Supplemental Materials for

An Epidemiologic, Longitudinal, and Discordant Twin Study of the Association Between Gambling Disorder and Suicidal Behaviors

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rable 51. Enterine prevalence of gamoning disorder symptoms and associations with sulcidar behaviors.											
	Lifetime prevalence		Assoc	viation with	Asso	ciation with	Association with				
Gambling disorder symptom			suicid	al thoughts	suio	cidal plans	suicide attempt				
			n = 21	n = 2169 affected		64 affected	n = 336 affected				
	%	n	OR	95% CI	OR	95% CI	OR	95% CI			
D5-1: tolerance	2.01	167	2.36	1.74, 3.22	2.37	1.51, 3.72	2.79	1.63, 4.77			
D5-2: restless or irritable	2.29	191	2.54	1.91, 3.38	3.47	2.38, 5.05	2.89	1.77, 4.74			
D5-3: efforts to control	1.21	101	2.83	1.93, 4.12	4.44	2.79, 7.05	2.97	1.51, 5.84			
D5-4: preoccupation	4.76	396	1.75	1.41, 2.17	2.30	1.69, 3.13	1.88	1.25, 2.84			
D5-5: gambles when distressed	5.15	429	2.85	2.34, 3.47	3.51	2.69, 4.58	2.89	2.06, 4.06			
D5-6: chases losses	5.33	444	1.83	1.49, 2.24	2.23	1.66, 3.03	2.01	1.37, 2.94			
D5-7: lies about gambling	3.11	259	1.43	1.09, 1.87	1.85	1.23, 2.77	1.94	1.17, 3.19			
D5-8: problems at home. school, or work	1.10	92	2.75	1.82, 4.16	4.46	2.73, 7.30	3.31	1.74, 6.28			
D5-9: bail out	1.22	102	2.66	1.78, 3.97	3.23	1.89, 5.50	4.60	2.64, 7.99			
D4-8: illegal acts (dropped from DSM-5)	0.31	26	2.44	1.13, 5.29	8.74	3.96, 19.30	7.25	2.89, 18.17			

Table S1. Lifetime prevalence of gambling disorder symptoms and associations with suicidal behaviors.

Note: ATR-II and ATR-III samples, N = 8,327; D5 = DSM-5, D4 = DSM-IV, OR = odds ratio, CI = confidence interval; all associations are significant at p < .05.

involvement in specific gambling activities (more than 100 days) with suicide plan or attempt.										
	Lifetime	prevalence	Asso	ciation with						
	Ever	More than 100 days	suicide $n = 4$	plan or attempt 24 affected						
Gambling activity	%	%	OR	95% CI						
lottery	90.25	24.66	0.88	0.70, 1.12						
scratch tickets	85.93	8.34	1.09	0.77, 1.54						
electronic gaming machines	87.78	7.73	1.66*	1.20, 2.29						
horse or dog races	75.32	5.48	0.84	0.53, 1.35						
casino table games	46.35	1.65	0.70	0.28, 1.74						
keno at a club, hotel, or casino	44.30	2.29	0.81	0.39, 1.69						
bingo at a club or hall	33.53	2.25	1.31	0.72, 2.41						
card games (not at a casino)	28.14	2.60	1.00	0.53, 1.89						
betting on sporting event	14.09	1.54	0.60	0.22, 1.66						
betting on games of skill	9.05	0.84	1.52	0.59, 3.92						
casino games on the internet	0.92	0.11	2.42	0.27, 21.74						
Note: ATR-II sample, $N = 4,542$; * $p = .002$										

Table S2. Lifetime gambling activity involvement and the association of recurrent involvement in specific gambling activities (more than 100 days) with suicide plan or attempt

	Lifetime number of disordered gambling symptoms									
	0 symptoms (n = 1168)	1-3 symptoms (n = 179)	4+ symptoms DSM-5 gambling disorder (n = 78)							
Current age	37.70	37.42	37.44							
Age peak gambling	23.77	25.58	27.29							
Hours spent	59.33	314.05	692.14							
Dollars spent	1,769.65	25,842.88	72,355.77							
Household income	87,873.79	83,502.86	70,266.23							
% of income spent	3%	40%	105%							

Table S3. Costliness of disordered gambling: time and money spent on gambling during the year when gambling participation was at its peak

Note: ATR-II sample; Household income was for the past year, time and money spent was for the year of peak gambling, disordered gambling symptoms are lifetime

Measures (Table S3)

The <u>age of peak gambling</u> was assessed with the question "Think about the 12-month period in your life when you were gambling the most. How old were you when that period began?"

The <u>number of days</u> gambling during the period of peak gambling was assessed with the question "how frequently were you gambling during that time?" with 14 available response options ranging from every day to 1 day. The variable ranged from 1-365.

The typical number of hours spent during the period of peak gambling was assessed with the question "during that period when you were gambling the most, how much time would you spend on gambling, on a typical day when you gambled?"

The typical number of dollars spent during the period of peak gambling was assessed with the question "during that period when you were gambling the most, how much money would you spend on gambling, on a typical day when you gambled? (By money spent on gambling, I mean the total amount that you started out with at the beginning of the day minus the total amount that you ended up with at the end of the day on a typical day during that period when you were gambling the most) with 10 response options ranging from less than \$1 to \$10,001 or more.

The <u>hours spent</u> during the peak gambling period was computed as the number of days multiplied by the typical number of hours.

The <u>dollars spent</u> during the peak gambling period was computed as the number of days multiplied by the typical number of dollars.

			Twin 2	2										
			disord	ered gar	nbling	sympto	m cour	nt						
			0	1	2	3	4	5	6	7	8	9		
n 1	unt	0	1940	87	20	14	6	5	6	4	5	1	2088	
Twi	m co	1	95	17	6	2	0	1	1	0	0	1	123	
	npto	2	23	6	0	3	0	0	3	2	1	0	38	
	g syr	g syn	3	12	3	0	1	0	2	1	0	0	0	19
	hlin	4	9	0	1	1	0	0	1	1	0	0	13	
	l gan	5	7	1	0	1	1	0	0	0	0	0	10	
	derec	6	2	0	0	1	0	0	1	0	0	0	4	
	lisor	7	2	0	2	0	0	1	0	0	0	1	6	
	0	8	2	0	0	0	0	0	0	0	0	0	2	
		9	7	0	0	0	0	0	1	1	0	0	9	
			2099	114	29	23	7	9	14	8	6	3	2312	

Table S4. Crosstabulation of twin pair disordered gambling symptom counts

Note: ATR-II and ATR-III same-sex twin pairs

Discordant pairs are in cells with yellow fill, concordant unaffected pairs are in cells with light gray fill, concordant affected pairs are in cells with dark gray fill.

Use of Continuous or Categorical Disordered Gambling Phenotypes to Identify Discordant **Twin Pairs (Table S4)**

There were essentially three types of discordant pairs: (1) the most common type of discordant twin pair was one in which one twin had zero symptoms and the other had one symptom (n=182), (2) the next most common type of discordant twin pair was one in which one twin had zero symptoms and the other had between 2-9 symptoms (n=125), (3) the least common type of discordant pair was one in which both twins had 1 or more symptoms, but differed on the number (n=65). Note that the first two types of discordant pairs based on symptom counts would also be considered discordant based on the designation of affected versus unaffected on a binary categorical disordered gambling phenotype. The only difference lies with the least common type of twin discordance. Because it was not clear that the difference between having, for example, 2 versus 1 symptoms was qualitatively equivalent to having 1 versus 0 symptoms, we elected to use a binary categorical disordered gambling phenotype to identify discordant pairs.

able 55. Results of Miz-only multilevel discordant twin analyses predicting suchdar moughts, plans, and attempts from disordered gamoning.													
	Suicidal thoughts				1	Suicide plan				Suicide attempt			
		n = 842	affected		Ţ	n = 2	5 affected		n = 136 affected				
Predictor	Base	model	Fully	adjusted	Bas	se model	Fully	v adjusted	Ba	ase model	Full	y adjusted	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	
Sex	1.51**	1.12, 2.04	1.19	0.85, 1.65	1.65	0.57, 4.73	1.68	0.50, 5.59	2.50	0.62, 10.07	4.66	0.80, 27.07	
Age	1.00	0.96, 1.04	1.00	0.96, 1.04	1.03	0.91, 1.17	1.04	0.91, 1.20	0.97	0.83, 1.13	0.99	0.83, 1.18	
Childhood SES	0.87	0.69, 1.11	0.96	0.76, 1.21	1.65	0.78, 3.47	1.91	0.87, 4.17	1.40	0.57, 3.46	1.45	0.56, 3.74	
Adult income	0.86***	0.81, 0.91	0.90***	0.85, 0.95	0.77**	0.66, 0.90	0.79**	0.66, 0.94	0.87	0.72, 1.05	0.97	0.78, 1.21	
Education	1.17**	1.05, 1.30	1.24***	1.11, 1.39	1.26	0.91, 1.74	1.37	0.96, 1.94	0.74	0.50, 1.10	0.81	0.53, 1.24	
WP disordered gambling	1.62	0.92, 2.86	1.54	0.85, 2.81	1.22	0.28, 5.34	0.94	0.20, 4.47	8.15*	1.17, 56.54	5.61	0.83, 37.85	
BP disordered gambling	4.73***	2.64, 8.45			3.71	0.69, 20.10	1.99	0.31, 12.91	1.68	0.18, 16.12	0.60	0.05, 7.12	
BP * sex interaction			3.36*	1.12, 10.09									
Major depression			6.56***	4.89, 8.81			13.54***	5.87, 31.25			13.22***	4.51, 38.73	
Alcohol use disorder			1.48**	1.10, 2.00			1.04	0.44, 2.49			1.40	0.48, 4.12	
Cannabis use disorder			1.97***	1.33, 2.93			2.87*	1.04, 7.91			4.95*	1.46, 16.75	
Nicotine dependence			1.30	0.96, 1.77			0.68	0.26, 1.80			1.89	0.60, 5.94	
Conduct disorder			3.37***	2.14, 5.30			6.45**	2.05, 20.27			7.01**	1.82, 27.04	

Table S5. Results of MZ-only multilevel discordant twin analyses predicting suicidal thoughts, plans, and attempts from disordered gambling.

Note: ATR-II and ATR-III samples; N=3,414 individual twins in each set of analyses, OR = odds ratio, CI = confidence interval, WP = within-pair, BP = between-pair.

* = p < .05, ** = p < .01, *** = p < .001

attempt from disordered gamoning in the full samples (All) and resulted to mose with a mistory of suicidal modglits (W/ST).										
		Suic	ide plan			Suicide	attempt			
	Base	model	Fully	adjusted	Base	model	Fully a	djusted		
	All	W/ST	All	W/ST	All	W/ST	All	W/ST		
PANEL A				Individual Lev	el Models					
N individuals	7,856	2,033	7,856	2,033	7,856	2033	7,856	2033		
N affected	531	531	531	531	317	314	317	314		
Predictor										
Sex	0.81	1.12	0.75	1.12	0.99	1.62	1.64	2.37		
Age	0.98	1.00	0.97	1.00	0.94	0.93	0.94	0.94		
Zygosity	0.84	0.93	1.02	1.06	0.91	0.90	1.01	1.13		
Childhood SES	1.07	0.91	1.51	0.95	0.90	0.65	0.94	0.73		
Adult income	0.76***	0.88***	0.77***	0.90***	0.74***	0.78**	0.80**	0.81*		
Education	1.21	1.04	1.24	1.07	0.89	0.80	0.93	0.83		
Disordered gambling	3.31***	1.49*	2.35*	1.09*	3.76**	2.31	1.98	1.20		
Major depression			52.61***	2.38***			50.23***	4.93**		
Alcohol use disorder			2.01*	1.32*			1.69	0.55		
Cannabis use disorder			1.89	1.08			4.31***	2.76		
Nicotine dependence			0.81	1.02			1.20	1.06		
Conduct disorder			5.60***	1.50*			5.25***	4.50*		
PANEL B			MZ and DZ	Z Multilevel Dis	cordant Tw	in Models				
N individuals	6,016	1,525	6,016	1,525	6,016	1,525	6,016	1,525		
N affected	382	382	382	382	233	234	233	234		
Predictor										
Sex	1.49	1.38	1.29	1.27	1.79	1.90	2.58	2.48		
Age	1.00	1.00	1.00	1.00	0.95	0.90	0.96	0.93		
Zygosity	0.87	0.94	0.86	0.94	1.08	1.09	1.14	1.06		
Childhood SES	1.05	0.84	1.31	0.90	1.19	0.91	1.48	1.17		
Adult income	0.74***	0.89***	0.76***	0.91**	0.74***	0.70***	0.81*	0.73*		
Education	1.29*	1.06	1.31*	1.09	0.88	0.72	0.93	0.75		
WP disordered gambling	1.48	0.86	1.07	0.86	5.63*	13.85*	2.70	12.48		
WP x sex interaction					0.04*	0.04*	0.25	0.25		
BP disordered gambling	3.76*	2.10*	1.9	1.79	1.78	0.71	0.88	0.46		
Major depression			22.99***	2.78***			20.88***	5.70**		
Alcohol use disorder			1.65	1.23			2.10	0.78		
Cannabis use disorder			1.32	1.04			4.59**	3.79		
Nicotine dependence			1.17	1.06			1.29	1.06		
Conduct disorder			3.23**	1.46			3.09*	3.20		

Table S6. Results of individual level (Panel A) and multilevel discordant twin (Panel B) analyses predicting suicide plan and attempt from disordered gambling in the full samples (All) and restricted to those with a history of suicidal thoughts (W/ST).

Note: ST = suicidal thoughts, WP = within-pair, BP = between-pair, * = p < .05, ** = p < .01, *** = p < .001

	Mono	zygotic	Dizy	gotic							
	Men	Women	Men	Women							
	N = 500	N = 903	N = 327	N = 647							
	pairs	pairs	pairs	pairs							
Within-trait correlations											
Disordered gambling	0.48	0.60	0.23	0.23							
Suicidal thoughts	0.41	0.59	0.12	0.13							
Suicidal plan	0.58	0.47	0.30	0.32							
Suicide attempt	0.57	0.41	0.28	0.47							
Cross-t	rait correlations with	h disordered ga	mbling	I							
Suicidal thoughts	0.09	0.25	-0.03	0.08							
Suicidal plan	0.13	0.23	0.19	0.12							
	0.03	0.17	0.03	0.17							

Twin correlations (Table S7)

Twin correlations in liability were estimated and biometric modeling was conducted in Mplus (Muthén & Muthén, 2017). In a twin study, one compares the similarity of MZ twins, who share 100% of their genetic information, to the similarity of DZ twins, who share on average 50% of their genetic information (specifically, the genetic information that varies in the population). When MZ twin pairs are more similar than DZ twin pairs, one can infer that there is a contribution of genetic factors to a trait. If the DZ twin similarity is greater than half the MZ twin similarity, then one can infer that shared environmental influences contribute to individual differences in a trait. A contribution of unique (individual-specific) environmental influences is inferred when the MZ twin similarity is less than 1.0 (this also includes measurement error). This is the contribution to individual differences that is not shared by twins and cannot be explained by genes or common environments.

The within-trait twin correlations for disordered gambling were greater among MZ twins than among DZ twins, indicating that genetic factors likely contribute to disordered gambling liability. The within-trait twin correlations for suicidal thoughts and plan were also greater among MZ than among DZ twins in both men and women, again supporting the importance of genetic factors. However, the MZ and DZ twin correlations for suicide attempt among women were nearly equivalent, suggesting the importance of shared environmental influences in the propensity to attempt suicide among women (top panel of Table S7).

Among women, the cross-trait twin correlations were larger among MZ than DZ pairs for suicidal thoughts and plan, but not for suicide attempt; this pattern of findings suggests that shared genetic influences may contribute to the overlap between disordered gambling and suicidal thoughts and suicide plan, but that shared environmental influences may contribute to the overlap between disordered gambling and suicide attempt. Among men, the cross-trait correlations were similarly modest and nonsignificant among both MZ and DZ pairs for all three suicidal behaviors; this pattern of findings suggests that familial (between-family factors) do not play a role in the overlap between disordered gambling and suicidal behaviors among men (bottom panel of Table S7).

Table S8. Estimates of variance components from univariate twin models of liability for lifetime disordered gambling and the	hree
suicidal behaviors (thoughts, plan, attempt).	

	Men				Women		Constrained across sex			
	A	С	E	A	С	Е	A	С	Е	
Disordered gambling	0.48	0	0.52	0.59	0	0.41	0.54	0	0.46	
95% CI	.37 – .61	0-0	.34 – .63	.42 – .70	0-0	.2854	.4268	0-0	.3356	
				Suic	idal behavio	ors				
Suicidal thoughts	0.39	0	0.61	0.56	0	0.44	.51	0	.49	
95% CI	.2251	012	.4978	.4965	0002	.3451	.3957	0 - 0	.4355	
Suicide plan	0.49	0.08	0.43	0.42	0.07	0.52	0.44	0.07	0.49	
95% CI	071	054	.2568	064	045	.3464	.1864	032	.3261	
Suicide attempt	0.57	0	0.43	0.002	0.43	0.57	0.32	0.17	0.52	
95% CI	083	044	.1578	0 - 52	.3159	.3867	.00258	036	.3164	

Note: ATR=II and ATR-III same-sex twin pairs; A = additive genetic influences, C = shared environmental influences, E = unique environmental influences, CI = confidence interval. Bold indicates significance.

Univariate twin models (Table S8)

Biometric model-fitting partitioned the variation in disordered gambling and suicidal behavior liability into genetic ("A") shared environmental ("C"), and unique environmental influences ("E", which also includes measurement error). Models were fitted by the method of robust weighted least squares directly to the raw twin data, which uses data from incomplete as well as complete twin pairs. An assumption was made that there existed latent liability continua underlying the disordered gambling and suicidality categories by employing a liability-threshold model (Neale & Cardon, 1992). In all models, the thresholds (prevalences) for men and women were allowed to differ. Bootstrapping was used to generate confidence intervals around parameter estimates. Evidence for quantitative sex differences (i.e., differences in the proportions of variation attributable to genetic, shared, and unique environmental influences) was assessed by constraining parameter estimates to be equal for men and women. Qualitative sex differences (i.e., differences in the sources of genetic variation for men and women) were evaluated by constraining the genetic correlation between opposite-sex twin pairs to that of same-sex twin pairs. Model comparisons were conducted using Wald chi-square tests. Because the correlations between age and disordered gambling (r = 0.05) and suicidality (r = .004) were very modest, we did not incorporate age in the biometric models.

Disordered gambling. A univariate model of disordered gambling allowing men's and women's parameter estimates to differ fit the data well ($\chi^2(8) = 6.14$, p = 0.63). Constraining the parameter estimates to be equal for men and women did not significantly reduce model fit (Wald $\chi^2(2) = 1.19$, p = 0.55). In this constrained model, genetic influences accounted for 53.9% of the variance in disordered gambling liability, with the remaining variance accounted for by unique environmental influences (46.1%).

Suicidal thoughts. The parameter estimates from a univariate model of suicidal thoughts allowing men's and women's parameter estimates to differ yielded significant estimates of genetic influences for both men and women. Constraining the parameter estimates to be equal for men and women did not significantly worsen model fit ($\Delta \chi^2(2) = 5.65$, p = 0.059). However, constraining the genetic correlation in opposite-sex twin pairs to 0.5 did ($\Delta \chi^2(1) = 4.19$, p = 0.041), suggesting potential qualitative sex differences in the genetic liability for suicidal thoughts. When the estimates for men and women were constrained, genetic influences

accounted for 51% of the variance in suicidality, with unique environmental influences accounting for the remaining variance (49%).

Suicide plan. The parameter estimates from a univariate model of suicide plan allowing men's and women's parameter estimates to differ yielded non-significant estimates of genetic and shared environmental influences. Constraining the parameter estimates to be equal for men and women did not significantly worsen model fit ($\Delta \chi^2(2) = 0.38$, p = 0.829). When the estimates for men and women were constrained, the contribution of genetic influences was significant, accounting for 44% of the variance in suicidal plans.

Suicide attempt. The parameter estimates from a univariate model of suicide attempt allowing men's and women's parameter estimates to differ also yielded mostly non-significant estimates of genetic and shared environmental influences; the exception was a significant influence of shared environmental influences, accounting for 43% of the variation in liability, among women. Although the parameter estimates for men and women did not significantly differ ($\Delta \chi^2(2) = 4.214$, p = 0.122), they were quite discrepant, with genetic influences accounting for 57% of the variation in liability among men, but none of the variation in liability among women, and shared environmental influences accounting for 43% of the variation in liability among women, but none of the variation in liability among men. When the parameter estimates for men and women were constrained, genetic influences accounted for 32%, shared environmental influences accounted for 17%, and unique environmental influences accounted for 52% of the variance in liability to make a suicide attempt.