



**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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Complete List of Authors:	Nichols, Melanie; Deakin University, Faculty of Health; Scarborough, Peter; University of Oxford, Department of Public Health Allender, Steven; Deakin University, Faculty of Health; University of Oxford, Department of Public Health Rayner, Mike; University of Oxford, Department of Public Health
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3 1 **What is the optimal level of population alcohol consumption for chronic disease prevention in**  
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5 2 **England? Modelling the impact of changes in consumption patterns**  
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8 3 Melanie Nichols<sup>1,2</sup>, Peter Scarborough<sup>2</sup>, Steven Allender<sup>1,2</sup>, Mike Rayner<sup>2</sup>  
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13

14 5 <sup>1</sup> Population Health Strategic Research Centre, Deakin University, Geelong, Australia  
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16

17 6 <sup>2</sup> British Heart Foundation Health Promotion Research Group, Department of Public Health,  
18  
19 7 University of Oxford, United Kingdom  
20  
21

22 8  
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24

25 9 Corresponding author:  
26  
27

28 10 Dr Melanie Nichols  
29  
30

31 11 British Heart Foundation Health Promotion Research Group  
32 12 Department of Public Health,  
33 13 University of Oxford  
34 14 Old Road Campus, Headington, Oxford, OX3 7LF  
35 15 Email: [melanie.nichols@deakin.edu.au](mailto:melanie.nichols@deakin.edu.au)  
36 16 Ph: +61 3 5227 8446  
37 17

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3 26 **Contributors:** PS conceived the study and developed the methods, with support from MN, SA and  
4  
5 27 MR. MN conducted literature searches to inform the model, PS and MN built the model and  
6  
7 28 conducted analysis. All authors contributed to interpretation of the results. MN prepared the initial  
8  
9 29 draft and led the preparation of the manuscript. All authors were involved in drafting and reviewing  
10  
11 30 the manuscript. MN and PS act as guarantors for the manuscript.  
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38  
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41 43 the submitted work  
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46

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48  
49

50  
51 46 **Data sharing:** The PRIME-Alcohol model is available for use upon request from PS  
52  
53 47 ([peter.scarborough@dph.ox.ac.uk](mailto:peter.scarborough@dph.ox.ac.uk)).  
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3 48 **Abstract**  
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6 49 **Objective** To estimate the impact of achieving alternative population alcohol consumption patterns  
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8 on chronic disease mortality in England.  
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11 51 **Design** A macro-simulation model was built to simultaneously estimate the number of deaths from  
12  
13 52 coronary heart disease, stroke, hypertensive disease, diabetes, liver cirrhosis, epilepsy and five  
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15 53 cancers that would be averted or delayed annually as result of changes in alcohol consumption  
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17 54 among English adults. Counterfactual scenarios assessed the impact on alcohol-related mortalities of  
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19 55 changing a) the percentage of non-drinkers; b) the median alcohol consumption of drinkers; c) both  
20  
21 56 factors simultaneously.  
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24  
25 57 **Data sources** Risk relationships were drawn from published meta-analyses. Age and sex specific  
26  
27 58 distributions of alcohol consumption (g/d) for the English population in 2006 were drawn from the  
28  
29 59 General Household Survey 2006, and age, sex and cause specific mortality data for 2006 were  
30  
31 60 provided by the Office for National Statistics.  
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34  
35 61 **Results** The optimum percentage of non-drinkers in the model was zero. If achieved, this would  
36  
37 62 avert or delay 4,160 (95% credible intervals: 908 to 6,962) chronic disease deaths per year. Increases  
38  
39 63 of 2,771 (2,443 to 3,898) deaths from cancer and 1,265 (1,166 to 1,360) deaths from liver cirrhosis  
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41 64 were more than offset by averting 7,705 (5,248 to 11,934) deaths from cardiovascular diseases. The  
42  
43 65 optimum median consumption level for drinkers in the model was 5g/d (about half a unit), which  
44  
45 66 would avert or delay 4,579 (2,544 to 6,590) deaths per year. Achieving both a median consumption  
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47 67 of 5g/d and zero non-drinkers would delay or avert 10,794 (6,601 to 14,504) deaths each year.  
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51 68 **Conclusions** Current government recommendations for alcohol consumption are well above the  
52  
53 69 level likely to minimise chronic disease. Public health targets should aim for a reduction in  
54  
55 70 population alcohol consumption to half a unit per day, in order to achieve the optimum level of  
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57 71 reduced chronic disease mortality.  
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3 72 **Article Summary**  
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6 73 **Article focus**  
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- 8 • Alcohol consumption is a risk factor for many chronic diseases, while providing protection  
9 from others. Assessments of the impact of alcohol on individual chronic diseases can  
10 therefore result in contradictory advice about the level of alcohol consumption that is  
11 optimal for health.  
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17 • The UK government currently recommends that men should consume no more than three to  
18 four units per day (24 to 32 g/d of pure alcohol) and women should drink no more than two  
19 to three units per day (16 to 24 g/d). However the true optimum population level of alcohol  
20 consumption is unclear.  
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25 • The aim of this study was to estimate the impact of achieving alternative population alcohol  
26 consumption patterns on chronic disease mortality in England.  
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30 84 **Key messages**  
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- 32  
33 • Results suggest that the optimum population level of alcohol consumption for minimising  
34 chronic disease mortality in England is 5g/day (approximately half a unit per day).  
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36  
37 • Current recommendations for alcohol consumption are well above this level and may not be  
38 compatible with optimum protection of public health. Substantial reductions in  
39 recommendations and in population alcohol consumption levels would be needed to  
40 minimise the chronic disease burden associated with alcohol consumption in England.  
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46 91 **Strengths and limitations of this study**  
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- 48  
49 • The study used a detailed modelling approach to synthesise the best available evidence from  
50 meta-analysis of prospective cohort studies and provide for the first time an estimate of the  
51 level of alcohol associated with theoretical minimum risk of a range of chronic diseases,  
52 considering both harmful and protective effects simultaneously.  
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- 96 • The approach used relies on chronic (average) consumption of alcohol and is not able to  
97 take account of to take account of patterns of drinking (e.g. binge drinking).
- 98 • Results are based on the assumption of a steady state relationship between alcohol  
99 consumption patterns and relative risk of disease, and cannot estimate the time required  
100 between changes in population alcohol consumption levels occurring and the achievement  
101 of changes in mortality rates.

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3 103 **Introduction**  
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6 104 Alcohol consumption has significant impacts on chronic disease risk.<sup>1-3</sup> In the UK, it has been  
7  
8 105 estimated that alcohol-related ill-health is responsible for £3.3 billion in direct costs to the National  
9  
10 106 Health Service annually.<sup>4</sup> The effects of episodes of heavy alcohol consumption are clearly  
11  
12 107 detrimental to health, for example increasing risk from injuries and violence.<sup>5-7</sup> Less is known about  
13  
14 108 the overall effects of long term alcohol consumption on chronic disease risk in the whole population,  
15  
16 109 due to alcohol consumption at various levels increasing risk for some chronic disease outcomes (e.g.  
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18 110 liver cirrhosis and cancer), yet decreasing risks of others (e.g. cardiovascular disease and diabetes).

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21 111 The World Cancer Research Fund has recommended that there is no safe level of alcohol  
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23 112 consumption in relation to cancer risk<sup>8</sup>, and Schutze and colleagues<sup>9</sup> report that up to 10% of all  
24  
25 113 cancers in men and 3% in women in some European countries may be attributable to alcohol  
26  
27 114 consumption. This has led to calls for public health messages to encourage abstinence or significant  
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29 115 reductions in alcohol consumption.<sup>9,10</sup> There is, however, a substantial body of evidence that  
30  
31 116 suggests that moderate alcohol consumption protects against other chronic diseases, including  
32  
33 117 cardiovascular disease (CVD) and diabetes.<sup>11-13</sup> Particularly in the case of CVD, which accounts for a  
34  
35 118 significant proportion of mortality in high income countries, this evidence suggests that significantly  
36  
37 119 reducing alcohol consumption could lead to an increase in mortality.

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40 120 Substantial research has examined the effects of alcohol consumption on various chronic diseases;  
41  
42 121 however there has been little integration of the findings across disease outcomes, thereby  
43  
44 122 precluding the development of comprehensive and evidence-based recommendations for  
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46 123 population alcohol consumption. The UK government currently recommends that men should  
47  
48 124 consume no more than three to four units per day (one unit = 8g of pure alcohol) and women should  
49  
50 125 drink no more than two to three units per day.<sup>14</sup> A large proportion of the literature supporting  
51  
52 126 alcohol policy in the UK, however, appears to focus on alcohol 'misuse', episodes of heavy drinking  
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3 127 and the social consequences of alcohol consumption<sup>14</sup>; it is not clear that there is evidence that the  
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5 128 UK Government recommended drinking levels offer the maximum protection for public health.  
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8 129 The aim of this study was to estimate the impact of achieving alternative population alcohol  
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10 130 consumption patterns on chronic disease mortality in England. The research question was: what  
11  
12 131 proportion of non-drinking in the English population and what level of alcohol consumption among  
13  
14 132 drinkers would result in the greatest number of chronic disease deaths delayed or averted in  
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16 133 England compared to recent levels?  
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## 21 22 135 **Methods**

23  
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25 136 A macro-simulation model was built that assessed the impact on mortality from chronic disease of  
26  
27 137 changing the distribution of alcohol consumption (g/day) within the population of England. The  
28  
29 138 Preventable Risk Integrated Model for Alcohol (PRIME-Alcohol) estimates the impact of population  
30  
31 139 changes in alcohol consumption on chronic disease mortality. Developing the PRIME-Alcohol model  
32  
33 140 involved: identifying chronic diseases associated with alcohol consumption; identifying the current  
34  
35 141 (baseline) distribution of alcohol consumption; and parameterising the association between alcohol  
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37 142 consumption and chronic disease.  
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### 40 41 143 *Selection of mortality outcomes*

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44 144 The initial list of chronic diseases was generated from those linked to alcohol consumption in the  
45  
46 145 World Health Organization Global Burden of Disease 'Global Health Risks' report<sup>15</sup> and the World  
47  
48 146 Cancer Research Fund Report<sup>8</sup> was used to select site-specific cancers associated with alcohol  
49  
50 147 consumption. Excluding those resulting in small numbers of deaths (fewer than 500 deaths in 2006  
51  
52 148 in England), 11 chronic diseases were included as outcomes in the PRIME-Alcohol model, including  
53  
54 149 five cancer sites.  
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3 150 The PubMed and Cochrane databases were searched for meta-analyses of prospective cohort or  
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5 151 case-control studies that quantified chronic disease risk for different levels of alcohol consumption.  
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7 152 The relationships between alcohol consumption were diverse, including protective effects, linear  
8  
9 153 increases in risk and 'U' or 'J' shaped relationships. Where multiple suitable meta-analyses were  
10  
11 154 available, preference was given to meta-analyses of cohort studies over case-control studies, and to  
12  
13 155 those using lifetime abstainers as the reference category. Age- and sex-specific estimates of risk  
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15 156 relationships and estimates adjusted for potential confounders were used where available.  
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19 157 Details of the chronic disease outcomes and the meta-analyses that were included in the model<sup>8 11 12</sup>  
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21 158 <sup>16-18</sup> are shown in table 1.

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23  
24 159 (table 1 here)

#### 25 26 27 160 *Identifying the current (baseline) distribution of alcohol consumption in England*

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30 161 The General Household Survey (GHS) from 2006<sup>19</sup> provided baseline distributions of alcohol  
31  
32 162 consumption for adults aged 16 years and over. The GHS is a multi-purpose survey conducted by the  
33  
34 163 Office for National Statistics in the UK. In 2006, it included 18,214 adults aged 16 years and over  
35  
36 164 (overall response rate 74%). To establish average weekly alcohol consumption, respondents were  
37  
38 165 asked how often over the last year they drank alcoholic beverages and the amount usually  
39  
40 166 consumed on any one day. This information is combined to give an estimate of the respondent's  
41  
42 167 weekly alcohol consumption in units of alcohol.<sup>20</sup> For the current analyses, units of alcohol per week  
43  
44 168 was converted to grams per day and only participants from England were included (n =15,616). The  
45  
46 169 distribution of alcohol consumption in the GHS is shown in supplementary figure S1 – there is a large  
47  
48 170 spike of non-drinkers and very low alcohol consumers (<=1g/d) and a long tail of higher alcohol  
49  
50 171 consumers. Non-drinkers and very low alcohol consumers were removed and analysed as a separate  
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52 172 category (referred to as non-drinkers henceforth). Excluding this group, alcohol consumption was  
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54 173 shown to be approximately log-normally distributed (supplementary figure S2).  
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175 The three parameters for the baseline distribution of alcohol consumption derived from the GHS for  
176 each of 30 age-sex groups were therefore: percentage of non-drinkers; the mean of ln-transformed  
177 alcohol consumption of drinkers; and the standard deviation of ln-transformed alcohol consumption  
178 of drinkers. Counterfactual scenarios were modelled by altering one or more of these parameters.

179

### 180 *Parameterising the association between alcohol consumption and chronic disease*

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

192

### 193 *Uncertainty analysis*

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

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3 197 computing requirements of the Monte Carlo iterations, credible intervals are only presented for key  
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5 198 results.  
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11 200 *Defining the counterfactual scenarios*  
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14 201 To assess the number of chronic disease mortalities in England under different alcohol consumption  
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16 202 scenarios, three counterfactual scenarios were analysed: 1) varying the proportion of non-drinkers in  
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18 203 the population while holding the median consumption among drinkers constant; 2) varying the  
19  
20 204 median consumption among drinkers while holding the proportion of non-drinkers constant; and 3)  
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22 205 varying both the proportion of non-drinkers and the median intake among drinkers.  
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25  
26 206 In the analysis of the first scenario, the total percentage of non-drinkers in the population was  
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28 207 allowed to vary between 0% and 100% such that the age-sex distribution of non-drinkers was  
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30 208 maintained, whilst the amount of alcohol consumed by drinkers remained constant. In the analysis  
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32 209 of the second scenario, the percentage of non-drinkers was kept constant while the amount of  
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34 210 alcohol consumed by drinkers in the population was varied between 1g/d and 48g/d (6 units), such  
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36 211 that the age-sex distribution of mean alcohol consumption was maintained. In the analysis of the  
37  
38 212 third scenario, both the percentage of non-drinkers and the amount consumed by drinkers were  
39  
40 213 varied. The aim of the analyses was to find the distribution of alcohol consumption for England that  
41  
42 214 would result in the lowest number of chronic disease mortalities. The funding bodies supporting the  
43  
44 215 authors of this work had no role in the present study.  
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3 217 **Results**  
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6 218 In 2006, 29% of English adults were non-drinkers according to the definitions used here (including  
7  
8 219 those who consume less than 1g/d). Rates of non-drinking varied substantially by age group and sex  
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10 220 (supplementary table S3). Overall, 20% of men and 36% of women were non-drinkers.  
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13 221 In the first counterfactual scenario, varying the proportion of non-drinkers in the whole population,  
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15 222 optimal results were achieved when there were zero non-drinkers in the population (figure 1 and  
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17 223 supplementary table S4), which resulted in 4,160 (95% credible intervals: 908 to 6,962) chronic  
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19 224 disease deaths averted or delayed compared to 2006 mortality rates. Although having the whole  
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21 225 population drinking some alcohol would increase deaths from cancer by 2,771 (2,443 to 3,898) and  
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23 226 from liver cirrhosis by 1,265 (1,166 to 1,360), this was more than offset by averting 7,705 (5,248 to  
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25 227 11,934) deaths from CVD. As the proportion of non-drinkers was increased in the counterfactual  
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27 228 scenarios, the reductions in mortality were attenuated. When the modelled rates of non-drinking  
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29 229 exceeded the 2006 levels there was a net increase in chronic disease mortality, up to an additional  
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31 230 3,160 (-436 to 6,409) lives lost annually if the entire population were to abstain from alcohol.  
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35 231 Analysis by gender showed that at low proportions of non-drinkers, greater numbers of deaths were  
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37 232 averted among women, while at higher proportions of non-drinkers there was a smaller increase in  
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39 233 mortality among women than among men, reflecting the fact that the baseline proportion of non-  
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41 234 drinkers is higher in women than in men. When premature deaths (before age 75) were examined,  
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43 235 the trend was opposite to that displayed for all ages: among people aged under 75 years, higher  
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45 236 levels of non-drinkers resulted in larger numbers of deaths delayed or averted (supplementary table  
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47 237 S4).  
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51 238 In the second counterfactual scenario, varying the median population level of alcohol consumption  
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53 239 among current drinkers between 1g and 48g per day, results showed that approximately 5g/day (just  
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55 240 over half of one unit) was the optimal level of alcohol consumption, resulting in 4,579 (2,544 to  
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3 241 6,590) deaths delayed or averted (figure 2 and supplementary table S5). In counterfactual scenarios  
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5 242 with lower levels of alcohol consumption, the shift of a large proportion of the population into the  
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7 243 non-drinker category resulted in an increase in deaths from cardiovascular disease, which was not  
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9 244 offset by reductions in cancer, liver cirrhosis and other chronic conditions. Above 5g/day the  
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11 245 additional protective effect of alcohol on CVD was not enough to offset the additional risk from  
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13 246 cancer, liver cirrhosis and other chronic conditions. For men and women aged under 75 years, the  
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15 247 optimum level of consumption was slightly lower than for the whole population, at 3g/d, at which  
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17 248 level 4,381 (3,327 to 5,400) deaths before age 75 would be delayed or averted each year.

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21 249 (table 2 here)

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24 250 In the third counterfactual scenario, the proportion of non-drinkers was set at the optimum level  
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26 251 (0%) and median alcohol consumption in drinkers was allowed to vary between 0g/d and 48g/d  
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28 252 (table 2). The optimal population median intake remained 5g/day, at which level 10,794 (6,601 to  
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30 253 14,504) deaths were averted or delayed. In this scenario, the increased risks of alcohol consumption  
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32 254 above optimal levels increased more rapidly due to all of the population being exposed to the risk.  
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34 255 There would be a simultaneous reduction in deaths from all three of the major alcohol-related  
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36 256 chronic disease categories under this scenario; deaths from CVD would be reduced by 6,064 (1,732  
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38 257 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).

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## 43 44 45 259 **Discussion**

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48 260 The PRIME-Alcohol model effectively demonstrates the impact of population usual alcohol  
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50 261 consumption on chronic disease mortality, bringing together a wide range of risk and protective  
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52 262 effects of alcohol, including the increased risks of many cancers and the protective effect of low to  
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54 263 moderate consumption on cardiovascular disease. Modelling demonstrated that the optimum  
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56 264 population median alcohol consumption level appears to be substantially lower than the

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3 265 recommended safe levels in current UK public health guidance. Reducing the median population  
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5 266 alcohol consumption among current drinkers to around half a unit (5g of alcohol) per day, would  
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7 267 result in around 4,600 fewer deaths annually, primarily due to reductions in cancers and liver  
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9 268 cirrhosis. If this same median consumption level were to be applied to the whole population (i.e.,  
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11 269 including current non-drinkers), more than double this number of deaths could be delayed or  
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13 270 averted. However, there are a number of reasons why it may not be prudent to encourage current  
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15 271 non-drinkers to start drinking. These include: encouraging abstainers to start drinking whilst  
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17 272 encouraging drinkers to reduce their alcohol consumption is a mixed message that may be difficult  
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19 273 to communicate and promote; reducing the number of non-drinkers may have an adverse impact on  
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21 274 non-chronic disease health (e.g. accidents and injuries); and the modelled results show that while  
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23 275 reducing the proportion of non-drinkers would decrease chronic disease deaths overall, it would  
24  
25 276 increase the number of premature deaths (before 75 years; see supplementary table 3). On this  
26  
27 277 basis, we recommend that the public health target for alcohol consumption in England should be to  
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29 278 reduce median alcohol consumption to half a unit per day for both men and women, and to  
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31 279 maintain the current level of non-drinkers within the population.

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36 280 Public health behavioural recommendations should ideally be based on the best available evidence  
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38 281 for optimising population health outcomes. In practice, public health goals in the UK have often  
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40 282 been based on a mixture of evidence of health risks and pragmatic considerations about setting a  
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42 283 goal that is considered achievable. A counterfactual modelling analysis such as the type reported in  
43  
44 284 this paper is particularly useful for setting public health goals, as its flexibility can provide results for  
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46 285 a range of counterfactual scenarios, which can then inform policy makers both of the optimum goal  
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48 286 and the strength of any pragmatic goal that they may consider.

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51  
52 287 A limitation of the PRIME-Alcohol model is that it is based on usual average levels of alcohol  
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54 288 consumption and is unable to take account of patterns of drinking (e.g. binge drinking). There is  
55  
56 289 evidence that patterns of drinking play an important role in disease risk<sup>21</sup>, and particularly in

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3 290 morbidity and mortality from accidents and injuries.<sup>25</sup> The central recommendation from the results  
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5 291 of this paper – that a target consumption level for England should be half a unit per day – is,  
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7 292 however, likely to be consistent with low levels of risk for accidents and injuries. In addition, it is not  
8  
9 293 possible to include wholly alcohol attributable conditions (e.g. mental and behavioural disorders due  
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11 294 to alcohol use) in the model. The PRIME-Alcohol model is necessarily limited by the availability of  
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13 295 robust meta-analytic estimates of relative risk for mortality. Sex-specific estimates of relative risk at  
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15 296 varying levels of alcohol consumption were available only for hypertensive disease and liver  
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17 297 cirrhosis, and no age-specific estimates were available, which limits the specificity of the  
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19 298 counterfactual scenarios analysed by the model. Furthermore, results are based on the assumption  
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21 299 of a steady state relationship between alcohol consumption patterns and relative risk of disease,  
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23 300 while in reality there is a lag time between changes in alcohol consumption levels and mortality risk.  
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25 301 For some conditions included in the model, relative risk estimates from appropriate meta-analysis  
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27 302 were available only for incidence of the disease, rather than mortality.  
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32 303 This study is an important addition to the current debate around alcohol consumption and public  
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34 304 health, combining and balancing risk and protective factors to identify an optimal population level of  
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36 305 alcohol consumption. This is in contrast to recent publications on the associations between alcohol  
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38 306 and specific conditions. For example, Schutze and colleagues concluded that their analyses of the  
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40 307 association between alcohol intake and cancer “support current political efforts to reduce or to  
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42 308 abstain from alcohol consumption to reduce the incidence of cancer”.<sup>9</sup> On behalf of the Australian  
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44 309 Cancer Council, Winstanley and colleagues recommend that “to reduce their risk of cancer, people  
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46 310 limit their consumption of alcohol, or better still avoid alcohol altogether”.<sup>10</sup> In contrast, a recent  
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48 311 systematic review of the impact of alcohol on cardiovascular disease concluded that “alcohol, in  
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50 312 moderation, may have overall health benefits that outweigh the risks in selected subsets of  
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52 313 patients”.<sup>11</sup> Only by systematically combining the effects of alcohol on all alcohol-related conditions  
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54 314 can appropriate public health messages be developed.  
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3 315 The findings from this paper are consistent with those from a meta-analysis of alcohol consumption  
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5 316 and total mortality<sup>22</sup>, which also found lowest mortality risk around 5g of alcohol per day, and a  
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7 317 Europe-wide study<sup>23</sup> which found minimum risk for alcohol attributable deaths at 10g per day or less  
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9 318 (the smallest consumption category included in that study). A strength of our modelling approach, in  
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11 319 comparison to cross-sectional studies or fixed meta-analyses of total mortality, is that it can account  
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13 320 for differences between populations in underlying risk of various chronic diseases, and can therefore  
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15 321 be used to predict population-specific curves of potential changes in chronic disease mortality for  
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17 322 international comparisons. Future work should therefore produce comparable results for  
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19 323 international populations with varying current levels of exposure and outcomes. Furthermore, there  
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21 324 is a significant interaction between alcohol consumption and other lifestyle risk factors for chronic  
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23 325 disease mortality, and future work should seek to integrate alcohol consumption with risk  
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25 326 behaviours such as poor nutrition, low physical activity and smoking to compare the relative  
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27 327 contributions that improvements in these risk factors, both independently and in combination, could  
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29 328 have on population health.  
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### 330 **Conclusions**

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

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3 398 **LIST OF FIGURES:**

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6  
7 400 **Figure 1 Deaths delayed or averted in the counterfactual scenario varying percentages of non-**  
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9 401 **drinkers.**

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11 402 The percentage of non-drinkers was allowed to vary between 0% and 100% of the total population  
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13 403 using England 2006 as the baseline. The median consumption of alcohol among those drinking was  
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15 404 held constant.  
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20 406 **Figure 2 Deaths delayed or averted in the counterfactual scenario varying median consumption of**  
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22 407 **alcohol in drinkers.**

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24 408 The median consumption of alcohol among drinkers was allowed to vary from 0g/d to 24g/d using  
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26 409 England 2006 as the baseline. The percentage of non-drinkers in the population was held constant.  
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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 <sup>11</sup> , 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 <sup>11</sup> , 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 <sup>16</sup> , 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 <sup>12</sup> , 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 <sup>17</sup> , 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 <sup>18</sup> , 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 <sup>8</sup> . 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 <sup>8</sup> . Adjusted for smoking.	Dose-response increased risk
Oesophagus (C15)	6,068	3,104 (51.2%)	WCRF/AICR 20 case-control studies <sup>8</sup> . 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 <sup>8</sup> . 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 <sup>8</sup> . 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

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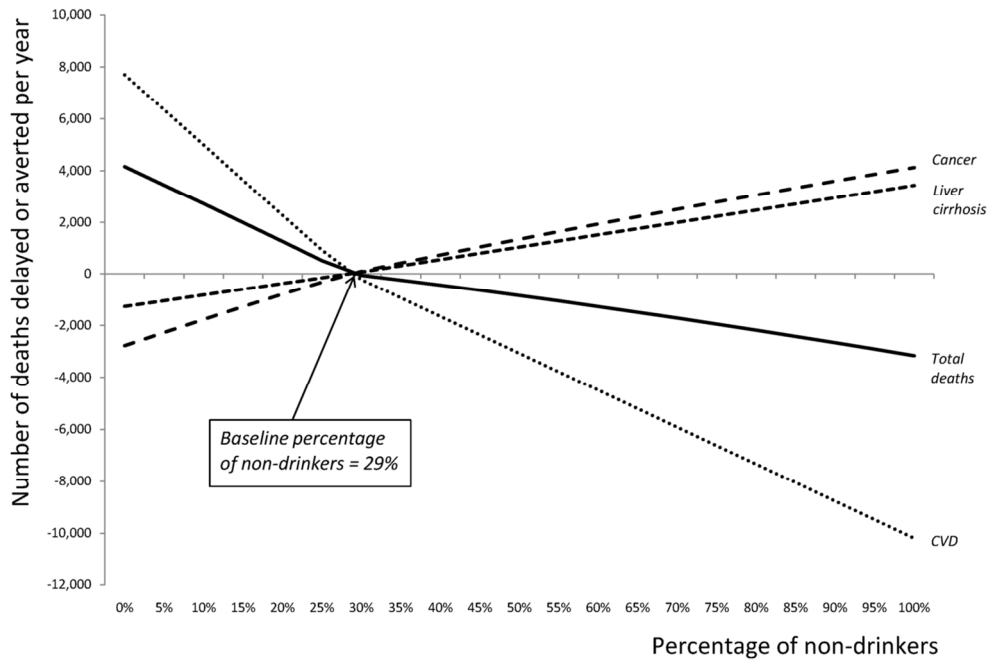


Figure 1. Deaths delayed or averted in the counterfactual scenario varying percentages of non-drinkers  
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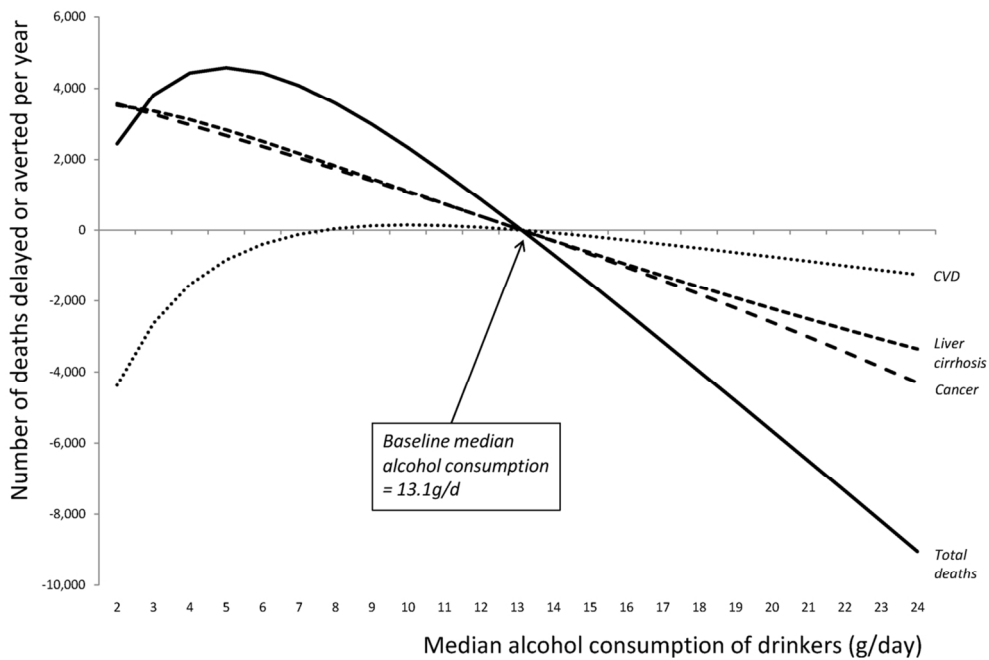


Figure 2. Deaths delayed or averted in the counterfactual scenario varying median consumption of alcohol in drinkers  
114x76mm (300 x 300 DPI)

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## Supplementary information

Table S1. Relative risks used in modelling

Outcome	Alcohol consumption level (g/day)	Relative Risk for mortality	
CHD (Ronksley et al., 2011)	0	1.00	
	<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 (Ronksley et al., 2011)	0	1.00	
	<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 (Koppes et al., 2005)	0	1.00	
	<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 (Samokhvalov et al., 2010)	0	1.00	
	<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 (Rehm et al., 2010)	0	1.00	
	<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 (Rehm et al., 2010)	0	1.00	
	<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 <sup>1</sup>	Baseline population <sup>2</sup>	Baseline deaths <sup>3</sup>	Mortality rate per 1,000 <sup>4</sup>	Counterfactual population <sup>5</sup>	Counterfactual deaths <sup>6</sup>
<=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
		<i>TOTAL</i>	<i>154</i>		<i>TOTAL</i>	<i>230</i>

<sup>1</sup> Taken from meta-analysis of prospective cohort studies (Rehm et al., 2010); <sup>2</sup> 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; <sup>3</sup> 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; <sup>4</sup> Mortality rates, which follow the relative risks shown in the earlier column; <sup>5</sup> The population of men aged 75-79 under the counterfactual scenario, in which all drinkers drink one unit per day more; <sup>6</sup> 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 <sup>1</sup>	Non-drinkers (<1g/day) <sup>2</sup>	Daily intake (g/day) among drinkers, median <sup>2</sup>
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
Female	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
	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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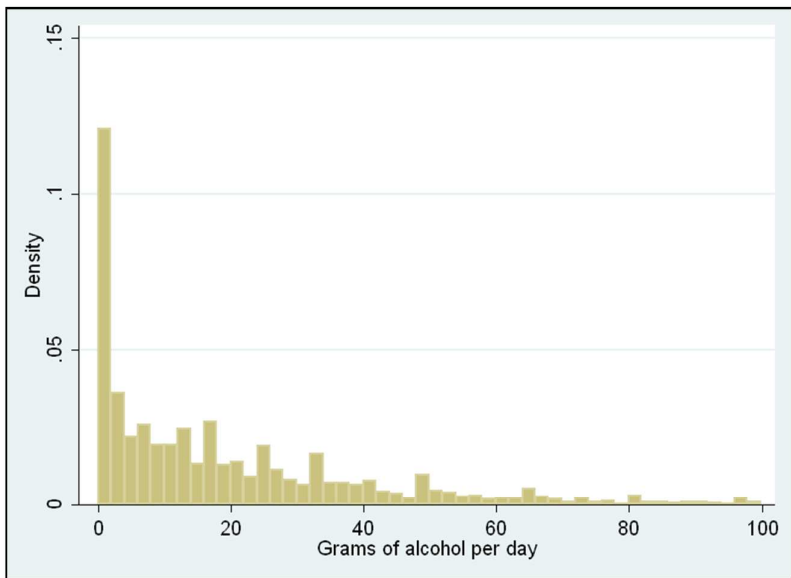
Table S5. Annual chronic disease deaths averted or delayed in counterfactual scenarios in which the median intake of alcohol in drinkers varies from 1g/day to 48g/day

	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

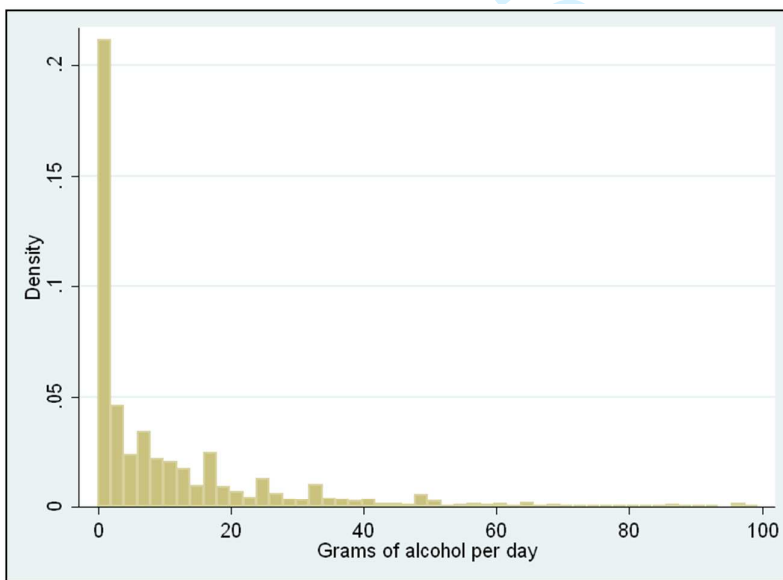
A positive number indicates lives saved compared to 2006 mortality, a negative number denotes a net increase in mortality compared to 2006. Assumes that the percentage of non-drinkers remains constant.

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

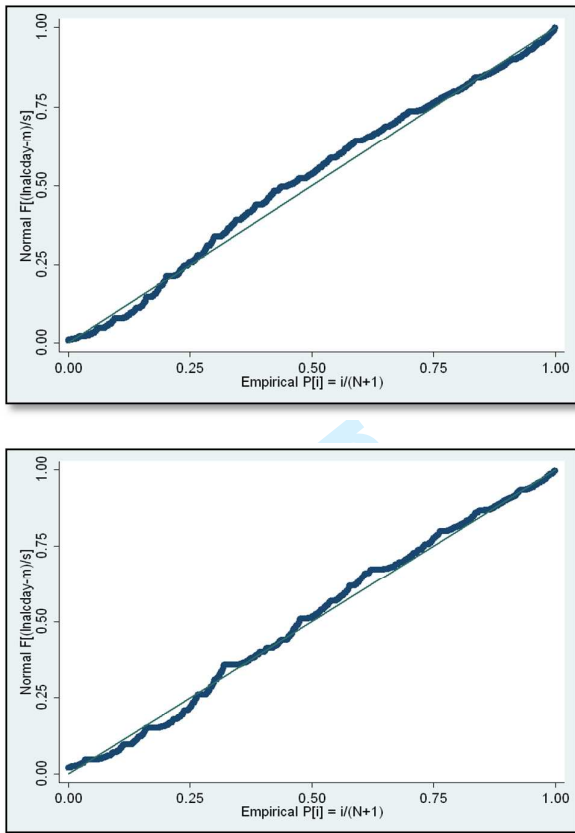


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Figure S2. P-norm plots for normality of ln-transformed variable of alcohol consumption among men and women, England, 2006: General Household Survey data (Office for National Statistics, 2008) (n = 14,306).



Review only



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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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Manuscript ID:	bmjopen-2012-000957.R1
Article Type:	Research
Date Submitted by the Author:	01-Apr-2012
Complete List of Authors:	Nichols, Melanie; Deakin University, Faculty of Health; Scarborough, Peter; University of Oxford, Department of Public Health Allender, Steven; Deakin University, Faculty of Health; University of Oxford, Department of Public Health Rayner, Mike; University of Oxford, Department of Public Health
<b>Primary Subject Heading</b>:	Public health
Secondary Subject Heading:	Epidemiology, Health policy
Keywords:	Alcohol, Chronic disease prevention, Cardiac Epidemiology < CARDIOLOGY, modelling, EPIDEMIOLOGY, PUBLIC HEALTH

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11 2 England? Modelling the impact of changes in average consumption levels

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14 3 Melanie Nichols<sup>1,2</sup>, Peter Scarborough<sup>2</sup>, Steven Allender<sup>1,2</sup>, Mike Rayner<sup>2</sup>

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19 5 <sup>1</sup> Population Health Strategic Research Centre, Deakin University, Geelong, Australia

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21 6 <sup>2</sup> British Heart Foundation Health Promotion Research Group, Department of Public Health,  
22 7 University of Oxford, United Kingdom

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28 9 Corresponding author:

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31 10 Dr Melanie Nichols

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33 11 British Heart Foundation Health Promotion Research Group  
34 12 Department of Public Health,  
35 13 University of Oxford  
36 14 Old Road Campus, Headington, Oxford, OX3 7LF  
37 15 Email: [melanie.nichols@deakin.edu.au](mailto:melanie.nichols@deakin.edu.au)  
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41 18 Word count (excluding abstract and references): 32~~69~~

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43 19 Number of references: 2~~8~~

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51 23 Keywords: Alcohol, chronic disease, prevention, modelling, cardiovascular disease, cancer, liver

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10 30 **Contributors:** PS conceived the study and developed the methods, with support from MN, SA and  
11 MR. MN conducted literature searches to inform the model, PS and MN built the model and  
12 conducted analysis. All authors contributed to interpretation of the results. MN prepared the initial  
13 draft and led the preparation of the manuscript. All authors were involved in drafting and reviewing  
14 the manuscript. MN and PS act as guarantors for the manuscript.  
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33 42 **Competing interests:** The authors declare no competing interests. All authors have completed the  
34 Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the  
35 corresponding author) and declare: there was no specific funding for the submitted work; no  
36 financial relationships with any organisations that might have an interest in the submitted work in  
37 the previous three years, no other relationships or activities that could appear to have influenced  
38 the submitted work  
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48 **Ethical approval** was not required, as no human or animal subjects were involved.  
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10 **Abstract**

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

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

Deleted: the percentage of non-drinkers;

Deleted: median alcohol consumption of drinkers; c) both factors simultaneously

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26 **Data sources** Risk relationships were drawn from published meta-analyses. Age and sex specific  
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28 distributions of alcohol consumption (g/d) for the English population in 2006 were drawn from the  
29  
30 General Household Survey 2006, and age, sex and cause specific mortality data for 2006 were  
31  
32 provided by the Office for National Statistics.

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34 **Results** The optimum median consumption level for drinkers in the model was 5g/d (about half a  
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36 unit), which would avert or delay 4,579 (2,544 to 6,590) deaths per year. Approximately equal  
37  
38 numbers of deaths from cancers and liver disease would be delayed or averted (~2800 for each),  
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40 while there was a small increase in cardiovascular mortality. The model showed, however, no  
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42 benefit in terms of reduced mortality when the proportion of non-drinkers in the population was  
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44 increased.

Deleted: 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

Deleted: . 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.

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

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98 **Article Summary**

99 **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.

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110 **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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10 127 **Strengths and limitations of this study**

- 11 128 • The study used a detailed modelling approach to synthesise the best available evidence from  
12 129 meta-analysis of prospective cohort studies and provide for the first time an estimate of the  
13 130 level of alcohol associated with theoretical minimum risk of a range of chronic diseases,  
14 131 considering both harmful and protective effects simultaneously.

15 132 • The model is dependent on the meta-analyses selected to define the parameters. Results  
16 133 may vary significantly in other contexts with varying levels of disease, alcohol consumption  
17 134 and other risk factors. Furthermore, results depend on the quality of the available  
18 135 epidemiological evidence, which remains contested in some areas.

- 19 136 • The approach used also relies on chronic (average) consumption of alcohol and is not able to  
20 137 take account of to take account of patterns of drinking (e.g. binge drinking). Furthermore,  
21 138 the results are based on the assumption of a steady state relationship between alcohol  
22 139 consumption patterns and relative risk of disease, and cannot estimate the time required  
23 140 between changes in population alcohol consumption levels occurring and the achievement  
24 141 of changes in mortality rates.

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148 **Introduction**

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

156 The World Cancer Research Fund has recommended that there is no safe level of alcohol  
 157 consumption in relation to cancer risk<sup>8</sup>, and Schutze and colleagues<sup>9</sup> report that up to 10% of all  
 158 cancers in men and 3% in women in some European countries may be attributable to alcohol  
 159 consumption. This has led to calls for public health messages to encourage abstinence or significant  
 160 reductions in alcohol consumption.<sup>9-10</sup> There is, however, a substantial body of evidence that

161 suggests that moderate alcohol consumption protects against other chronic diseases, including  
 162 cardiovascular disease (CVD) and diabetes, which are responsible for a substantial burden of  
 163 disease.<sup>11-13</sup>

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

171 literature supporting alcohol policy in the UK, however, appears to focus on alcohol 'misuse',

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Deleted: 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.

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10 179 episodes of heavy drinking and the social consequences of alcohol consumption<sup>14</sup>; it is not clear that  
11 180 there is evidence that the UK Government recommended drinking levels offer the maximum  
12 181 protection for public health.

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16 182 The aim of this study was to estimate the impact of achieving alternative population average alcohol  
17 183 consumption levels on chronic disease mortality in England. The research question was: what  
18 184 proportion of non-drinking in the English population and what level of alcohol consumption among  
19 185 drinkers would result in the greatest number of chronic disease deaths delayed or averted in  
20 186 England compared to recent levels?  
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## 188 **Methods**

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30 189 A macro-simulation model was built that assessed the impact on mortality from chronic disease of  
31 190 changing the distribution of alcohol consumption (g/day) within the population of England. The  
32 191 Preventable Risk Integrated ModEl for Alcohol (PRIME-Alcohol) estimates the impact of population  
33 192 changes in alcohol consumption on chronic disease mortality. Developing the PRIME-Alcohol model  
34 193 involved: identifying chronic diseases associated with alcohol consumption; identifying the current  
35 194 (baseline) distribution of alcohol consumption; and parameterising the association between alcohol  
36 195 consumption and chronic disease.  
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### 43 196 *Selection of mortality outcomes*

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46 197 The initial list of chronic diseases was generated from those linked to alcohol consumption in the  
47 198 World Health Organization Global Burden of Disease 'Global Health Risks' report<sup>15</sup> and the World  
48 199 Cancer Research Fund Report<sup>8</sup> was used to select site-specific cancers associated with alcohol  
49 200 consumption. Excluding those resulting in small numbers of deaths (fewer than 500 deaths in 2006  
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202 in England), 11 chronic diseases were included as outcomes in the PRIME-Alcohol model, including  
203 five cancer sites.

204 The PubMed and Cochrane databases were searched for meta-analyses of prospective cohort or  
205 case-control studies that quantified chronic disease risk for different levels of alcohol consumption.

206 The relationships between alcohol consumption were diverse, including protective effects, linear  
207 increases in risk and 'U' or 'J' shaped relationships. Where multiple suitable meta-analyses were  
208 available, preference was given to meta-analyses of cohort studies over case-control studies, and to  
209 those using lifetime abstainers as the reference category. Age- and sex-specific estimates of risk  
210 relationships and estimates adjusted for potential confounders were used where available.

211 Details of the chronic disease outcomes and the meta-analyses that were included in the model <sup>8,11-12</sup>

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212 <sup>16-18</sup> are shown in table 1.

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213 (table 1 here)

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

215 The General Household Survey (GHS) from 2006<sup>19</sup> provided baseline distributions of alcohol  
216 consumption for adults aged 16 years and over. The GHS is a multi-purpose survey conducted by the  
217 Office for National Statistics in the UK. In 2006, it included 18,214 adults aged 16 years and over  
218 (overall response rate 74%). To establish average weekly alcohol consumption, respondents were  
219 asked how often over the last year they drank alcoholic beverages and the amount usually  
220 consumed on any one day. This information is combined to give an estimate of the respondent's  
221 weekly alcohol consumption in units of alcohol.<sup>20</sup> For the current analyses, units of alcohol per week  
222 was converted to grams per day and only participants from England were included (n =15,616).

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223 Non-drinkers and very low alcohol consumers were removed and analysed as a separate category  
224 (referred to as non-drinkers henceforth). Excluding this group, alcohol consumption was shown to be  
225 approximately log-normally distributed.

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.

Deleted: (supplementary figure S2)

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12 235 The three parameters for the baseline distribution of alcohol consumption derived from the GHS for  
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14 236 each of 30 age-sex groups were therefore: percentage of non-drinkers; the mean of ln-transformed  
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16 237 alcohol consumption of drinkers; and the standard deviation of ln-transformed alcohol consumption  
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18 238 of drinkers. Counterfactual scenarios were modelled by altering one or more of these parameters.

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22 240 *Parameterising the association between alcohol consumption and chronic disease*

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25 241 The meta-analyses identified by the literature search provided estimates of the relative risk of  
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27 242 different levels of alcohol consumption on chronic disease (table 1). The relative risks used in the  
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29 243 PRIME-Alcohol model are shown in supplementary table S1. These risks were used in conjunction  
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31 244 with the baseline distribution of alcohol consumption to attribute risk for chronic disease  
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33 245 throughout the age-sex specific populations. Baseline age, sex and cause specific number of  
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35 246 mortalities (England 2006) were provided by the Office for National Statistics. For each chronic  
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37 247 disease and age-sex group, mortality rates were assigned to each level of alcohol consumption such  
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39 248 that the relative risks from the meta-analyses were maintained, and the total risk in the population  
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41 249 produced the recorded number of mortalities. These mortality rates were then applied to the  
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43 250 counterfactual distributions to calculate the number of deaths that would be expected under the  
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45 251 counterfactual scenario. An example is provided in supplementary table S2.

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48 253 *Uncertainty analysis*

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50 254 The alcohol-chronic disease association parameters were allowed to vary stochastically according to  
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52 255 the distributions reported in the literature. Five thousand Monte Carlo iterations were run, and the  
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54 256 results were used to calculate 95% credible intervals around the estimates. Because of the

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

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### 260 *Defining the counterfactual scenarios*

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

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

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

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**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.

**Deleted:** 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.

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294 **Results**

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

299 In the first counterfactual scenario, varying the median population level of alcohol consumption  
 300 among current drinkers between 1g and 48g per day, results showed that approximately 5g/day (just  
 301 over half of one unit) was the optimal level of alcohol consumption, resulting in 4,579 (2,544 to  
 302 6,590) deaths delayed or averted (table 2 and figure 1), or approximately 3% of all deaths from  
 303 partially alcohol-related chronic diseases. At this level of consumption, a small predicted increase in  
 304 risk of CVD (843 additional deaths per year, +0.7% from 2006 levels) is counteracted by large  
 305 decreases in cancer (2668 fewer deaths, -8%) and liver disease (2828 fewer deaths, -49%). At this  
 306 level of consumption, the vast majority (90%) of deaths delayed or averted were premature (before  
 307 age 75).

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

316 (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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10 362 In the second counterfactual scenario, varying the proportion of non-drinkers in the whole  
11 363 population, the model showed a net increase in mortality in all versions of the scenario for which the  
12 364 modelled rates of non-drinking exceeded the 2006 levels, up to an additional 3,160 (-436 to 6,409)  
13 365 lives lost annually if the entire population were to abstain from alcohol.  
14  
15 366 Theoretically optimal results were achieved when there were zero non-drinkers in the population  
16 367 (figure 2 and supplementary table S4), which resulted in 4,160 (95% credible intervals: 908 to 6,962)  
17 368 chronic disease deaths averted or delayed compared to 2006 mortality rates. Although a modelled  
18 369 situation in which the whole population consumes some alcohol would increase predicted deaths  
19 370 from cancer by 2,771 (credible interval 2,443 to 3,898, +8% from 2006 levels) and from liver cirrhosis  
20 371 by 1,265 (1,166 to 1,360, +22%), this was more than offset by averting 7,705 (5,248 to 11,934, -6%)  
21 372 deaths from CVD. As the proportion of non-drinkers was increased in the counterfactual scenarios,  
22 373 the reductions in mortality were attenuated.  
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## 375 Discussion

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

**Deleted:** In the third counterfactual scenario, age-sex 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). ¶

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10 407 The model showed no additional benefit to chronic disease mortality if the proportion of the  
11 408 population abstaining from alcohol were to be increased. Results indicated that increasing the  
12 409 proportion of alcohol consumers in the population (drinking moderately) would result in reduced  
13 410 cardiovascular disease mortality, however this is of little practical relevance given that there are  
14 411 safer and more socially acceptable means of reducing cardiovascular disease risk, and there are a  
15 412 number of reasons why it would be imprudent to encourage current non-drinkers to start drinking.  
16  
17 413 These include: encouraging abstainers to start drinking whilst encouraging drinkers to reduce their  
18 414 alcohol consumption is a mixed message that may be difficult to communicate and promote;  
19 415 reducing the number of non-drinkers may have an adverse impact on non-chronic disease health  
20 416 (e.g. accidents and injuries). Furthermore, modelled results show that while reducing the proportion  
21 417 of non-drinkers would decrease chronic disease deaths overall, it would increase the number of  
22 418 premature deaths (before 75 years; see supplementary table 4), increasing the impact on years of  
23 419 life lost. On this basis, we recommend that the public health target for alcohol consumption in  
24 420 England should be to reduce median alcohol consumption to half a unit per day for both men and  
25 421 women, and to maintain the current level of non-drinkers within the population. The  
26 422 recommendations and public messages around restriction of alcohol consumption that would be  
27 423 required to achieve this target median level of consumption are beyond the scope of this work, but  
28 424 should take account of the likely impacts on chronic disease as modelled here, as well as aiming to  
29 425 reduce other known risks and address patterns of consumption.  
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33 426 Public health behavioural recommendations should ideally be based on the best available evidence  
34 427 for optimising population health outcomes. In practice, public health goals in the UK have often  
35 428 been based on a mixture of evidence of health risks and pragmatic considerations about setting a  
36 429 goal that is considered achievable. A counterfactual modelling analysis such as the type reported in  
37 430 this paper is particularly useful for setting public health goals, as its flexibility can provide predicted

Deleted: 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,

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10 440 impacts for a range of counterfactual scenarios, which can then inform policy makers both of the  
11 441 optimum goal and the strength of any pragmatic goal that they may consider.

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14 442 A limitation of the PRIME-Alcohol model is that it is based on usual average levels of alcohol

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16 443 consumption and is unable to take account of patterns of drinking (e.g. binge drinking) or provide

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18 444 any evidence about the least harmful pattern of alcohol consumption. There is evidence that

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20 445 patterns of drinking play an important role in disease risk<sup>21</sup>, and particularly in morbidity and

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22 446 mortality from accidents and injuries.<sup>25</sup> The central recommendation from the results of this paper –

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24 447 that a target consumption level for England should be half a unit per day – is, however, likely to be

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26 448 consistent with low levels of risk for accidents and injuries. Heavy, irregular drinking has also been

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28 449 linked with increased risk of CVD<sup>21</sup>. Guidance to the public about avoiding heavy drinking sessions

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30 450 remains a very important component of any public health guidance around alcohol consumption. In

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32 451 addition, it is not possible to include wholly alcohol attributable conditions (e.g. mental and

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34 452 behavioural disorders due to alcohol use) in the model.

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36 453 The PRIME-Alcohol model is necessarily limited by the availability of robust meta-analytic estimates

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38 454 of relative risk for mortality and estimates generated are limited by the quality of available evidence

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40 455 to parameterise the model. The observational studies included in the meta-analyses used to

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42 456 parameterise the PRIME-Alcohol model used self-report of alcohol consumption, which may result in

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44 457 an under-estimate of actual alcohol consumption<sup>22</sup>, and results from observational studies cannot

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46 458 account for within-individual variability in alcohol consumption. Although there is a strong body of

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48 459 epidemiological evidence over many years linking moderate alcohol consumption with lower rates of

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50 460 CVD<sup>23-25</sup>, concerns remain about possible residual confounding or other methodological explanations

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52 461 for the observed relationship<sup>25-26</sup>.

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54 462 Sex-specific estimates of relative risk at varying levels of alcohol consumption were available only for

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56 463 hypertensive disease and liver cirrhosis, and no age-specific estimates were available, which limits



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10 465 the specificity of the counterfactual scenarios analysed by the model. Furthermore, results are based  
11 466 on the assumption of a steady state relationship between alcohol consumption levels and relative  
12 467 risk of disease, while in reality there is a lag time between changes in alcohol consumption levels and  
13 468 mortality risk. For some conditions included in the model, relative risk estimates from appropriate  
14 469 meta-analysis were available only for incidence of the disease, rather than mortality, however this is  
15 470 unlikely to significantly impact on the accuracy of estimates unless there was an additional effect of  
16 471 alcohol consumption on case-fatality ratios for the included conditions.

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17 472 The predicted results, in terms of increases or decreases in mortality expected at varying levels of  
18 473 alcohol consumption, are entirely dependent upon the baseline population inputs – particularly  
19 474 current alcohol consumption levels and current levels of mortality from the included chronic  
20 475 diseases (which will reflect among other things, prevalence of other risk factors and both treatment  
21 476 and prevention related health care variables). The level of alcohol consumption associated with the  
22 477 most favourable predicted change from existing mortality levels may vary substantially between  
23 478 populations. It is also important to emphasise that the results indicate predicted impacts on  
24 479 mortality only, and do not account for alcohol-related chronic disease morbidity, which has a  
25 480 significant impact on population health and the health system.

26 481 This study is an important addition to the current debate around alcohol consumption and public  
27 482 health, combining and balancing risk and protective factors to identify an optimal population level of  
28 483 alcohol consumption associated with reduced levels of chronic disease mortality. This is in contrast  
29 484 to recent publications focusing on the associations between alcohol and specific conditions. For  
30 485 example, Schutze and colleagues concluded that their analyses of the association between alcohol  
31 486 intake and cancer “support current political efforts to reduce or to abstain from alcohol  
32 487 consumption to reduce the incidence of cancer”.<sup>9</sup> In contrast, a recent systematic review of the  
33 488 impact of alcohol on cardiovascular disease concluded that “alcohol, in moderation, may have  
34 489 overall health benefits that outweigh the risks in selected subsets of patients”.<sup>11</sup> Only by

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Deleted: 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”.<sup>10</sup>

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10 497 systematically combining the effects of alcohol on all alcohol-related conditions can appropriate  
11 498 public health messages be developed. The results of this modelling exercise contribute to further  
12 499 building all of the evidence required to make such an assessment.  
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16 500 The findings from this paper are consistent with those from a meta-analysis of alcohol consumption  
17 501 and total mortality<sup>27</sup>, which also found lowest mortality risk around 5g of alcohol per day, and a  
18 502 Europe-wide study<sup>28</sup>, which found minimum risk for alcohol attributable deaths at 10g per day or less  
19 503 (the smallest consumption category included in that study). A strength of our modelling approach, in  
20 504 comparison to cross-sectional studies or fixed meta-analyses of total mortality, is that it can account  
21 505 for differences between populations in underlying risk of various chronic diseases, and can therefore  
22 506 be used to predict population-specific curves of potential changes in chronic disease mortality for  
23 507 international comparisons. Future work should therefore produce comparable results for  
24 508 international populations with varying current levels of exposure and outcomes. Furthermore, there  
25 509 is a significant interaction between alcohol consumption and other lifestyle risk factors for chronic  
26 510 disease mortality, and future work should seek to integrate alcohol consumption with risk  
27 511 behaviours such as poor nutrition, low physical activity and smoking to compare the relative  
28 512 contributions that improvements in these risk factors, both independently and in combination, could  
29 513 have on population health.  
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#### 515 Conclusions

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46 516 Our modelling suggests that the optimum level of reduced chronic disease mortality in England  
47 517 would be achieved at an average alcohol consumption level of around 5g per day, which should be  
48 518 taken into account in the formulation of health guidance. It is likely that government  
49 519 recommendations would need to be set at a much lower level than the current 'low risk' drinking  
50 520 guidelines in order to achieve this level.  
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Deleted: Current government recommendations for alcohol consumption are well above the level likely to minimise chronic disease.

Deleted: 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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## 734 LIST OF FIGURES:

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737 **Figure 1 Deaths delayed or averted in the counterfactual scenario varying median consumption of**738 **alcohol in drinkers.**

739 The median consumption of alcohol among drinkers was allowed to vary from 0g/d to 24g/d using

740 England 2006 as the baseline. The percentage of non-drinkers in the population was held constant.

741

742 **Figure 2 Deaths delayed or averted in the counterfactual scenario varying percentages of non-**743 **drinkers.**744 **The percentage of non-drinkers was allowed to vary between 0% and 100% of the total population**745 **using England 2006 as the baseline. The median consumption of alcohol among those drinking was**746 **held constant.**

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Deleted: 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. ¶

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759 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 <sup>11</sup> , 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 <sup>11</sup> , 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 <sup>16</sup> , 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 <sup>12</sup> , 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 <sup>17</sup> , 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 <sup>18</sup> , 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 <sup>8</sup> . 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 <sup>8</sup> . Adjusted for smoking.	Dose-response increased risk
Oesophagus (C15)	6,068	3,104 (51.2%)	WCRF/AICR 20 case-control studies <sup>8</sup> . 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 <sup>8</sup> . 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 <sup>8</sup> . 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
<b>Total</b>	-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
<b>Males</b>	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
<b>Females</b>	-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
<b>Males under 75 years</b>	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
<b>Females under 75 years</b>	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
<b>CVD</b>	-7,150	-4,377	-2,639	-1,543	-843	-397	-120	42	80	-283	-759	-1,259	-2,223	-3,108	-3,923
<b>Cancer</b>	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
<b>Liver disease</b>	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.

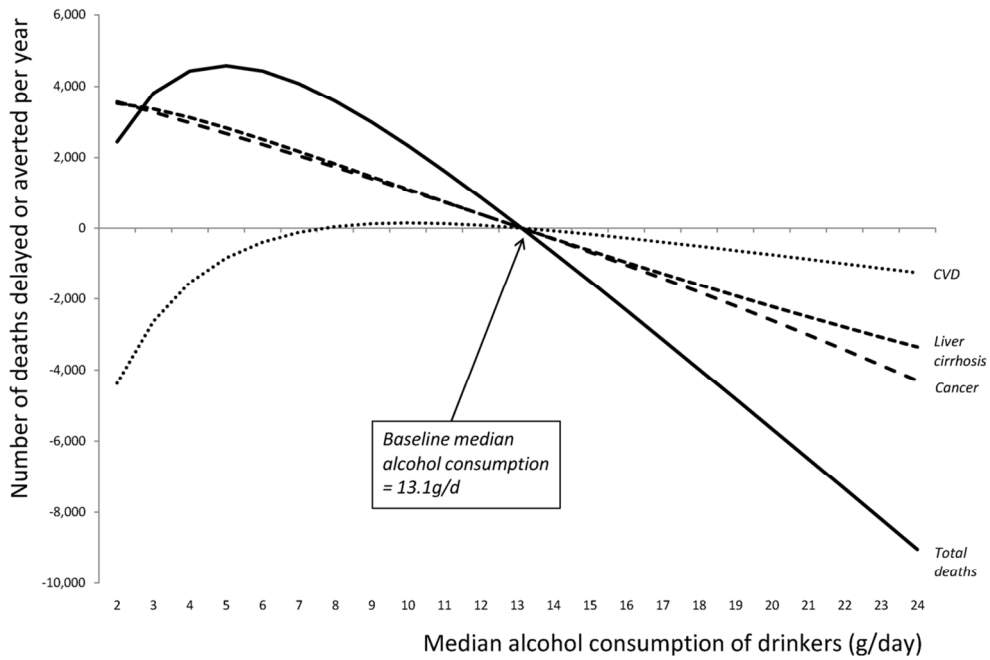
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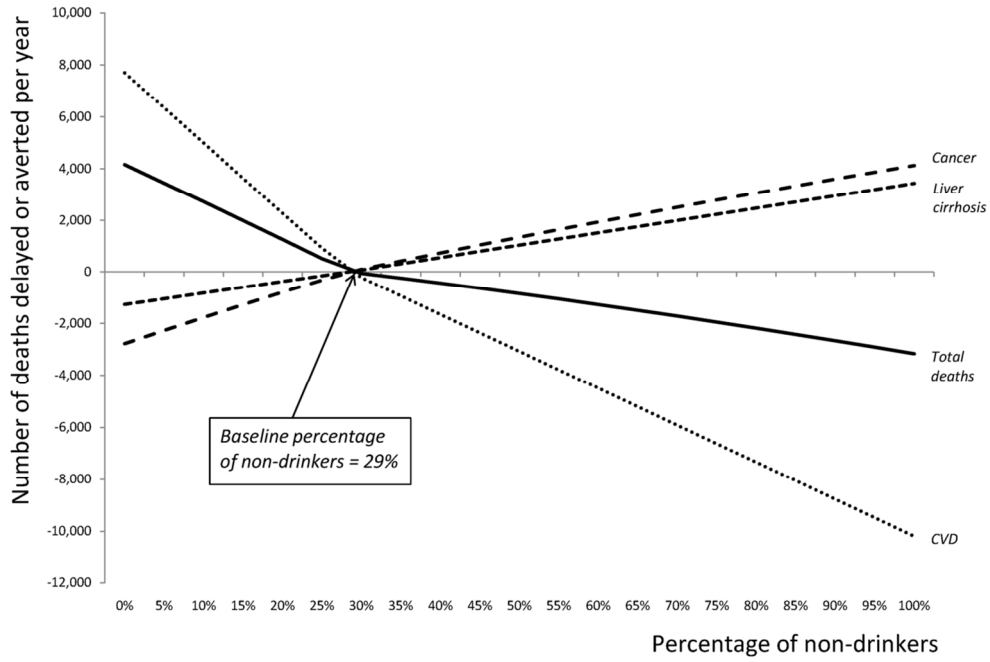


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## Supplementary information

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 (Ronsley et al., 2011)	0	1.00
	<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)
Stroke (Ronsley et al., 2011)	>60	0.75 (0.63 to 0.89)
	0	1.00
	<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)
Diabetes (Koppes et al., 2005)	30 – 60	1.10 (0.85 to 1.45)
	>60	1.44 (0.99 to 2.10)
	0	1.00
	<6	0.88 (0.80 to 0.95)
	6-12	0.73 (0.62 to 0.86)
Hypertensive disease – men (Taylor et al., 2009)	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)
	per 10g	1.09 (1.07 to 1.12)
	Hypertensive disease – women (Taylor et al., 2009)	per 10g
Epilepsy (Samokhvalov et al., 2010)	0	1.00
	<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)
Liver cirrhosis – men (Rehm et al., 2010)	>96	3.27 (2.52 to 4.26)
	0	1.00
	<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)
Liver cirrhosis – women (Rehm et al., 2010)	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)
	0	1.00
	<12	1.9 (1.1 to 3.1)
Cancer (WCRF / AICR, 2007)	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)
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 <sup>1</sup>	Baseline population <sup>2</sup>	Baseline deaths <sup>3</sup>	Mortality rate per 1,000 <sup>4</sup>	Counterfactual population <sup>5</sup>	Counterfactual deaths <sup>6</sup>
<=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
		<b>TOTAL</b>	<b>154</b>		<b>TOTAL</b>	<b>230</b>

<sup>1</sup> Taken from meta-analysis of prospective cohort studies (Rehm et al., 2010); <sup>2</sup> 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; <sup>3</sup> 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; <sup>4</sup> Mortality rates, which follow the relative risks shown in the earlier column; <sup>5</sup> The population of men aged 75-79 under the counterfactual scenario, in which all drinkers drink one unit per day more; <sup>6</sup> 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 <sup>1</sup>	Non-drinkers (<1g/day) <sup>2</sup>	Daily intake (g/day) among drinkers, median <sup>2</sup>
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%

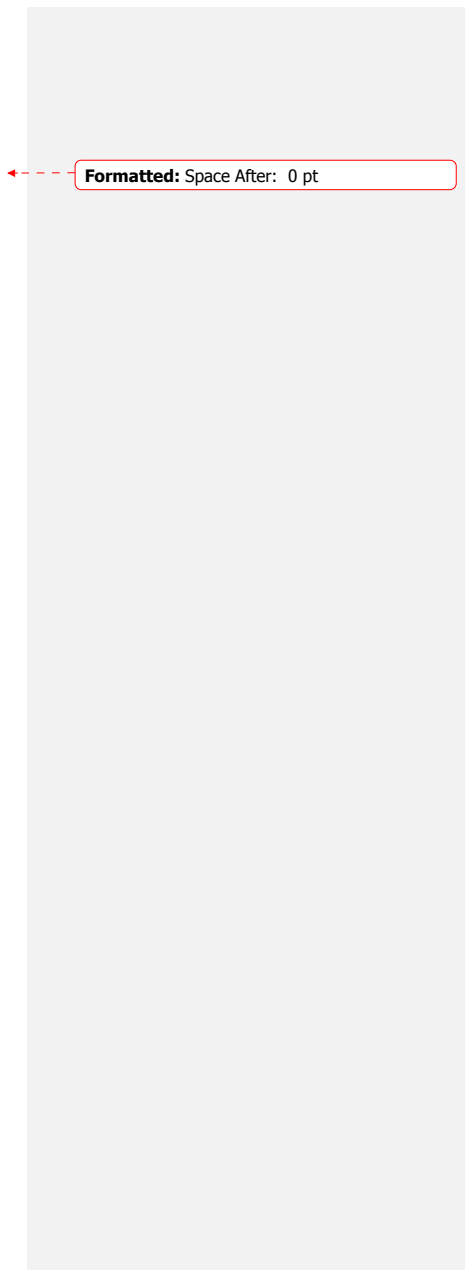
	0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
Total	4,160	2,727	1,259	-59	-441	-844	-1,269	-1,714	-2,178	-2,660	-3,160
Males	1,462	960	444	-42	-312	-602	-910	-1,236	-1,578	-1,936	-2,309
Females	2,698	1,767	815	-18	-129	-243	-359	-479	-600	-725	-851
Males under 75 years	-201	-124	-54	23	157	276	379	468	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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