Supplementary Material for:

Investigating the Influence of Prenatal Androgen Exposure and Sibling Effects on Alcohol Use and Alcohol Use Disorders in Females from Opposite Sex Twin Pairs

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Table S2: Mean and variance difference tests of drinking phenotypes across dizygotic opposite-sex & dizygotic same-sex females matched for the presence of a close-in-age older brother (i.e., the prenatal effects of having a male cotwin, above the postnatal effects of having a close-in-age older brother).

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Table S1: Frequencies and odds ratios of alcohol use disorder symptoms in dizygotic opposite-sex females, dizygotic same-sex females, and dizygotic same-sex females with a close-in-age older (CAO) brother.

	Frequency of Endorsement			Odds Ratios (95% CI)	
Symptom	**Opposite-Sex Females [a]**	**Same-Sex Females [b]**	**Same-Sex Females with a COA Brother [c]**	**Overall Effect**	**Prenatal Effect**
Tolerance (e.g., need for markedly increased amounts of alcohol to achieve desired effect)	18.8%	15.7%	14.7%	1.24 (0.92, 1.68)	1.35 (0.73, 2.49)
Withdrawal (e.g., alcohol is taken to relieve withdrawal symptoms)	5.3%	4.0%	3.9%	1.33 (0.83, 2.15)	1.39 (0.54, 3.57)
Alcohol taken in larger amounts or over a longer period than intended.	44.8%	39.1%	37.2%	1.26 (1.02, 1.56)*	1.37 (0.90, 2.09)
A persistent desire or unsuccessful efforts to cut down or control use.	8.1%	5.8%	8.5%	1.42 (0.95, 2.13)	0.94 (0.49, 1.82)
A great deal of time is spent obtaining, using, or recovering from use.	8.8%	5.0%	3.7%	1.84 (1.16, 2.90)*	2.54 (0.92, 7.06)
Important activities (e.g., occupational) are given up or reduced because of use.	4.0%	3.3%	2.8%	1.25 (0.69, 2.26)	1.48 (0.44, 4.98)

Use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is caused or exacerbated by alcohol use.	7.5%	6.9%	8.3%	1.09	(0.71, 1.68)	0.90	(0.40, 2.00)
Recurrent use resulting in failure to fulfill major role obligations (e.g., repeated absences or poor work performance).	12.1%	7.8%	10.1%	1.63	(1.16, 2.31)*	1.23	(0.65, 2.32)
Recurrent use in situations in which it is physically hazardous (e.g., driving an automobile).	12.7%	9.5%	11.6%	1.39	(1.00, 1.93)	1.11	(0.61, 2.03)
Recurrent alcohol-related legal problems.	1.6%	0.8%	0.8%	2.12	(0.81, 5.60)	2.10	(0.27, 16.41)
Continued use despite persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of use.	6.4%	5.4%	3.9%	1.22	(0.79, 1.87)	1.71	(0.67, 4.33)

[a] 621 twin pairs

[b] 459 twin pairs

[c] 65 twin pairs

* $p < .05$

Overall Effect: Opposite-sex females vs. same-sex females

Prenatal Effect: Opposite-sex females vs. same-sex females with a close-in-age older brother

NOTE: Frequencies were obtained using PROC SURVEYFREQ and odds ratios were obtained using PROC SURVEYLOGISTIC in SAS (version 9.2), both accounting for participants clustered within families (SAS Institute Inc., Cary, North Carolina). All odds ratios are presented such that an estimate greater than one indicates a greater prevalence in the group hypothesized to be masculinized (opposite-sex females). For the overall effect, there were significant differences in the endorsement of three symptoms, all of which were more prevalent in opposite-sex females: (1) Alcohol taken in larger amounts or over a longer period than intended; (2) A great deal of time is spent obtaining, using, or recovering from use; and (3) Recurrent use resulting in failure to fulfill major role obligations. For the prenatal effect, there were no significant differences in the endorsement of any symptom, but the magnitude of odds ratio estimates was the same size or larger for several symptoms.

Table S2: Mean and variance difference tests of drinking phenotypes across dizygotic opposite-sex & dizygotic same-sex females matched for the presence of a close-in-age older (CAO) brother.

	Means (SD)				Mean Differences Tests		Variance Differences Tests		Effect Sizes
Phenotype	**Opposite-Sex Females with a CAO Brother [a]**		**Same-Sex Females with a CAO Brother [b]**		χ^2	***p*-value**	χ^2	***p*-value**	***d***
Drinking Frequency [c]	158.28	(114.94)	133.89	(111.00)	1.06	0.30	0.09	0.76	0.16
Intoxication Frequency [c]	44.26	(75.92)	34.78	(65.19)	0.45	0.50	0.05	0.83	0.10
Hangover Frequency [c]	32.40	(59.76)	27.08	(55.97)	0.29	0.59	0.02	0.90	0.08
Drink Quantity	4.28	(3.30)	3.75	(2.99)	0.44	0.51	0.14	0.71	0.10
Max Drinks	12.71	(8.49)	10.09	(6.43)	5.90	0.02	0.16	0.69	0.37
Lifetime AUD Symptoms	1.47	(2.06)	1.01	(1.74)	3.35	0.07	0.88	0.35	0.27

[a] 83 twin pairs

[b] 65 twin pairs

[c] All frequency phenotypes are measured in days per year.

NOTE: Means and standard deviations presented are based on raw data, statistical tests and effect sizes were based on log-transformed data. The twin pair covariance was included in all analyses to account for the non-independence of having data for two participants from the same family. Results suggest that prenatal androgenization (i.e., hypermasculinization of opposite-sex females) has medium effects on max drinks and lifetime AUD symptoms, above the postnatal effects of having a CAO brother.

Table S3: Mean and variance difference tests of drinking phenotypes across dizygotic opposite-sex females with a close-in-age older (CAO) brother and without any brother.

	Means (SD)				Mean Differences Tests		Variance Differences Tests		Effect Sizes
Phenotype	**Opposite-Sex Females with a CAO Brother [a]**		**Opposite-Sex Females without a Brother [b]**		χ^2	***p*-value**	χ^2	***p*-value**	***d***
Drinking Frequency [c]	158.28	(114.94)	132.14	(106.2)	2.38	0.12	0.48	0.49	0.20
Intoxication Frequency [c]	44.26	(75.92)	26.58	(52.95)	1.68	0.20	2.29	0.13	0.18
Hangover Frequency [c]	32.40	(59.76)	19.63	(45.28)	2.56	0.11	0.06	0.81	0.21
Drink Quantity	4.28	(3.3)	3.42	(2.61)	3.37	0.07	0.97	0.33	0.25
Max Drinks	12.71	(8.49)	9.69	(7.24)	12.34	<.01	1.18	0.28	0.45
Lifetime AUD Symptoms	1.47	(2.06)	1.18	(1.92)	1.50	0.22	0.51	0.48	0.13

[a] 83 twin pairs

[b] 199 twin pairs

[c] All frequency phenotypes are measured in days per year.

NOTE: Means and standard deviations presented are based on raw data, statistical tests and effect sizes were based on log-transformed data. The twin pair covariance was included in all analyses to account for the non-independence of having data for two participants from the same family. Results suggest that having a CAO brother has medium (e.g., drinking quantity and frequency) to large (max drinks) effects, above the prenatal effects of having a male-cotwin.

Table S4: Mean and variance difference tests of drinking phenotypes across dizygotic opposite-sex & dizygotic same-sex males.

	Means (SD)				Mean Differences Tests		Variance Differences Tests		Effect Sizes
Phenotype	**Opposite-Sex Males** [a]		**Same-Sex Males** [b]		χ^2	***p*-value**	χ^2	***p*-value**	***d***
Drinking Frequency [c]	174.15	(115.36)	164.20	(109.78)	0.48	0.49	0.16	0.69	-0.03
Intoxication Frequency [c]	50.35	(76.32)	51.31	(71.22)	0.52	0.47	0.62	0.43	0.04
Hangover Frequency [c]	31.26	(53.07)	34.53	(54.55)	0.86	0.35	0.06	0.81	0.05
Drink Quantity	5.38	(4.01)	5.71	(4.18)	0.99	0.32	0.04	0.83	0.06
Max Drinks	23.86	(14.26)	23.60	(13.72)	0.02	0.89	0.03	0.86	-0.01
Lifetime AUD Symptoms	1.86	(2.32)	1.91	(2.28)	0.91	0.34	0.05	0.82	0.06

[a] 520 twin pairs

[b] 443 twin pairs

[c] All frequency phenotypes are measured in days per year.

NOTE: Means and standard deviations presented are based on raw data, and statistical tests and effect sizes were based on log-transformed data. The twin pair covariance was included in all analyses to account for the non-independence of having data for two participants from the same family. Analyses yielded no significant differences between opposite-sex males (OSMs) and same-sex males (SSMs). Results are inconsistent with an effect of prenatal androgenization (i.e., hypermasculinization of SSMs) or prenatal estrogenization (i.e., feminization of OSMs) on alcohol use or lifetime AUD symptoms.

Table S5: Mean and variance difference tests of drinking phenotypes across dizygotic opposite-sex & dizygotic same-sex males matched for the presence of a close-in-age older (CAO) brother.

	Means (SD)				Mean Differences Tests		Variance Differences Tests		Effect Sizes
Phenotype	**Opposite-Sex Males with a CAO Brother [a]**		**Same-Sex Males with a CAO Brother [b]**		χ^2	***p*-value**	χ^2	***p*-value**	***d***
Drinking Frequency [c]	180.93	(115.17)	156.20	(106.44)	2.00	0.16	1.94	0.16	-0.22
Intoxication Frequency [c]	54.68	(77.36)	48.41	(62.37)	0.14	0.71	0.02	0.90	-0.06
Hangover Frequency [c]	29.81	(42.33)	27.82	(42.45)	0.01	0.94	0.03	0.85	-0.01
Drink Quantity	5.43	(4.20)	5.74	(3.57)	0.04	0.85	0.09	0.77	-0.03
Max Drinks	22.91	(13.8)	25.17	(15.00)	0.03	0.87	12.35	<.01	0.02
Lifetime AUD Symptoms	1.78	(2.09)	1.92	(2.20)	0.12	0.72	0.07	0.79	0.05

[a] 74 twin pairs

[b] 74 twin pairs

[c] All frequency phenotypes are measured in days per year.

NOTE: Means and standard deviations presented are based on raw data, and statistical tests and effect sizes were based on log-transformed data. The twin pair covariance was included in all analyses to account for the non-independence of having data for two participants from the same family. Analyses yielded no significant differences between opposite-sex males (OSMs) and same-sex males (SSMs). Results are inconsistent with an effect of prenatal androgenization (i.e., hypermasculinization of SSMs) or prenatal estrogenization (i.e., feminization of OSMs) on alcohol use or lifetime AUD symptoms.