13 and 43; 9–15 and 54 (tuberculosis)
103–07 and 110–14; 148–56 and 160–64 (pneumonia, etc)
30 and 122–23; 41–43 and 173–75 (liver disease, not cancer)
126; 178 (pancreatic disease, not cancer)
92–97; 122–32 (heart disease, other than myocardial infarction [acute and chronic were not separable])
158–59; 226–28 (ill-specified disease)
73, 75, and 160–75; 97, 98, and 239–55 (external causes, including alcoholic psychosis and poisoning)

alcohol-related causes than in those dying from other causes. For men who died at ages 15–39 years and were drinkers of less than one, one to less than three, or three or more bottles of vodka (or equivalent) per week, the respective proportions of deaths with non-beverage alcohol use reported were 1% (18/1306), 6% (70/1106), and 20% (250/1257) for the strongly alcohol-related causes and 1% (3/313), 5% (8/168), and 28% (34/120) for the other causes. These findings suggest that for a given amount of ethanol consumption its source was not strongly predictive of cause of death. For women, the corresponding percentages were based on much smaller numbers: 2% (8/405), 6% (9/153) and 20% (38/192) for strongly alcohol-related causes and 0% (0/240), 0% (0/23) and 39% (9/23) for other causes, respectively.

Figure 2 shows the regional mortality trends (1990–2001) in mortality from all causes, from the main causes strongly associated with alcohol use in this study (approximately as in table 2), and from the other causes. Because of the changes in Russian death coding in 1999, the strongly alcohol-related causes had to include chronic heart disease and exclude liver cancer (see panel 2). In both sexes and all age-groups there was a much sharper increase during 1992–94 in mortality from the strongly alcohol-related causes than from other causes. Fluctuations in these alcohol-related causes were the main determinants of the large fluctuations in all-cause mortality in the study areas, particularly at ages 15–34 years and 35–54 years. Thus, at these ages, the ratio of mortality from the strongly alcohol-related causes to mortality from all other causes fluctuated sharply, and was at a maximum in 1994. This was true for the whole study region (figure 2) and for the individuals in our study (data not shown).

Discussion

We found strong dose-response associations between alcohol consumption and mortality from accidents, violence, and several disease groupings. If these associations are mainly causal, then alcohol was responsible for more than half of all deaths in younger men (15–54 years) in our study areas during 1990–2001, and was a major cause of death in older men (55–74 years) and in women. Additionally, large fluctuations in mortality from alcohol-related diseases were major determinants of the extreme fluctuations in overall adult mortality after 1991, so the proportion of deaths caused by alcohol would be much greater in some years than in others.

Our study of residents in three industrial cities populated mainly by European Russians was large and population based. The interviewers were local physicians; therefore, few families refused to be interviewed and cooperation was generally good. Information was unavailable only when the address no longer existed or no family member was found there. This excludes deaths in families that subsequently moved, deaths of those who (perhaps partly because of alcohol) were isolated or without a registered address, and deaths of migrants to the study cities. Otherwise, selection bias is unlikely to have had any major affect on the results.

Cases were those adults who had died from causes we judged beforehand likely to be related to drinking or smoking, and controls were those who had died from other causes. This designation of controls was somewhat arbitrary, but is supported by the cancer results. The extensive epidemiological evidence on alcohol and cancer, as summarised by the WHO International Agency for Research on Cancer (IARC),[19] shows that the only major types of cancer much affected by alcohol in men are those of the liver and upper aerodigestive tract. This evidence helps validate the case–control results from our study (table 2), which show a highly significant effect of alcohol on mortality from cancers of the liver and upper aerodigestive tract, but not from lung cancer or stomach cancer. Few women consumed more than three bottles of vodka (or equivalent) per week, but among those who did, the only conventionally significant excess cancer risks were for those of the liver and upper aerodigestive tract.

Use of deceased people as controls was intended to limit the effects of recall and reporting bias, with the expectation that there would be no large systematic bias between people with similar drinking habits who had died of different diseases. (Similarly, many epidemiological studies of hospitalised cases use hospitalised controls.) Although families in our study are likely to misreport alcohol consumption, we had hoped that such misreporting would merely dilute the strengths of any associations. We found, however, that under-reporting of moderate alcohol consumption was particularly common for those who had died from accidents, violence, and the diseases strongly related to drinking. This under-reporting could substantially

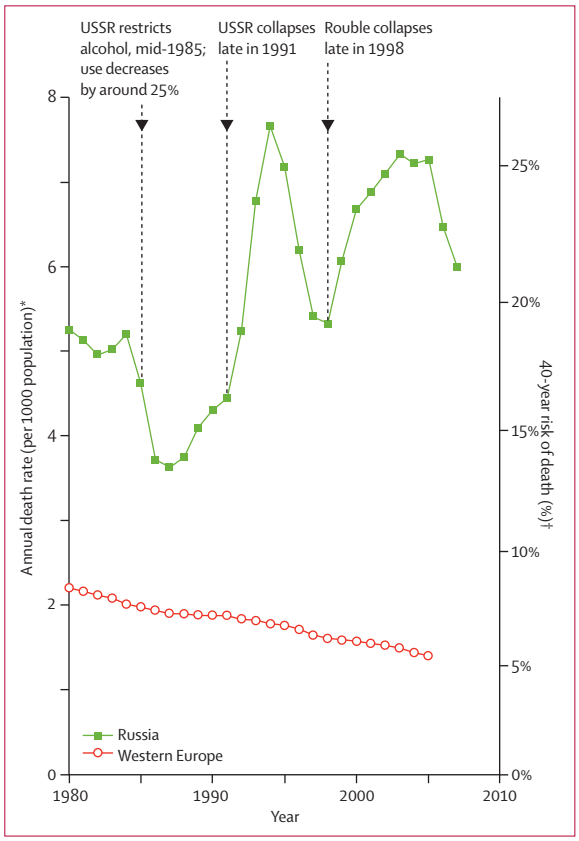

Figure 3: **Mortality from all causes and 40-year risks of death in men and women aged 15–54 years in Russia (1980–2007) and western Europe (to 2005)**
USSR=Union of Soviet Socialist Republics. Alcohol consumption had been increasing slowly for many years, then decreased suddenly in mid-1985, was minimal during 1986–87 at about three-quarters of pre-1985 levels, increased (slowly, then steeply), and was at a maximum in 1994.[7,8] During 1992–94, Russian industrial output halved, accompanied by hyperinflation; the rouble then stabilised (1995–98), collapsed (1998–99), and stabilised again. *The death rate (R per 1000) is the mean of 16 male and female age-specific death rates in the eight component 5-year age-groups (15–19 years to 50–54 years). †The 40-year risk is the probability, 1–exp (–40R/1000), that a 15-year-old would die before 55 years of age, if exposed over next 40 years to the mean of the male and female age-specific death rates of one particular calendar year. Source: WHO death numbers and UN population estimates.[1,2]

distort relative risks comparing never-drinkers with reference drinkers, but should have less of an effect on the corrected dose-related excess, on which our main conclusions are based. Moreover, sensitivity analyses that combined never-drinkers with the lowest two groups of ever-drinkers yielded similar corrected estimates of excess mortality. To include a reasonably representative sample of all deaths, including those of alcoholics, we settled for the imperfect, and potentially slightly biased, exposure information that families can provide. It is only because the effects of alcohol on mortality in Russia are so great that our crude methods can provide useful estimates of them; in less severely affected populations such methods might not yield useful results.

For those who died before the age of 40 years, we asked about regular non-beverage alcohol use. Such practice was common only in the highest alcoholic beverage consumption category, and was not independently predictive of risk. Thus, as others have suggested,[20] non-beverage alcohol use should perhaps be seen mainly as a source of ethanol rather than of other toxins.

Apart from liver cancer and upper aerodigestive cancer, the strongly positive associations were with mortality (in both men and women) from liver disease, pancreatic disease, tuberculosis, pneumonia, ill-specified disease, acute IHD other than myocardial infarction, and external causes (alcohol poisoning, accidents, and violence). At ages 15–54 years, these strongly positive associations accounted for a substantial proportion of all deaths (figure 2), and for about 90% of the excess mortality (tables 4 and 5); vascular disease accounted for most of the remainder. The only significantly inverse association was with mortality from breast cancer, which was substantially lower in the few women in the highest alcohol category (mean more than five bottles of vodka or equivalent per week) than in women from the lower alcohol consumption categories. In other populations, moderate alcohol consumption (all levels of which would be within our reference category) appears to increase the incidence of breast cancer.[19,21] The reasons for this apparent discrepancy are unclear, because information on many other potentially relevant factors was unavailable; however, the inverse association with breast cancer would, even if causal, account for only 0·1% of all deaths.

The excess mortality from liver cancer, upper aerodigestive cancer, liver disease, and pancreatic disease is largely or wholly because alcohol caused the disease that caused death.[19,22–27] The excess mortality from tuberculosis and pneumonia may be partly a result of increased exposure to infection, reduced immunocompetence, or decreased likelihood of cure;[28,29] in each case, however, alcohol use could be a direct or indirect cause of the excess. Some of the excess mortality from stroke and other vascular diseases must reflect the ability of alcohol to increase blood pressure.

The relative risks for mortality from ill-specified diseases were particularly extreme, perhaps partly because alcohol use was associated with inadequate post-mortem assessment of causes. The largest single contributor to the alcohol-associated excess mortality from disease was acute IHD other than myocardial infarction. In a survey of forensic autopsies in Barnaul during 1990–2004 at which post-mortem blood alcohol was recorded, half of those who died aged 15–69 years with non-myocardial infarction acute IHD (ICD-10 code I24) as the certified cause did not have raised blood alcohol concentrations, but 15% had concentrations over 4 g/L, which is potentially lethal.[6] In other populations, unspecified ICD codes could usually, with better data, be reassigned to more specific codes in the same disease group.[30] In Russia, however, unspecified cardiovascular disease codes are common, and probably mask large numbers of deaths from acute alcohol poisoning or from acute outcomes of chronic

alcoholic cardiotoxicity. This hypothesis is strongly supported by the sharp fluctuations in some but not all vascular causes of death during 1990–2006 in Russia as a whole; in men aged 35–69 years there was little variation in the national mortality attributed to acute myocardial infarction, but there was extreme variation in the much greater mortality attributed to other acute IHD, with a large increase after 1991 that peaked sharply in 1994.[6]

The largest contributors to alcohol-associated excess mortality were accidents and violence (including assault and suicide). The excess of accidental deaths in alcohol users could be largely or wholly causal. The excess of deaths from violence by others could be partly from the effects of alcohol on the behaviour of the dead person and partly from exposure to other drinkers. (Fluctuations in population alcohol consumption match those in population homicide rates.[31]) Finally, alcohol can cause depression,[22] impulsivity, and suicidal behaviour,[24,32] and many people who committed suicide had raised blood ethanol concentrations.[6] The relative risks for death from assault and suicide were both so extreme in the highest male and two highest female alcohol consumption categories that most of the excess must be causal.[32]

A case–control study with live controls estimated that 43% of all deaths in men aged 25–54 years in Izhevsk in 2003–05 were from alcohol (including non-beverage alcohol).[14] Our study (after correction to include all deaths from alcohol poisoning) attributed to alcohol 59% of all male and 33% of all female study deaths at ages 15–54 years; and, our corrected percentages might still underestimate the alcohol-attributable proportion of all deaths in the study areas, since they were calculated only for non-migrants with families still available at the same address years later, and exclude some deaths due to alcohol use by others. Moreover, they average the whole study period (1990–2001); alcohol-attributable proportions would have been greater in the central years (1993–97) than in 1990–91 or 1998–99, since the large temporal fluctuations in overall mortality (and, in particular, the large increase during 1992–93) were mainly caused by sudden large changes in the causes we found to be strongly associated with alcohol (figure 2).

For adult mortality in Russia as a whole, the large fluctuations since 1990 (with, again, a particularly sharp increase during 1992–93) were due to much the same causes as the fluctuations in our study area;[6] therefore, the proportion of adult Russian mortality caused by alcohol must, as in our study, have been large and have varied greatly (figures 1 and 2).

Figure 3 compares the all-cause mortality rates (averaging male and female) at ages 15–54 years in Russia and western Europe since 1980. Because our study, and other studies of individuals,[11–14] show alcohol to have been a major determinant of overall mortality in Russia, the sharp changes in alcohol and in mortality in the mid-1980s are particularly informative, and they are well documented[3–8] and uncomplicated by the social upheavals of later decades. Because of the restrictions suddenly placed on alcohol in mid-1985, total consumption (legal plus other) dropped suddenly by about a quarter,[7,8] as did overall mortality at ages 15–54 years (figures 1 and 3). Still, however, during the period of lowest alcohol consumption (1986–87), about three-quarters of pre-1985 consumption remained.[7] Thus, although Russian mortality was then at its lowest, a great deal of the alcohol-attributable mortality must also have remained.[8] If, therefore, the 1985 decrease of only about a quarter in alcohol consumption was largely responsible for the 1984–86 decrease of almost a quarter in Russian mortality at ages 15–54 years, then in the (hypothetical) absence of all deaths from alcohol, Russian and west European death rates at these ages could well have been similar in 1986. This suggests that, in Russia, alcohol has been of even greater importance than tobacco as a cause of premature death. In western Europe in the mid-1980s, smoking was responsible for about a quarter of all mortality (and a third of all male mortality) in middle age, and in Russia male lung cancer mortality was then about 50% greater than in western Europe.[1–3,33,34] Even if the overall mortality rate from smoking was also somewhat greater in Russia, however, it would still have been much smaller, at least at ages 15–54 years, than the probable effects of alcohol in Russia since 1991 (figures 1 and 3).

If, without alcohol, mortality at these ages would have been similar in Russia and western Europe in the mid-1980s, then (without alcohol in either population) it would probably still be similar in the present decade. If so, then Russian death rates at these ages would now be much less than double the corresponding rates in western Europe (figure 3). The actual Russian mortality rate in people aged 15–54 years in 2006 was, however, more than five times (for men) and three times (for women) the rate in western Europe (figure 1).[1–3] This large discrepancy is consistent with alcohol being responsible in the current decade for about three-quarters of all male Russian deaths at ages 15–54 years and about half of all female Russian deaths at these ages—ie, proportions even greater than in our study population. Whatever the exact alcohol-attributed proportion may have been at particular times since 1980, however, it was always high, has fluctuated greatly, and is still high.

We conclude that alcohol is the main cause (and perhaps the only major cause) of the large fluctuations in Russian adult mortality since 1980, and that alcohol and tobacco account for most or all of the large difference in premature adult mortality between Russia and western Europe.

Contributors

DZ, RP, PBo, and PBr designed the study, DZ and AB coordinated its conduct, RK, AL, IK, VI, and TT coordinated the fieldwork, AB and JB prepared the final database, JB and RP undertook the statistical analyses, and DZ, RP, and PBr drafted the manuscript. All authors contributed to the final paper.

Conflicts of interest

We declare that we have no conflicts of interest.

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