SUPPLEMENTAL METHODS

Initial screening and enrollment: screening measures

Candidates underwent medical screening with a brief physical assessment, vital signs, a blood draw to confirm normal liver enzyme levels ($\leq$2 SD of normal range), and a urine toxicology screen (cocaine, opiates, benzodiazepines, amphetamines, barbiturates, and PCP) as well as urine pregnancy test for women. They also participated in a series of surveys and interviews to provide background information (see King et al., 2011 for details), drinking patterns [Timeline Follow-back (Sobell et al., 1996) and Alcohol Quantity-Frequency Interview (Cahalan et al., 1969)], and mental health status [Structured Clinical Interview (SCID) non-patient version, alcohol use disorders module (First et al., 2002)].

Laboratory Procedures: pre-session measure details

Participants were also interviewed to confirm their compliance with 3-hour abstinence from food, caffeine, and cigarette use, as well as 24-hour abstinence from alcohol and drugs, with objective verification via breathalyzer (BrAC <.003 g/dl) and urine toxicology (barbiturates, opiates, benzodiazepines, PCP, amphetamines) on at least one randomly selected session. After these procedures, the participant consumed a standard snack at 20% of daily kilocalorie needs per body weight (55% carbohydrates, 10% protein, and 35% fat) (Schofield et al., 1985) followed by a short rest break and completion of the baseline subjective, objective and performance measures.

Beverages: The beverages contained 190-proof ethanol (1% volume for placebo as a taste mask, 16% volume for alcohol beverage) mixed with water, a flavored drink mix, and a sucralose-based sugar substitute. Doses for women were adjusted to 85% of those for men to adjust for sex differences in total body water (Frezza et al., 1990; Sutker et al., 1983). Across the three testing phases, the average total beverage volume prepared was 471 mL,

492 mL, and 500 mL, respectively, reflecting the small increase in weight in participants over time.

Secondary Measures: Secondary measures were general drug and physiological responses, including the DEQ feel drug item ("do you FEEL any drug effects?"), heart rate measured by an automated monitor (General Electric Dynamap® ProCare Auscultatory 100, Tampa, FL USA), and cortisol levels assessed from salivary samples (Salivettes®, Sarstedt AG & Company; Nümbrecht, Germany). The saliva samples were stored at –20°C, and later assayed via an enzyme immunoassay at the University of Chicago CRC Core Laboratory. The inter- and intra-assay coefficients of variation ranged from 6.6 - 7.9% across testing phases.

SUPPLEMENTARY FIGURES AND TABLE

Figure S1: CONSORT diagram of enrollment, follow-up and reexamination phases

Table S1: GEE analysis results of secondary outcomes. Data include feel drug, cortisol, and heart rate at initial, 5- and 10-year reexaminations in AUD+ and AUD- groups at Year 10 AUD symptom trajectory subgroups

Figure S2: BrAC curves. At initial, 5- and 10-year reexaminations in A) AUD+ and AUD- subgroups at Year 10 and B) AUD symptom trajectory subgroups.

Figure S3: Secondary outcomes (feel drug, cortisol, and heart rate) at initial, 5- and 10-year re-examinations in AUD+ and AUD- groups at Year 10. Data are shown as means (SEM) for AUD- and AUD+ groups at initial and reexamination phases. Group assignments were identified based on AUD symptom counts per the DSM-5 at Year 10 of follow-up. Data are change scores (alcohol session minus placebo session) at each time point. GEE results are depicted for group-by-phase, group-by-time, and group-by-phase-by-time effects, see Table S1 for post-estimation testing results.

Fig S4: Secondary outcomes (feel drug, cortisol, and heart rate) at initial, 5- and 10-year reexaminations for AUD symptom trajectory subgroups. Data are shown as means (SEM) for the trajectory subgroups (low/no, intermediate and high AUD symptoms) at initial and reexamination phases. Group assignments were determined based on trajectory analysis of DSM-IV AUD symptom counts over all follow-ups. Data are change scores (alcohol session minus placebo session) at each time point. GEE results are depicted for group-by-phase, group-by-time, and group-by-phase-by-time effects, see Table S1 for post-estimation testing results.

Fig S1: CONSORT

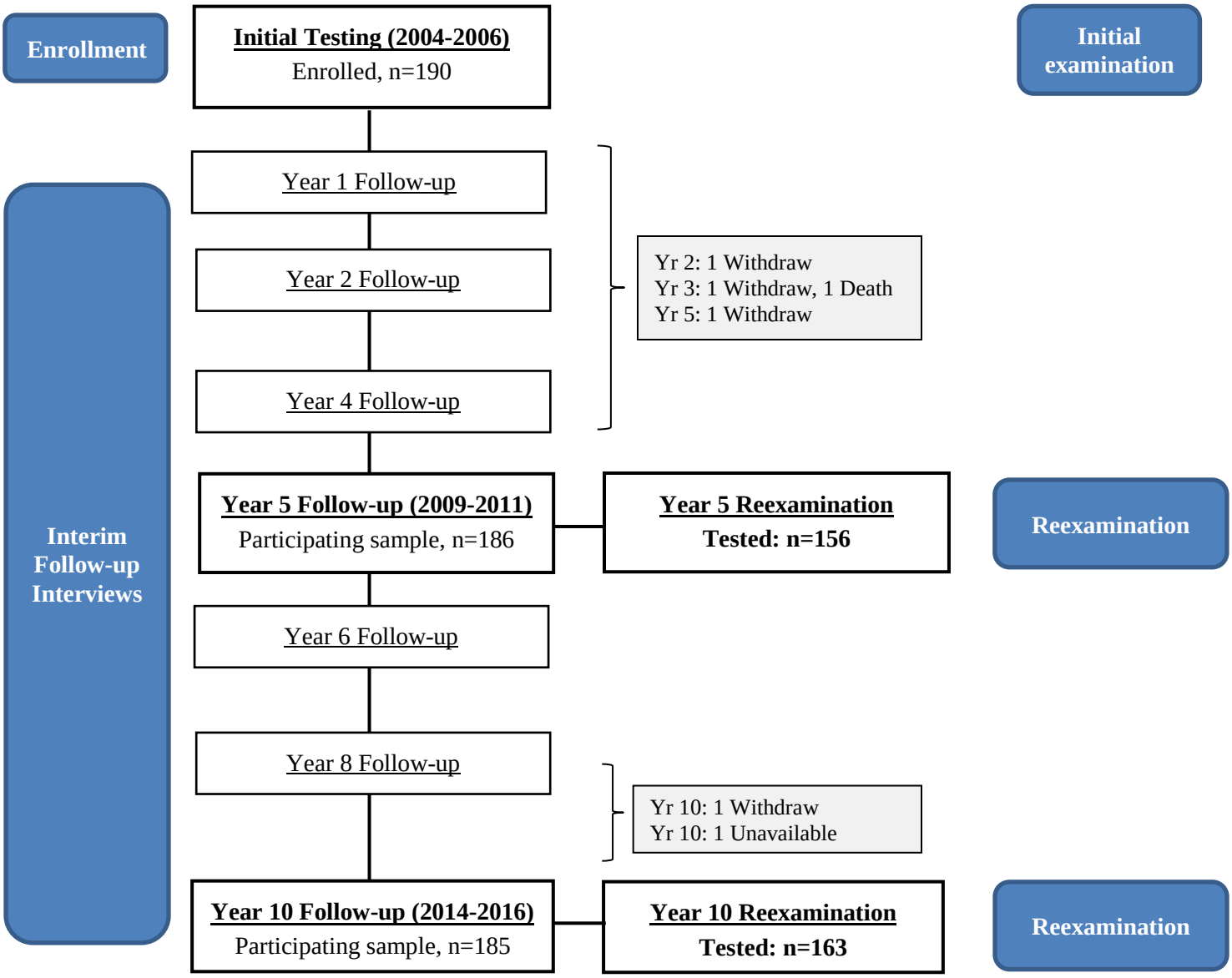

Table S1: GEE Analysis summary of primary and secondary alcohol response outcomes in AUD +/- groups at Year 10 and AUD symptom trajectory subgroups

Secondary Outcomes	AUD group			Time			Phase			AUD group-by-phase interaction			AUD group-by-time interaction			AUD group-by-time-by-phase interaction		
	Coef	**SE**	**p**	**Coef**	**SE**	**p**	**Coef**	**SE**	**p**	**Coef**	**SE**	**p**	**Coef**	**SE**	**p**	**Coef**	**SE**	**p**
Heart Rate	1.103	1.280	0.389	1.627	0.251	**<0.001**	-0.192	0.067	0.004	0.112	0.141	0.428	0.030	0.531	0.955	-0.027	0.083	0.743
Cortisol	0.022	0.037	0.554	0.025	0.009	**0.004**	0.000	0.002	0.977	-0.001	0.005	0.905	-0.016	0.018	0.372	0.001	0.003	0.715
Feeling	-5.335	4.566	0.243	-9.266	0.953	**<0.001**	-0.546	0.270	**0.043**	1.661	0.572	**0.004**	0.855	1.929	0.658	-0.366	0.302	0.226
Secondary Outcomes	**AUD symptom trajectory subgroup**			**Time**			**Phase**			**AUD symptom group-by-phase interaction**			**AUD symptom group-by-time interaction**			**AUD symptom group-by-time-by-phase**		
	Coef	**SE**	**p**	**Coef**	**SE**	**p**	**Coef**	**SE**	**p**	**Coef**	**SE**	**p**	**Coef**	**SE**	**p**	**Coef**	**SE**	**p**
Heart Rate	1.424	0.822	0.083	1.472	0.547	**0.007**	-0.093	0.146	0.524	-0.047	0.086	0.587	0.105	0.323	0.745	-0.006	0.051	0.903
Cortisol	0.031	0.024	0.198	0.060	0.019	**0.002**	0.001	0.005	0.792	-0.001	0.003	0.770	-0.024	0.011	**0.028**	0.002	0.002	0.258
Feeling	-4.791	2.906	0.099	-11.97	1.996	**<0.001**	-1.633	0.591	**0.006**	0.947	0.349	**0.007**	1.902	1.174	0.105	-0.293	0.185	0.112

Note. Generalized Estimating Equations (GEE) analysis. All GEE analysis controlled baseline AUD count, BrAC

Figure S2: BrAC curves. At initial, 5- and 10-year reexaminations in A) AUD+ and AUD- subgroups at Year 10 and B) AUD symptom trajectory subgroups

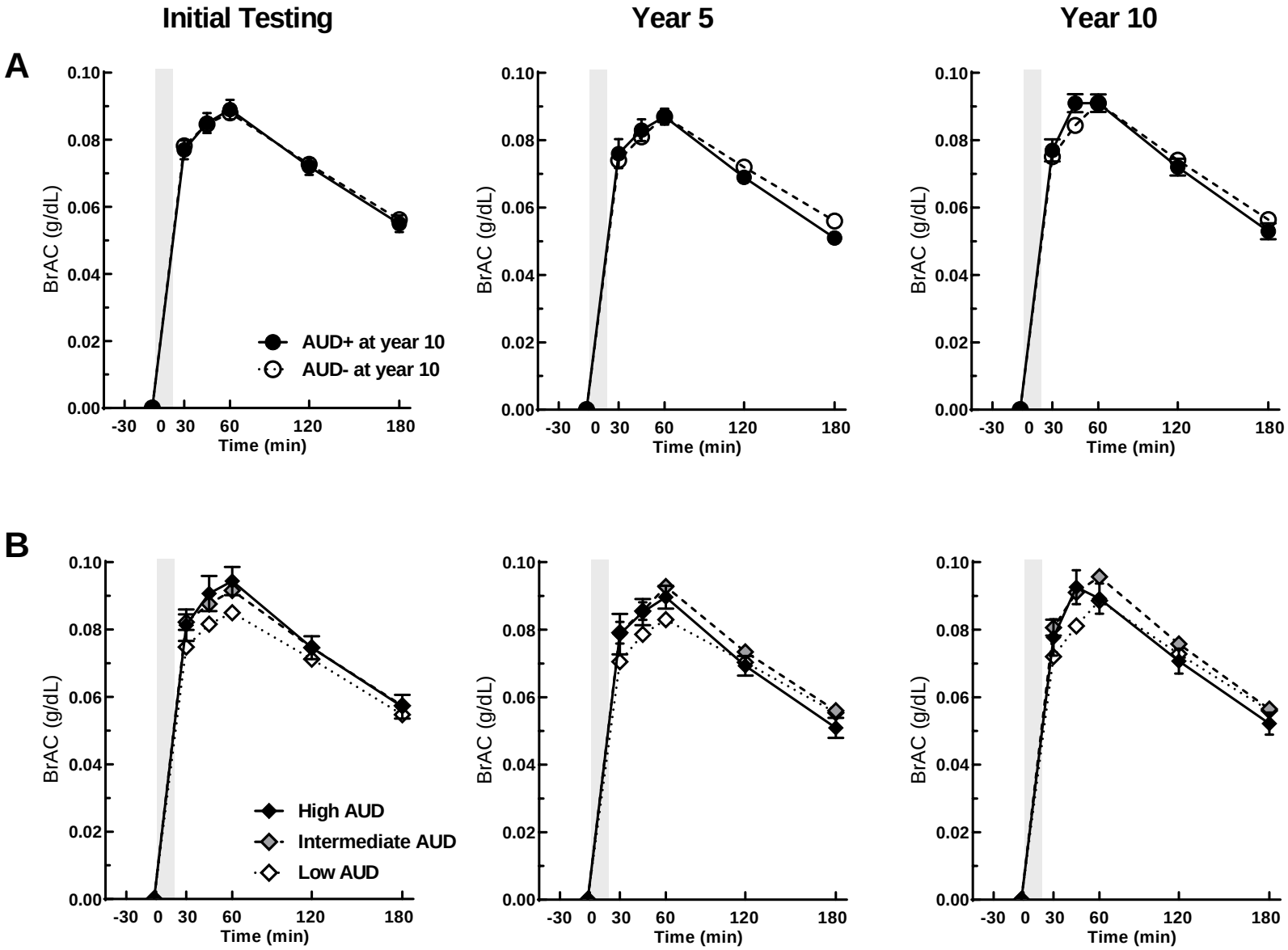

Figure S3: Secondary alcohol responses at initial, 5- and 10-year reexaminations in AUD+ and AUD- subgroups at Year 10

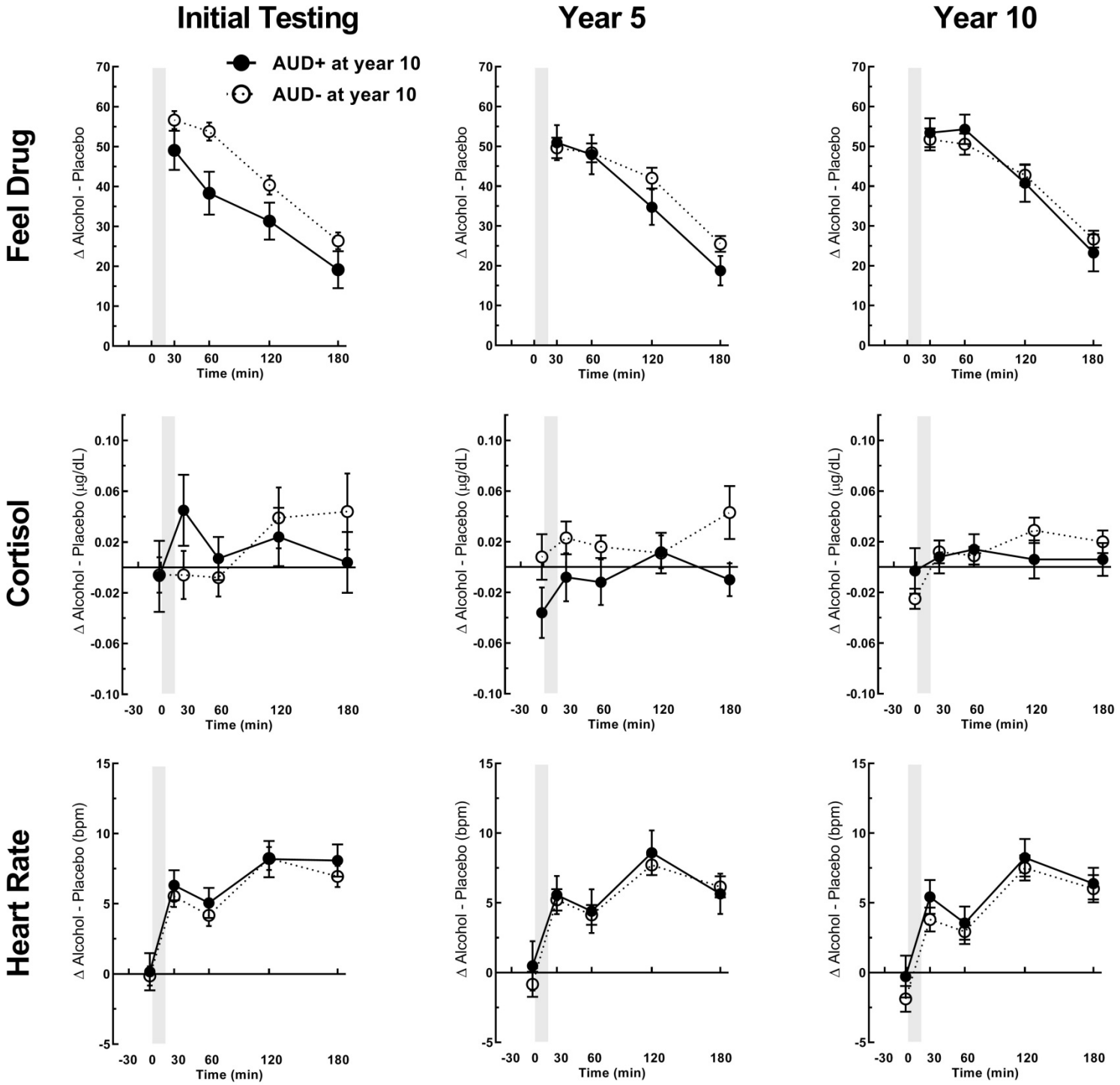

Fig S4: Secondary alcohol responses at initial, 5- and 10-year reexaminations for AUD symptom trajectory subgroups