

Table S1. Association between ADH1B (rs1229984), ALDH2 (rs671), and drinking intensity in ever drinkers expressed as mean of ml of ethanol consumed per week.

| | All | | | Controls | | | Cases | | |
|--------------------------|-----|--------|---------------|----------|--------|---------------|-------|--------|---------------|
| | n | mean* | 95% CI | n | mean | 95% CI | n | mean | 95% CI |
| ADH1B (rs1229984) | | | | | | | | | |
| A/A (fast) | 507 | 541.37 | 483.92-598.81 | 276 | 493.01 | 441.42-544.60 | 231 | 601.32 | 492.62-710.01 |
| A/G | 420 | 573.07 | 509.92-636.23 | 233 | 521.97 | 465.95-577.99 | 187 | 627.29 | 506.15-748.43 |
| G/G (slow) | 157 | 620.01 | 516.56-723.47 | 64 | 587.12 | 479.99-694.25 | 93 | 656.29 | 484.38-828.20 |
| <i>P</i> for trend | | | 0.0327 | | | 0.0351 | | | 0.5003 |
| ADH1C (rs698) | | | | | | | | | |
| A/A (fast) | 908 | 571.18 | 528.40-613.96 | 472 | 520.83 | 481.48-560.17 | 436 | 628.42 | 549.62-707.22 |
| A/G | 166 | 541.00 | 440.79-641.22 | 95 | 506.86 | 419.00-594.72 | 71 | 567.57 | 371.74-763.40 |
| G/G (slow) | 14 | 514.74 | 169.66-859.83 | 6 | 329.01 | -20.85-678.87 | 8 | 674.56 | 88.81-1260.31 |
| <i>P</i> for trend | | | 0.5224 | | | 0.9759 | | | 0.4036 |
| ALDH2 (rs671) | | | | | | | | | |
| G/G (fast) | 817 | 602.61 | 557.58-647.64 | 450 | 561.02 | 521.33-600.70 | 367 | 648.94 | 562.53-735.36 |
| A/G | 254 | 461.82 | 380.64-543.01 | 119 | 367.38 | 290.00-444.75 | 135 | 554.28 | 410.40-698.16 |
| A/A (slow) | 20 | 430.87 | 140.80-720.94 | 8 | 272.90 | -30.36-576.16 | 12 | 575.53 | 97.26-1053.79 |
| <i>P</i> for trend | | | <0.001 | | | <0.001 | | | 0.2228 |

Mean of ml ethanol per week was derived from ANOVA with adjustment on age, gender, study area, smoking pack-years, and case/control status (when appropriate).

P for trend was derived from linear regression with log(ml of ethanol per week) as outcome using a log-additive genetic model.

Table S2. Association between ADH1B (rs1229984), ALDH2 (rs671), and drinking intensity in ever drinkers expressed as mean of ml of ethanol consumed per week, stratified on alcohol drinking intensity.

| | All | | | Controls | | | Cases | | |
|--|-----|--------|----------------|----------|--------|---------------|-------|--------|----------------|
| | n | mean | 95% CI | n | mean | 95% CI | n | mean | 95% CI |
| <u>Light Drinkers (< 250ml/wk)</u> | | | | | | | | | |
| ADH1B (rs1229984) | | | | | | | | | |
| A/A (fast) | 113 | 122.60 | 112.49-132.71 | 77 | 126.43 | 113.48-139.38 | 36 | 113.99 | 97.77-130.21 |
| A/G | 96 | 136.97 | 125.97-147.96 | 63 | 142.99 | 128.69-157.30 | 33 | 126.25 | 109.16-143.34 |
| G/G (slow) | 24 | 141.53 | 119.52-163.55 | 18 | 145.12 | 118.41-171.83 | 6 | 128.98 | 87.79-170.17 |
| <i>P</i> for trend | | | 0.0154 | | | 0.0420 | | | 0.2213 |
| ADH1C (rs698) | | | | | | | | | |
| A/A (fast) | 194 | 126.66 | 119.08-134.25 | 123 | 129.83 | 119.92-139.75 | 71 | 119.29 | 107.82-130.76 |
| A/G | 37 | 152.44 | 134.88-170.01 | 32 | 160.13 | 140.68-179.59 | 5 | 126.81 | 83.05-170.56 |
| G/G (slow) | 2 | 100.65 | 24.64-176.65 | 2 | 108.64 | 28.14-189.15 | 0 | | |
| <i>P</i> for trend | | | 0.0276 | | | 0.0223 | | | 0.7595 |
| ALDH2 (rs671) | | | | | | | | | |
| G/G (fast) | 171 | 131.51 | 123.21-139.84 | 114 | 137.86 | 127.18-148.54 | 57 | 117.75 | 104.98-130.52 |
| A/G | 57 | 125.84 | 111.28-140.40 | 42 | 126.65 | 108.93-144.38 | 15 | 128.07 | 102.51-153.63 |
| A/A (slow) | 4 | 100.79 | 45.39-156.18 | 2 | 143.19 | 60.19-226.20 | 2 | 55.01 | -13.87-123.90 |
| <i>P</i> for trend | | | 0.2763 | | | 0.4912 | | | 0.3290 |
| <u>Moderate/heavy (≥ 250ml/wk)</u> | | | | | | | | | |
| ADH1B (rs1229984) | | | | | | | | | |
| A/A (fast) | 394 | 655.96 | 585.48-726.45 | 199 | 630.11 | 566.81-693.42 | 195 | 689.56 | 564.07-815.05 |
| A/G | 324 | 701.19 | 623.37-779.02 | 170 | 664.49 | 596.14-732.83 | 154 | 727.81 | 586.05-869.58 |
| G/G (slow) | 133 | 725.34 | 603.73-846.96 | 46 | 772.91 | 641.82-903.89 | 87 | 708.62 | 520.30-896.94 |
| <i>P</i> for trend | | | 0.2713 | | | 0.0171 | | | 0.4245 |
| ADH1C (rs698) | | | | | | | | | |
| A/A (fast) | 714 | 691.89 | 639.85-743.94 | 349 | 660.27 | 612.85-707.69 | 365 | 722.55 | 631.30-813.80 |
| A/G | 129 | 647.79 | 525.03-770.56 | 63 | 668.43 | 556.55-780.32 | 66 | 623.44 | 408.10-838.79 |
| G/G (slow) | 12 | 637.40 | 235.46-1039.34 | 4 | 525.15 | 81.10-969.19 | 8 | 712.83 | 92.12-1333.53 |
| <i>P</i> for trend | | | 0.7450 | | | 0.8408 | | | 0.4560 |
| ALDH2 (rs671) | | | | | | | | | |
| G/G (fast) | 646 | 720.44 | 665.71-775.16 | 336 | 701.26 | 653.62-748.90 | 310 | 737.73 | 638.08-837.38 |
| A/G | 197 | 578.06 | 478.04-678.09 | 77 | 509.39 | 409.33-609.44 | 120 | 628.64 | 466.78-790.50 |
| A/A (slow) | 16 | 556.78 | 207.59-905.97 | 6 | 365.03 | 2.89-727.18 | 10 | 702.11 | 148.15-1256.06 |
| <i>P</i> for trend | | | 0.0002 | | | <0.001 | | | 0.2009 |

Mean of ml ethanol per week was derived from ANOVA with adjustment on age, gender, study area, smoking pack-years, and case/control status (when appropriate).

P for trend was derived from linear regression with log(ml of ethanol per week) as outcome using a log-additive genetic model.