

Table S.1. Hazard ratio estimates for age-based models for drunkenness, regular drinking, first symptom, reported and perceived tolerance onsets including zygosity and gender interactions.

| Variable                             | Drunk Onset | Regular Drinking Onset | First Symptom Onset | Reported Tolerance Onset | Perceived Tolerance Onset |
|--------------------------------------|-------------|------------------------|---------------------|--------------------------|---------------------------|
| Zygosity                             | 1.02        | 1.04                   | 1.07                | 1.00                     | 1.04                      |
| Gender                               | 1.05        | 1.04                   | 1.03                | 1.05                     | 1.07                      |
| Birth Year                           | 1.00        | 1.00                   | 1.03**              | 1.09**                   | 1.08**                    |
| Initial Alcohol Sensitivity          | 1.01*       | 1.00                   | 1.01                | 1.03**                   | 1.03*                     |
| L1 (WT) Drinking Onset               | 0.93**      | 0.96                   | 1.01                | 1.04                     | 1.01                      |
| L1 (WT) Drinking Onset x Gender      | 0.97        | 0.96                   | 0.95                | 1.00                     | 1.02                      |
| L1 (WT) Drinking Onset x Zygosity    | 0.97        | 0.97                   | 1.09                | 1.04                     | 1.05                      |
| L2 (BT) Drinking Onset               | 0.84**      | 0.96*                  | 1.00                | 0.98                     | 0.98                      |
| L2 (BT) Drinking Onset x Gender      | 0.98        | 0.98                   | 1.02                | 1.00                     | 1.01                      |
| L2 (BT) Drinking Onset x Zygosity    | 0.96**      | 0.99                   | 1.01                | 0.99                     | 0.98                      |
| L1 (WT) Drunkenness Onset            |             | 0.95**                 | 0.91**              | 0.92*                    | 0.92                      |
| L1 (WT) Drunkenness Onset x Gender   |             | 1.01                   | 0.97                | 1.00                     | 1.01                      |
| L1 (WT) Drunkenness Onset x Zygosity |             | 0.97                   | 0.98                | 1.05                     | 1.01                      |
| L2 (BT) Drunkenness Onset            |             | 0.91**                 | 0.88**              | 1.00                     | 0.97                      |
| L2 (BT) Drunkenness Onset x Gender   |             | 0.96*                  | 1.01                | 1.00                     | 0.99                      |
| L2 (BT) Drunkenness Onset x Zygosity |             | 0.94**                 | 0.98                | 1.03                     | 1.00                      |
| L1 (WT) Regular Drinking Onset       |             |                        | 0.91*               | 0.94                     | 0.87**                    |
| L1 (WT) Regular Onset x Gender       |             |                        | 1.03                | 0.99                     | 0.98                      |
| L1 (WT) Regular Onset x Zygosity     |             |                        | 0.93                | 0.95                     | 0.92                      |
| L2 (BT) Regular Drinking Onset       |             |                        | 0.92**              | 0.86**                   | 0.85**                    |
| L2 (BT) Regular Onset x Gender       |             |                        | 0.94                | 0.99                     | 1.01                      |
| L2 (BT) Regular Onset x Zygosity     |             |                        | 1.00                | 1.02                     | 0.97                      |

Note: L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between- twin; \*  $p < .05$ ; \*\*  $p < .01$

Table S.2. Hazard ratio estimates for age-based models for AUD onset including zygosity and gender interactions.

| Variable                                   | AUD   |
|--|-------|
| Zygoty                                     | 0.87  |
| Gender                                     | 0.93  |
| Birth Year                                 | 1.05  |
| Initial Alcohol Sensitivity                | 1.03  |
| L1 (WT) Drinking Onset                     | 0.96  |
| L1 (WT) Drinking Onset x Gender            | 0.96  |
| L1 (WT) Drinking Onset x Zygoty            | 1.14  |
| L2 (BT) Drinking Onset                     | 0.65* |
| L2 (BT) Drinking Onset x Gender            | 1.55* |
| L2 (BT) Drinking Onset x Zygoty            | 0.96  |
| L1 (WT) Drunkenness Onset                  | 1.02  |
| L1 (WT) Drunk Onset x Gender               | 1.12  |
| L1 (WT) Drunk Onset x Zygoty               | 0.98  |
| L2 (BT) Drunkenness Onset                  | 1.63* |
| L2 (BT) Drunk Onset x Gender               | 0.64* |
| L2 (BT) Drunk Onset x Zygoty               | 0.69  |
| L1 (WT) Regular Drinking Onset             | 0.91  |
| L1 (WT) Regular Onset x Gender             | 0.99  |
| L1 (WT) Regular Onset x Zygoty             | 1.00  |
| L2 (BT) Regular Drinking Onset             | 0.76  |
| L2 (BT) Regular Onset x Gender             | 1.08  |
| L2 (BT) Regular Onset x Zygoty             | 1.21  |
| L1 (WT) Reported Tolerance Onset           | 0.93  |
| L1 (WT) Reported Tolerance Onset x Gender  | 1.00  |
| L1 (WT) Reported Tolerance Onset x Zygoty  | 0.92  |
| L2 (BT) Reported Tolerance Onset           | 1.01  |
| L2 (BT) Reported Tolerance Onset x Gender  | 0.88  |
| L2 (BT) Reported Tolerance Onset x Zygoty  | 0.91  |
| L1 (WT) Perceived Tolerance Onset          | 0.88  |
| L1 (WT) Perceived Tolerance Onset x Gender | 0.93  |
| L1 (WT) Perceived Tolerance Onset x Zygoty | 1.21  |

|  |       |
|--|-------|
| L2 (BT) Perceived Tolerance Onset          | 0.74* |
| L2 (BT) Perceived Tolerance Onset x Gender | 1.10  |
| L2 (BT) Perceived Tolerance Onset x Zygoty | 1.11  |
| L1 (WT) First Symptom Onset                | 0.94  |
| L1 (WT) First Symptom Onset x Gender       | 0.97  |
| L1 (WT) First Symptom Onset x Zygoty       | 1.04  |
| L2 (BT) First Symptom Onset                | 0.89* |
| L2 (BT) First Symptom Onset x Gender       | 0.91  |
| L2 (BT) First Symptom Onset x Zygoty       | 0.83  |

Note: L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between- twin; \*  $p < .05$ ; \*\*  $p < .01$

Table S.3. Hazard ratio estimates for original models and models in which predictors and outcome are not equal (model without predictor-outcome ties) for age-based models for drunkenness, regular drinking, first symptom, perceived and reported tolerance.

| Variable                    | Drunkenness Onset |                    | Regular Drinking Onset |                    | First Symptom Onset |                    | Perceived Tolerance Onset |                    | Reported Tolerance Onset |                    |
|-----------------------------|-------------------|--------------------|------------------------|--------------------|---------------------|--------------------|---------------------------|--------------------|--------------------------|--------------------|
|                             | Original Model    | Model Without ties | Original Model         | Model Without ties | Original Model      | Model Without Ties | Original Model            | Model Without Ties | Original Model           | Model Without Ties |
| Zygoty                      | 1.01              | 1.02               | 1.00                   | 1.07               | 1.04                | 1.00               | 1.06                      | 1.05               | 1.01                     | 1.01               |
| Gender                      | 1.01              | 1.05               | 1.00                   | 1.17**             | 1.07                | 1.16*              | 1.08                      | 1.10               | 1.03                     | 1.07               |
| Birth Year                  | 3.37**            | 1.01               | 1.00                   | 1.00               | 0.98**              | 1.06**             | 1.02**                    | 1.08**             | 1.01                     | 1.10**             |
| Initial Alcohol Sensitivity | 1.00              | 1.02**             | 1.00                   | 1.00               | 1.01                | 1.02               | 1.03**                    | 1.02               | 1.02*                    | 1.02*              |
| L1 (WT) Drinking Onset      | 0.96**            | 0.90**             | 0.94**                 | 0.93**             | 0.98**              | 0.97               | 1.02                      | 1.01               | 1.02                     | 1.04*              |
| L2 (BT) Drinking Onset      | 0.96 **           | .81**              | 0.95**                 | 0.91**             | 1.04                | 0.99               | 0.97                      | 0.98               | 0.99                     | 1.00               |
| L1 (WT) Drunkenness Onset   | -                 | -                  | 0.93**                 | 0.96**             | 0.92 **             | 0.89**             | 0.95*                     | 0.96               | 0.96                     | 0.94**             |
| L2 (BT) Drunkenness Onset   | -                 | -                  | 0.95**                 | 0.90**             | 0.90 **             | 0.88**             | 0.98                      | 0.96               | 0.99                     | 0.98               |

|                                   |   |   |   |   |        |        |        |        |        |        |
|-----------------------------------|---|---|---|---|--------|--------|--------|--------|--------|--------|
| L1 (WT) Regular<br>Drinking Onset | - | - | - | - | 0.90** | 0.90** | 0.85** | 0.94** | 0.92** | 0.90** |
| L2 (BT) Regular<br>Drinking Onset | - | - | - | - | 0.89** | 0.90** | 0.83** | 0.83** | 0.88** | 0.86** |

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Note: L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between-twin; \*  $p < .05$ ; \*\*  $p < .01$

Table S.4. Hazard ratio estimates original models and models in which predictors and outcome are not equal (model without predictor-outcome ties) for age-based models AUD onset.

| Variable                          | AUD Onset      |                    |
|-----------------------------------|----------------|--------------------|
|                                   | Original Model | Model Without Ties |
| Zygoty                            | 0.95           | 0.76               |
| Gender                            | 1.08           | 0.91               |
| Birth Year                        | 1.00           | 1.11               |
| Initial Alcohol Sensitivity       | 1.00           | 1.08               |
| L1 (WT) Drinking Onset            | 0.95           | 1.06               |
| L2 (BT) Drinking Onset            | 0.95           | 0.89               |
| L1 (WT) Drunkenness Onset         | 1.15**         | 0.88               |
| L2 (BT) Drunkenness Onset         | 1.07           | 1.26               |
| L1 (WT) Regular Drinking Onset    | 0.97           | 1.09               |
| L2 (BT) Regular Drinking Onset    | 0.98           | 0.81               |
| L1 (WT) Perceived Tolerance Onset | 0.08 **        | 0.98               |
| L2 (BT) Perceived Tolerance Onset | 0.91**         | 0.77**             |
| L1 (WT) Reported Tolerance Onset  | 0.91**         | 1.08               |
| L2 (BT) Reported Tolerance Onset  | 0.88 **        | 1.06               |
| L1 (WT) First symptom Onset       | 0.20 **        | 0.93               |
| L2 (BT) First Symptom Onset       | 0.05 **        | 0.84               |

Note: L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between- twin; \*  $p < .05$ ; \*\*  $p < .01$

Table S.5. Percentage of individuals reporting specific pair-orders of alcohol use milestones.

|                     | Milestone B      |       |       |                |       |       |                    |       |       |                     |       |       |       |       |       |
|---------------------|------------------|-------|-------|----------------|-------|-------|--------------------|-------|-------|---------------------|-------|-------|-------|-------|-------|
|                     | Regular Drinking |       |       | First Symptom* |       |       | Reported Tolerance |       |       | Perceived Tolerance |       |       | AUD   |       |       |
|                     | A < B            | A > B | A = B | A < B          | A > B | A = B | A < B              | A > B | A = B | A < B               | A > B | A = B | A < B | A > B | A = B |
| <b>Milestone A</b>  |                  |       |       |                |       |       |                    |       |       |                     |       |       |       |       |       |
| Drunkenness         | 49.76            | 11.01 | 39.23 | 58.20          | 3.80  | 38.00 | 95.86              | 0.62  | 3.52  | 95.15               | 0.91  | 3.94  | 95.37 | .14   | 4.49  |
| Regular Drinking    | -                | -     | -     | -              | -     | -     | -                  | -     | -     | -                   | -     | -     | -     | -     | -     |
| First Symptom       | 46.46            | 19.72 | 33.82 | -              | -     | -     | -                  | -     | -     | -                   | -     | -     | -     | -     | -     |
| Reported Tolerance  | 93.31            | 0.91  | 5.78  | 7.92           | 78.46 | 13.62 | -                  | -     | -     | -                   | -     | -     | -     | -     | -     |
| Perceived Tolerance | 93.33            | 0.54  | 6.13  | 11.13          | 73.74 | 15.13 | 45.46              | 20.11 | 35.43 | -                   | -     | -     | -     | -     | -     |
| AUD                 | 90.43            | 1.51  | 8.06  | 81.05          | 0.41  | 19.54 | 30.30              | 32.16 | 37.54 | 19.41               | 39.39 | 41.20 | -     | -     | -     |

Note: “Stage A” refers to the first symptom in an A-B order, and “Stage B” refers to the second symptom. L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between- twin; \*  $p < .05$ ; \*\*  $p < .01$ .

\* As “first symptom” is first symptom besides tolerance, there were some negative numbers (in which they did not report another first symptom beyond tolerance)

Table S.6. Hazard ratio estimates for alternative pattern age-based models for perceived and reported tolerance in which AUD is a predictor

| Variable                    | Perceived Tolerance | Reported Tolerance |
|-----------------------------|---------------------|--------------------|
|                             | Onset               | Onset              |
| Zygoty                      | 0.85                | 1.01               |
| Gender                      | 0.88                | 1.06               |
| Birth Year                  | 1.04                | 1.01               |
| Initial Alcohol Sensitivity | 1.01                | 1.00               |

|                                |        |        |
|--------------------------------|--------|--------|
| L1 (WT) Drinking Onset         | 1.05   | 1.03   |
| L2 (BT) Drinking Onset         | 0.97   | 0.99   |
| L1 (WT) Drunkenness Onset      | 0.95   | 1.03   |
| L2 (BT) Drunkenness Onset      | 0.97   | 0.98   |
| L1 (WT) Regular Drinking Onset | 0.87*  | 0.94   |
| L2 (BT) Regular Drinking Onset | 0.91   | 0.99   |
| L1 (WT) AUD Onset              | 0.93*  | 0.92** |
| L2 (BT) AUD Onset              | 0.87** | 0.88** |

Note: L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between- twin; \*  $p < .05$ ; \*\*  $p < .01$

Table S.7. Hazard ratio estimates for time to event models for drunkenness and regular drinking, onsets including zygosity and gender interactions.

| Variable                          | Drinking To Drunkenness | Drinking to Regular Drinking | Drunkenness to Regular Drinking |
|-----------------------------------|-------------------------|------------------------------|---------------------------------|
| Zygosity                          | 1.07                    | 1.04                         | 1.02                            |
| Gender                            | 1.15**                  | 1.07                         | 1.12*                           |
| Birth Year                        | 1.01**                  | 1.00                         | 1.01*                           |
| Initial Alcohol Sensitivity       | 1.02*                   | 1.01                         | 1.01                            |
| L1 (WT) Drinking Onset            | 1.18**                  | 1.35**                       | 1.02                            |
| L1 (WT) Drinking Onset x Time     | 0.96**                  | 0.89**                       | 0.95*                           |
| L1 (WT) Drinking Onset x Gender   | 1.01                    | 1.07*^                       | 0.98                            |
| L1 (WT) Drinking Onset x Zygosity | 0.99                    | 1.03                         | 1.00                            |
| L2 (BT) Drinking Onset            | 1.08**                  | 0.93*                        | 1.03                            |
| L2 (BT) Drinking Onset x Time     | 0.97**                  | 0.85**                       | -                               |
| L2 (BT) Drinking Onset x Gender   | 1.05**                  | 1.06**^                      | 1.01                            |

|                                   |      |        |        |
|-----------------------------------|------|--------|--------|
| L2 (BT) Drinking Onset x Zygosity | 1.01 | 1.03   | 1.00   |
| L1 (WT) Drunkenness Onset         | -    | 0.93*  | 1.14** |
| L1 (WT) Drunk Onset x Time        | -    | -      | -      |
| L1 (WT) Drunk Onset x Gender      | -    | 0.99   | 1.06   |
| L1 (WT) Drunk Onset x Zygosity    | -    | 0.97   | 0.99   |
| L2 (BT) Drunkenness Onset         | -    | 0.85** | 1.05   |
| L2 (BT) Drunk Onset x Time        | -    | 1.07** | -      |
| L2 (BT) Drunk Onset x Gender      | -    | 0.95** | 0.99   |
| L2 (BT) Drunk Onset x Zygosity    | -    | 0.94** | 0.96   |

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^Not significant when all nonsignificant interactions removed from the model, therefore this was not included in the formal models (effect in Drinking to Regular drinking model = HR = 1.04, 95% CI = 1.00 – 1.09;  $p > .05$ )

Note: L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between-twin; \*  $p < .05$ ; \*\*  $p < .01$



Table S.8. Hazard ratio estimates for time to event models for reported and perceived tolerance onsets including zygosity and gender interactions.

| Variable                        | Drinking to Reported Tolerance | Drunkenness to Reported Tolerance | Regular Drinking to Reported Tolerance | Drinking to Perceived Tolerance | Drunkenness to Perceived Tolerance | Regular Drinking to Perceived Tolerance |
|---------------------------------|--------------------------------|-----------------------------------|--|---------------------------------|------------------------------------|---|
| Zygoty                          | 1.00                           | 1.01                              | 1.03                                   | 1.05                            | 1.06                               | 1.05                                    |
| Gender                          | 1.06                           | 1.05                              | 1.03                                   | 1.09                            | 1.08                               | 1.06                                    |
| Birth Year                      | 0.97                           | 1.03                              | 1.06*                                  | 1.08**                          | 1.07**                             | 1.07**                                  |
| Initial Alcohol Sensitivity     | 1.03**                         | 1.03**                            | 1.02**                                 | 1.03*                           | 1.03*                              | 1.03*                                   |
| L1 (WT) Drinking Onset          | 1.28**                         | 1.06                              | 1.10                                   | 1.29**                          | 1.03                               | 1.01                                    |
| L1 (WT) Drinking Onset x Gender | 1.05                           | 1.00                              | 1.02                                   | 1.04                            | 0.99                               | 1.01                                    |
| L1 (WT) Drinking Onset x Zygoty | 1.03                           | 0.99                              | 1.00                                   | 1.01                            | 1.03                               | 1.02                                    |
| L2 (BT) Drinking Onset          | 1.26**                         | 1.12**                            | 1.09                                   | 1.66**                          | 1.09                               | 0.94                                    |
| L2 (BT) Drinking Onset x Time   | -                              | 0.92**                            | 0.94*                                  | 0.87**                          | 0.96                               | 1.01                                    |
| L2 (BT) Drinking Onset x Gender | 1.01                           | 0.99                              | 1.00                                   | 1.00                            | 0.96                               | 0.97                                    |
| L2 (BT) Drinking Onset x Zygoty | 1.02                           | 1.02                              | 1.00                                   | 1.04                            | 0.95                               | 0.99                                    |
| L1 (WT) Drunkenness Onset       | 0.96                           | 1.15**                            | 0.88                                   | 0.94                            | 1.16**                             | 0.93                                    |
| L1 (WT) Drunk Onset x Gender    | 0.98                           | 1.03                              | 1.00                                   | 1.01                            | 1.05                               | 1.02                                    |
| L1 (WT) Drunk Onset x Zygoty    | 1.01                           | 1.05                              | 1.04                                   | 1.04                            | 1.07                               | 1.05                                    |
| L2 (BT) Drunkenness Onset       | 0.99                           | 1.25**                            | 0.89*                                  | 0.97                            | 1.37**                             | 0.94                                    |
| L2 (BT) Drunk Onset x Time      | -                              | -                                 | 1.07*                                  | -                               | 0.91**                             | 1.01                                    |
| L2 (BT) Drunk Onset x Gender    | 1.01                           | 1.04                              | 1.02                                   | 1.00                            | 1.07                               | 1.02                                    |
| L2 (BT) Drunk Onset x Zygoty    | 1.00                           | 1.02                              | 0.97                                   | 1.00                            | 1.01                               | 0.99                                    |
| L1 (WT) Regular Drinking Onset  | 0.96                           | 0.95                              | 1.22**                                 | 0.88**                          | 0.88**                             | 1.11*                                   |
| L1 (WT) Regular Onset x Gender  | 0.97                           | 0.98                              | 1.00                                   | 0.98                            | 0.98                               | 1.02                                    |
| L1 (WT) Regular Onset x Zygoty  | 0.95                           | 0.96                              | 0.93                                   | 0.92                            | 0.93                               | 0.92                                    |
| L2 (BT) Regular Drinking Onset  | 0.85**                         | 0.85                              | 1.17**                                 | 0.85**                          | 0.75**                             | 1.10**                                  |
| L2 (BT) Regular Onset x Time    | -                              | 1.04                              | 0.97                                   | -                               | 1.11**                             | -                                       |
| L2 (BT) Regular Onset x Gender  | 0.98                           | 0.96                              | 0.93                                   | 0.98                            | 0.96                               | 1.02                                    |
| L2 (BT) Regular Onset x Zygoty  | 1.01                           | 0.98                              | 1.02                                   | 1.04                            | 1.01                               | 0.92                                    |

Note: L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between-twin; \*  $p < .05$ ; \*\*  $p < .01$

Table S.9. Hazard ratios for time to event models for first symptom onset including zygoty and gender interactions.

| Variable                         | Drinking to First Symptom | Drunkenness to First Symptom | Regular Drinking to First Symptom |
|----------------------------------|---------------------------|------------------------------|-----------------------------------|
| Zygoty                           | 1.04                      | 1.02                         | 0.97                              |
| Gender                           | 1.08                      | 1.14                         | 1.12                              |
| Birth Year                       | 0.98                      | 1.00                         | 1.02                              |
| Initial Alcohol Sensitivity      | 1.02                      | 1.02                         | 1.01                              |
| L1 (WT) Drinking Onset           | 1.29**                    | 1.07                         | 1.11                              |
| L1 (WT) Drinking Onset x time    | 1.03                      | -                            | -                                 |
| L1 (WT) Drinking Onset x Gender  | 1.02                      | 0.91                         | 0.86*^                            |
| L1 (WT) Drinking Onset x Zygoty  | 1.05                      | 0.97                         | 0.96                              |
| L2 (BT) Drinking Onset           | 1.44**                    | 1.05                         | 1.04                              |
| L2 (BT) Drinking Onset x Time    | 1.07                      | -                            | -                                 |
| L2 (BT) Drinking Onset x Gender  | 1.07*                     | 1.00                         | 0.97                              |
| L2 (BT) Drinking Onset x Zygoty  | 1.01                      | 0.99                         | 1.01                              |
| L1 (WT) Drunkenness Onset        | 0.94**                    | 1.08                         | 0.99                              |
| L1 (WT) Drunkenness Onset x time | 1.03                      | -                            | -                                 |
| L1 (WT) Drunk Onset x Gender     | 0.98                      | 1.04                         | 0.98                              |
| L1 (WT) Drunk Onset x Zygoty     | 0.87                      | 1.02                         | 1.03                              |
| L2 (BT) Drunkenness Onset        | 0.86**                    | 1.17**                       | 0.95                              |
| L2 (BT) Drunk Onset x Time       | 1.07**                    | 0.93**                       | -                                 |
| L2 (BT) Drunk Onset x Gender     | 0.99                      | 1.03                         | 1.03                              |
| L2 (BT) Drunk Onset x Zygoty     | 1.01                      | 1.02                         | 1.07                              |
| L1 (WT) Regular Drinking Onset   | 0.90*                     | 0.91                         | 0.97                              |
| L1 (WT) Regular Onset x Gender   | 1.00                      | 1.04                         | 1.12                              |
| L1 (WT) Regular Onset x Zygoty   | 0.95                      | 0.94                         | 0.95                              |
| L2 (BT) Regular Drinking Onset   | 0.86**                    | 0.82**                       | 1.00                              |
| L2 (BT) Regular Onset x Time     | 1.05*                     | 1.09**                       | -                                 |
| L2 (BT) Regular Onset x Gender   | 0.95                      | 0.98                         | 1.00                              |
| L2 (BT) Regular Onset x Zygoty   | 0.97                      | 1.00                         | 0.96                              |

^Not significant when all nonsignificant interactions removed from the model, therefore this was not included in the formal models (effect in Drinking to Regular drinking model = HR = 0.97, 95%CI = 1.00 – 1.09; p>.05. Note: L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between- twin; \* p<.05; \*\* p<.01

Table S.10. Hazard ratio estimates for time to event models for first symptom onset including zygoty and gender interactions.

| Variable                                  | Drinking to AUD | Drunkenness To AUD | Regular drinking to AUD | Reported Tolerance To AUD | Perceived Tolerance to AUD | First Symptom To AUD |
|---|-----------------|--------------------|-------------------------|---------------------------|----------------------------|----------------------|
| Zygoty                                    | 0.85            | 0.74               | 0.99                    | 1.28                      | 0.99                       | 0.79                 |
| Gender                                    | 1.12            | 1.12               | 0.94                    | 0.91                      | 1.12                       | 1.12                 |
| Birth Year                                | 1.06            | 1.07               | 1.08                    | 1.07                      | 1.06                       | 1.09                 |
| Initial Alcohol Sensitivity               | 1.02            | 1.02               | 1.02                    | 1.18                      | 1.08*                      | 1.03                 |
| L1 (WT) Drinking Onset                    | 1.62*           | 0.92               | 0.85                    | 0.21                      | 0.67*                      | 0.83                 |
| L1 (WT) Drinking Onset x Gender           | 0.84            | 0.94               | 1.06                    | 8.15                      | 1.44                       | 0.98                 |
| L1 (WT) Drinking Onset x Zygoty           | 1.21            | 1.25               | 1.19                    | 0.73                      | 1.19                       | 1.42*                |
| L2 (BT) Drinking Onset                    | 1.65            | 0.60*              | 0.72                    | 2.76                      | 1.00                       | 0.58*                |
| L2 (BT) Drinking Onset x Time             | 0.73**          | -                  | -                       | -                         | -                          | -                    |
| L2 (BT) Drinking Onset x Gender           | 1.72*           | 1.64*              | 1.03                    | 2.03                      | 0.98                       | 1.93**               |
| L2 (BT) Drinking Onset x Zygoty           | 0.95            | 1.06               | 1.39                    | 0.55                      | 0.93                       | 0.94                 |
| L1 (WT) Drunkenness Onset                 | 0.95            | 2.08**             | 1.10                    | 0.50                      | 1.27                       | 0.93                 |
| L1 (WT) Drunk Onset x Gender              | 0.60*           | 1.16               | 0.90                    | 1.48                      | 0.85                       | 1.23                 |
| L1 (WT) Drunk Onset x Zygoty              | 0.98*           | 0.92               | 1.15                    | 0.55                      | 0.86                       | 0.94                 |
| L2 (BT) Drunkenness Onset                 | 1.72*           | 1.02               | 1.49                    | 2.76                      | 1.00                       | 1.51                 |
| L2 (BT) Drunk Onset x Gender              | 1.14            | 0.64               | 0.70                    | 0.56                      | 0.97                       | 0.62                 |
| L2 (BT) Drunk Onset x Zygoty              | 1.03            | 0.84               | 0.95                    | 0.56                      | 1.13                       | 0.86                 |
| L1 (WT) Regular Drinking Onset            | 0.94            | 0.88               | 2.24**                  | 5.11                      | 0.78                       | 1.13                 |
| L1 (WT) Regular Onset x Gender            | 1.06            | 1.03               | 0.96                    | 0.28                      | 1.09                       | 0.87                 |
| L1 (WT) Regular Onset x Zygoty            | 0.92            | 0.85               | 0.91                    | 5.97                      | 1.29                       | 0.90                 |
| L2 (BT) Regular Drinking Onset            | 0.78            | 0.82               | 1.66**                  | 0.21                      | 1.04                       | 0.90                 |
| L2 (BT) Regular Onset x Gender            | 1.16            | 1.14               | 1.04                    | 2.69                      | 1.10                       | 1.01                 |
| L2 (BT) Regular Onset x Zygoty            | 1.17            | 1.14               | 1.24                    | 3.79                      | 1.26                       | 1.19                 |
| L1 (WT) Reported Tolerance Onset          | 0.92            | 0.88               | 0.95                    | 2.07                      | 0.96                       | 0.86                 |
| L1 (WT) Reported Tolerance Onset x Gender | 1.01            | 1.07               | 1.02                    | 0.82                      | 0.97                       | 1.12                 |
| L1 (WT) Reported Tolerance Onset x Zygoty | 0.88            | 0.87               | 0.88                    | 0.88                      | 1.08                       | 0.92                 |
| L2 (BT) Reported Tolerance Onset          | 1.02            | 1.01               | 1.00                    | 3.23                      | 1.04                       | 0.98                 |
| L2 (BT) Reported Tolerance Onset x Gender | 0.90            | 0.93               | 0.93                    | 0.40                      | 0.97                       | 1.02                 |
| L2 (BT) Reported Tolerance Onset x Zygoty | 0.90            | 0.89               | 0.92                    | 2.60                      | 0.89                       | 0.86                 |
| L1 (WT) Perceived Tolerance Onset         | 0.92            | 0.95               | 0.63*                   | 0.62                      | 0.99                       | 0.66*                |

|  |       |        |        |      |       |        |
|--|-------|--------|--------|------|-------|--------|
| L1 (WT) Perceived Tolerance Onset x Gender | 0.88  | 0.86   | 0.98   | 1.93 | 1.25  | 0.92   |
| L1 (WT) Perceived Tolerance Onset x Zygoty | 1.18  | 1.21   | 1.09   | 1.35 | 0.89  | 1.17   |
| L2 (BT) Perceived Tolerance Onset          | 0.70* | 0.67** | 0.55** | 0.23 | 0.76* | 0.60** |
| L2 (BT) Perceived Tolerance Onset x Gender | 1.08  | 1.07   | 1.12   | 2.70 | 1.35* | 1.08   |
| L2 (BT) Perceived Tolerance Onset x Zygoty | 1.21  | 1.30*  | 1.14   | 1.13 | 1.13  | 1.31*  |
| L1 (WT) First Symptom Onset                | 0.66* | 0.76   | 0.84   | 1.15 | 1.06  | 1.36*  |
| L1 (WT) First Symptom Onset x Gender       | 0.96  | 0.94   | 0.93   | 0.64 | 0.88  | 0.94   |
| L1 (WT) First Symptom Onset x Zygoty       | 1.06  | 1.05   | 1.07   | 1.70 | 1.10  | 1.15   |
| L2 (BT) First Symptom Onset                | 0.61* | 1.02   | 1.00   | 1.05 | 1.12  | 1.92** |
| L2 (BT) First Symptom Onset x Gender       | 0.90  | 0.91   | 0.93   | 0.55 | 0.91  | 0.81   |
| L2 (BT) First Symptom Onset x Zygoty       | 0.91  | 0.87   | 0.88   | 2.43 | 0.92  | 0.88   |

Note: L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between-twin; \*  $p < .05$ ; \*\*  $p < .01$

Table S.11. Hazard ratio estimates for original models and models in which predictors and outcome are not equal (model without predictor-outcome ties) for time-to-event for drunkenness and regular drinking.

| Milestone A → Milestone B | Drinking → Drunkenness |                    | Drinking → Regular Drinking |                    | Drunkenness → Regular Drinking |                    |
|---------------------------|------------------------|--------------------|-----------------------------|--------------------|--------------------------------|--------------------|
|                           | Original Model         | Model Without ties | Original Model              | Model Without ties | Original Model                 | Model Without Ties |
| Variable                  |                        |                    |                             |                    |                                |                    |
| Birth year                | 1.01* *                | 1.02**             | 1.00                        | 1.01               | 1.01*                          | 1.01*              |
| Gender                    | 1.07                   | 1.18**             | 1.06                        | 1.10*              | 1.11**                         | 1.11*              |
| Zyosity                   | 1.12**                 | 1.05               | 1.02                        | 1.04               | 1.04                           | 1.04               |
| Drinking Sensitivity      | 1.02*                  | 1.02*              | 1.01                        | 1.01               | 1.01                           | 1.01               |
| L1 Drinking Onset         | 1.18**                 | 1.14**             | 1.55**                      | 1.40**             | 1.02                           | 1.01               |
| L2 Drinking Onset         | 1.10**                 | 1.04*              | 1.64**                      | 1.50**             | 1.04*                          | 1.04*              |
| L1 Drunk Onset            | -                      | -                  | 0.85 **                     | .094*              | 1.17**                         | 1.17**             |
| L2 Drunk Onset            | -                      | -                  | 1.64**                      | 0.83**             | 1.03                           | 1.03               |

Note: all time interactions accounting for violations of proportional hazards as modeled in original models are also included in without-tie models. L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between- twin; \*  $p < .05$ ; \*\*  $p < .01$

Table S.12. Hazard ratio estimates for original models and models in which predictors and outcome are not equal (model without predictor-outcome ties) for time-to-event for perceived tolerance.

| Milestone A → Milestone B | Drinking→ Perceived Tolerance |                    | Drunkenness → Perceived Tolerance |                    | Regular Drinking→ Perceived Tolerance |                    |
|---------------------------|-------------------------------|--------------------|-----------------------------------|--------------------|---------------------------------------|--------------------|
|                           | Original Model                | Model Without ties | Original Model                    | Model Without ties | Original Model                        | Model Without Ties |
| Variable                  |                               |                    |                                   |                    |                                       |                    |
| Birth year                | 1.08**                        | 1.08**             | 1.08**                            | 1.08**             | 1.07**                                | 1.08**             |
| Gender                    | 1.08**                        | 1.11               | 1.12**                            | 1.11               | 1.08                                  | 1.09               |
| Zyosity                   | 1.04                          | 1.05               | 1.08                              | 1.06               | 1.05                                  | 1.04               |
| Drinking Sensitivity      | 1.03**                        | 1.02               | 1.03*                             | 1.03*              | 1.03*                                 | 1.03*              |
| L1 Drinking Onset         | 1.33**                        | 1.32**             | 1.03                              | 1.01               | 1.03                                  | 1.02               |
| L2 Drinking Onset         | 1.56**                        | 1.72**             | 1.01                              | 1.02               | 0.99                                  | 1.00               |
| L1 Drunk Onset            | 0.96                          | 0.96               | 1.24**                            | 1.24**             | 0.96                                  | 0.95               |
| L2 Drunk Onset            | 0.97                          | 0.97               | 1.60**                            | 1.51**             | 0.95                                  | 0.94               |
| L1 Regular Drinking Onset | 0.84**                        | 0.85**             | 0.83**                            | 0.85**             | 1.08**                                | 1.12**             |
| L2 Regular Drinking Onset | 0.85**                        | 0.83**             | 0.66**                            | 0.70**             | 1.10**                                | 1.10**             |

Note: all time interactions accounting for violations of proportional hazards as modeled in original models are also included in without-tie models. L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between- twin; \*  $p < .05$ ; \*\*  $p < .01$

Table S.13. Hazard ratio estimates for original models and models in which predictors and outcome are not equal (model without predictor-outcome ties) for time-to-event for reported tolerance.

| Milestone A → Milestone B<br>Variable | Drinking→ Reported Tolerance |                    | Drunkenness→ Reported Tolerance |                    | Regular Drinking→ Reported Tolerance |                    |
|---------------------------------------|------------------------------|--------------------|---------------------------------|--------------------|--------------------------------------|--------------------|
|                                       | Original Model               | Model Without ties | Original Model                  | Model Without ties | Original Model                       | Model Without Ties |
| Birth year                            | 0.96                         | 0.97               | 1.03                            | 1.00               | 1.06**                               | 1.06*              |
| Gender                                | 1.06                         | 1.07               | 1.07                            | 1.15               | 1.05                                 | 1.06               |
| Zyosity                               | 0.99                         | 1.01               | 1.00                            | 1.00               | 1.00                                 | 1.01               |
| Drinking Sensitivity                  | 1.03**                       | 1.03*              | 1.03**                          | 1.01               | 1.03*                                | 1.02*              |
| L1 Drinking Onset                     | 1.34**                       | 1.35**             | 1.05*                           | 0.99               | 1.12*                                | 1.14*              |
| L2 Drinking Onset                     | 1.29**                       | 1.29**             | 1.13**                          | 1.01               | 1.08*                                | 1.09*              |
| L1 Drunk Onset                        | 0.94*                        | 0.93**             | 1.20**                          | 1.12**             | 0.89*                                | 0.86**             |
| L2 Drunk Onset                        | 1.00                         | 0.99               | 1.28**                          | 1.20**             | 0.90**                               | 0.88**             |
| L1 Regular Drinking Onset             | 0.92**                       | 0.91**             | 0.92**                          | 0.91**             | 1.18**                               | 1.19**             |
| L2 Regular Drinking Onset             | 0.87**                       | 0.86**             | 0.79**                          | 0.81**             | 1.18**                               | 1.18**             |

Note: all time interactions accounting for violations of proportional hazards as modeled in original models are also included in without-tie models L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between- twin; \*  $p < .05$ ; \*\*  $p < .01$

Table S.14. Hazard ratio estimates for original models and models in which predictors and outcome are not equal (model without predictor-outcome ties) for time-to-event for first symptom.

| Milestone A → Milestone B<br>Variable | First Symptom → Drinking |                    | First Symptom → Drunkenness |                    | First Symptom → Regular Drinking |                    |
|---------------------------------------|--------------------------|--------------------|-----------------------------|--------------------|----------------------------------|--------------------|
|                                       | Original Model           | Model Without ties | Original Model              | Model Without ties | Original Model                   | Model Without Ties |
| Birth year                            | 0.98                     | 0.94               | 1.00                        | 1.00               | 1.02                             | 1.02               |
| Gender                                | 1.06                     | 1.11               | 1.13*                       | 1.16               | 1.12                             | 1.15               |
| Zyosity                               | 1.04                     | 1.00               | 1.03                        | 1.00               | 1.00                             | 1.01               |
| Drinking Sensitivity                  | 1.02                     | 1.02               | 1.02                        | 1.01               | 1.00                             | 1.01               |
| L1 Drinking Onset                     | 1.49**                   | 1.30**             | 1.00                        | 0.99               | 0.99                             | 1.01               |
| L2 Drinking Onset                     | 1.66**                   | 1.61**             | 1.04                        | 1.01               | 1.03                             | 1.03               |
| L1 Drunk Onset                        | 0.86**                   | 0.88               | 1.10**                      | 1.12**             | 0.99                             | 0.96               |
| L2 Drunk Onset                        | 0.80**                   | 0.73**             | 1.21**                      | 1.20**             | 0.99                             | 0.98               |
| L1 Regular Drinking Onset             | 0.82**                   | 0.85*              | 0.90**                      | 0.91**             | 1.01                             | 1.02               |
| L2 Regular Drinking Onset             | 0.80**                   | 0.84**             | 0.80**                      | 0.81**             | 0.99                             | 1.00               |

Note: all time interactions accounting for violations of proportional hazards as modeled in original models are also included in without-tie models. L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between-twin; \*  $p < .05$ ; \*\*  $p < .01$



Table S.15. Hazard ratio estimates for original models and models in which predictors and outcome are not equal (model without predictor-outcome ties) for time-to-event for AUD.

| Variable                          | Drinking → AUD |                    | Drunkenness→ AUD |                    | Regular Drinking→ AUD |                    | Reported Tolerance→ AUD |                    | Perceived Tolerance→ AUD |                    | First Symptom→ AUD |                    |
|-----------------------------------|----------------|--------------------|------------------|--------------------|-----------------------|--------------------|-------------------------|--------------------|--------------------------|--------------------|--------------------|--------------------|
|                                   | Original Model | Model Without ties | Original Model   | Model Without ties | Original Model        | Model Without ties | Original Model          | Model Without ties | Original Model           | Model Without ties | Original Model     | Model Without ties |
| Milestone A → Milestone B         |                |                    |                  |                    |                       |                    |                         |                    |                          |                    |                    |                    |
| Zygoty                            | 1.07           | 0.69               | 1.06             | 0.75               | 1.07*                 | 0.85               | 1.10                    | 0.88               | 1.07                     | 0.95               | 1.09*              | 0.80               |
| Gender                            | 0.96           | 0.98               | 0.93             | 1.00               | 0.98                  | 0.88               | 0.75                    | 0.51               | 0.99                     | 0.73               | 0.95               | 1.03               |
| Birth Year                        | 0.88           | 1.12               | 0.86             | 1.10               | 0.85                  | 1.08               | 0.97                    | 1.10               | 0.77                     | 1.09               | 0.81               | 1.10               |
| Initial Alcohol Sensitivity       | 1.02           | 1.07               | 1.03             | 1.07               | 1.02                  | 1.06               | 1.06                    | 1.17               | 1.07**                   | 1.15**             | 1.02               | 1.05               |
| L1 (WT) Drinking Onset            | 1.45**         | 1.67**             | 1.00             | 1.04               | 0.97                  | 1.04               | 1.14                    | 1.07               | 1.00                     | 1.03               | 0.99               | 1.01               |
| L2 (BT) Drinking Onset            | 2.25**         | 4.53**             | 0.93             | 0.92               | 0.94                  | 0.89               | 1.08                    | 0.95               | 0.93                     | 0.79               | 0.94               | 0.91               |
| L1 (WT) Drunkenness Onset         | 1.02           | 0.76               | 2.03**           | 1.62               | 1.06                  | 1.13               | 0.85                    | 0.83               | 1.02                     | 0.92               | 0.98               | 0.89               |
| L2 (BT) Drunkenness Onset         | 1.13           | 1.17               | 1.58**           | 1.77**             | 1.10                  | 1.26               | 1.16                    | 1.39               | 1.05                     | 1.32               | 1.07               | 1.19               |
| L1 (WT) Regular Drinking Onset    | 0.99           | 1.15               | 1.00             | 1.14               | 1.94** <sup>G</sup>   | 1.29               | 1.15                    | 1.68               | 0.95                     | 1.57               | 1.04               | 1.17               |
| L2 (BT) Regular Drinking Onset    | 0.91           | 0.82               | 0.91             | 0.85               | 1.93**                | 1.73               | 0.86                    | 0.91               | 0.93                     | 0.90               | 0.96               | 0.88               |
| L1 (WT) Perceived Tolerance Onset | 0.86**         | 0.99               | 0.87**           | 1.00               | 0.91*                 | 0.96               | 1.10                    | 0.93               | 0.99                     | 1.26*              | 0.90**             | 0.85               |
| L2 (BT) Perceived Tolerance Onset | 0.89**         | 0.77**             | 0.90**           | 0.74**             | 0.92*                 | 0.60**             | 1.17                    | 0.75               | 0.96                     | 0.99               | 0.95               | 0.75**             |

|                                  |        |        |        |      |        |      |      |      |      |      |        |        |
|----------------------------------|--------|--------|--------|------|--------|------|------|------|------|------|--------|--------|
| L1 (WT) Reported Tolerance Onset | 0.90*  | 1.02   | 0.92   | 1.01 | 0.62** | 1.01 | 0.98 | 1.28 | 1.08 | 1.06 | 0.68** | 0.97   |
| L2 (BT) Reported Tolerance Onset | 0.88** | 1.05   | 0.86** | 1.03 | 0.62** | 1.73 | 0.92 | 1.29 | 1.05 | 1.03 | 0.81** | 1.04   |
| L1 (WT) First symptom Onset      | 0.72** | 1.00   | 0.75** | 0.88 | 0.95   | 0.80 | 1.06 | 0.93 | 0.99 | 0.87 | 1.28** | 1.29** |
| L2 (BT) First Symptom Onset      | 0.54** | 0.35** | 0.90** | 0.83 | 0.91** | 0.85 | 1.03 | 1.00 | 0.98 | 0.95 | 1.43** | 1.17   |

Note: all time interactions accounting for violations of proportional hazards as modeled in original models are also included in without-tie models. L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between- twin; \*  $p < .05$ ; \*\*  $p < .01$

Table S.16. Hazard ratio estimates for alternative pattern time-to-event models for perceived and reported tolerance in which AUD is a predictor.

| Milestone A → Milestone B      | Drinking Onset -><br>Perceived<br>Tolerance | Drunkenness -<br>> Perceived<br>Tolerance | Regular Drinking -><br>Perceived Tolerance | Drinking Onset -<br>> Reported<br>Tolerance | Drunkenness Onset -<br>> Reported<br>Tolerance | Regular Drinking<br>Onset -> Reported<br>Tolerance |
|--------------------------------|---|---|--|---|--|--|
| Zygoty                         | 0.87  | 0.93                                      | 0.93                                       | 1.04  | 1.07   | 1.07   |
| Gender                         | 0.92  | 0.91                                      | 0.94                                       | 1.10  | 1.12   | 1.05   |
| Birth Year                     | 1.04  | 1.04                                      | 1.04                                       | 0.89  | 0.99   | 1.02   |
| Initial Alcohol Sensitivity    | 1.00  | 1.00                                      | 1.00                                       | 0.99  | 1.00   | 0.99   |
| L1 (WT) Drinking Onset         | 1.45**                                      | 1.04                                      | 1.03                                       | 1.36**                                      | 1.04   | 1.14   |
| L2 (BT) Drinking Onset         | 1.78**                                      | 0.95                                      | 0.98                                       | 1.34**                                      | 1.33**   | 1.14   |
| L1 (WT) Drunkenness Onset      | 0.96  | 1.34**                                    | 0.95                                       | 1.03  | 1.37**   | 0.86   |
| L2 (BT) Drunkenness Onset      | 0.99  | 2.02**                                    | 1.00                                       | 0.95  | 1.35**   | 0.85   |
| L1 (WT) Regular Drinking Onset | 0.88  | 0.89                                      | 1.23**                                     | 0.94  | 0.91   | 1.24   |
| L2 (BT) Regular Drinking Onset | 0.89*                                       | 0.65**                                    | 1.27**                                     | 0.99  | 0.74*  | 1.34**   |
| L1 (WT) AUD Onset              | 0.92*                                       | 0.93*                                     | 0.94                                       | 0.91**                                      | 0.91**   | 0.91**   |
| L2 (BT) AUD Onset              | 0.88**                                      | 0.88**                                    | 0.88**                                     | 0.87**                                      | 0.87**   | 0.87**   |

Note: L1 = Level 1; L2 = Level 2; WT = Within-twin; BT = between-twin; \*  $p < .05$ ; \*\*  $p < .01$