Hazardous alcohol drinking and premature mortality in Russia: a population based case-control study

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Summary

Background The reason for the low life expectancy in Russian men and large fluctuations in mortality are unknown. We investigated the contribution of alcohol, and hazardous drinking in particular, to male mortality in a typical Russian city.

Methods Cases were all deaths in men aged 25–54 years living in Izhevsk occurring between Oct 20, 2003, to Oct 3, 2005. Controls were selected at random from the city population and were frequency matched to deaths by age. Interviews with proxy informants living in the same household as cases were done between Dec 11, 2003, and Nov, 16 2005, and were obtained for 62% (1750/2835) of cases and 57% (1750/3078) of controls. We ascertained frequency and usual amount of beer, wine, and spirits consumed and frequency of consumption of manufactured ethanol-based liquids not intended to be drunk (non-beverage alcohol), and markers of problem drinking. Complete information on markers of problem drinking, frequency of alcohol consumption, education, and smoking was available for 1468 cases and 1496 controls.

Findings 751 (51%) cases were classed as problem drinkers or drank non-beverage alcohol, compared with 192 (13%) controls. The mortality odds ratio (OR) for these men, compared with those who either abstained or were non-problematic beverage drinkers, was 6·0 (95% CI 5·0–7·3) after adjustment for smoking and education. The mortality ORs for drinking non-beverage alcohol in the past year (yes *vs* no) was 9·2 (7·2–11·7) after adjustment for age. Adjustment for volume of ethanol consumed from beverages lowered the OR to 8·3 (6·5–10·7), and further adjustment for education and smoking reduced it to 7·0 (5·5–9·0). A strong direct gradient with mortality was seen for frequency of non-beverage alcohol drinking independent of volume of beverage ethanol consumed. 43% of mortality was attributable to hazardous drinking (problem drinking or non-beverage alcohol consumption, or both) adjusted for smoking and education.

Interpretation Almost half of all deaths in working age men in a typical Russian city may be accounted for by hazardous drinking. Our analyses provide indirect support for the contention that the sharp fluctuations seen in Russian mortality in the early 1990s could be related to hazardous drinking as indicated by consumption of non-beverage alcohol.

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See **Comment** page 1975

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Introduction

Russia has exceptionally low life expectancy for an industrialised country. In 2004, life expectancy was 59 years for males and 72 years for females, mainly because of very high mortality at working ages.[1] Russian men have a probability of dying between 25 and 65 years of 0·55 compared with 0·15 for men in England and Wales.[2] This low life expectancy, coupled with a low birthrate, means that the Russian population is falling by 700 000 people per year.

Mortality rates in Russia have greatly fluctuated over the past 20 years,[2] as in other countries of the former Soviet Union.[3] Although these fluctuations have been greatest for men, much the same trends are seen for women of working age.[4,5] Previous studies suggest that alcohol has had an important role.[4,6] President Gorbachev's anti-alcohol campaign in the mid 1980s was associated with an immediate rise in life expectancy,[7] whereas increased alcohol consumption has been linked to rising mortality in the early 1990s during the transition from communism.[8,9] Deaths obviously related to alcohol, such as acute alcohol poisoning and liver cirrhosis, showed the greatest fluctuations, with similar trends for other causes plausibly linked to alcohol consumption.

A worldwide assessment of drinking patterns in 2000, showed that the European subregion containing Russia and other parts of the former Soviet Union had the most hazardous pattern of (binge) drinking and the highest consumption of alcohol per head (13·9 L of pure ethanol per year in people aged ≥15 years).[10] 2001–03 estimates from the same source show a figure of 15·2 L per head,[11] which is consistent with indirect Russian estimates for the 1990s of 14–15 L per person every year.[12] Although population surveys generally underestimate alcohol consumption,[13] cross sectional studies in Russia in the 1990s show frequent consumption of large quantities of ethanol (mainly vodka) on single occasions.[14–18] A study in Arkhangelsk, Russia, (1999–2000) classified 75% of male industrial workers as harmful or hazardous drinkers using AUDIT criteria.[19]

In 2002, in the European subregion containing Russia, 19% of male mortality was attributable to alcohol compared with 3% in western Europe,[20] with almost identical attributable fractions estimated for Russia alone.[11]

Manufactured ethanol-based liquids not intended for consumption (from now on referred to as non-beverage alcohols), including eau de colognes, medicinal tinctures, and cleaning agents, are not classed as alcoholic drinks. They therefore avoid excise duty and are up to six times cheaper per unit of ethanol than vodka. Toxicological analyses of non-beverage alcohols bought in Izhevsk (Russia) showed no traces of methanol and only very low concentrations of long-chain alcohols.[21] However, many non-beverage alcohols have very high concentrations of ethanol. Russian vodka contains on average 43% ethanol by volume, whereas the tinctures and eau de colognes bought for drinking varied between 60% and 97% ethanol.[21]

The need for more rigorous assessment of the association of mortality in Russia with alcohol, and hazardous alcohol consumption in particular, overcoming the limitations of previous work, led to the Izhevsk Family Study, which focused on working age men. We investigated the contribution of alcohol, particularly hazardous drinking, to male mortality in a typical Russian city.

Methods

Population and study design

We used a population-based case-control design. Our study was undertaken in Izhevsk, an industrial city on the western side of the Ural mountains in Russia. Our earlier work[22] in the region showed the feasibility of undertaking such a complex investigation in this location. It is a typical Russian city of its size (population 632 000 at the 2002 all Russia Census) with average life expectancy for Russia and a distribution of deaths by cause in working age men that is much the same as that for Russia overall. Cases were deceased men aged 25–54 years who had died from any cause from Oct 20, 2003, to Oct 3, 2005, and had lived in households in Izhevsk with at least one other person. Deaths were notified by the registrar of deaths. Cause of death was coded by the certifying doctor or pathologist using the tenth revision of the International Classification of Diseases. Controls were live men selected from a 2002 population register. Every month new controls were randomly selected from within 5-year age bands from the sampling frame, such that the control sample with proxy interviews was the same age as the accumulating series of cases with proxy interviews.

	Cases (n=2835)	Controls (n=3078)
Proxy interviewed	1750 (62%)	1750 (57%)
Proxy refused or unavailable	323 (11%)	646 (21%)
Man lived alone*	312 (11%)	157 (5%)
Control dead	..	16 (1%)
No answer at address	74 (3%)	76 (3%)
Problem with address	339 (12%)	404 (13%)
Other reason for no proxy interview	37 (1%)	29 (1%)

Data are number (%). *No proxy to interview.

Table 1: **Outcome of questionnaire survey in cases and controls**

A team of 34 trained interviewers used a structured questionnaire to obtain information about cases and controls from proxy respondents living in the same household. Nearly all case proxy interviews took place 6–8 weeks after death. Proxy interviews were done between Dec 11, 2003 and Nov 16, 2005. Control and case proxy interviews were done at the same rate throughout the data accumulation period. Interviewers returned to an address up to three times to get a response. When more than one proxy was available, a pre-specified priority order was used, with wives or partners being first choice. For validation purposes we obtained proxy interviews from two informants living in the same household in a subset of 200 cases and 200 controls. Interviewers did interviews in private to avoid contamination of responses.

The questionnaire covered a range of characteristics including alcohol consumption, smoking, and socioeconomic and demographic variables. Most questions were derived from established and validated instruments. A systematic review of the validity of proxy informant data undertaken at the design stage[23] noted that average drinking frequency and usual number of drinks per occasion showed high index-proxy agreement when classified into ordinal categories.[24,25] A key conclusion was that the validity of proxy responses was improved if they were restricted to questions on behaviours that were directly observable, and we therefore adopted this approach.

Information about beverage alcohol consumption (beer, wine, and spirits) was obtained by the standard quantity-frequency approach[26] with a reference period of the previous year. Respondents were asked about the frequency of consumption of all beverage types (everyday or more often, nearly every day, 3–4 times per week, once or twice per week, 1–3 times per month, a few times per year, never, or almost never). The amount of each beverage type drunk on a usual occasion was obtained for categories defined in quantity units commonly used by Russians (bottles of beer, grams of wine and spirits). Volume of pure ethanol from beer, wine, and spirits consumed in the previous year was estimated from frequency and usual amount drunk of every beverage. Ethanol concentrations for every beverage type were measured after inspection of what was available in Izhevsk plus laboratory analysis of locally purchased vodkas.[21] Beer was taken as 4·5% ethanol by volume, wine 12%, and spirits 43%. For non-beverage alcohols, only frequency of consumption was obtained since there are no standard measures of volume consumed.

Information about several adverse alcohol related behaviours was obtained. *Zapoi* is a Russian term used to describe a period of 2 or more days of continuous drunkenness when the person is withdrawn from

	Proxy interviewed	Proxy not interviewed
Cases		
n	1750	1085
Age at death (years)		
25–29	131 (8%)	88 (8%)
30–34	144 (8%)	110 (10%)
35–39	137 (8%)	106 (10%)
40–44	305 (17%)	190 (18%)
45–49	441 (25%)	295 (27%)
50–54	592 (34%)	296 (27%)
Registered with narcology clinic	292 (17%)	188 (17%)
Highest educational level at death registration		
Incomplete secondary and less	209 (12%)	120 (11%)
Secondary	1316 (75%)	753 (69%)
Higher and incomplete higher	137 (8%)	136 (13%)
Not known	88 (5%)	76 (7%)
Civil status at death registration		
Married	1098 (63%)	457 (42%)
Single	312 (18%)	257 (24%)
Widowed	33 (2%)	33 (3%)
Divorced	270 (15%)	285 (26%)
Not known	37 (2%)	53 (5%)
Controls		
n	1750	1328
Age at interview (years)		
25–29	132 (8%)	119 (9%)
30–34	145 (8%)	104 (8%)
35–39	140 (8%)	147 (11%)
40–44	294 (17%)	234 (18%)
45–49	434 (25%)	310 (23%)
50–54	605 (35%)	414 (31%)
Registered with narcology clinic	71 (4%)	48 (4%)

Data are number (%).

Table 2: **Distribution of cases and controls by outcome of proxy questionnaire interview**

normal social life.[12] A single indicator of problem drinking was constructed on the basis of having one or more episodes of *zapoi* in the past year or twice a week or more occurrence of excessive drunkenness, hangover, or going to sleep at night clothed because of being drunk.

For all cases and controls, irrespective of whether or not an interview was done, we obtained information about ever having been registered at the city's Narcology Clinic, the main treatment facility for alcohol problems. This information was abstracted from clinical records blind to case-control status. Since 99% of registrations for men aged 25–54 years had an alcohol related diagnosis, we obtained information about alcohol problems without observer and recall bias. Logistic regression was used to estimate the strength of association of factors with mortality, with all analyses done with STATA (version 9.1). In all models, age was included in six 5-year categories. Education, smoking, and marital status were treated as potential confounders, and where appropriate were introduced into models as categorical variables.

Oral consent was obtained from proxy informants. Ethical approval for the study was obtained from the committees of the Izhevsk Medical Academy and the London School of Hygiene and Tropical Medicine.

Role of the funding source

The sponsor of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all anonymised data in the study and had final responsibility for the decision to submit for publication.

Results

The proportion of interviews obtained from case proxies and control proxies was much the same (table 1). More cases than controls lived alone so no proxy was available, although refusals by proxies were more common for controls than for cases (table 1). Table 2 shows that success in obtaining a proxy interview for cases varied by education and marital status (as derived from the death certificate). Equivalent information about number of years in education and marital status of non-responding controls was not available. The percentage of cases and controls registered with the narcology clinic was the same irrespective of whether or not a proxy interview was obtained (table 2). Most proxy interviews were with wives or partners (1036 [59%]

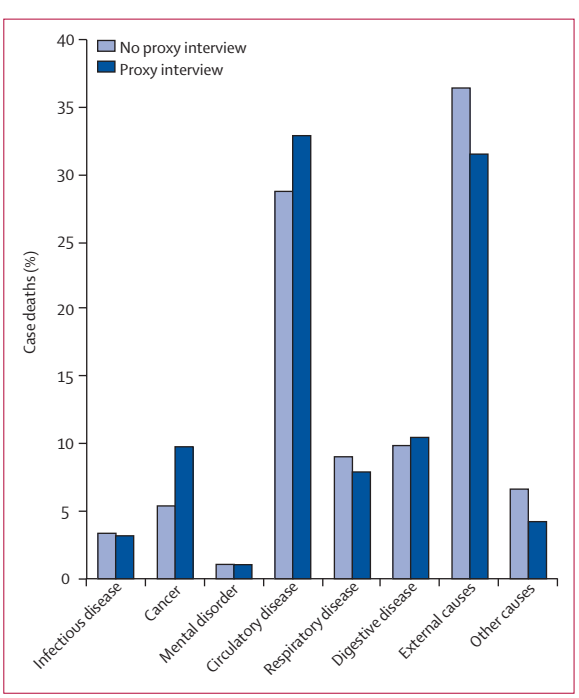

Figure 1: **Distribution of case deaths by cause**
Deaths identified by proxy interview.

	Number of cases and controls		Mean ethanol intake/ week from beverages in 10 mL units*		Non-beverage alcohol drinkers		Problem drinkers†		Registered with narcology clinic	
	Cases n=1750	Controls n=1750	Cases n=1451	Controls n=1529	Cases n=1705	Controls n=1725	Cases n=1656	Controls n=1682	Cases n=1750	Controls n=1750
Educational level										
Incomplete secondary or lower	209	100	38·8 (72·8)	26·5 (57·0)	104/199 (52%)	22/97 (23%)	99/197 (50%)	25/98 (26%)	39/209 (19%)	8/100 (8%)
Secondary specialised and professional	1342	1239	33·2 (52·6)	19·2 (31·5)	555/1310 (42%)	103/1219 (8%)	573/1268 (45%)	158/1186 (13%)	228/1342 (17%)	58/1239 (5%)
Higher (complete & incomplete)	171	397	26·4 (38·8)	13·0 (22·3)	39/168 (23%)	9/395 (2%)	55/164 (34%)	16/385 (4%)	16/171 (9%)	4/397 (1%)
Difficult/refused to answer	28	14	79·9(120·3)	14·7 (21·9)	19/28 (68%)	1/14 (7%)	18/27 (67%)	2/13 (15%)	9/28 (32%)	1/14 (7%)
Smoking										
Never smoker	133	373	30·3 (51·1)	11·7 (30·2)	38/132 (29%)	9/369 (2%)	41/128 (32%)	16/365 (4%)	9/133 (7%)	3/373 (1%)
Ex-smoker	149	218	20·2 (41·0)	13·3 (21·7)	30/145 (21%)	5/217 (2%)	34/141 (24%)	10/214 (5%)	16/149 (11%)	2/218 (1%)
1–10 per day	370	265	28·0 (48·5)	16·1 (22·8)	135/361 (37%)	23/262 (9%)	134/352 (38%)	28/252 (11%)	56/370 (15%)	12/265 (5%)
11-20 per day	710	571	34·1 (50·4)	21·9 (33·4)	325/690 (47%)	68/562 (12%)	339/672 (50%)	84/549 (15%)	136/710 (19%)	39/571 (7%)
≥20 per day	294	174	49·5 (75·3)	30·1 (45·5)	155/287 (54%)	15/168 (9%)	160/277 (58%)	44/170 (26%)	54/294 (18%)	8/174 (5%)
Difficult/refused to answer	94	149	32·4 (68·8)	17·0 (31·4)	34/90 (38%)	15/147 (10%)	37/86 (43%)	19/132 (14%)	21/94 (22%)	7/149 (5%)
Mean ethanol intake per week from beverages (700 mL vodka bottle equivalents)										
≥4 bottles	96	18	200·2 (82·1)	211·7 (98·4)	72/96 (75%)	12/18 (67%)	85/91 (93%)	15/18 (83%)	15/96 (16%)	2/18 (11%)
2–4 bottles	149	82	86·0 (17·7)	84·5 (19·1)	83/149 (56%)	25/82 (31%)	110/145 (76%)	42/76 (55%)	18/149 (12%)	7/82 (9%)
1–2 bottles	197	171	44·1 (7·7)	41·3 (8·0)	80/197 (41%)	18/171 (11%)	100/185 (54%)	34/162 (21%)	30/197 (15%)	2/171 (1%)
0·5–1 bottle	215	244	21·5 (4·2)	21·3 (4·3)	78/215 (36%)	11/244 (5%)	87/209 (42%)	23/237 (10%)	35/215 (16%)	11/244 (5%)
<0·5 bottle	608	801	6·1 (3·9)	5·9 (4·0)	203/608 (33%)	36/801 (5%)	175/590 (30%)	47/785 (6%)	97/608 (16%)	22/801 (3%)
Beverage non-drinker	186	213	..	..	46/186 (25%)	2/213 (1%)	39/184 (21%)	2/213 (1%)	27/186 (15%)	13/213 (6%)
Volume not calculable (missing data)	299	221	..	..	155/254 (61%)	31/196 (16%)	149/252 (59%)	38/191 (20%)	70/299 (23%)	14/221 (6%)
Non-beverage alcohol drinking frequency										
Daily	160	12	60·0(102·8)	170·4 (180·6)	-	-	147/150 (98%)	10/10 (100%)	57/160 (36%)	2/12 (17%)
5–6 times per week	254	29	68·0 (84·0)	66·9 (54·5)	-	-	231/240 (96%)	27/28 (96%)	69/254 (27%)	10/29 (35%)
3–4 times per week	102	19	47·1 (43·5)	45·8 (41·0)	-	-	79/94 (84%)	13/18 (72%)	29/102 (28%)	3/19 (16%)
1–2 times per week	104	23	30·5 (34·0)	33·6 (35·2)	-	-	62/96 (65%)	16/22 (73%)	23/104 (22%)	6/23 (26%)
1–3 times per month or less	97	52	31·9 (45·2)	45·1 (52·2)	-	-	48/93 (52%)	30/48 (63%)	21/97 (22%)	4/52 (8%)
Never or almost never	988	1590	22·2 (33·9)	15·2 (23·7)	-	-	167/947 (18%)	97/1534 (6%)	84/988 (9%)	41/1590 (3%)
Difficult/refused to answer	45	25	-	-	-	-	11/36 (31%)	8/22 (36%)	9/45 (20%)	5/25 (20%)
Problem drinker†										
Yes	745	201	57·3 (72·3)	12·9 (17·9)	567/734 (77%)	96/193 (50%)	-	-	192/745 (26%)	27/201 (13%)
No	911	1481	15·3 (23·5)	57·7 (69·7)	106/886 (12%)	30/1467 (2%)	-	-	79/911 (9%)	39/1481 (3%)
Difficult/refused to answer	94	68	52·3 (84·1)	30·1 (30·8)	44/85 (52%)	9/65 (14%)	-	-	21/94 (22%)	5/68 (7%)
Narcology registration										
Yes	292	71	33·5 (60·1)	22·9 (34·8)	199/283 (70%)	25/66 (38%)	192/271 (71%)	27/66 (41%)	-	-
No	1458	1679	33·8 (55·0)	17·9 (31·7)	518/1422 (36%)	110/1659 (7%)	553/1385 (40%)	174/1616 (11%)	-	-
Total	1750	1750	33·8 (55·8)	18·1 (31·8)	717/1705 (42%)	135/1725 (8%)	745/1656 (45%)	201/1682 (12%)	292/1750 (17%)	71/1750 (4%)

Total number of cases and controls varies according to alcohol measure due to missing data. Data are mean (SD) or n/N (%) where n is number of men with characteristic and N is corresponding denominator. *Ethanol volume from beer, wine, and spirits (not non-beverage alcohols). †Problem drinking defined as having one or more episodes of *zapoi* in the past year and/or twice a week or more occurrence of excessive drunkenness, hangover, or going to sleep at night clothed because of being drunk.

Table 3: **Indicators of alcohol consumption and problems in cases and controls**

cases and 1486 [85%] controls), followed by mothers (368 [21%] cases and 156 [9%] controls). Other informants were adult offspring, siblings, fathers, or other relatives.

Of the 1750 cases with a proxy interview, cause of death was established in 1257 (72%) by forensic autopsy, 190 (11%) by non-forensic pathologist, 185 (11%) by a doctor who had treated the man, and 94 (5%) by a doctor

who had not. The distribution of cases by cause of death was virtually the same irrespective of whether a proxy interview was obtained (figure 1).

Cases were less educated and smoked more than controls (table 3). Cases were also more likely to be divorced or separated (342 [20%] *vs* 106 [6%]) and never married (215 [12%] *vs* 104 [6%]) than controls.

Complete proxy information on frequency of drinking beer, wine, spirits, and non-beverage alcohol was available for 1638 (94%) cases and 1696 (97%) controls. Over the previous year, 1332 (81%) cases and 1343 (79%) controls drank spirits. Drinking beer was less common (1147 [70%] cases *vs* 1286 [76%] controls), and wine drinking was least common (664 [41%] *vs* 651 [38%]). The largest contrast between cases and controls was for non-beverage alcohol drinking (677 [41%] *vs* 128 [8%]).

Table 3 shows the association of indicators of alcohol consumption with each other and with education and smoking. Lower levels of education and smoking were both associated with increased volume of ethanol consumed, non-beverage alcohol drinking, and markers of problem drinking. The probability of narcology registration was positively associated with non-beverage alcohol drinking, and the correlation was much the same in cases and controls (r=0·26 *vs* 0·22). Narcology registration was not associated with volume of ethanol from beverages. Volume of ethanol consumed was positively associated with concentration of ethanol detected at forensic autopsy in blood (p=0·014) and urine (p=0·008) for men certified as dying from causes explicitly implicating alcohol but not from other causes (data not shown).

Table 4 shows the associations of all cause mortality with mean volume of ethanol consumed per week (from beverages) and frequency of non-beverage alcohol consumption. Model 1 shows the effects of every factor on mortality adjusted for age alone. Although there is evidence of a positive dose response effect for total volume of beverage ethanol consumed, the association of non-beverage alcohol frequency with mortality was far stronger. Model 2 shows the effect of mutual adjustment of each of these variables for the other. Adjustment for non-beverage alcohol frequency substantially reduced the strength of association of mortality with beverage ethanol volume. Additional adjustment for education, smoking, and marital status (model 3) had little further effect on this association. By contrast, adjustment for mean volume of beverage ethanol consumed per week had only a small effect on the mortality odds ratios (OR) for frequency of non-beverage alcohol consumption. Adjustment for education, smoking, and marital status (models 3 and 4) attenuated these effects. However, even in the fully adjusted model there remained a steep and graded association between frequency of non-beverage alcohol consumption and mortality. A summary of the non-beverage alcohol mortality association is provided by the ORs for drinking non-beverage alcohol (yes *vs* no) in the past year. For the equivalent models in table 4, the OR was 9·2 (95% CI 7·2–11·7) for model 1, 8·3 (6·5–10·7) for model 2, 7·0 (5·5–9·0) for model 3, and 5·8 (4·5–7·4) for model 4.

A strong positive association of mortality with beverage ethanol volume (adjusted for education and smoking) was seen for men reported to never or almost never drink non-beverage alcohols. However, for those who did drink non-beverage alcohols there was no association with volume of ethanol consumed (table 5).

	Cases (n=1366)	Controls (n=1401)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 4 OR (95% CI)
Mean volume ethanol consumed per week from beverages (700 mL vodka bottle equivalents) *						
≥4 bottles	89	17	6·8 (4·0–11·6)	2·7 (1·5–4·8)	2·5 (1·4–4·6)	2·8 (1·5–5·1)
2–4 bottles	140	77	2·4 (1·8–3·2)	1·4 (1·0–2·0)	1·3 (0·9–1·8)	1·3 (0·9–1·9)
1–2 bottles	186	157	1·5 (1·2–2·0)	1·4 (1·1–1·8)	1·2 (0·9–1·6)	1·2 (0·9–1·6)
0·5–1 bottle	206	221	1·2 (1·0–1·5)	1·2 (0·9–1·5)	1·1 (0·8–1·4)	1·1 (0·8–1·4)
<0·5 bottle	572	742	1·0 [ref]	1·0 [ref]	1·0 [ref]	1·0 [ref]
Beverage non-drinker	173	187	1·2 (0·9–1·5)	1·3 (1·0–1·7)	1·3 (1·0–1·6)	1·2 (0·9–1·6)
Frequency of non-beverage alcohol drinking						
Daily	120	5	38·5 (15·7–94·7)	34·9 (14·2–86·0)	28·8 (11·7–71·3)	23·2 (9·3–57·8)
5–6 times per week	176	23	12·1 (7·8–18·9)	10·4 (6·6–16·3)	8·5 (5·4–13·4)	6·9 (4·4–11·1)
3–4 times per week	72	11	10·5 (5·5–20·0)	9·7 (5·1–18·5)	8·3 (4·3–15·9)	6·5 (3·3–12·6)
1–2 times per week	79	18	7·0 (4·1–11·7)	6·6 (3·9–11·2)	5·7 (3·3–9·7)	4·8 (2·8–8·2)
1–3 times per month or less	85	35	3·8 (2·6–5·7)	3·7 (2·5–5·6)	3·2 (2·1–4·8)	2·8 (1·8–4·3)
Never or almost never	834	1309	1·0 [ref]	1·0	1·0 [ref]	1·0 [ref]

*Ethanol volume from beer, wine, and spirits (not including non-beverage alcohol). Model 1: adjusted for age; model 2: adjusted for age and other variable in table (ie, frequency of non-beverage alcohol adjusted for volume ethanol and vice versa); model 3: adjusted for all variables in model 2 plus smoking and education (as categorical variables—education 3 levels, smoking 5 levels); model 4: adjusted for all variables in model 3 plus marital status (as categorical variable—registered marriage, living together unregistered marriage, single, divorced, widowed). Data restricted to men with full information on smoking and education, and frequency and usual amount drunk of every beverage and frequency of non-beverage alcohol drinking.

Table 4: **Association of mortality from all causes with frequency of non-beverage alcohol drinking and mean volume ethanol consumed from beverages**

	Never or almost never drank non-beverage alcohol			Non-beverage alcohol drinker		
	Cases	Controls	OR (95% CI)	Cases	Controls	OR (95% CI)
≥4 bottles*	24	6	7·6 (3·0–19·2)	65	11	0·9 (0·4–2·0)
2–4 bottles	60	54	1·8 (1·2–2·6)	80	23	0·6 (0·3–1·1)
1–2 bottles	111	144	1·3 (0·9–1·7)	75	13	1·0 (0·5–2·0)
0·5–1 bottle	130	210	1·1 (0·8–1·4)	76	11	1·3 (0·6–2·8)
<0·5 bottle	377	709	1·0 [ref]	195	33	1·0 [ref]
Beverage non-drinker	132	186	1·2 (0·9–1·6)	41	1	7·6 (1·0–57·8)
Total	834	1309		532	92	

*700 mL vodka bottle equivalents. †Ethanol volume from beer, wine, and spirits (not including non-beverage alcohols). All ORs adjusted for age, smoking, and education. Data restricted to men with full information on smoking and education, and frequency and usual amount drunk of every beverage and frequency of non-beverage alcohol drinking.

***Table 5:* Association of beverage ethanol volume drunk per week stratified by non-beverage alcohol drinking status†**

	Cases (n=1633)	Controls (n=1587)	OR (95% CI)
Abstains	132	186	1·3 (1·0–1·7)
Beverage alcohol drinker only (no problem drinking*)	585	1118	1·0 [ref]
Beverage alcohol drinker only (problem drinking)	152	85	3·0 (2·2–4·0)
Non-beverage alcohol drinker (no problem drinking)	99	25	6·3 (4·0–10·0)
Non-beverage alcohol drinker (problem drinking)	500	82	9·7 (7·5–12·6)
Difficult or refuse to answer†	165	91	3·0 (2·3–4·0)

*Problem drinking defined as having one or more episodes of *zapoi* in the past year or twice per week or more occurrence of excessive drunkenness, hangover, or going to sleep at night clothed because of being drunk. †Includes all men for whom data were missing on frequency of drinking, *zapoi*, frequency of hangover, excessive drunkenness, or going to sleep with clothes on at night because drunk. All data restricted to men with complete data for education and smoking.

***Table 6:* Association of mortality from all causes with alcohol drinking pattern and problem drinking adjusted for smoking and education**

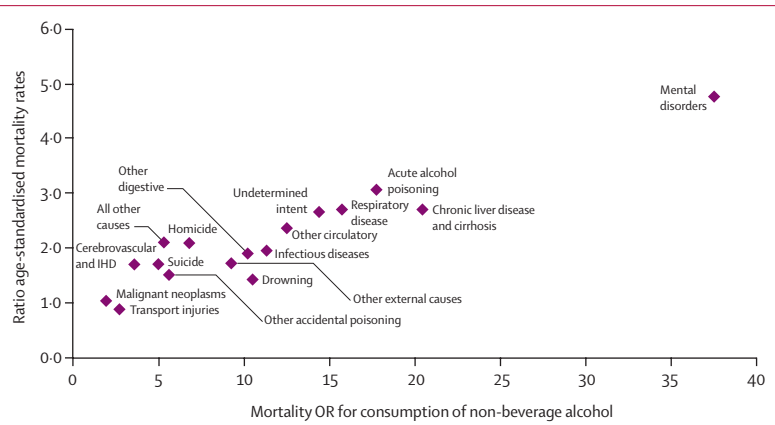

***Figure 2:* Cause-specific mortality odds ratios for non-beverage alcohol drinkers in our study compared with relative changes in age-standardised mortality rates in men aged 25–54 in Russia, 1994–1991**
IHD=Ischaemic heart disease. Mortality OR=ever versus never in the past year. Pearson r=0·93. Spearman ⍰=0·85.

Table 6 combines several different dimensions of alcohol intake and behaviours. Men were classified according to whether they consumed only beverage alcohols or additionally non-beverage alcohols and whether they were reported as being problem drinkers. Beverage only drinkers who were problem drinkers had a three-fold increased risk of death compared with those drinking beverages but without these adverse behaviours. Much larger ORs are seen for non-beverage alcohol drinkers than for beverage drinkers, especially for men who were problem drinkers.

In men with full data for drinking behaviours in table 6, over half (51%) of those who died had drunk either non-beverage alcohols or were classed as problem drinkers with adverse behaviours, compared with 13% of controls. The mortality OR for this group of hazardous drinkers, relative to men who either abstained or were beverage only drinkers without adverse behaviours, was 6·0 (5·0–7·3) adjusted for smoking and education. On the basis of these results, we estimate (with Greenland's method[27]) that 43% of deaths in men aged 25–54 years in Izhevsk might be attributable to hazardous drinking defined by non-beverage alcohol consumption or problem drinking, or both. With an OR additionally adjusted for marital status, the percentage of attributable deaths falls very slightly to 41%.

307 of 1750 (18%) deaths were from causes explicitly implicating alcohol—ie, alcoholic psychoses, alcoholic cardiomyopathy, alcoholic liver disease and cirrhosis, or acute alcohol poisoning. Non-beverage alcohol drinking in the past year (yes *vs* no) was very strongly associated with mortality from the aggregate of these directly alcohol-related causes with an OR of 25·5 (17·4–37·6) adjusted for volume of ethanol consumed from beer, wine, and spirits; education; and smoking. The equivalent adjusted OR for mortality from the aggregate of all other causes was less than this result—5·3 (4·1–6·9).

Figure 2 shows that the cause-specific mortality OR for non-beverage drinkers in our study is very similar to the trend for cause-specific mortality rates for Russia as a whole during the early 1990s.

Since more wives or partners were proxies for controls than for cases, we repeated various analyses restricted to cases and controls where the informant was a wife or partner. The results were much the same. For example, the mortality OR for non-beverage alcohol drinking (yes *vs* no) adjusted for education, smoking, and beverage ethanol volume was 7·0 (5·5–9·0) for all men and 5·6 (4·2–7·4) when restricted to those whose wives or partners were the proxy. A formal test of interaction of this OR with informant type (spouse *vs* non-spouse) was not significant (p=0·39).

In the subset of 200 case and 200 control households in which two informants were interviewed about the same man, Cohen's κ for whether non-beverage alcohol was consumed in the past year (yes *vs* no) was 0·85 for cases and 0·83 for controls, whereas for frequency of non-beverage alcohol drinking it was 0·81 for cases and 0·80 for controls. This level of agreement is high and is conventionally described as almost perfect (κ>0·80) or substantial (κ=0·61–0·80).[28] However, agreement for the composite variable of total beverage ethanol was lower than for non-beverage ethanol (0·51 for cases and controls) and described as moderate (κ=0·41–0·60).

Narcology registration provides a marker of serious alcohol problems without proxy reporting bias. Adjusted for age alone, narcology registration had an all cause mortality OR of 4·8 (95% CI 3·6–6·2). However, this effect was almost halved to 2·6 (1·9–3·5) on adjustment for non-beverage alcohol use (yes or no) in the past year, whereas that for non-beverage alcohol after adjustment for narcology registration fell from 8·7 to 7·5. Adjustment for volume of beverage ethanol consumed per week had almost no effect on the OR for narcology registration (OR=4·7 [3·5–6·1]).

The mortality OR for narcology registration versus non-registration was 5·1 (4·1–6·3) on the basis of all 2835 cases and 3078 controls (table 1) compared with 4·8 (3·6–6·2) on the basis of those with interviews.

Of the cases in which a proxy interview was obtained, 118 (7%) could not be found in the population register sampling frame used to select controls. Excluding these cases, the mortality OR for non-beverage alcohols (yes or no) was 8·8 (7·2–10·8) adjusted for age only. This OR is almost identical to that found without such exclusions (OR=8·7 [7·1–10·6]).

Discussion

We have shown that mortality in working-age men in a typical city in Russia is strongly associated with hazardous patterns of alcohol consumption. In particular, we have identified drinking of non-beverage alcohols as a potentially major contributor to mortality. Frequency of consumption of such beverages was strongly associated with all cause mortality in a graded fashion, and was statistically independent of volume of consumption of beverage alcohols. Mortality was also associated with a composite marker of problem drinking independently of non-beverage alcohol consumption and total volume of beverage ethanol consumed. However, there was a reduced but consistent increased risk of death with increasing total volume of ethanol consumed in men who did not drink non-beverage alcohol.

The mortality ORs for consumption of non-beverage alcohols are unusually large compared with those generally observed in epidemiology (excluding those associated with smoking and the effects of exposure to communicable agents). How biased are these ORs? Could case proxies overestimate the amount and extent of hazardous drinking compared with control proxies? Differential reporting of this sort is inconsistent with our finding that the correlation between non-beverage alcohol drinking and narcology registration is almost the same in cases and controls. Furthermore, we have shown that the same independent external data for registration at the narcology clinic are also strongly associated with all cause mortality. Importantly, this effect is substantially attenuated on adjustment for non-beverage alcohol drinking, which is consistent with it being a causal mediator of the association. However, we cannot exclude the possibility that there is some degree of over-reporting of non-beverage alcohol use in case proxies compared with control proxies.

The few epidemiological studies of alcohol and mortality in Russia undertaken over the past 20 years have methodological limitations. The Novosibirsk cohort[15] recruited people willing to participate in a medical examination, potentially selectively excluding heavy drinkers.[13] Nevertheless they reported that frequent heavy drinking increased mortality from cardiovascular disease. A case-control study[29] of men aged 20–55 years in the Udmurt Republic established that periods of heavy drinking were associated with an increased risk of death from cardiovascular disease and external causes, but the choice of controls was questionable. Only weak associations between alcohol and mortality were seen in a study applying indirect demographic estimations to a 2002 cross sectional survey in selected Russian regions.[30] This study depended on relatives' reports of drinking by family members who had died up to 30 years previously. None of these studies used indicators of problem drinking such as frequent hangover, which has been advocated for the Russian context.[31] Additionally, none had explicitly considered consumption of non-beverage alcohols.

A particular strength of our study is that it was population based. We started with all deaths in men aged 25–54 years who were residents of the city, and in parallel selected controls randomly from a register of the city population. Although we were not able to obtain proxy interviews with all cases and controls, we noted that the association of mortality with narcology registration for all men (irrespective of whether they were interviewed) was almost identical to that obtained with the subset of men for whom a proxy interview was obtained. This result suggests that selection bias is unlikely to play much of a part in explanation of our key findings with respect to non-beverage alcohols and problem drinking, which are both strongly related to probability of narcology registration.

If a substantial part of the association of non-beverage alcohol drinking with mortality is not a result of design difficulties or selection bias, how can it be explained? Adjustment for two important confounders (smoking and education) leads to negligible attenuation of the associations. Pronounced effects of non-beverage alcohol drinking on mortality are seen even after further adjustment for marital status. However, treating marital status as a confounder might lead to over-adjustment, because marital status is partly determined by alcohol problems[32,33] and therefore probably carries information about the severity of alcohol problems that are not adequately captured by the questions we asked about alcohol itself.

An unavoidable weakness of the study was the use of proxy reports. Consistent with previous research, proxy reporting of very obvious features of behaviour of the case or control—eg, non-beverage alcohol consumption—seems reliable. Conversely, total volume of ethanol from

beverage sources is less well reported than is non-beverage alcohol drinking since accurate information is needed not only about frequency of consumption but also about usual amount drunk on typical occasions. Nevertheless, total volume of ethanol is related to mortality especially in men not drinking non-beverage alcohols. However, there is probably some residual confounding from ethanol volume consumed because of measurement error in this variable. Since all cause mortality ORs associated with non-beverage alcohols are much larger than are those reported for ethanol volume, residual confounding is highly unlikely to account for much of this effect.

How far do these associations show a direct causal role for non-beverage alcohols that is independent from the heavy binge drinking of spirits that is a feature of Russian drinking? Could non-beverage alcohol drinking simply be a good marker of an extended history of heavy and hazardous alcohol drinking? Men might only regularly drink non-beverage alcohols when they already have an established history of heavy and frequent beverage drinking. These medicinal tinctures, eau de colognes, and other non-beverage alcohols are a cheap and highly concentrated source of ethanol.[21] They could thus be especially attractive to heavy drinkers who are not well off. Moreover, for men who become impoverished because of heavy drinking (eg, through unemployment) they could be the only affordable source of ethanol. We have some evidence for this tenet, since 47% of controls who drank non-beverage alcohols were unemployed compared with 13% of those who did not drink non-beverage alcohols. Further analyses of socioeconomic factors associated hazardous drinking in this study have been reported elsewhere.[34]

Men who drink non-beverage alcohols will have had a higher cumulative consumption of ethanol for any particular length of drinking history than would those who drink only beer, wine, or spirits. They are also likely to have had more episodes of very high blood concentrations of ethanol and its metabolites and corresponding increased toxic effects[35] because of the high concentration of ethanol in these liquids, than heavy drinkers who consume only beverage alcohols.

What is the relevance of our results for Russia as a whole? We have shown that cause-specific variations in the strength of association of mortality with non-beverage alcohol drinking (as a powerful indicator of hazardous alcohol consumption) in Izhevsk nowadays, are much the same as the pattern of mortality variation by cause seen during the first half of the 1990s in Russia as a whole (figure 2). This trend accords with the contention that the factors of this sharp increase in mortality could be related not just to variations in general alcohol consumption[4,7] but in particular to the sort of hazardous alcohol consumption represented in Izhevsk nowadays by drinking of non-beverage alcohol. However, on the basis of our study we are unable to generalise our quantitative estimate of mortality attributable to non-beverage alcohol or hazardous drinking in Izhevsk to the whole of Russia. To estimate these deaths we would need to have exposure information from a representative sample of the Russian population. If such a generalisation was justified, the 43% of mortality attributable to non-beverage alcohols or hazardous drinking in Izhevsk would translate to 170 000 excess deaths in Russia per year for men aged 25–54 years.

What does this study add to what is already known? In the European subregion containing Russia, Rehm and colleagues[20] have estimated that 27% of deaths in men aged 15–59 years in 2002 were attributable to alcohol. However, we have estimated that 43% of deaths in men aged 25–54 years in Izhevsk were attributable to hazardous drinking alone. Additionally, we report much stronger associations with alcohol than do other epidemiological studies. Most of these differences are probably explained by the fact we quantified the effect of hazardous patterns of alcohol drinking on mortality, especially consumption of non-beverage alcohol, as well as factors such as heavy binge drinking exhibited by episodic and extended periods of drunkenness (*zapoi*) and frequent hangover.

Development of policy interventions to address this serious problem will need major shifts in how alcohol is perceived in Russian life. Addressing the consumption of non-beverage alcohols might be a good starting point, and there could be lessons to be learnt from Finland, where non-beverage alcohols were once a major problem.[36] However, a focus on non-beverage alcohols might only be effective in reducing alcohol-related harm and mortality if developed within a broader framework of policies and interventions aimed at reducing harmful patterns of ethanol consumption irrespective of source.

Contributors

The idea of the study was developed by VS with input from DL and MM. All authors contributed to the detailed design of the protocol. LS was responsible for the conduct of the interview field work, NK for coordination of all other data collection in Izhevsk, EA for data capture systems and monitoring of field work progress, ST for the detailed design of the questionnaire (including the systematic review of proxy validity) and coordination of the project and management of the final data set, and MM for the autopsy and setting up of the surrogate toxicological analyses. DL and VS developed the analysis plan and all authors contributed to the interpretation of data. DL undertook the main analyses and drafted the text which was commented on by all authors.

Conflict of interest statement

We declare that we have no conflict of interest.

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References

1 Shkolnikov VM, Andreev EM, Leon DA, McKee M, Meslé F, Vallin J. Mortality Reversal in Russia: the story so far. *Hygiea Internationalis* 2004; **4:** 29–80.

2 Human Mortality Database. http://www.mortality.org (accessed March 15, 2007).

3 Meslé F. Mortality in Central and Eastern Europe: long-term trends and recent upturns. *Demogr Res* 2004; **S2:** 45–70.

4 Leon DA, Chenet L, Shkolnikov VM, et al. Huge variation in Russian mortality rates 1984-94: artefact, alcohol, or what? *Lancet* 1997; **350:** 383–88.

5 Shkolnikov V, McKee M, Leon DA. Changes in life expectancy in Russia in the mid-1990s. *Lancet* 2001; **357:** 917–21.

6 McKee M, Shkolnikov V, Leon DA. Alcohol is implicated in the fluctuations in cardiovascular disease in Russia since the 1980s. *Ann Epidemiol* 2001; **11:** 1–6.

7 Nemtsov AV. Alcohol-related human losses in Russia in the 1980s and 1990s. *Addiction* 2002; **97:** 1413–25.

8 Leon DA, Shkolnikov VM. Social stress and the Russian mortality crisis. *JAMA* 1998; **279:** 790–91.

9 Walberg P, McKee M, Shkolnikov V, Chenet L, Leon DA. Economic change, crime, and mortality crisis in Russia : regional analysis. *BMJ* 1998; **317:** 312–18.

10 Rehm J, Rehn N, Room R, et al. The global distribution of average volume of alcohol consumption and patterns of drinking. *Eur Addict Res* 2003; **9:** 147–56.

11 Rehm J, Patra J, Baliunas D, Popova M, Roerecke M, Taylor B. Russian Federation. Toronto: Centre for Addiction and Mental Health, 2006.

12 Treml V. Soviet and Russian statistics on alcohol consumption and abuse. In: Bobadilla J-L, Costello C, Mitchell F, eds. Premature death in the New Independent States. Washington DC: National Academy Press, 1997: 220–38.

13 Gmel G, Rehm J. Measuring alcohol consumption. *Contemp Drug Probl* 2004; **31:** 467–540.

14 Bobak M, Room R, Pikhart H, et al. Contribution of drinking patterns to differences in rates of alcohol related problems between three urban populations. *J Epidemiol Community Health* 2004; **58:** 238–42.

15 Malyutina S, Bobak M, Kurilovitch S, et al. Relation between heavy and binge drinking and all-cause and cardiovascular mortality in Novosibirsk, Russia: a prospective cohort study. *Lancet* 2002; **360:** 1448–54.

16 Carlson P. Risk behaviours and self rated health in Russia 1998. *J Epidemiol Community Health* 2001; **55:** 806–17.

17 Bobak M, McKee M, Rose R, Marmot M. Alcohol consumption in a national sample of the Russian population. *Addiction* 1999; **94:** 857–66.

18 Malyutina S, Bobak M, Kurilovitch S, Ryizova E, Nikitin Y, Marmot M. Alcohol consumption and binge drinking in Novosibirsk, Russia, 1985–95. *Addiction* 2001; **96:** 987–95.

19 Nilssen O, Averina M, Brenn T, Brox J, Kalinin A, Archipovski V. Alcohol consumption and its relation to risk factors for cardiovascular disease in the north-west of Russia: the Arkhangelsk study. *Int J Epidemiol* 2005: **34:** 781–88.

20 Rehm J, Taylor B, Patra J. Volume of alcohol consumption, patterns of drinking and burden of disease in the European region 2002. *Addiction* 2006; **101:** 1086–95.

21 McKee M, Suzcs S, Sarvary A, et al. The composition of surrogate alcohols consumed in Russia. *Alcohol Clin Exp Res* 2005; **29:** 1884–88.

22 Shkolnikov V, Meslé F, Leon DA. Premature cardiovascular mortality in Russia in the light of population- and individual-level evidence. In: Weidner G, Kopp SM, Kristenson M, eds. Heart disease: environment, stress and gender. Nato Science Series, Series I: life and behavioural sciences, vol 327. Amsterdam: NATO, 2001.

23 Tomkins S. Proxy respondents in a case-control study: validity, reliability and impact. PhD thesis, London School of Hygiene & Tropical Medicine, University of London; 2006.

24 Graham P, Jackson R. Primary versus proxy respondents: comparability of questionnaire data on alcohol consumption. *Am J Epidemiol* 1993; **138:** 443–52.

25 Nelson LM, Longstreth WT Jr, Koepsell TD, Checkoway H, van Belle G. Completeness and accuracy of interview data from proxy respondents: demographic, medical, and life-style factors. *Epidemiology* 1994; **5:** 204–17.

26 Dawson DA, Room R. Towards agreement on ways to measure and report drinking patterns and alcohol-related problems in adult general population surveys: the Skarpo conference overview. *J Subst Abuse* 2000; **12:** 1–21.

27 Greenland S. Variance estimators for attributable fraction estimates consistent in both large strata and sparse data. *Statist Med* 1987; **6:** 701–08.

28 Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977; **33:** 159–74.

29 Shkolnikov V, Chervyakov VV, McKee M, Leon DA. Russian mortality beyond vital statistics: effects of social status and behaviours on deaths from circulatory disease and external causes—a case-control study of men aged 20–55 years in Udmurtia, 1998–99. *Demogr Res* 2004; **S2:** 71–104.

30 Nicholson A, Bobak M, Murphy M, Rose R, Marmot M. Alcohol consumption and increased mortality in Russian men and women: a cohort study based on the mortality of relatives. *Bull World Health Organ* 2005; **83:** 812–19.

31 Room R. Commentary: pattern of drinking and the Russian heart. *Int J Epidemiol* 2005; **34:** 788–90.

32 Stack S, Bankowski E. Divorce and drinking: an analysis of Russian data. *J Marriage Fam* 1994; **56:** 805–12.

33 Vannoy D, Rimashevskaya N, Cubbins L, Malysheva M, Mesherkina E, Pisklakova M. Marriages in Russia. Couples during the economic transition. Westport: Praeger, 1999.

34 Tomkins S, Saburova L, Kiryanov N, et al. Prevalence and socio-economic distribution of hazardous patterns of alcohol drinking: study of alcohol consumption in men aged 25–54 years in Izhevsk, Russia. *Addiction* 2007; **102:** 544–53.

35 Lebach WK. Organic pathology related to volume and pattern of alcohol use. In: Gibbins RJ, Israel Y, Kalant H, Popham RE, Schmidt W, Smart RG, eds. Research advances in alcohol and drug problems, vol 1. New York: John Wiley & Sons, 1974: 93–198.

36 Mäkelä K. Unrecorded consumption of alcohol in Finland, 1950–1975. Helsinki: Social Research Institute of Alcohol Studies, 1979.