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What is the optimal level of population alcohol consumption for chronic disease prevention in England? Modelling the impact of changes in consumption patterns

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Abstract

Objective To estimate the impact of achieving alternative population alcohol consumption patterns on chronic disease mortality in England.

Design A macro-simulation model was built to simultaneously estimate the number of deaths from coronary heart disease, stroke, hypertensive disease, diabetes, liver cirrhosis, epilepsy and five cancers that would be averted or delayed annually as result of changes in alcohol consumption among English adults. Counterfactual scenarios assessed the impact on alcohol-related mortalities of changing a) the percentage of non-drinkers; b) the median alcohol consumption of drinkers; c) both factors simultaneously.

Data sources Risk relationships were drawn from published meta-analyses. Age and sex specific distributions of alcohol consumption (g/d) for the English population in 2006 were drawn from the General Household Survey 2006, and age, sex and cause specific mortality data for 2006 were provided by the Office for National Statistics.

Results The optimum percentage of non-drinkers in the model was zero. If achieved, this would avert or delay 4,160 (95% credible intervals: 908 to 6,962) chronic disease deaths per year. Increases of 2,771 (2,443 to 3,898) deaths from cancer and 1,265 (1,166 to 1,360) deaths from liver cirrhosis were more than offset by averting 7,705 (5,248 to 11,934) deaths from cardiovascular diseases. The optimum median consumption level for drinkers in the model was 5g/d (about half a unit), which would avert or delay 4,579 (2,544 to 6,590) deaths per year. Achieving both a median consumption of 5g/d and zero non-drinkers would delay or avert 10,794 (6,601 to 14,504) deaths each year.

Conclusions Current government recommendations for alcohol consumption are well above the level likely to minimise chronic disease. Public health targets should aim for a reduction in population alcohol consumption to half a unit per day, in order to achieve the optimum level of reduced chronic disease mortality.

Article Summary

Article focus

- Alcohol consumption is a risk factor for many chronic diseases, while providing protection from others. Assessments of the impact of alcohol on individual chronic diseases can therefore result in contradictory advice about the level of alcohol consumption that is optimal for health.
- The UK government currently recommends that men should consume no more than three to four units per day (24 to 32 g/d of pure alcohol) and women should drink no more than two to three units per day (16 to 24 g/d). However the true optimum population level of alcohol consumption is unclear.
- The aim of this study was to estimate the impact of achieving alternative population alcohol consumption patterns on chronic disease mortality in England.

Key messages

- Results suggest that the optimum population level of alcohol consumption for minimising chronic disease mortality in England is 5g/day (approximately half a unit per day).
- Current recommendations for alcohol consumption are well above this level and may not be compatible with optimum protection of public health. Substantial reductions in recommendations and in population alcohol consumption levels would be needed to minimise the chronic disease burden associated with alcohol consumption in England.

Strengths and limitations of this study

- The study used a detailed modelling approach to synthesise the best available evidence from meta-analysis of prospective cohort studies and provide for the first time an estimate of the level of alcohol associated with theoretical minimum risk of a range of chronic diseases, considering both harmful and protective effects simultaneously.

- The approach used relies on chronic (average) consumption of alcohol and is not able to take account of to take account of patterns of drinking (e.g. binge drinking).
- Results are based on the assumption of a steady state relationship between alcohol consumption patterns and relative risk of disease, and cannot estimate the time required between changes in population alcohol consumption levels occurring and the achievement of changes in mortality rates.

Introduction

Alcohol consumption has significant impacts on chronic disease risk. [1-3] In the UK, it has been estimated that alcohol-related ill-health is responsible for £3.3 billion in direct costs to the National Health Service annually. [4] The effects of episodes of heavy alcohol consumption are clearly detrimental to health, for example increasing risk from injuries and violence.[5-7] Less is known about the overall effects of long term alcohol consumption on chronic disease risk in the whole population, due to alcohol consumption at various levels increasing risk for some chronic disease outcomes (e.g. liver cirrhosis and cancer), yet decreasing risks of others (e.g. cardiovascular disease and diabetes).

The World Cancer Research Fund has recommended that there is no safe level of alcohol consumption in relation to cancer risk[8], and Schutze and colleagues[9] report that up to 10% of all cancers in men and 3% in women in some European countries may be attributable to alcohol consumption. This has led to calls for public health messages to encourage abstinence or significant reductions in alcohol consumption.[9 10] There is, however, a substantial body of evidence that suggests that moderate alcohol consumption protects against other chronic diseases, including cardiovascular disease (CVD) and diabetes.[11-13] Particularly in the case of CVD, which accounts for a significant proportion of mortality in high income countries, this evidence suggests that significantly reducing alcohol consumption could lead to an increase in mortality.

Substantial research has examined the effects of alcohol consumption on various chronic diseases; however there has been little integration of the findings across disease outcomes, thereby precluding the development of comprehensive and evidence-based recommendations for population alcohol consumption. The UK government currently recommends that men should consume no more than three to four units per day (one unit = 8g of pure alcohol) and women should drink no more than two to three units per day.[14] A large proportion of the literature supporting alcohol policy in the UK, however, appears to focus on alcohol 'misuse', episodes of heavy drinking

and the social consequences of alcohol consumption[14]; it is not clear that there is evidence that the UK Government recommended drinking levels offer the maximum protection for public health.

The aim of this study was to estimate the impact of achieving alternative population alcohol consumption patterns on chronic disease mortality in England. The research question was: what proportion of non-drinking in the English population and what level of alcohol consumption among drinkers would result in the greatest number of chronic disease deaths delayed or averted in England compared to recent levels?

Methods

A macro-simulation model was built that assessed the impact on mortality from chronic disease of changing the distribution of alcohol consumption (g/day) within the population of England. The Preventable Risk Integrated ModEl for Alcohol (PRIME-Alcohol) estimates the impact of population changes in alcohol consumption on chronic disease mortality. Developing the PRIME-Alcohol model involved: identifying chronic diseases associated with alcohol consumption; identifying the current (baseline) distribution of alcohol consumption; and parameterising the association between alcohol consumption and chronic disease.

Selection of mortality outcomes

The initial list of chronic diseases was generated from those linked to alcohol consumption in the World Health Organization Global Burden of Disease 'Global Health Risks' report[15] and the World Cancer Research Fund Report[8] was used to select site-specific cancers associated with alcohol consumption. Excluding those resulting in small numbers of deaths (fewer than 500 deaths in 2006 in England), 11 chronic diseases were included as outcomes in the PRIME-Alcohol model, including five cancer sites.

The PubMed and Cochrane databases were searched for meta-analyses of prospective cohort or case-control studies that quantified chronic disease risk for different levels of alcohol consumption. The relationships between alcohol consumption were diverse, including protective effects, linear increases in risk and 'U' or 'J' shaped relationships. Where multiple suitable meta-analyses were available, preference was given to meta-analyses of cohort studies over case-control studies, and to those using lifetime abstainers as the reference category. Age- and sex-specific estimates of risk relationships and estimates adjusted for potential confounders were used where available.

Details of the chronic disease outcomes and the meta-analyses that were included in the model[8 11 12 16-18] are shown in table 1.

(table 1 here)

Identifying the current (baseline) distribution of alcohol consumption in England

The General Household Survey (GHS) from 2006[19] provided baseline distributions of alcohol consumption for adults aged 16 years and over. The GHS is a multi-purpose survey conducted by the Office for National Statistics in the UK. In 2006, it included 18,214 adults aged 16 years and over (overall response rate 74%). To establish average weekly alcohol consumption, respondents were asked how often over the last year they drank alcoholic beverages and the amount usually consumed on any one day. This information is combined to give an estimate of the respondent's weekly alcohol consumption in units of alcohol.[20] For the current analyses, units of alcohol per week was converted to grams per day and only participants from England were included (n =15,616). The distribution of alcohol consumption in the GHS is shown in supplementary figure S1 – there is a large spike of non-drinkers and very low alcohol consumers (<=1g/d) and a long tail of higher alcohol consumers. Non-drinkers and very low alcohol consumers were removed and analysed as a separate category (referred to as non-drinkers henceforth). Excluding this group, alcohol consumption was shown to be approximately log-normally distributed (supplementary figure S2).

The three parameters for the baseline distribution of alcohol consumption derived from the GHS for each of 30 age-sex groups were therefore: percentage of non-drinkers; the mean of ln-transformed alcohol consumption of drinkers; and the standard deviation of ln-transformed alcohol consumption of drinkers. Counterfactual scenarios were modelled by altering one or more of these parameters.

Parameterising the association between alcohol consumption and chronic disease

The meta-analyses identified by the literature search provided estimates of the relative risk of different levels of alcohol consumption on chronic disease (table 1). The relative risks used in the PRIME-Alcohol model are shown in supplementary table S1. These risks were used in conjunction with the baseline distribution of alcohol consumption to attribute risk for chronic disease throughout the age-sex specific populations. Baseline age, sex and cause specific number of mortalities (England 2006) were provided by the Office for National Statistics. For each chronic disease and age-sex group, mortality rates were assigned to each level of alcohol consumption such that the relative risks from the meta-analyses were maintained, and the total risk in the population produced the recorded number of mortalities. These mortality rates were then applied to the counterfactual distributions to calculate the number of deaths that would be expected under the counterfactual scenario. An example is provided in supplementary table S2.

Uncertainty analysis

The alcohol-chronic disease association parameters were allowed to vary stochastically according to the distributions reported in the literature. Five thousand Monte Carlo iterations were run, and the results were used to calculate 95% credible intervals around the estimates. Because of the

computing requirements of the Monte Carlo iterations, credible intervals are only presented for key results.

Defining the counterfactual scenarios

To assess the number of chronic disease mortalities in England under different alcohol consumption scenarios, three counterfactual scenarios were analysed: 1) varying the proportion of non-drinkers in the population while holding the median consumption among drinkers constant; 2) varying the median consumption among drinkers while holding the proportion of non-drinkers constant; and 3) varying both the proportion of non-drinkers and the median intake among drinkers.

In the analysis of the first scenario, the total percentage of non-drinkers in the population was allowed to vary between 0% and 100% such that the age-sex distribution of non-drinkers was maintained, whilst the amount of alcohol consumed by drinkers remained constant. In the analysis of the second scenario, the percentage of non-drinkers was kept constant while the amount of alcohol consumed by drinkers in the population was varied between 1g/d and 48g/d (6 units), such that the age-sex distribution of mean alcohol consumption was maintained. In the analysis of the third scenario, both the percentage of non-drinkers and the amount consumed by drinkers were varied. The aim of the analyses was to find the distribution of alcohol consumption for England that would result in the lowest number of chronic disease mortalities. The funding bodies supporting the authors of this work had no role in the present study.

Results

In 2006, 29% of English adults were non-drinkers according to the definitions used here (including those who consume less than 1g/d). Rates of non-drinking varied substantially by age group and sex (supplementary table S3). Overall, 20% of men and 36% of women were non-drinkers.

In the first counterfactual scenario, varying the proportion of non-drinkers in the whole population, optimal results were achieved when there were zero non-drinkers in the population (figure 1 and supplementary table S4), which resulted in 4,160 (95% credible intervals: 908 to 6,962) chronic disease deaths averted or delayed compared to 2006 mortality rates. Although having the whole population drinking some alcohol would increase deaths from cancer by 2,771 (2,443 to 3,898) and from liver cirrhosis by 1,265 (1,166 to 1,360), this was more than offset by averting 7,705 (5,248 to 11,934) deaths from CVD. As the proportion of non-drinkers was increased in the counterfactual scenarios, the reductions in mortality were attenuated. When the modelled rates of non-drinking exceeded the 2006 levels there was a net increase in chronic disease mortality, up to an additional 3,160 (-436 to 6,409) lives lost annually if the entire population were to abstain from alcohol.

Analysis by gender showed that at low proportions of non-drinkers, greater numbers of deaths were averted among women, while at higher proportions of non-drinkers there was a smaller increase in mortality among women than among men, reflecting the fact that the baseline proportion of non-drinkers is higher in women than in men. When premature deaths (before age 75) were examined, the trend was opposite to that displayed for all ages: among people aged under 75 years, higher levels of non-drinkers resulted in larger numbers of deaths delayed or averted (supplementary table S4).

In the second counterfactual scenario, varying the median population level of alcohol consumption among current drinkers between 1g and 48g per day, results showed that approximately 5g/day (just over half of one unit) was the optimal level of alcohol consumption, resulting in 4,579 (2,544 to

6,590) deaths delayed or averted (figure 2 and supplementary table S5). In counterfactual scenarios with lower levels of alcohol consumption, the shift of a large proportion of the population into the non-drinker category resulted in an increase in deaths from cardiovascular disease, which was not offset by reductions in cancer, liver cirrhosis and other chronic conditions. Above 5g/day the additional protective effect of alcohol on CVD was not enough to offset the additional risk from cancer, liver cirrhosis and other chronic conditions. For men and women aged under 75 years, the optimum level of consumption was slightly lower than for the whole population, at 3g/d, at which level 4,381 (3,327 to 5,400) deaths before age 75 would be delayed or averted each year.

(table 2 here)

In the third counterfactual scenario, the proportion of non-drinkers was set at the optimum level (0%) and median alcohol consumption in drinkers was allowed to vary between 0g/d and 48g/d (table 2). The optimal population median intake remained 5g/day, at which level 10,794 (6,601 to 14,504) deaths were averted or delayed. In this scenario, the increased risks of alcohol consumption above optimal levels increased more rapidly due to all of the population being exposed to the risk. There would be a simultaneous reduction in deaths from all three of the major alcohol-related chronic disease categories under this scenario; deaths from CVD would be reduced by 6,064 (1,732 to 9,791), from cancer by 1,735 (1,355 to 2,078) and from liver cirrhosis by 2,704 (2,296 to 2,994).

Discussion

The PRIME-Alcohol model effectively demonstrates the impact of population usual alcohol consumption on chronic disease mortality, bringing together a wide range of risk and protective effects of alcohol, including the increased risks of many cancers and the protective effect of low to moderate consumption on cardiovascular disease. Modelling demonstrated that the optimum population median alcohol consumption level appears to be substantially lower than the

recommended safe levels in current UK public health guidance. Reducing the median population alcohol consumption among current drinkers to around half a unit (5g of alcohol) per day, would result in around 4,600 fewer deaths annually, primarily due to reductions in cancers and liver cirrhosis. If this same median consumption level were to be applied to the whole population (i.e., including current non-drinkers), more than double this number of deaths could be delayed or averted. However, there are a number of reasons why it may not be prudent to encourage current non-drinkers to start drinking. These include: encouraging abstainers to start drinking whilst encouraging drinkers to reduce their alcohol consumption is a mixed message that may be difficult to communicate and promote; reducing the number of non-drinkers may have an adverse impact on non-chronic disease health (e.g. accidents and injuries); and the modelled results show that while reducing the proportion of non-drinkers would decrease chronic disease deaths overall, it would increase the number of premature deaths (before 75 years; see supplementary table 3). On this basis, we recommend that the public health target for alcohol consumption in England should be to reduce median alcohol consumption to half a unit per day for both men and women, and to maintain the current level of non-drinkers within the population.

Public health behavioural recommendations should ideally be based on the best available evidence for optimising population health outcomes. In practice, public health goals in the UK have often been based on a mixture of evidence of health risks and pragmatic considerations about setting a goal that is considered achievable. A counterfactual modelling analysis such as the type reported in this paper is particularly useful for setting public health goals, as its flexibility can provide results for a range of counterfactual scenarios, which can then inform policy makers both of the optimum goal and the strength of any pragmatic goal that they may consider.

A limitation of the PRIME-Alcohol model is that it is based on usual average levels of alcohol consumption and is unable to take account of patterns of drinking (e.g. binge drinking). There is evidence that patterns of drinking play an important role in disease risk[21], and particularly in

morbidity and mortality from accidents and injuries.[2 5] The central recommendation from the results of this paper – that a target consumption level for England should be half a unit per day – is, however, likely to be consistent with low levels of risk for accidents and injuries. In addition, it is not possible to include wholly alcohol attributable conditions (e.g. mental and behavioural disorders due to alcohol use) in the model. The PRIME-Alcohol model is necessarily limited by the availability of robust meta-analytic estimates of relative risk for mortality. Sex-specific estimates of relative risk at varying levels of alcohol consumption were available only for hypertensive disease and liver cirrhosis, and no age-specific estimates were available, which limits the specificity of the counterfactual scenarios analysed by the model. Furthermore, results are based on the assumption of a steady state relationship between alcohol consumption patterns and relative risk of disease, while in reality there is a lag time between changes in alcohol consumption levels and mortality risk. For some conditions included in the model, relative risk estimates from appropriate meta-analysis were available only for incidence of the disease, rather than mortality.

This study is an important addition to the current debate around alcohol consumption and public health, combining and balancing risk and protective factors to identify an optimal population level of alcohol consumption. This is in contrast to recent publications on the associations between alcohol and specific conditions. For example, Schutze and colleagues concluded that their analyses of the association between alcohol intake and cancer "support current political efforts to reduce or to abstain from alcohol consumption to reduce the incidence of cancer".[9] On behalf of the Australian Cancer Council, Winstanley and colleagues recommend that "to reduce their risk of cancer, people limit their consumption of alcohol, or better still avoid alcohol altogether".[10] In contrast, a recent systematic review of the impact of alcohol on cardiovascular disease concluded that "alcohol, in moderation, may have overall health benefits that outweigh the risks in selected subsets of patients".[11] Only by systematically combining the effects of alcohol on all alcohol-related conditions can appropriate public health messages be developed.

The findings from this paper are consistent with those from a meta-analysis of alcohol consumption and total mortality[22], which also found lowest mortality risk around 5g of alcohol per day, and a Europe-wide study[23] which found minimum risk for alcohol attributable deaths at 10g per day or less (the smallest consumption category included in that study). A strength of our modelling approach, in comparison to cross-sectional studies or fixed meta-analyses of total mortality, is that it can account for differences between populations in underlying risk of various chronic diseases, and can therefore be used to predict population-specific curves of potential changes in chronic disease mortality for international comparisons. Future work should therefore produce comparable results for international populations with varying current levels of exposure and outcomes. Furthermore, there is a significant interaction between alcohol consumption and other lifestyle risk factors for chronic disease mortality, and future work should seek to integrate alcohol consumption with risk behaviours such as poor nutrition, low physical activity and smoking to compare the relative contributions that improvements in these risk factors, both independently and in combination, could have on population health.

Conclusions

Current government recommendations for alcohol consumption are well above the level likely to minimise chronic disease. Public health targets for alcohol should aim for a reduction in population level alcohol consumption to half a unit per day, in order to achieve the optimum level of reduced chronic disease mortality.

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LIST OF FIGURES:

Figure 1 Deaths delayed or averted in the counterfactual scenario varying percentages of non-drinkers.

The percentage of non-drinkers was allowed to vary between 0% and 100% of the total population using England 2006 as the baseline. The median consumption of alcohol among those drinking was held constant.

Figure 2 Deaths delayed or averted in the counterfactual scenario varying median consumption of alcohol in drinkers.

The median consumption of alcohol among drinkers was allowed to vary from 0g/d to 24g/d using England 2006 as the baseline. The percentage of non-drinkers in the population was held constant.

412 Table 1: Details of mortality outcomes included in the model

Outcome (ICD-10 codes)	Total deaths, England 2006	Deaths <75years, England 2006 n (%)	Meta-analysis details	Nature of risk relationship
Coronary Heart Disease (I20-25)	76,806	24,364 (31.7%)	31 cohort studies[11], total 1,925,106 subjects. Adjusted for up to 18 confounders by study. 23 studies adjusted for smoking.	Protective at all levels of consumption
Stroke (I60-69)	45,219	7,966 (17.6%)	10 cohort studies[11], total 723,571 subjects. Adjusted for up to 18 confounders by study. 8 studies adjusted for smoking.	'U' or 'J' shaped: protection only at low to moderate consumption
Hypertensive disease (I10-15)	3,742	995 (26.6%)	12 cohort studies[16], 27,603 cases. Adjusted for age, BMI and up to 5 others by study. 4 studies adjusted for smoking.	Dose-response increased risk
Diabetes (E11,E14)	4,831	1,450 (30.0%)	15 cohort studies[12], 11,959 cases among 369,862 subjects. Adjusted for up to 14 confounders by study. 8 studies adjusted for smoking.	Protective 'U'-shaped: greatest protection at low to moderate consumption
Epilepsy (G40-41)	932	715 (76.7%)	4 case-control studies[17], 698 cases, 1,162 controls. Not adjusted for smoking. Other adjustments varied by study.	Dose-response increased risk
Liver cirrhosis (K70,K74)	5,783	5,137 (88.8%)	13 cohort and case-control studies[18], 2383 cases among 1,469,323 subjects. Adjusted for age and gender plus others by study. 11 studies adjusted for smoking.	Dose-response increased risk
Cancer				
Liver (C22)	2,486	1,305 (52.5%)	WCRF/AICR 6 cohort studies[8]. Adjustment varied by study. 4 adjusted for smoking.	Dose-response increased risk
Mouth, larynx, pharynx (C00-14)	1,572	1,033 (65.7%)	WCRF/AICR 2 cohort studies[8]. Adjusted for smoking.	Dose-response increased risk
Oesophagus (C15)	6,068	3,104 (51.2%)	WCRF/AICR 20 case-control studies[8]. Adjustment varied by study. All adjusted for smoking.	Dose-response increased risk
Breast (C50)	10,302	5,644 (54.8%)	WCRF/AICR 9 cohort studies[8]. Adjustment varied by study (including age and reproductive factors). Not adjusted for smoking.	Dose-response increased risk
Colo-rectum (C18-20)	12,876	5,587 (43.4%)	WCRF/AICR 9 cohort studies[8]. Adjustments varied by study. 6 adjusted for smoking.	Dose-response increased risk

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Table 2: Annual chronic disease deaths averted or delayed if there were no non-drinkers in the population, by population median intake of alcohol in g/day

		1	2	3	4	5	6	7	8	12	16	20	24	32	40	48
Total		1,742	6,333	8,954	10,288	10,794	10,754	10,341	9,668	5,539	386	-5,154	-10,910	-23,046	-36,436	-51,897
Sex – all ages	Males	964	3,566	4,895	5,481	5,622	5,483	5,159	4,710	2,252	-675	-3,803	-7,086	-14,239	-22,610	-32,948
	Females	777	2,766	4,060	4,807	5,172	5,272	5,182	4,957	3,287	1,061	-1,351	-3,824	-8,807	-13,826	-18,949
Sex – age <75 years only	Males <75y	2,274	3,197	3,508	3,504	3,320	3,027	2,663	2,253	365	-1,699	-3,857	-6,114	-11,086	-17,071	-24,731
	Females <75y	1,346	1,730	1,875	1,860	1,742	1,558	1,329	1,069	-120	-1,393	-2,672	-3,939	-6,434	-8,918	-11,453
Major conditions	CVD	-5,267	-432	2,712	4,743	6,064	6,917	7,454	7,772	7,861	7,144	6,185	5,168	3,179	1,328	-397
	Cancer	3,670	3,202	2,723	2,234	1,735	1,223	701	166	-2,099	-4,590	-7,339	-10,387	-17,573	-26,642	-38,309
	Liver cirrhosis	3,622	3,620	3,421	3,101	2,704	2,259	1,785	1,293	-714	-2,640	-4,416	-6,032	-8,823	-11,120	-13,027

A positive number indicates lives saved, a decrease in mortality compared to 2006 rates, a negative number denotes a net increase in mortality compared to 2006 rates

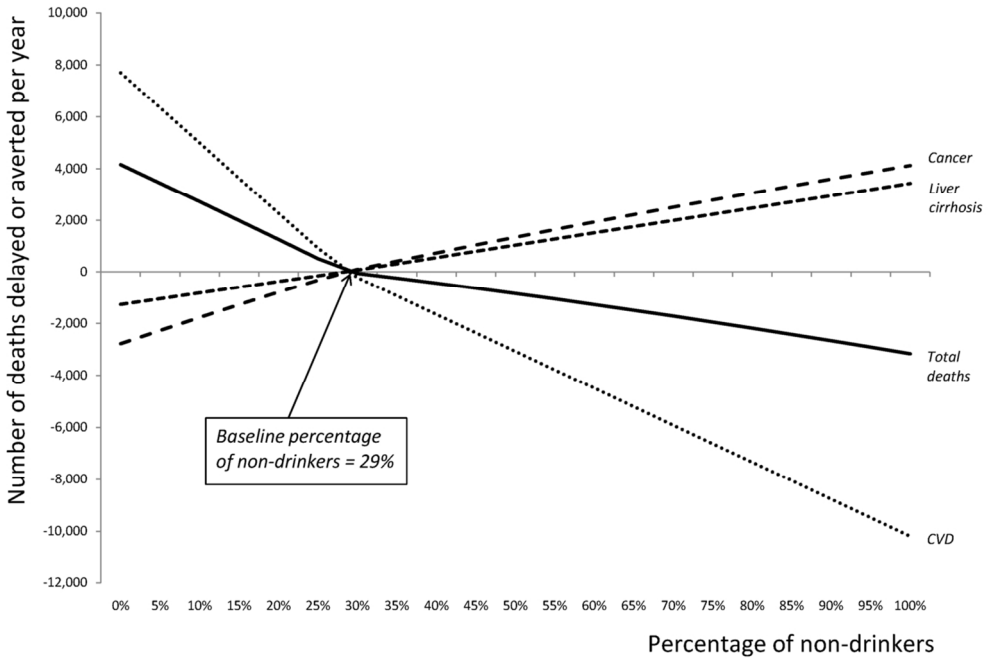

Figure 1. Deaths delayed or averted in the counterfactual scenario varying percentages of non-drinkers
114x76mm (300 x 300 DPI)

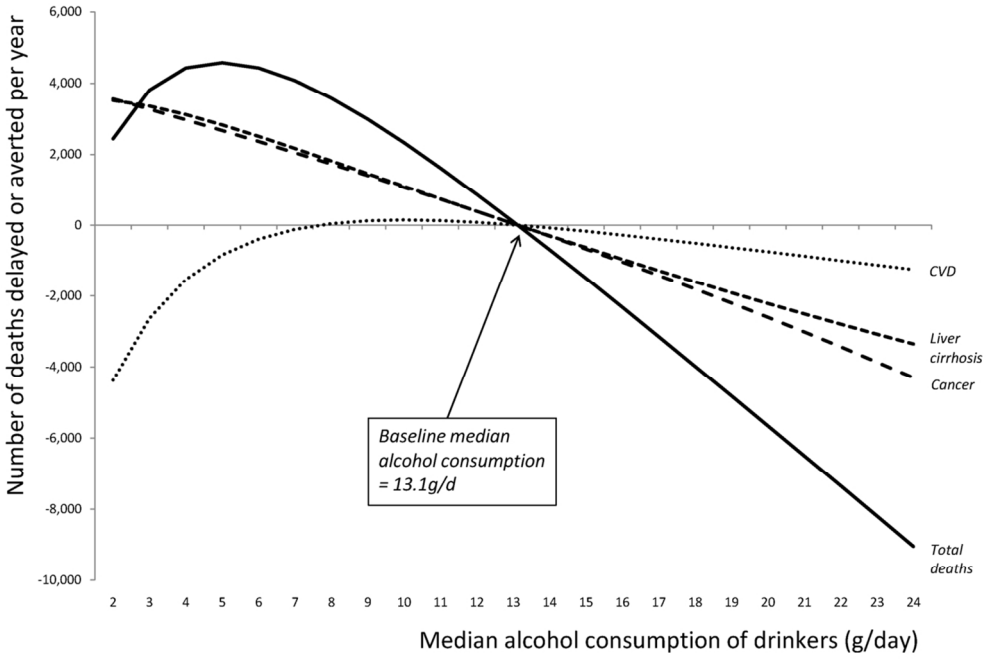

Figure 2. Deaths delayed or averted in the counterfactual scenario varying median consumption of alcohol in drinkers
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Supplementary information

Table S1. Relative risks used in modelling

Outcome	Alcohol consumption level (g/day)	Relative Risk for mortality
CHD	0	1·00
(Ronksley et al., 2011)	<2·5	0·92 (0·80 to 1·06)
	2·5 – 15	0·79 (0·73 to 0·86)
	15 – 30	0·79 (0·71 to 0·88)
	30 – 60	0·77 (0·72 to 0·83)
	>60	0·75 (0·63 to 0·89)
Stroke	0	1·00
(Ronksley et al., 2011)	<2·5	1·00 (0·75 to 1·34)
	2·5 – 15	0·86 (0·75 to 0·99)
	15 – 30	1·15 (0·86 to 1·54)
	30 – 60	1·10 (0·85 to 1·45)
	>60	1·44 (0·99 to 2·10)
Diabetes	0	1·00
(Koppes et al., 2005)	<6	0·88 (0·80 to 0·95)
	6-12	0·73 (0·62 to 0·86)
	12-24	0·66 (0·59 to 0·75)
	24-48	0·74 (0·63 to 0·88)
	>48	0·93 (0·74 to 1·18)
Hypertensive disease – men (Taylor et al., 2009)	per 10g	1·09 (1·07 to 1·12)
Hypertensive disease – women (Taylor et al., 2009)	per 10g	1·10 (1·06 to 1·14)
Epilepsy	0	1·00
(Samokhvalov et al., 2010)	<12	1·00
	12 – 48	1·17 (1·13 to 1·21)
	48 – 72	1·81 (1·59 to 2·07)
	72 -96	2·44 (2·00 to 2·97)
	>96	3·27 (2·52 to 4·26)
Liver cirrhosis – men	0	1·00
(Rehm et al., 2010)	<12	1·0 (0·6 to 1·6)
	12-24	1·6 (1·4 to 2·0)
	24-36	2·8 (2·3 to 3·4)
	36-48	5·6 (4·5 to 7·0)
	48-60	7·0 (5·8 to 8·5)
	>60	14 (11·7 to 16·7)
Liver cirrhosis – women	0	1·00
(Rehm et al., 2010)	<12	1·9 (1·1 to 3·1)
	12-24	5·6 (4·5 to 6·9)
	24-36	7·7 (6·3 to 9·5)
	36-48	10·1 (7·5 to 13·5)
	48-60	14·7 (11·0 to 19·6)
	>60	22·7 (17·2 to 30·1)
Cancer (WCRF / AICR, 2007)		
Liver	Per 10g	1·10 (1·02 to 1·07)
Mouth, larynx, pharynx	Per drink per week	1·24 (1·18 to 1·30)
Oesophagus	Per drink per week	1·04 (1·03 to 1·05)
Breast	10g	1·10 (1·06 to 1·14)
Colorectum	10g	1·09 (1·03 to 1·14)

Table S2. Calculating impact on deaths from liver cirrhosis of increasing consumption of alcohol by 8g/d (one unit). Results shown for men aged 75-79 as example

Alcohol consumption (g/d)	Relative risk[1]	Baseline population[2]	Baseline deaths[3]	Mortality rate per 1,000[4]	Counterfactual population[5]	Counterfactual deaths[6]
<=1	1·0	229,532	24	0·11	229,532	24
1 - <=12	1·0	232,024	24	0·11	146,491	15
12 - <=24	1·6	126,930	21	0·17	130,440	22
24 - <=36	2·8	54,831	16	0·29	73,789	22
36 - <=48	5·6	27,303	16	0·59	43,678	26
48 - <=60	7·0	15,076	11	0·74	27,400	20
>60	14·0	28,404	42	1·47	68,950	101
		TOTAL	*154*		*TOTAL*	*230*

[1] Taken from meta-analysis of prospective cohort studies(Rehm et al., 2010); [2] The total population of men aged 75-79 in England in 2006, following the distribution of alcohol consumption described by the General Household Survey 2006; [3] The total number of deaths from liver cirrhosis in men aged 75-59 in England in 2006, split so that mortality rates respect the relative risks; [4] Mortality rates, which follow the relative risks shown in the earlier column; [5] The population of men aged 75-79 under the counterfactual scenario, in which all drinkers drink one unit per day more; [6] The counterfactual number of deaths, calculated using the mortality rates and the counterfactual population.

Table S3. Population size and alcohol consumption in England, 2006

Sex	Age group, years	Population size[1]	Non-drinkers (<1g/day)[2]	Daily intake (g/day) among drinkers, median[2]
Male	15-19	1,719,800	30·9%	14·9
	20-24	1,716,200	15·3%	18·0
	25-29	1,636,900	16·5%	19·3
	30-34	1,714,100	16·2%	14·8
	35-39	1,933,300	16·5%	17·3
	40-44	1,939,700	16·5%	17·5
	45-49	1,717,700	15·6%	17·0
	50-54	1,511,900	18·6%	18·0
	55-59	1,608,900	17·4%	17·5
	60-64	1,320,600	18·3%	17·4
	65-69	1,074,300	20·6%	14·8
	70-74	906,300	23·4%	13·3
	75-79	714,100	31·6%	12·5
	80-84	476,000	32·7%	10·9
	85+	323,700	43·7%	10·1
Female	15-19	1,614,800	33·4%	10·4
	20-24	1,654,200	25·6%	10·9
	25-29	1,633,900	26·4%	9·9
	30-34	1,719,100	33·3%	10·9
	35-39	1,946,400	30·1%	10·0
	40-44	1,971,700	27·2%	9·8
	45-49	1,740,000	30·5%	11·0
	50-54	1,546,900	29·4%	11·3
	55-59	1,652,000	36·3%	10·6
	60-64	1,376,400	41·7%	9·9
	65-69	1,155,800	54·5%	9·4
	70-74	1,034,900	49·7%	8·2
	75-79	923,800	54·6%	7·8
	80-84	746,000	61·2%	7·2
	85+	731,200	68·7%	7·9

1 Population estimates from Office for National Statistics; 2 Estimates taken from the General Household Survey 2006(Office for National Statistics, 2008) (n = 14,306)

Table S4. Annual chronic disease deaths averted or delayed in counterfactual scenarios in which the percentage of non-drinkers in the population varies from 0% to 100%

	0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
Total	4,160	2,727	1,259	-59	-441	-844	-1,269	-1,714	-2,178	-2,660	-3,160
Males	1,462	960	444	-42	-312	-602	-910	-1,236	-1,578	-1,936	-2,309
Females	2,698	1,767	815	-18	-129	-243	-359	-479	-600	-725	-851
Males under 75 years	-201	-124	-54	23	157	276	379	468	544	607	659
Females under 75 years	-472	-300	-134	22	159	293	426	557	685	812	937
CVD	7,705	4,994	2,280	-228	-1,649	-3,071	-4,494	-5,918	-7,342	-8,767	-10,193
Cancer	-2,771	-1,765	-792	104	738	1,351	1,943	2,516	3,071	3,608	4,129
Liver disease	-1,265	-819	-374	77	558	1,039	1,521	2,002	2,483	2,964	3,445

A positive number indicates lives saved compared to 2006 mortality, a negative number denotes a net increase in mortality compared to 2006· Assumes that the distribution of consumption in drinkers remains constant·

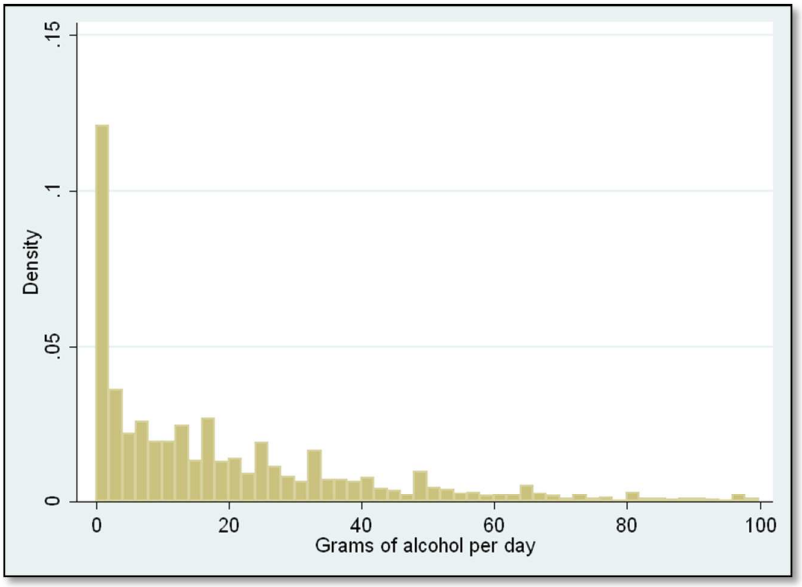
Table S5. Annual chronic disease deaths averted or delayed in counterfactual scenarios in which the median intake of alcohol in drinkers varies from 1g/day to 48g/day

	1	2	3	4	5	6	7	8	12	16	20	24	32	40	48
Total	-148	2,436	3,808	4,428	4,579	4,427	4,073	3,579	867	-2,327	-5,661	-9,043	-15,936	-23,180	-31,097
Males	43	1,847	2,739	3,107	3,164	3,027	2,763	2,414	577	-1,543	-3,754	-6,015	-10,725	-15,873	-21,758
Females	-191	589	1,069	1,321	1,415	1,400	1,310	1,165	290	-784	-1,907	-3,028	-5,211	-7,307	-9,339
Males under 75 years	1,953	2,690	2,936	2,930	2,781	2,546	2,256	1,929	441	-1,158	-2,793	-4,458	-7,952	-11,850	-16,430
Females under 75 years	1,170	1,377	1,445	1,421	1,340	1,222	1,080	921	208	-539	-1,277	-1,995	-3,370	-4,682	-5,956
CVD	-7,150	-4,377	-2,639	-1,543	-843	-397	-120	42	80	-283	-759	-1,259	-2,223	-3,108	-3,923
Cancer	3,846	3,559	3,267	2,970	2,668	2,360	-1,159	1,728	392	-1,050	-2,610	-4,304	-8,166	-12,817	-18,500
Liver disease	3,543	3,514	3,356	3,117	2,828	2,507	2,167	1,816	390	-971	-2,221	-3,354	-5,301	-6,893	-8,208

A positive number indicates lives saved compared to 2006 mortality, a negative number denotes a net increase in mortality compared to 2006· Assumes that the percentage of non-drinkers remains constant·

Figure S1. Population distribution of alcohol consumption for men and women, England, 2006: General Household Survey data (Office for National Statistics, 2008) (n = 14,306)

Men



Women

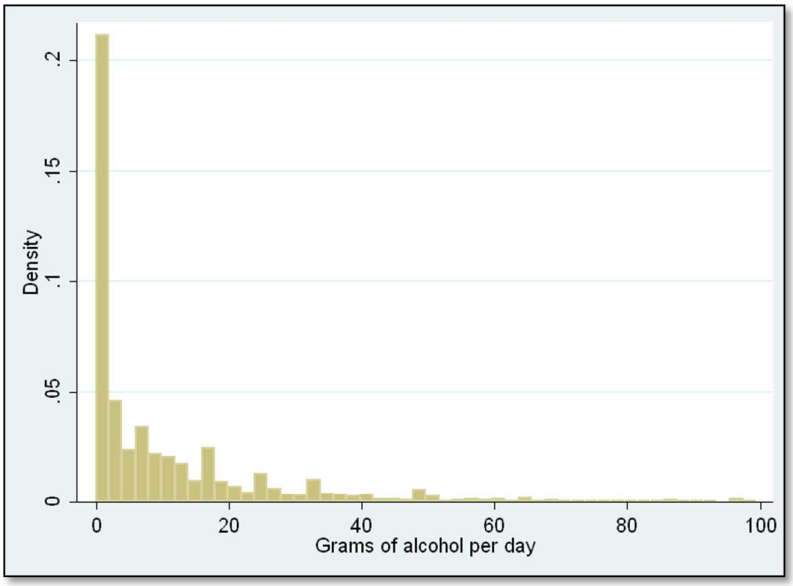
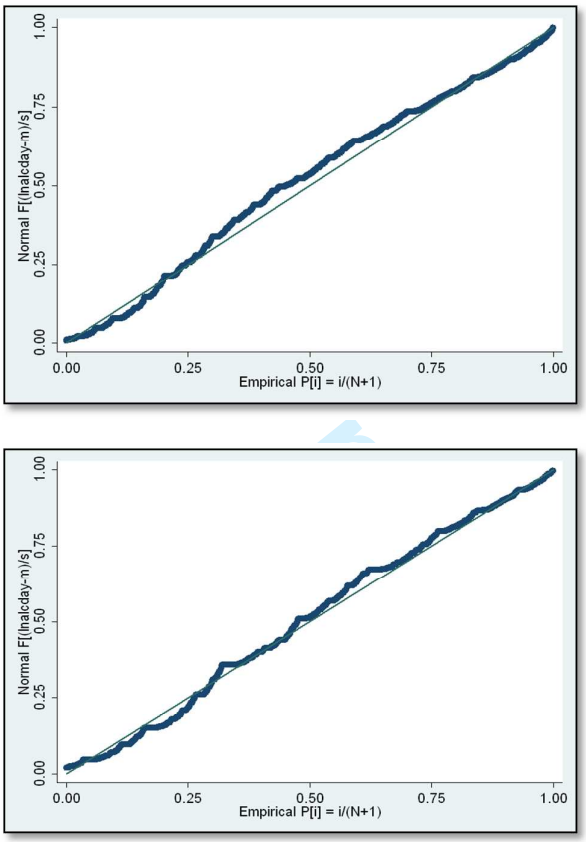


Figure S2. P-norm plots for normality of ln-transformed variable of alcohol consumption among men and women, England, 2006: General Household Survey data (Office for National Statistics, 2008) (n = 14,306)·



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What is the optimal level of population alcohol consumption for chronic disease prevention in England? Modelling the impact of changes in average consumption levels

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What is the optimal level of population alcohol consumption for chronic disease prevention in England? Modelling the impact of changes in average consumption levels

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Contributors: PS conceived the study and developed the methods, with support from MN, SA and MR. MN conducted literature searches to inform the model, PS and MN built the model and conducted analysis. All authors contributed to interpretation of the results. MN prepared the initial draft and led the preparation of the manuscript. All authors were involved in drafting and reviewing the manuscript. MN and PS act as guarantors for the manuscript.

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Ethical approval was not required, as no human or animal subjects were involved.

Study sponsors – None.

Data sharing: The PRIME-Alcohol model is available for use upon request from PS (peter.scarborough@dph.ox.ac.uk).

Abstract

Objective To estimate the impact of achieving alternative average population alcohol consumption levels on chronic disease mortality in England.

Design A macro-simulation model was built to simultaneously estimate the number of deaths from coronary heart disease, stroke, hypertensive disease, diabetes, liver cirrhosis, epilepsy and five cancers that would be averted or delayed annually as result of changes in alcohol consumption among English adults. Counterfactual scenarios assessed the impact on alcohol-related mortalities of changing a) the median alcohol consumption of drinkers; b) the percentage of non-drinkers.

Data sources Risk relationships were drawn from published meta-analyses. Age and sex specific distributions of alcohol consumption (g/d) for the English population in 2006 were drawn from the General Household Survey 2006, and age, sex and cause specific mortality data for 2006 were provided by the Office for National Statistics.

Results The optimum median consumption level for drinkers in the model was 5g/d (about half a unit), which would avert or delay 4,579 (2,544 to 6,590) deaths per year. Approximately equal numbers of deaths from cancers and liver disease would be delayed or averted (~2800 for each), while there was a small increase in cardiovascular mortality. The model showed, however, no benefit in terms of reduced mortality when the proportion of non-drinkers in the population was increased.

Conclusions Current government recommendations for alcohol consumption are well above the level likely to minimise chronic disease. Public health targets should aim for a reduction in population alcohol consumption to half a unit per day, in order to achieve the optimum level of reduced chronic disease mortality.

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Article Summary

Article focus

- Alcohol consumption is a risk factor for many chronic diseases, while providing modest protection from others. Assessments of the impact of alcohol on individual chronic diseases can therefore result in contradictory advice about the level of alcohol consumption that is optimal for health.
- The UK government currently recommends that men should consume no more than three to four units per day (24 to 32 g/d of pure alcohol) and women should drink no more than two to three units per day (16 to 24 g/d). However the net impact of this level of consumption on chronic disease mortality is unclear.
- The aim of this study was to estimate the impact of achieving alternative population alcohol consumption levels on chronic disease mortality in England.

Key messages

- Results suggest that the optimum population level of alcohol consumption for minimising chronic disease mortality in England is just 5g (approximately half a unit) per day.
- Current recommendations for alcohol consumption are well above this level and may not be compatible with optimum protection of public health. Substantial reductions in recommendations and in population alcohol consumption levels would be needed to minimise the chronic disease burden associated with alcohol consumption in England.
- Community beliefs in the protective role of alcohol in cardiovascular disease is widespread, however our modelling shows that when multiple conditions are considered simultaneously, the levels of alcohol that would actually be likely to be associated with reduced risk of chronic disease, are much lower than is generally accepted, or recommended by government.

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Strengths and limitations of this study

- The study used a detailed modelling approach to synthesise the best available evidence from meta-analysis of prospective cohort studies and provide for the first time an estimate of the level of alcohol associated with theoretical minimum risk of a range of chronic diseases, considering both harmful and protective effects simultaneously.
- The model is dependent on the meta-analyses selected to define the parameters. Results may vary significantly in other contexts with varying levels of disease, alcohol consumption and other risk factors. Furthermore, results depend on the quality of the available epidemiological evidence, which remains contested in some areas.
- The approach used also relies on chronic (average) consumption of alcohol and is not able to take account of to take account of patterns of drinking (e.g. binge drinking). Furthermore, the results are based on the assumption of a steady state relationship between alcohol consumption patterns and relative risk of disease, and cannot estimate the time required between changes in population alcohol consumption levels occurring and the achievement of changes in mortality rates.

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Introduction

Alcohol consumption has significant impacts on chronic disease risk.[1-3] In the UK, it has been estimated that alcohol-related ill-health is responsible for £3.3 billion in direct costs to the National Health Service annually.[4] The effects of episodes of heavy alcohol consumption are clearly detrimental to health, for example increasing risk from injuries and violence.[5-7] Less is known about the overall effects of long term alcohol consumption on chronic disease risk in the whole population, due to alcohol consumption at various levels increasing risk for some chronic disease outcomes (e.g. liver cirrhosis and cancer), yet decreasing risks of others (e.g. cardiovascular disease and diabetes).

The World Cancer Research Fund has recommended that there is no safe level of alcohol consumption in relation to cancer risk[8], and Schutze and colleagues[9] report that up to 10% of all cancers in men and 3% in women in some European countries may be attributable to alcohol consumption. This has led to calls for public health messages to encourage abstinence or significant reductions in alcohol consumption.[9-10] There is, however, a substantial body of evidence that suggests that moderate alcohol consumption protects against other chronic diseases, including cardiovascular disease (CVD) and diabetes, which are responsible for a substantial burden of disease.[11-13]

Substantial research has examined the effects of alcohol consumption on various chronic diseases; however there has been little integration of the findings across disease outcomes, thereby precluding the development of comprehensive and evidence-based recommendations for population alcohol consumption. The UK government currently recommends that men should consume no more than three to four units per day (one unit = 8g (10ml) of pure alcohol, one pint of standard beer usually contains between 2 and 3 units, and a 175ml glass of wine approximately 2 units) and women should drink no more than two to three units per day.[14] A large proportion of the literature supporting alcohol policy in the UK, however, appears to focus on alcohol 'misuse',

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episodes of heavy drinking and the social consequences of alcohol consumption[14]; it is not clear that there is evidence that the UK Government recommended drinking levels offer the maximum protection for public health.

The aim of this study was to estimate the impact of achieving alternative population average alcohol consumption levels on chronic disease mortality in England. The research question was: what proportion of non-drinking in the English population and what level of alcohol consumption among drinkers would result in the greatest number of chronic disease deaths delayed or averted in England compared to recent levels?

Methods

A macro-simulation model was built that assessed the impact on mortality from chronic disease of changing the distribution of alcohol consumption (g/day) within the population of England. The Preventable Risk Integrated ModEl for Alcohol (PRIME-Alcohol) estimates the impact of population changes in alcohol consumption on chronic disease mortality. Developing the PRIME-Alcohol model involved: identifying chronic diseases associated with alcohol consumption; identifying the current (baseline) distribution of alcohol consumption; and parameterising the association between alcohol consumption and chronic disease.

Selection of mortality outcomes

The initial list of chronic diseases was generated from those linked to alcohol consumption in the World Health Organization Global Burden of Disease 'Global Health Risks' report[15] and the World Cancer Research Fund Report[8] was used to select site-specific cancers associated with alcohol consumption. Excluding those resulting in small numbers of deaths (fewer than 500 deaths in 2006

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in England), 11 chronic diseases were included as outcomes in the PRIME-Alcohol model, including five cancer sites.

The PubMed and Cochrane databases were searched for meta-analyses of prospective cohort or case-control studies that quantified chronic disease risk for different levels of alcohol consumption. The relationships between alcohol consumption were diverse, including protective effects, linear increases in risk and 'U' or 'J' shaped relationships. Where multiple suitable meta-analyses were available, preference was given to meta-analyses of cohort studies over case-control studies, and to those using lifetime abstainers as the reference category. Age- and sex-specific estimates of risk relationships and estimates adjusted for potential confounders were used where available.

Details of the chronic disease outcomes and the meta-analyses that were included in the model [8 11-12 16-18] are shown in table 1.

(table 1 here)

Identifying the current (baseline) distribution of alcohol consumption in England

The General Household Survey (GHS) from 2006[19] provided baseline distributions of alcohol consumption for adults aged 16 years and over. The GHS is a multi-purpose survey conducted by the Office for National Statistics in the UK. In 2006, it included 18,214 adults aged 16 years and over (overall response rate 74%). To establish average weekly alcohol consumption, respondents were asked how often over the last year they drank alcoholic beverages and the amount usually consumed on any one day. This information is combined to give an estimate of the respondent's weekly alcohol consumption in units of alcohol.[20] For the current analyses, units of alcohol per week was converted to grams per day and only participants from England were included (n =15,616). Non-drinkers and very low alcohol consumers were removed and analysed as a separate category (referred to as non-drinkers henceforth). Excluding this group, alcohol consumption was shown to be approximately log-normally distributed.

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Deleted: The distribution of alcohol consumption in the GHS is shown in supplementary figure S1 – there is a large spike of non-drinkers and very low alcohol consumers (<=1g/d) and a long tail of higher alcohol consumers.

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The three parameters for the baseline distribution of alcohol consumption derived from the GHS for each of 30 age-sex groups were therefore: percentage of non-drinkers; the mean of ln-transformed alcohol consumption of drinkers; and the standard deviation of ln-transformed alcohol consumption of drinkers. Counterfactual scenarios were modelled by altering one or more of these parameters.

Parameterising the association between alcohol consumption and chronic disease

The meta-analyses identified by the literature search provided estimates of the relative risk of different levels of alcohol consumption on chronic disease (table 1). The relative risks used in the PRIME-Alcohol model are shown in supplementary table S1. These risks were used in conjunction with the baseline distribution of alcohol consumption to attribute risk for chronic disease throughout the age-sex specific populations. Baseline age, sex and cause specific number of mortalities (England 2006) were provided by the Office for National Statistics. For each chronic disease and age-sex group, mortality rates were assigned to each level of alcohol consumption such that the relative risks from the meta-analyses were maintained, and the total risk in the population produced the recorded number of mortalities. These mortality rates were then applied to the counterfactual distributions to calculate the number of deaths that would be expected under the counterfactual scenario. An example is provided in supplementary table S2.

Uncertainty analysis

The alcohol-chronic disease association parameters were allowed to vary stochastically according to the distributions reported in the literature. Five thousand Monte Carlo iterations were run, and the results were used to calculate 95% credible intervals around the estimates. Because of the

computing requirements of the Monte Carlo iterations, credible intervals are only presented for key results.

Defining the counterfactual scenarios

To assess the number of chronic disease mortalities in England under different alcohol consumption scenarios, three counterfactual scenarios were analysed: 1) varying the median consumption among drinkers while holding the proportion of non-drinkers and the distribution of consumption levels constant; and 2) varying the proportion of non-drinkers in the population while holding the median consumption among drinkers constant.

In the analysis of the first scenario, the percentage of non-drinkers was kept constant while the amount of alcohol consumed by drinkers in the population was varied between 1g/d and 48g/d (6 units), such that the age-sex distribution of mean alcohol consumption was maintained. In the analysis of the second scenario, the total percentage of non-drinkers in the population was allowed to vary between 0% and 100% such that the age-sex distribution of non-drinkers was maintained, whilst the amount of alcohol consumed by drinkers remained constant. The aim of the analyses was to find the median level of average alcohol consumption for England that would be likely to result in the lowest number of chronic disease mortalities.

The funding bodies supporting the authors of this work had no role in the present study.

Deleted: ; 2) varying the median consumption among drinkers while holding the proportion of non-drinkers constant; and 3) varying both the proportion of non-drinkers and the median intake among drinkers.

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Results

In 2006, 29% of English adults were non-drinkers according to the definitions used here (including those who consume less than 1g/d). Rates of non-drinking varied substantially by age group and sex (supplementary table S3). Overall, 20% of men and 36% of women were non-drinkers. In total, there were 170,558 deaths in England in 2006 from the causes of death considered in this study.

In the first counterfactual scenario, varying the median population level of alcohol consumption among current drinkers between 1g and 48g per day, results showed that approximately 5g/day (just over half of one unit) was the optimal level of alcohol consumption, resulting in 4,579 (2,544 to 6,590) deaths delayed or averted (table 2 and figure 1), or approximately 3% of all deaths from partially alcohol-related chronic diseases. At this level of consumption, a small predicted increase in risk of CVD (843 additional deaths per year, +0.7% from 2006 levels) is counteracted by large decreases in cancer (2668 fewer deaths, -8%) and liver disease (2828 fewer deaths, -49%). At this level of consumption, the vast majority (90%) of deaths delayed or averted were premature (before age 75).

In variations of the scenario with lower levels of median alcohol consumption, the shift of a large proportion of the population into the non-drinker category resulted in a modelled increase in deaths from cardiovascular disease, which was not offset by reductions in cancer, liver cirrhosis and other chronic conditions. Above 5g/day the additional protective effect of alcohol on CVD was not enough to offset the additional risk from cancer, liver cirrhosis and other chronic conditions. For men and women aged under 75 years, the optimum level of consumption was slightly lower than for the whole population, at 3g/d, at which level 4,381 (3,327 to 5,400) deaths before age 75 would be delayed or averted each year, a decrease of 8% from 2006 levels.

(table 2 here)

Deleted: In the first counterfactual scenario, varying the proportion of non-drinkers in the whole population, optimal results were achieved when there were zero non-drinkers in the population (figure 1 and supplementary table S4), which resulted in 4,160 (95% credible intervals: 908 to 6,962) chronic disease deaths averted or delayed compared to 2006 mortality rates. Although having the whole population drinking some alcohol would increase deaths from cancer by 2,771 (2,443 to 3,898) and from liver cirrhosis by 1,265 (1,166 to 1,360), this was more than offset by averting 7,705 (5,248 to 11,934) deaths from CVD. As the proportion of non-drinkers was increased in the counterfactual scenarios, the reductions in mortality were attenuated. When the modelled rates of non-drinking exceeded the 2006 levels there was a net increase in chronic disease mortality, up to an additional 3,160 (-436 to 6,409) lives lost annually if the entire population were to abstain from alcohol. ¶
Analysis by gender showed that at low proportions of non-drinkers, greater numbers of deaths were averted among women, while at higher proportions of non-drinkers there was a smaller increase in mortality among women than among men, reflecting the fact that the baseline proportion of non-drinkers is higher in women than in men. When premature deaths (before age 75) were examined, the trend was opposite to that displayed for all ages: among people aged under 75 years, higher levels of non-drinkers resulted in larger numbers of deaths delayed or averted (supplementary table S4). ¶

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In the second counterfactual scenario, varying the proportion of non-drinkers in the whole population, the model showed a net increase in mortality in all versions of the scenario for which the modelled rates of non-drinking exceeded the 2006 levels, up to an additional 3,160 (-436 to 6,409) lives lost annually if the entire population were to abstain from alcohol.

Theoretically optimal results were achieved when there were zero non-drinkers in the population (figure 2 and supplementary table S4), which resulted in 4,160 (95% credible intervals: 908 to 6,962) chronic disease deaths averted or delayed compared to 2006 mortality rates. Although a modelled situation in which the whole population consumes some alcohol would increase predicted deaths from cancer by 2,771 (credible interval 2,443 to 3,898, +8% from 2006 levels) and from liver cirrhosis by 1,265 (1,166 to 1,360, +22%), this was more than offset by averting 7,705 (5,248 to 11,934, -6%) deaths from CVD. As the proportion of non-drinkers was increased in the counterfactual scenarios, the reductions in mortality were attenuated.

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Discussion

The PRIME-Alcohol model effectively demonstrates the potential impact of population usual alcohol consumption on chronic disease mortality, bringing together a wide range of risk and protective effects of alcohol, including the increased risks of many cancers and the protective effect of low to moderate consumption on cardiovascular disease. Modelling demonstrated that the optimum population median alcohol consumption level appears to be substantially lower than the currently recommended safe levels in current UK public health guidance. Based on this model, reducing the median population alcohol consumption among current drinkers to around half a unit (5g of alcohol) per day, would result in around 4,600 fewer deaths annually, primarily due to reductions in cancers and liver cirrhosis. This level of consumption would equate to as little as one-quarter of a glass of wine, or one-fifth of a pint of beer per day on average.

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The model showed no additional benefit to chronic disease mortality if the proportion of the population abstaining from alcohol were to be increased. Results indicated that increasing the proportion of alcohol consumers in the population (drinking moderately) would result in reduced cardiovascular disease mortality, however this is of little practical relevance given that there are safer and more socially acceptable means of reducing cardiovascular disease risk, and there are a number of reasons why it would be imprudent to encourage current non-drinkers to start drinking. These include: encouraging abstainers to start drinking whilst encouraging drinkers to reduce their alcohol consumption is a mixed message that may be difficult to communicate and promote; reducing the number of non-drinkers may have an adverse impact on non-chronic disease health (e.g. accidents and injuries). Furthermore, modelled results show that while reducing the proportion of non-drinkers would decrease chronic disease deaths overall, it would increase the number of premature deaths (before 75 years; see supplementary table 4), increasing the impact on years of life lost. On this basis, we recommend that the public health target for alcohol consumption in England should be to reduce median alcohol consumption to half a unit per day for both men and women, and to maintain the current level of non-drinkers within the population. The recommendations and public messages around restriction of alcohol consumption that would be required to achieve this target median level of consumption are beyond the scope of this work, but should take account of the likely impacts on chronic disease as modelled here, as well as aiming to reduce other known risks and address patterns of consumption.

Public health behavioural recommendations should ideally be based on the best available evidence for optimising population health outcomes. In practice, public health goals in the UK have often been based on a mixture of evidence of health risks and pragmatic considerations about setting a goal that is considered achievable. A counterfactual modelling analysis such as the type reported in this paper is particularly useful for setting public health goals, as its flexibility can provide predicted

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impacts for a range of counterfactual scenarios, which can then inform policy makers both of the optimum goal and the strength of any pragmatic goal that they may consider.

A limitation of the PRIME-Alcohol model is that it is based on usual average levels of alcohol consumption and is unable to take account of patterns of drinking (e.g. binge drinking) or provide any evidence about the least harmful pattern of alcohol consumption. There is evidence that patterns of drinking play an important role in disease risk[21], and particularly in morbidity and mortality from accidents and injuries.[2 5] The central recommendation from the results of this paper – that a target consumption level for England should be half a unit per day – is, however, likely to be consistent with low levels of risk for accidents and injuries. Heavy, irregular drinking has also been linked with increased risk of CVD[21]. Guidance to the public about avoiding heavy drinking sessions remains a very important component of any public health guidance around alcohol consumption. In addition, it is not possible to include wholly alcohol attributable conditions (e.g. mental and behavioural disorders due to alcohol use) in the model.

The PRIME-Alcohol model is necessarily limited by the availability of robust meta-analytic estimates of relative risk for mortality and estimates generated are limited by the quality of available evidence to parameterise the model. The observational studies included in the meta-analyses used to parameterise the PRIME-Alcohol model used self-report of alcohol consumption, which may result in an under-estimate of actual alcohol consumption[22], and results from observational studies cannot account for within-individual variability in alcohol consumption. Although there is a strong body of epidemiological evidence over many years linking moderate alcohol consumption with lower rates of CVD[23-25], concerns remain about possible residual confounding or other methodological explanations for the observed relationship[25-26].

Sex-specific estimates of relative risk at varying levels of alcohol consumption were available only for hypertensive disease and liver cirrhosis, and no age-specific estimates were available, which limits

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the specificity of the counterfactual scenarios analysed by the model. Furthermore, results are based on the assumption of a steady state relationship between alcohol consumption levels and relative risk of disease, while in reality there is a lag time between changes in alcohol consumption levels and mortality risk. For some conditions included in the model, relative risk estimates from appropriate meta-analysis were available only for incidence of the disease, rather than mortality, however this is unlikely to significantly impact on the accuracy of estimates unless there was an additional effect of alcohol consumption on case-fatality ratios for the included conditions.

The predicted results, in terms of increases or decreases in mortality expected at varying levels of alcohol consumption, are entirely dependent upon the baseline population inputs – particularly current alcohol consumption levels and current levels of mortality from the included chronic diseases (which will reflect among other things, prevalence of other risk factors and both treatment and prevention related health care variables). The level of alcohol consumption associated with the most favourable predicted change from existing mortality levels may vary substantially between populations. It is also important to emphasise that the results indicate predicted impacts on mortality only, and do not account for alcohol-related chronic disease morbidity, which has a significant impact on population health and the health system.

This study is an important addition to the current debate around alcohol consumption and public health, combining and balancing risk and protective factors to identify an optimal population level of alcohol consumption associated with reduced levels of chronic disease mortality. This is in contrast to recent publications focusing on the associations between alcohol and specific conditions. For example, Schutze and colleagues concluded that their analyses of the association between alcohol intake and cancer "support current political efforts to reduce or to abstain from alcohol consumption to reduce the incidence of cancer".[9] In contrast, a recent systematic review of the impact of alcohol on cardiovascular disease concluded that "alcohol, in moderation, may have overall health benefits that outweigh the risks in selected subsets of patients".[11] Only by

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systematically combining the effects of alcohol on all alcohol-related conditions can appropriate public health messages be developed. The results of this modelling exercise contribute to further building all of the evidence required to make such an assessment.

The findings from this paper are consistent with those from a meta-analysis of alcohol consumption and total mortality[27] which also found lowest mortality risk around 5g of alcohol per day, and a Europe-wide study[28] which found minimum risk for alcohol attributable deaths at 10g per day or less (the smallest consumption category included in that study). A strength of our modelling approach, in comparison to cross-sectional studies or fixed meta-analyses of total mortality, is that it can account for differences between populations in underlying risk of various chronic diseases, and can therefore be used to predict population-specific curves of potential changes in chronic disease mortality for international comparisons. Future work should therefore produce comparable results for international populations with varying current levels of exposure and outcomes. Furthermore, there is a significant interaction between alcohol consumption and other lifestyle risk factors for chronic disease mortality, and future work should seek to integrate alcohol consumption with risk behaviours such as poor nutrition, low physical activity and smoking to compare the relative contributions that improvements in these risk factors, both independently and in combination, could have on population health.

Conclusions

Our modelling suggests that the optimum level of reduced chronic disease mortality in England would be achieved at an average alcohol consumption level of around 5g per day, which should be taken into account in the formulation of health guidance. It is likely that government recommendations would need to be set at a much lower level than the current 'low risk' drinking guidelines in order to achieve this level.

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LIST OF FIGURES:

Figure 1 Deaths delayed or averted in the counterfactual scenario varying median consumption of alcohol in drinkers.

The median consumption of alcohol among drinkers was allowed to vary from 0g/d to 24g/d using England 2006 as the baseline. The percentage of non-drinkers in the population was held constant.

Figure 2 Deaths delayed or averted in the counterfactual scenario varying percentages of non-drinkers.

The percentage of non-drinkers was allowed to vary between 0% and 100% of the total population using England 2006 as the baseline. The median consumption of alcohol among those drinking was held constant.

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Table 1: Details of mortality outcomes included in the model

Outcome (ICD-10 codes)	Total deaths, England 2006	Deaths <75years, England 2006 n (%)	Meta-analysis details	Nature of risk relationship
Coronary Heart Disease (I20-25)	76,806	24,364 (31.7%)	31 cohort studies[11], total 1,925,106 subjects. Adjusted for up to 18 confounders by study. 23 studies adjusted for smoking.	Protective at all levels of consumption
Stroke (I60-69)	45,219	7,966 (17.6%)	10 cohort studies[11], total 723,571 subjects. Adjusted for up to 18 confounders by study. 8 studies adjusted for smoking.	'U' or 'J' shaped: protection only at low to moderate consumption
Hypertensive disease (I10-15)	3,742	995 (26.6%)	12 cohort studies[16], 27,603 cases. Adjusted for age, BMI and up to 5 others by study. 4 studies adjusted for smoking.	Dose-response increased risk
Diabetes (E11,E14)	4,831	1,450 (30.0%)	15 cohort studies[12], 11,959 cases among 369,862 subjects. Adjusted for up to 14 confounders by study. 8 studies adjusted for smoking.	Protective 'U'-shaped: greatest protection at low to moderate consumption
Epilepsy (G40-41)	932	715 (76.7%)	4 case-control studies[17], 698 cases, 1,162 controls. Not adjusted for smoking. Other adjustments varied by study.	Dose-response increased risk
Liver cirrhosis (K70,K74)	5,783	5,137 (88.8%)	13 cohort and case-control studies[18], 2383 cases among 1,469,323 subjects. Adjusted for age and gender plus others by study. 11 studies adjusted for smoking.	Dose-response increased risk
Cancer				
Liver (C22)	2,486	1,305 (52.5%)	WCRF/AICR 6 cohort studies[8]. Adjustment varied by study. 4 adjusted for smoking.	Dose-response increased risk
Mouth, larynx, pharynx (C00-14)	1,572	1,033 (65.7%)	WCRF/AICR 2 cohort studies[8]. Adjusted for smoking.	Dose-response increased risk
Oesophagus (C15)	6,068	3,104 (51.2%)	WCRF/AICR 20 case-control studies[8]. Adjustment varied by study. All adjusted for smoking.	Dose-response increased risk
Breast (C50)	10,302	5,644 (54.8%)	WCRF/AICR 9 cohort studies[8]. Adjustment varied by study (including age and reproductive factors). Not adjusted for smoking.	Dose-response increased risk
Colo-rectum (C18-20)	12,876	5,587 (43.4%)	WCRF/AICR 9 cohort studies[8]. Adjustments varied by study. 6 adjusted for smoking.	Dose-response increased risk

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Table 2. Annual chronic disease deaths averted or delayed in counterfactual scenarios in which the median intake of alcohol in drinkers varies from 1g/day to 48g/day

	1	2	3	4	5	6	7	8	12	16	20	24	32	40	48
Total	-148	2,436	3,808	4,428	4,579	4,427	4,073	3,579	867	-2,327	-5,661	-9,043	-15,936	-23,180	-31,097
Males	43	1,847	2,739	3,107	3,164	3,027	2,763	2,414	577	-1,543	-3,754	-6,015	-10,725	-15,873	-21,758
Females	-191	589	1,069	1,321	1,415	1,400	1,310	1,165	290	-784	-1,907	-3,028	-5,211	-7,307	-9,339
Males under 75 years	1,953	2,690	2,936	2,930	2,781	2,546	2,256	1,929	441	-1,158	-2,793	-4,458	-7,952	-11,850	-16,430
Females under 75 years	1,170	1,377	1,445	1,421	1,340	1,222	1,080	921	208	-539	-1,277	-1,995	-3,370	-4,682	-5,956
CVD	-7,150	-4,377	-2,639	-1,543	-843	-397	-120	42	80	-283	-759	-1,259	-2,223	-3,108	-3,923
Cancer	3,846	3,559	3,267	2,970	2,668	2,360	-1,159	1,728	392	-1,050	-2,610	-4,304	-8,166	-12,817	-18,500
Liver disease	3,543	3,514	3,356	3,117	2,828	2,507	2,167	1,816	390	-971	-2,221	-3,354	-5,301	-6,893	-8,208

A positive number indicates lives saved compared to 2006 mortality, a negative number denotes a net increase in mortality compared to 2006.

Analysis assumes that the percentage of non-drinkers, and the distribution of average consumption levels among drinkers remains constant.

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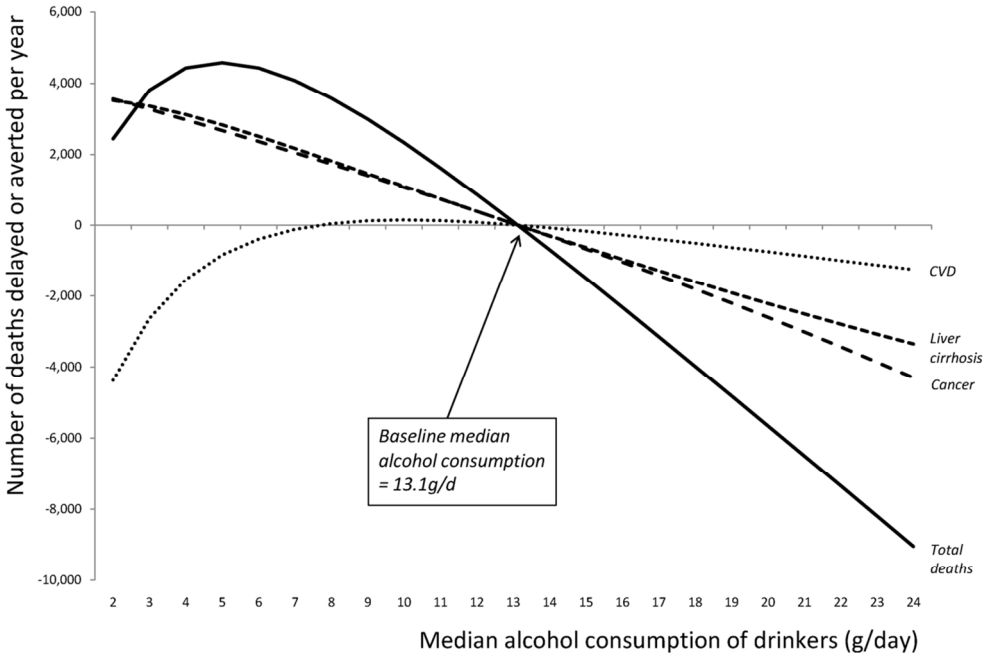

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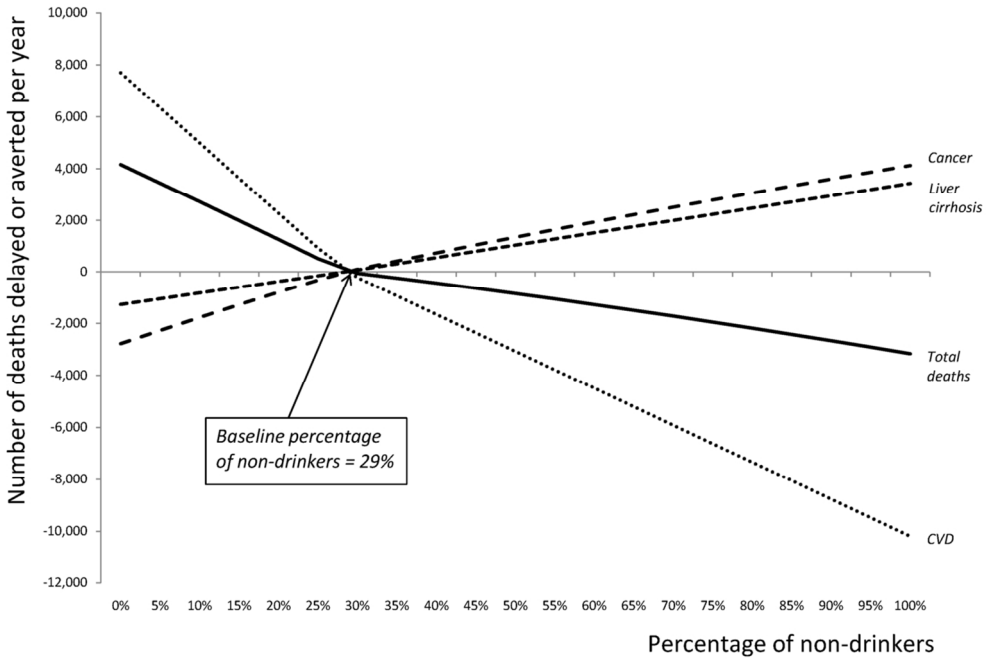

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Supplementary information

Table S1. Relative risks used in modelling relationships between average alcohol consumption levels and chronic disease mortality in PRIME-Alcohol

Outcome	Alcohol consumption level (g/day)	Relative Risk for mortality
CHD	0	1·00
(Ronksley et al., 2011)	<2·5	0·92 (0·80 to 1·06)
	2·5 – 15	0·79 (0·73 to 0·86)
	15 – 30	0·79 (0·71 to 0·88)
	30 – 60	0·77 (0·72 to 0·83)
	>60	0·75 (0·63 to 0·89)
Stroke	0	1·00
(Ronksley et al., 2011)	<2·5	1·00 (0·75 to 1·34)
	2·5 – 15	0·86 (0·75 to 0·99)
	15 – 30	1·15 (0·86 to 1·54)
	30 – 60	1·10 (0·85 to 1·45)
	>60	1·44 (0·99 to 2·10)
Diabetes	0	1·00
(Koppes et al., 2005)	<6	0·88 (0·80 to 0·95)
	6-12	0·73 (0·62 to 0·86)
	12-24	0·66 (0·59 to 0·75)
	24-48	0·74 (0·63 to 0·88)
	>48	0·93 (0·74 to 1·18)
Hypertensive disease – men	per 10g	1·09 (1·07 to 1·12)
(Taylor et al., 2009)		
Hypertensive disease – women	per 10g	1·10 (1·06 to 1·14)
(Taylor et al., 2009)		
Epilepsy	0	1·00
(Samokhvalov et al., 2010)	<12	1·00
	12 – 48	1·17 (1·13 to 1·21)
	48 – 72	1·81 (1·59 to 2·07)
	72 -96	2·44 (2·00 to 2·97)
	>96	3·27 (2·52 to 4·26)
Liver cirrhosis – men	0	1·00
(Rehm et al., 2010)	<12	1·0 (0·6 to 1·6)
	12-24	1·6 (1·4 to 2·0)
	24-36	2·8 (2·3 to 3·4)
	36-48	5·6 (4·5 to 7·0)
	48-60	7·0 (5·8 to 8·5)
	>60	14 (11·7 to 16·7)
Liver cirrhosis – women	0	1·00
(Rehm et al., 2010)	<12	1·9 (1·1 to 3·1)
	12-24	5·6 (4·5 to 6·9)
	24-36	7·7 (6·3 to 9·5)
	36-48	10·1 (7·5 to 13·5)
	48-60	14·7 (11·0 to 19·6)
	>60	22·7 (17·2 to 30·1)
Cancer		
(WCRF / AICR, 2007)		
Liver	Per 10g	1·10 (1·02 to 1·07)
Mouth, larynx, pharynx	Per drink per week	1·24 (1·18 to 1·30)
Oesophagus	Per drink per week	1·04 (1·03 to 1·05)
Breast	10g	1·10 (1·06 to 1·14)
Colorectum	10g	1·09 (1·03 to 1·14)

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Table S2. Calculating impact on deaths from liver cirrhosis of increasing consumption of alcohol by 8g/d (one unit). Results shown for men aged 75-79 as example

Alcohol consumption (g/d)	Relative risk[1]	Baseline population[2]	Baseline deaths[3]	Mortality rate per 1,000[4]	Counterfactual population[5]	Counterfactual deaths[6]
<=1	1·0	229,532	24	0·11	229,532	24
1 - <=12	1·0	232,024	24	0·11	146,491	15
12 - <=24	1·6	126,930	21	0·17	130,440	22
24 - <=36	2·8	54,831	16	0·29	73,789	22
36 - <=48	5·6	27,303	16	0·59	43,678	26
48 - <=60	7·0	15,076	11	0·74	27,400	20
>60	14·0	28,404	42	1·47	68,950	101
		TOTAL	*154*		*TOTAL*	*230*

[1] Taken from meta-analysis of prospective cohort studies(Rehm et al., 2010); [2] The total population of men aged 75-79 in England in 2006, following the distribution of alcohol consumption described by the General Household Survey 2006; [3] The total number of deaths from liver cirrhosis in men aged 75-59 in England in 2006, split so that mortality rates respect the relative risks; [4] Mortality rates, which follow the relative risks shown in the earlier column; [5] The population of men aged 75-79 under the counterfactual scenario, in which all drinkers drink one unit per day more; [6] The counterfactual number of deaths, calculated using the mortality rates and the counterfactual population.

Table S3. Population size and alcohol consumption characteristics by sex and 5-year age group in England, 2006

Sex	Age group, years	Population size[1]	Non-drinkers (<1g/day)[2]	Daily intake (g/day) among drinkers, median[2]
Male	15-19	1,719,800	30·9%	14·9
	20-24	1,716,200	15·3%	18·0
	25-29	1,636,900	16·5%	19·3
	30-34	1,714,100	16·2%	14·8
	35-39	1,933,300	16·5%	17·3
	40-44	1,939,700	16·5%	17·5
	45-49	1,717,700	15·6%	17·0
	50-54	1,511,900	18·6%	18·0
	55-59	1,608,900	17·4%	17·5
	60-64	1,320,600	18·3%	17·4
	65-69	1,074,300	20·6%	14·8
	70-74	906,300	23·4%	13·3
	75-79	714,100	31·6%	12·5
	80-84	476,000	32·7%	10·9
	85+	323,700	43·7%	10·1
Female	15-19	1,614,800	33·4%	10·4
	20-24	1,654,200	25·6%	10·9
	25-29	1,633,900	26·4%	9·9
	30-34	1,719,100	33·3%	10·9
	35-39	1,946,400	30·1%	10·0
	40-44	1,971,700	27·2%	9·8
	45-49	1,740,000	30·5%	11·0
	50-54	1,546,900	29·4%	11·3
	55-59	1,652,000	36·3%	10·6
	60-64	1,376,400	41·7%	9·9
	65-69	1,155,800	54·5%	9·4
	70-74	1,034,900	49·7%	8·2
	75-79	923,800	54·6%	7·8
	80-84	746,000	61·2%	7·2
	85+	731,200	68·7%	7·9

1 Population estimates from Office for National Statistics; 2 Estimates taken from the General Household Survey 2006(Office for National Statistics, 2008) (n = 14,306)

Table S4. Annual chronic disease deaths averted or delayed in counterfactual scenarios in which the percentage of non-drinkers in the population varies from 0% to 100%

	0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
Total	4,160	2,727	1,259	-59	-441	-844	-1,269	-1,714	-2,178	-2,660	-3,160
Males	1,462	960	444	-42	-312	-602	-910	-1,236	-1,578	-1,936	-2,309
Females	2,698	1,767	815	-18	-129	-243	-359	-479	-600	-725	-851
Males under 75 years	-201	-124	-54	23	157	276	379	468	544	607	659
Females under 75 years	-472	-300	-134	22	159	293	426	557	685	812	937
CVD	7,705	4,994	2,280	-228	-1,649	-3,071	-4,494	-5,918	-7,342	-8,767	-10,193
Cancer	-2,771	-1,765	-792	104	738	1,351	1,943	2,516	3,071	3,608	4,129
Liver disease	-1,265	-819	-374	77	558	1,039	1,521	2,002	2,483	2,964	3,445

A positive number indicates lives saved compared to 2006 mortality, a negative number denotes a net increase in mortality compared to 2006· Assumes that the distribution of consumption in drinkers remains constant

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