Alcohol consumption is associated with increased all-cause mortality in Russian men and women: a cohort study based on the mortality of relatives

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Drs Bobak, Murphy and Nicholson had full access to all the data in the study. Dr Nicholson takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Abstract

Objectives: To examine the relationships between frequency of alcohol consumption and of binge drinking and adult mortality in Russian men and women.

Methods : Using modified indirect demographic techniques, a convenience cohort was constructed based on survey respondents' information about their close relatives.

A random sample general population of the Russian Federation of 7172 respondents (response rate 61%) provided information on 10475 male and 3129 female relatives, including age, vital status and frequency of alcohol consumption and binge drinking. These relatives formed the cohort analysed in this report. The outcome measure was all-cause mortality after the age of 30 years.

Findings: There was a strong linear relationship between frequency of drinking and of binge drinking and all-cause mortality in men; after controlling for smoking and calendar period of birth, the relative risk of death in daily drinkers compared to occasional drinkers was 1.52 (95% CI 1.33 –1.75). Male binge drinkers had higher mortality than drinkers who did not binge, which persisted after adjustment for drinking frequency (adjusted RR 1.09 (1.00-1.19). In women, the increased mortality was confined to a small group of those who binged at least once a month (adjusted relative risk 2.68, 1.54-4.66).

Conclusions: The results suggest a positive association between alcohol and mortality in Russia. There was no evidence for the protective effect of drinking seen in western populations. Alcohol appears to have contributed to the high long-term mortality rates in Russian men, but it is unlikely to be a major cause of female mortality.

Abstract word count = 248. Key words: Russia, alcohol consumption, mortality

The dramatic mortality fluctuations in Russia since the mid 1980s have attracted considerable attention*(1,2)*. During the societal transformation that followed the fall of communism, Russian mortality increased dramatically between 1990 and 1994 and it has been fluctuating since then. The scale of the mortality changes is striking; between 1990–1994 alone, the rise in mortality was equivalent to more than 2 million additional deaths above long-term mortality rates(*3*).

While it has been recognised that the causes of the mortality crisis are complex(*3,4*), it has been proposed that alcohol was an important proximal cause of these changes*(1,5).* Although moderate drinking has been shown to reduce mortality*(6)*, there is evidence from US and Finland that a pattern of binge drinking is related to increased mortality *(7-11)*. The hypothesised powerful role of alcohol has been attributed to the binge drinking pattern common in Russia*(12-14)*.

It is unclear whether alcohol consumption in Russia has any beneficial effects or whether the adverse effect of heavy drinking predominates*(15)*. To our knowledge, there have been four individual-level studies with data on the relation between alcohol and mortality in Russia, with inconsistent results*(16-19)*. However, these studies were relatively small, and the inconsistency of the findings could be due to the limited statistical power of these studies. Studies in Russia are urgently needed.

We have previously developed and piloted a quick and effective approach to assess risk factors for mortality in a population. It borrows from demographers' indirect

methodology to estimate mortality in countries without vital statistics. Such indirect demographic methods using survey or census data, often called "Brass techniques" *(20,21)*, have been used to estimate mortality from information on the survival of close kin (such as spouses and parents) where conventional data are unavailable. These methods use simple information on the number of close kin and on how many of them have died. We modified this method for literate and numerate populations, and showed that the method, based on spouses and siblings, is a useful tool to study mortality and its individual level determinants in Russia*(22,23)*.

MATERIALS AND METHODS

Subjects

We conducted a cross-sectional survey of a national sample of the Russian population, conducted in 3 waves in July, September and November 2002. The data were collected in collaboration with the Russian Centre for Public Opinion Research (VCIOM), under the direction of Professor Levada, and the New Russian Barometer survey program*(24)*. The population sample was selected in a multi-stage process. The whole Russian Federation was first stratified into 22 regions, and each region was further stratified into urban and rural areas. Within this framework, towns and settlements were randomly selected proportionately to population size. Within these locations, primary sampling units (locations) were randomly drawn. In each primary sampling unit, an address was randomly selected, and interviewers were instructed to seek a face-to-face interview at every n-th eligible household. At each address, the interviewer asked for a respondent matching an age-sex-education grid, and if more than one respondent was eligible, the

person with the most recent birthday was selected. The questions on alcohol consumption and survival of relatives were added to an existing survey on the social and economic impact of transition. 3 waves were needed to obtain the required sample size.

In total, 11,776 households containing an eligible respondent were identified. Of these 3837 declined to be interviewed, 608 were unable to answer due to bad health or other reasons, 159 interviews were interrupted or rejected during control, yielding an overall response rate of 61 percent. Response rates were similar in all 3 waves. The 7172 respondents were asked to provide information about their parents, eldest two siblings and first husbands, a total of 26,709 relatives, who formed the population analysed in this paper. Wives were not included as our pilot study had found that husbands underestimated wives' mortality*(22)*. These analyses do not include the siblings from the pilot study, reported previously*(23)*.

Measurements

Information collected about each relative included year of birth, whether they were alive or dead, and, if applicable, year of (or age at) death. Further details including cause of death and other details of relatives' lifestyle were sought for parents (except those who died before 1972 because it was considered that recall of behaviour from over 30 years previously would be inaccurate), siblings aged 20 years and older, and husbands. Two questions concerning alcohol consumption were asked about all relatives except mothers, for whom we judged such information would be unreliable, given the social convention of low alcohol consumption in women. First, the frequency of drinking vodka or other

strong spirits, and second, the frequency of drinking more than 0.5 l (half bottle) of vodka or strong spirits in one evening (binge drinking). Data on the consumption of other alcoholic beverages were not collected due to the predominance of vodka and spirit consumption in Russian drinking behaviour. Additional data collected on relatives included smoking (all relatives), education (sibs and husbands), frequency of contact with respondent and marital status (sibs only). Respondents also answered questions concerning their own age, sex, socio-economic characteristics, and social and political attitudes, childhood circumstances, such as lack of food, and family size.

Statistical analyses

Since we were interested in determinants of adult mortality, only relatives who had reached 30 years of age were included in these analyses. As alcohol data were not collected on mothers, the analyses on women were therefore restricted to siblings. Fathers who died before 1972, on whom covariate data were not collected, were not included.

We calculated the Cox proportional hazard ratios (relative risks) to assess the effect of relatives' characteristics on their risk of death from all causes. The proportional hazards assumptions were fulfilled. Since we relied on survey responders' reports about their relatives, relatives with unknown vital status or age were excluded from the analyses. 1884 men and 210 women were excluded because this information was missing. Data were left-censored at respondent's birth for fathers and year of marriage for husbands since time prior to these events should not be considered time at risk of death. Husbands who were separated or divorced from the respondent and whose vital status was unknown

were right-censored at the year of separation. Since the results on different types of relatives were similar, although somewhat stronger in siblings, we analysed pooled data on different relatives and included relative type as an adjustment factor.

For drinking and other variables, we included the response "unknown" as a separate category. For drinking frequency in men, we used those who drank "occasionally, up to once a month" as the reference group (because the use of abstainers as the reference category in studies of the effects of alcohol has been criticized, as this group can contain ex-drinkers in poor health). In women, never drinkers were the reference category since this was by far the largest group. For binge drinking, we used "drinkers who never binged" as the reference category. We also used drinking and binge frequency as a linear variable excluding the unknown category, to assess the significance of linear trends. In addition, in order to investigate if binge drinking had an effect on mortality beyond that of drinking frequency, binge frequency estimates were adjusted for drinking frequency and the effect of drinking frequency on mortality was stratified by bingeing behaviour .

The study design means that the data are clustered, with one respondent potentially giving information on up to four relatives. As this may influence standard error estimates, the adjusted analyses were repeated with robust sandwich estimates*(25)* to calculate standard errors. The resulting confidence intervals (not shown) were virtually identical to those presented in the tables for men, and with minimal changes only for women. Results of the conventional analyses are therefore reported. In addition, characteristics of the respondent may influence reporting and hence results. Respondent sex, education and

drinking behavior were examined in relation to reported relatives' mortality and drinking behaviour. There was no evidence that these features were distorting the results and so results of the simpler models are reported.

RESULTS

Alcohol data were available for 10475 male and 3129 female relatives with 3852 and 441 deaths reported respectively (Table 1). Cardiovascular disease was the most common reported cause of death. There were, as expected, marked differences in drinking pattern between men and women. Only 14% of men never drank and 41% were occasional and 6% daily drinkers. The prevalence of weekly or more frequent binge drinking (amongst male drinkers) was 13%. Amongst women, 54% never drank and only 5% drank several times a month or more. 17% of female drinkers were reported as ever binge drinking. Over 50% of the male population was described as regular smokers, compared to 5% of women.

In men, there was a strong association between frequency of drinking vodka or spirits and mortality (Table 2). Compared with occasional drinkers, the hazard ratio for death in never drinkers was 0.70 (95% confidence interval (CI): 0.62-0.77) increasing to 1.95 (1.71-2.23) in daily drinkers. Among male drinkers, there was a strong association between the frequency of binge drinking and mortality; the hazard ratio for men who binged weekly compared with drinkers who never binged was 2.05 (1.84-2.29). Adjustment for drinking frequency and then smoking, relative type and decade of birth reduced the effect size to 1.27 (1.10-1.48). Further adjustment was possible only in

subgroups of male relatives: for education (husbands and siblings), marital status and contact with respondent (siblings only). However, adjusting for these additional variables did not alter the estimates.

In women, small numbers meant that the frequency groups were combined, but there was an increased risk of mortality in women who drank several times a month or more (Table 3). There was no statistically significant difference in mortality between women who never drank and occasional drinkers. Binge drinking increased mortality risk in women drinkers with the hazard ratio larger than in men. Adjustment for smoking reduced the mortality risk in women who drank regularly; the adjusted relative risk associated with bingeing among drinkers was 1.70 (1.03-2.82). As in men, further adjustment did not reduce the estimates. Further analyses by group of cause of death (as reported by the respondents) found that the effect in women was due to violent or alcohol-related deaths (not shown).

In order to account for residual confounding by inaccurate estimates of smoking, adjusted analyses were repeated restricted to never smokers. Effect sizes for drinking were similar to the adjusted results in Tables 2 and 3 and for bingeing were larger. Amongst men who had never smoked the adjusted linear drinking and bingeing variables were 1.16 (1.10-1.22) and 1.25 (1.09-1.43) respectively and in women who never smoked the linear drinking variable was 1.19 (0.98-1.44) and the effect of bingeing was 1.87 (.1.07-3.27).

Table 4 examines the contribution of binge drinking to the mortality risk in drinkers stratifying by bingeing behaviour. Never drinkers were used a reference point for both sexes. In men, increasing mortality with increasing drinking frequency was observed in drinkers who were reported as never bingeing, with a similar increase seen in bingers. A statistical test for interaction between binge and drinking frequency was not significant (p=0.29). In women the increased mortality risk was limited to women who binged but, due to small numbers, the formal test for interaction was not significant (p=0.26). Interestingly, of 21 deaths in women who drank several times a month, 18 were among binge drinkers, and 12 of these 18 deaths were reported as due to violence or alcohol-related, giving a relative risk of 30.4 for external causes of deaths.

DISCUSSION

This study, the largest individual-level study of alcohol and mortality in Russia to date, found strong and robust positive associations between frequency of drinking and of binge drinking and all-cause mortality in men and women. In men the associations were linear; there was no suggestion of the U- or J-shaped association usually seen in western populations.

The design of this study offers great advantages in terms of time and expense, but several potential limitations need to be considered. Firstly a formal validation study of the indirect methodology in this context has not been undertaken but there is good evidence to suggest both that the methodology provides good estimates of overall mortality and temporal changes in mortality (*22*), and that the approach is sufficiently sensitive to study

differences in mortality between socio-economic subgroups within populations (*23*) and the temporal trends in such differences (Murphy et al, manuscript under review 2005).

In terms of studying the effect of alcohol, the methodology has not been formally validated. It is possible that respondents were more likely to over-estimate alcohol consumption in dead relatives, which would account for the associations observed. However, the fact that the reported alcohol consumption in relatives is similar to other reports in the Russian population suggests that this method should give reliable estimates of the association between drinking and mortality. In men we were able to examine the associations between alcohol and mortality within different groups of relatives. The associations were stronger in siblings but the pattern of results was similar. Since reports on husband drinking could be expected to be the most reliable, a similar pattern of associations in all relatives argues for the validity of our findings. We are aware of the potential for inaccurate reporting of alcohol which led us to exclude all mothers and fathers who died before 1972.

Secondly, the questionnaire asked about alcohol consumption of the relative without specifying time-period and replies may refer to drinking habits immediately preceding death. Changes in alcohol behaviour prior to death may therefore influence the results, but one would expect that this type of misclassification would tend to underestimate the underlying relative risks.

Thirdly, mortality of fathers was underestimated in the dataset since alcohol consumption was not obtained for father who died before 1972, while those in the same birth cohort

and still alive were included. We assessed the effect of this potential bias by analysing only fathers born after 1941; the results were similar to, but marginally stronger than, those in all fathers. Deaths at younger ages are more likely to be due to alcohol; this indicates that the effects are, if anything, under-estimated in the full dataset.

Finally, frequent contact with sibling was associated with higher reported mortality in siblings. This observation is probably due to increased contact with sick relatives and to under-reporting of mortality in sibs with less contact. However, adjustment for the frequency of contact did not materially alter the results. When analyses were restricted to siblings in more frequent contact, the associations between drinking and mortality were similar in men and stronger in women.

These potential biases are unlikely to explain our findings. The pattern of drinking in this study was similar to that previously reported for Russia*(12,14)*. Men drank relatively infrequently but many drinking occasions tended to be high intake episodes, whereas the frequency of any drinking and of binge drinking in women was low.

Previous studies of alcohol and mortality in Russia have produced inconsistent results. One cohort study found no relation between alcohol and mortality at all*(16)*; another cohort study found increased mortality among frequent heavy drinkers only*(17)*; and one cohort study found that men drinking >150g of alcohol per week had 42 percent higher mortality from all causes then men drinking less than 150 g per week (calculations based on Plavinski et al*(19)*). One case-control study found increased CVD mortality risk

among binge drinkers*(18)* but the authors were concerned with selection bias. Only one study included women*(16)*, and reported a weak protective effect in females.

This study, larger than previous reports, shows an effect of both drinking and binge frequency on mortality in men, with no evidence of any protective effect of drinking. In women, there was also no protective effect of drinking, but the adverse risk associated with drinking was restricted to a small group of frequent drinkers (only about 5% of the female population). These analyses focus on all-cause mortality whereas the U-shaped curve has been most clearly demonstrated for CVD deaths. Although we had information from the relative on cause of death, and preliminary analyses showed similar or weaker associations with CVD deaths, it is possible that the report of cause of death is imprecise or incorrect. Analyses by cause of death have not been reported in details because of uncertainty over the relatives' recall or accurate knowledge of the causes of death, especially in heavy drinkers where alcohol may have been given as cause of death that was actually due to heart disease.

The role of drinking pattern in determining the health risks associated with alcohol consumption is increasingly recognised*(7,8,26)*. It has been suggested that the absence of a protective effect of drinking in Eastern Europe might be due to binge drinking *(13)*. This notion has been supported by data in Russia showing that risk was restricted to heavy drinkers *(17,18)*. Existing data on the U-shaped curve has used volume of alcohol consumption, rather than just frequency. It is possible that drinkers who drink rarely but heavily have a similar total volume intake to those who drink smaller amounts more

regularly, which might account for the lack of a protective effect in these data. However, the present results indicate that men who never binged and drank only moderately are also at increased risk of death. Inaccuracy in the reporting of binge drinking may account for these findings in men since informants' knowledge of the quantity of alcohol consumed may be less accurate than that of the frequency of drinking episodes. Hence the group of men we classified as never binge drinking may include those who did in fact drink large quantities at a time, accounting for their increased risk. Data in women are more consistent with the adverse effect of drinking restricted to binge drinkers, but as in men, fail to show any benefit from drinking.

Rather than providing an unequivocal support for the binge drinking hypothesis, our results are consistent with the concept of a recently developed hazardous drinking pattern scores that indicate, on a country level, the degree of hazard associated with each extra per capita liter consumed *(27,28)*.In the most recent version, Russia has been assigned the most hazardous score*(29)*. A recent population study in three eastern European countries confirmed this scoring. Russia had the highest rates of problem drinking and negative social consequences of drinking, despite relatively low volume of alcohol consumption, and only part of this excess was explained by binge drinking *(30)*.

This suggests that aspects of alcohol consumption other than binge drinking also contribute to the harmful nature of drinking in Russia. This could be related to the nature, content and type of the alcohol beverages consumed in Russia. Vodka accounts for more than four fifths of all alcohol consumption in Russia*(31)*. Although some studies report

stronger beneficial effects for wine*(32,33)* than for spirits, there is debate as to the role confounding in these observations*(34,35)*. However, a considerable proportion of vodka, especially until about the mid 1990s, came from home or illicit production and was of questionable quality, and this may have further increased the hazard related to drinking.

Alcohol has been proposed to have underpinned the fluctuations in mortality since 1991 *(36)* but this hypothesis has been disputed *(37,38)*. This study estimated the association of alcohol with long-term term mortality risk, rather than with short-term fluctuations. We are aware of the fact that factors affecting long-term mortality risk may have no relation to short-term mortality changes and vice versa*(39)*. However, the results on women, where the adverse effect of drinking is restricted to a very small proportion of the population, make it more difficult to argue that changes in mortality of the whole population (that were of similar magnitude in men and women) could be accounted for by changes in alcohol consumption.

In conclusion, the findings indicate that alcohol has contributed to the high long-term mortality rates in Russian men. The pattern of results in women suggests that alcohol is unlikely to be a major contributor to female mortality in Russia. The relation between alcohol and the short-term fluctuations in mortality and deaths from different causes remains unclear.

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Table 1. Descriptive data on male and female relatives

	Men	**Women**
Number	**10475**	**3129**
Relation to informant		
Father	4456 (42.5)	
Sibling	3087 (29.5)	3129 (100)
Husband	2932 (28.0)	
Alive – yes	6623 (63.2)	2688 (86.0)
- no	3852 (36.8)	441 (14.0)
Year of birth N=	**10475**	**3129**
Pre 1921	1223 (11.7)	137 (4.4)
1921-30	1709 (16.3)	470 (15.0)
1931-40	2165 (20.7)	625 (20.0)
1941-50	1828 (17.5)	523 (16.7)
1951-60	2175 (20.8)	718 (23.0)
After 1960	1375 (13.1)	656 (21.0)
Drinking frequency N=	**10475**	**3129**
Never	1472(14.1)	1674 (53.5)
Occasional, up to once/mnth	4288 (40.9)	1080 (34.5)
Several times a month	1614 (15.4)	
Weekly / more often	1990 (19.0)	} 170 (5.4)[1]
Daily	619 (5.9)	
Don't know	492 (4.7)	205 (6.6)
Frequency of bingeing N=	**8509**	**1250**
Never	2704 (31.8)	841 (67.3)
Occasional	2428 (28.5)	
Several times a month	942 (11.1)	} 216 (17.3)[2]
Weekly / more often	1070 (12.6)	
Don't know	1365 (16.0)	193 (15.4)
Cause of death N=	**3852**	**441**
CVD	1511(39.2)	165 (37.4)
Cancer	721 (18.7)	99 (22.5)
Accident /alcohol	598 (15.5)	37 (8.4)
Other illnesses	912 (23.7)	129 (29.3)
Don't know	110 (2.9)	11 (2.5)

1- several times / month or more frequent. 2-occasionally or more often

Table 2. Hazard ratios (95% confidence intervals) for alcohol consumption and all-cause mortality after the age of 30 years in men.

	N	Events	HR (age adj.)	95% confidence interval	Adjusted HR[b]	95% confidence interval	Adjusted HR[c]	95% confidence interval
Drinking frequency								
Never	1472	443	0.70	0.62, 0.77			0.79	0.71, 0.88
Occasional	4288	1454	1	Referent			1	Referent
Several times a month	1614	654	1.39	1.27, 1.53			1.26	1.15, 1.38
Weekly / more often	1990	878	1.63	1.50, 1.77			1.37	1.25, 1.49
Daily	619	263	1.95	1.71, 2.23			1.52	1.33, 1.75
Don't know			1.15	0.98, 1.36			1.05	0.87, 1.26
Linear variable[a]			1.23	1.20, 1.25			1.14	1.11, 1.16
Frequency of binge drinking (amongst drinkers)								
Never	2704	1044	1	Referent	1	Referent	1	Referent
Occasional	2428	823	1.19	1.08, 1.30	1.13	1.03, 1.24	1.01	0.92, 1.11
Several times a monthly	942	386	1.67	1.48, 1.87	1.41	1.24, 1.60	1.24	1.09, 1.42
Weekly / more often	1070	477	2.05	1.84, 2.29	1.51	1.31, 1.75	1.27	1.09, 1.47
Don't know	1365	518	1.30	1.17, 1.44	1.23	1.11, 1.37	1.18	1.05, 1.31
Linear variable[a]			1.28	1.24, 1.32	1.19	1.13, 1.25	1.11	1.06, 1.17
Ever vs never binge			1.45	1.34, 1.57	1.22	1.12, 1.34	1.09	1.00, 1.19

a HR for one category change excluding don't know category
[b] adjusted for drinking frequency
[c] adjusted for relative, smoking behaviour (& drinking frequency for binge variables) and stratified by decade of birth

Table 3. Hazard ratios (95% confidence intervals) for alcohol consumption and all-cause mortality after the age of 30 years in women.

	N	Events	HR (age adj.)	95% confidence interval			Adjusted HR[c]	95% confidence interval
Drinking frequency								
Never	1674	281	1	Referent			1	Referent
Occasional	1080	118	1.07	0.86, 1.33			1.07	0.86, 1.33
Several times a month	170	23	1.94	1.26, 2.97			1.74	1.09, 2.77
Don't know	205	19	0.76	0.48, 1.21			0.76	0.47, 1.24
Linear variable[a]			1.21	1.02, 1.44			1.18	0.98, 1.40
					Adjusted HR[b]	95% confidence interval		
Frequency of binge drinking (amongst drinkers)								
Never	841	92	1	Referent	1	Referent	1	Referent
Does binge	216	28	1.94	1.26, 2.97	1.68	1.03, 2.73	1.70	1.03, 2.82
Don't know	193	21	1.09	0.68, 1.76	1.07	0.66, 1.72	1.10	0.67, 1.81

[a] HR for one category change excluding don't know category
[b] adjusted for drinking frequency
[c] adjusted for smoking behaviour (& drinking frequency for binge frequency) and stratified by decade of birth

Table 4. Adjusted hazard ratios (95% confidence intervals) for mortality from all causes by drinking frequency and binge drinking.

Drinking frequency	Binge drinking			
	No		Yes	
	HR	95% confidence interval	HR	95% confidence interval
Men				
Never	1	Referent		-
Occasionally	1.24	1.10, 1.40	1.33	1.15, 1.52
Several times a month	1.50	1.25, 1.81	1.59	1.38, 1.84
Weekly	1.57	1.25, 1.97	1.73	1.52, 1.97
Daily	1.31	0.75, 2.28	2.06	1.73, 2.45
Women				
Never	1	Referent	-	
Occasionally	1.03	0.81, 1.31	1.29	0.68, 2.45
Several times a month or more	1.28	0.47, 3.45	2.68	1.54, 4.66

HR adjusted for relative (men only), smoking behaviour and decade of birth