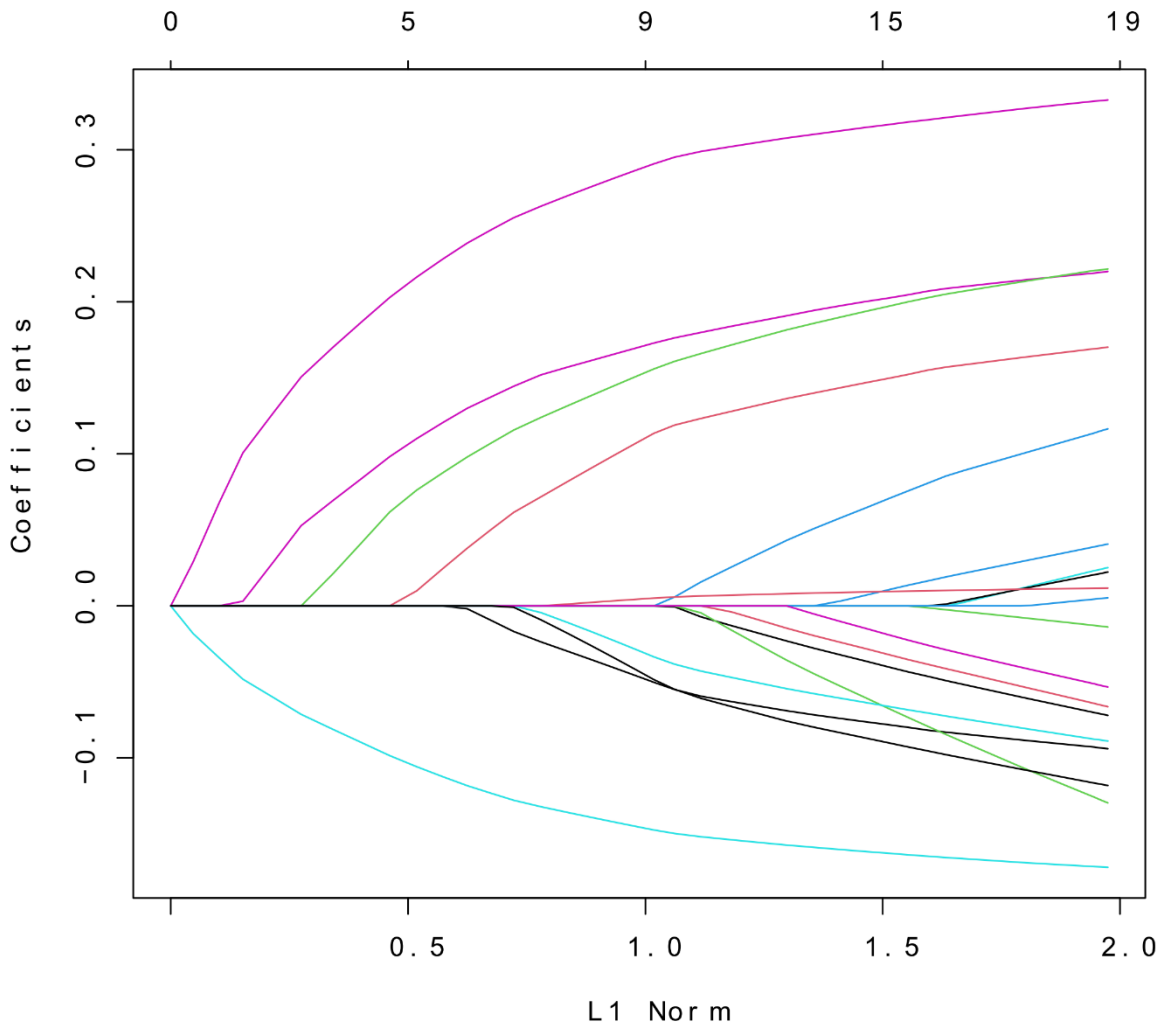
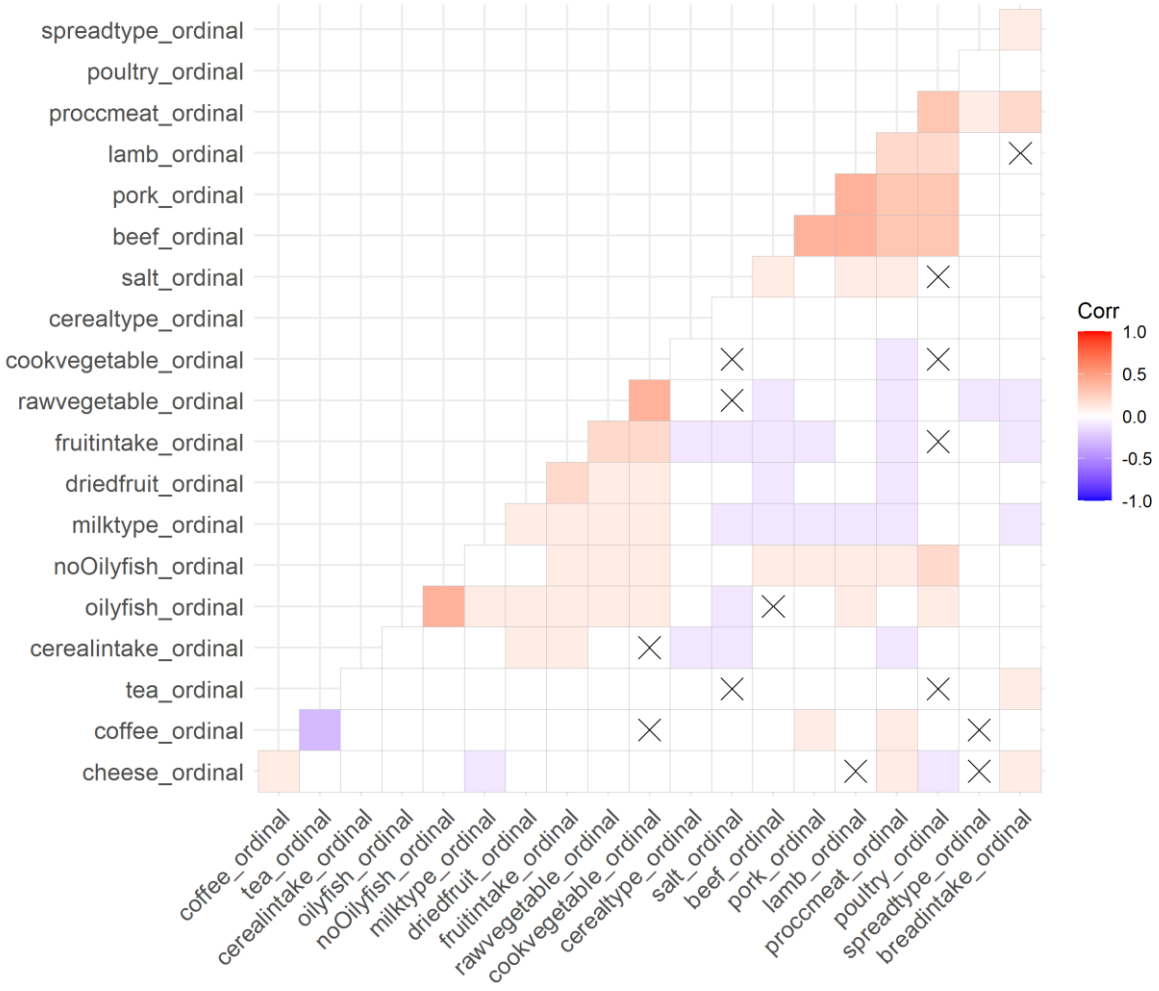
**Supplementary Material**

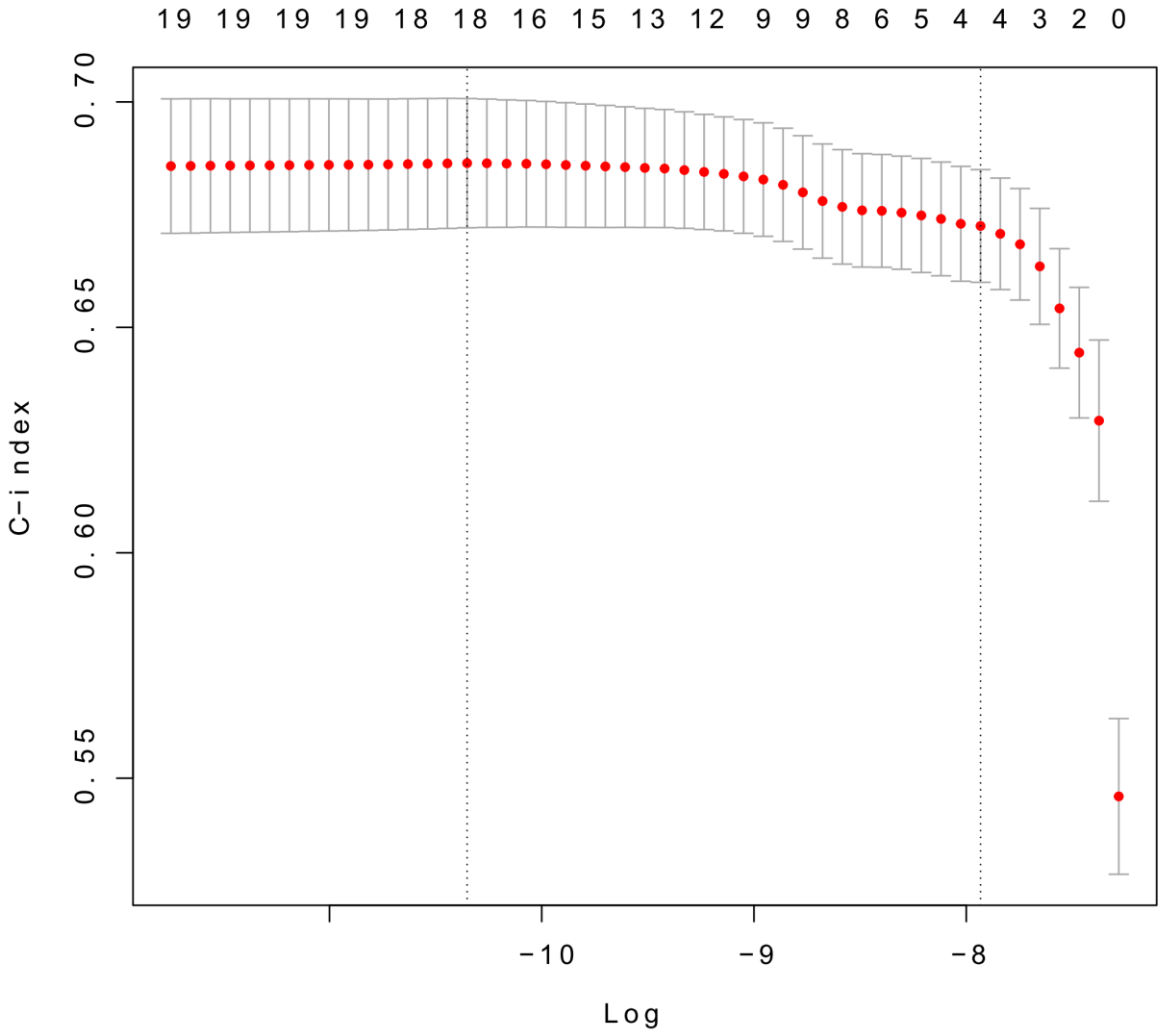
# Diet modifies the association between alcohol and severe alcohol-related liver disease: findings from UK Biobank




**Supplementary Figure 1. Coefficients of included dietary items in models with different lambda values (L1 Norm).**
Coloured lines shown are the reduction in the dietary items' reduction in coefficient as L1 norm is reduced. Purple, cyan, magenta, green, orange, and two black lines showed the coefficients of salt added to food, cereal, processed meat, beef, lamb, coffee and tea intake. Analyses were estimated by Cox regression models using the LASSO algorithm.




**Supplementary Figure 2. Correlation matrix among the 20 dietary items**
The coloured showed are the Spearman's correlation coefficients. Xs represent non-significant correlation. Analyses were estimated by Cox regression models using the LASSO algorithm.




**Supplementary Figure 3. Cross-validated C-index of the optimal λ values**
Numbers on top showed the number of dietary items being selected for different lambda values. The two dotted lines showed the maximal (left) and the within 1-SD C indices. This validation aimed to maximise Harrel´s C-index, where a higher C-index indicates superior risk discrimination performance. Analyses were estimated by Cox regression models using the LASSO algorithm.

**Supplementary Table 1. Pathologies and drug use disorder at/before baseline excluded from the analyses.**

| **Diagnosis** | **ICD-10** |
|---|---|
| **Excluding at baseline** | |
| ALD | K70 (all: from 70.0 to 70.9) |
| Viral Hepatitis | B16, B17, B18, B19 |
| Autoimmune liver disease (AIH, PBC, PSC) | K83.0A, K83.0F, K74.3, K75.4 |
| Hemochromatosis | E83.1 |
| Wilson | E.83.0B |
| Alpha-1-antirypsin deficiency | E88.0A, E88.0B |
| Budd-Chiari | I82.0, K76.5 |
| Chronic hepatitis, unspecified | K73.9, K73.2 |
| Secondary or unspecified biliary cirrhosis | K74.4, K74.5 |
| NAFLD/NASH | K76.0 & K75.8 |
| **Excluding drug use disorders at/before baseline** | |
| Codes associated with drug use disorders except nicotine/caffeine | F11-F14, F16, F18, F19 |

**Supplementary Table 2. Individual association between dietary items and severe ALD.**

| Dietary item | Unit | HR (95% CI) | p-value |
|---|---|---|---|
| Cooked vegetable intake | Portions/day | 0.96 (0.87; 1.06) | 0.401 |
| Salad/raw vegetable intake | Portions/day | 1.04 (0.96; 1.12) | 0.354 |
| Fresh fruit intake | Portions/day | 0.94 (0.89; 1.00) | 0.065 |
| Dried fruit intake | Portions/day | 0.94 (0.87; 1.01) | 0.086 |
| Oily fish intake | Frequency/week | 1.01 (0.92; 1.11) | 0.804 |
| Non-oily fish intake | Frequency/week | 1.03 (0.92; 1.14) | 0.611 |
| Processed meat intake | Frequency/week | 1.10 (1.01; 1.19) | 0.003 |
| Poultry intake | Frequency/week | 0.97 (0.88; 1.07) | 0.564 |
| Beef intake | Frequency/week | 1.14 (1.04; 1.26) | 0.010 |
| Lamb intake | Frequency/week | 1.12 (1.00; 1.26) | 0.044 |
| Pork intake | Frequency/week | 1.05 (0.94; 1.18) | 0.357 |
| Cheese intake | Frequency/week | 0.95 (0.88; 1.03) | 0.257 |
| Milk type | Full cream, semi-skimmed, skimmed, alternative milk, never/rarely have milk | 1.04 (0.96; 1.13) | 0.315 |
| Spread type | Butter, others, rarely use spread | 0.98 (0.91; 1.06) | 0.567 |
| Bread type | White, brown, wholemeal, others | 0.99 (0.98; 1.00) | 0.033 |
| Cereal intake | Bowls/week | 0.88 (0.86; 0.91) | <0.001 |
| Cereal type | Bran, biscuit, oat, muesli, others | 1.03 (0.96; 1.11) | 0.375 |
| Salt added to food | Always, usually, sometimes, rarely/never | 1.25 (1.15; 1.36) | <0.001 |
| Tea intake | Cups/day | 0.95 (0.92; 0.98) | 0.001 |
| Coffee intake | Cups/day | 0.91 (0.87; 0.95) | <0.001 |

Data are presented as hazard ratio and their 95% confidence intervals (95% CI). All analyses were performed excluding people who developed the disease during the first two years of follow-up. Individual analyses were adjusted for age, sex, deprivation, ethnicity, the five components of the metabolic syndrome, alcohol intake at baseline, smoking and physical activity. Analyses were estimated using Cox proportional hazard models. There was no comparison among dietary items.

**Supplementary Table 3. Coefficients of the LASSO model at the chosen lambda.**

| Dietary items | Coefficient |
|---|---|
| Processed meat intake | 0.098 |
| Beef intake | 0.061 |
| Cereal intake | -0.098 |
| Salt added to food | 0.202 |

Estimated from the LASSO model selected from Supplementary Figure 3. There is small correlation between the included food items (Supplementary Figure 2) which might have affected the stability of the coefficients.

**Supplementary Table 4. Interaction between per 7-units/week of alcohol intake (continuous variable) and diet score with severe ALD**

| | HR (95% CI) | RERI (95% CI) | Multiplicative interaction (95% CI) |
|---|---|---|---|
| **Overall** | | 0.19 (0.08-0.31) | 0.94 (0.90-0.97) |
| *Lower ALD diet score (< median)* | | | |
| *7 units lower alcohol intake* | 1 (Reference) | | |
| *7 units higher alcohol intake* | 2.23 (1.65-3.01) | | |
| *Higher ALD diet score (≥ median)* | | | |
| *7 units lower alcohol intake* | 1.31 (1.26-1.36) | | |
| *7 units higher alcohol intake* | 2.74 (2.04-3.67) | | |

Data are presented as hazard ratio and their 95% confidence intervals (95% CI). All analyses were performed excluding people who developed the disease during the first two years of follow-up. Analyses were adjusted for age, sex, deprivation, ethnicity, the five components of the metabolic syndrome, alcohol intake at baseline, smoking and physical activity, and alcohol drinking frequency. RERI: relative risk due to interaction. Calculation of RERI based on Cox proportional model requires comparison between two points of the continuous variable. In this analysis the two points chosen were by 7-unit difference in alcohol intake.

**Supplementary Table 5. Interaction between alcohol intake and diet score with specific ALD outcomes**

| | HR (95% CI) | RERI (95% CI) | Multiplicative interaction (95% CI) |
|---|---|---|---|
| **Alcohol-related cirrhosis** | | 2.34 (0.54-4.14) | 1.68 (0.92-3.09) |
| *Lower ALD diet score (< median)* | | | |
| Lower alcohol risk | 1 (Reference) | | |
| Increasing alcohol risk | 1.86 (0.85-4.07) | | |
| Higher alcohol risk | 10.42 (4.72-22.98) | | |
| *Higher ALD diet score (≥ median)* | | | |
| Lower alcohol risk | 1.09 (0.64-1.86) | | |
| Increasing alcohol risk | 4.30 (2.15-8.61) | | |
| Higher alcohol risk | 10.87 (5.15-22.96) | | |
| **Alcohol-related hepatitis** | | 1.14 (-6.26, 8.53) | 0.27 (0.05-1.33) |
| *Lower ALD diet score (< median)* | | | |
| Lower alcohol risk | 1 (Reference) | | |
| Increasing alcohol risk | 7.07 (1.60-31.12) | | |
| Higher alcohol risk | 26.52 (4.42-159.08) | | |
| *Higher ALD diet score (≥ median)* | | | |
| Lower alcohol risk | 1.50 (0.18-12.43) | | |
| Increasing alcohol risk | 8.39 (1.57-44.83) | | |
| Higher alcohol risk | 33.14 (5.26-208.96) | | |

Data are presented as hazard ratio and their 95% confidence intervals (95% CI). All analyses were performed excluding people who developed the disease during the first two years of follow-up. Analyses were adjusted for age, sex, deprivation, ethnicity, the five components of the metabolic syndrome, alcohol intake at baseline, smoking and physical activity, and alcohol drinking frequency. RERI: relative risk due to interaction. Analyses were estimated using Cox proportional hazard models.

**Supplementary Table 6. Population attributable fraction of ALD diet score and units/week of alcohol consumption (continuous variable)**

| | HR (95% CI) | Population attributable fraction, % (95% CI) |
|---|---|---|
| **ALD diet score** | 1.55 (1.25-1.92) | 28.7 (15.7-39.7) |
| **Alcohol consumption (per 7 units/week)** | 1.23 (1.20-1.27) | 55.3 (50.6-59.5) |

Population attributable fractions assume the HR shown to be causal which could not be shown in this study. All analyses were performed excluding people who developed the disease during the first two years of follow-up. Analyses were mutually adjusted, and adjusted for age, sex, deprivation, ethnicity, the five components of the metabolic syndrome, frequency of alcohol consumption, smoking and physical activity. Analyses were estimated using Cox proportional hazard models.