

## Supplementary Online Content

Weissman MM, Berry OO, Warner V, et al. A 30-year study of 3 generations at high risk and low risk for depression. *JAMA Psychiatry*. Published online August 10, 2016. doi:10.1001/jamapsychiatry.2016.1586.

**eMethods.** Interviewers and Best-Estimate Procedures

**eTable 1.** Demographic Characteristics of Grandchildren (Generation 3) by Grandparental (Generation 1) and Parental (Generation 2) Depression Status

**eTable 2.** The Effect of Adjusting for Various Potential Confounders on the Association Between Parental MDD and Grandchild Outcomes

This supplementary material has been provided by the authors to give readers additional information about their work.

## **eMethods.** Interviewers and Best-Estimate Procedures

The diagnostic assessments were administered by trained doctoral and master's level mental health professionals blind to the clinical status of the parents and other generations. Based on a best-estimate procedure using all available information, final diagnoses were made by experienced clinicians, either a psychiatrist or Ph.D. psychologist, who was not involved in the interviewing and was blind to the clinical status of previous generations.<sup>1</sup> For information on interrater reliabilities, please see Weissman et al.<sup>2</sup>

## **eReferences**

1. Leckman JF, Sholomskas D, Thompson WD, Belanger A, Weissman MM. Best estimate of lifetime psychiatric diagnosis: a methodological study. *Arch Gen Psychiatry*. 1982;39(8):879-883.
2. Weissman M, Wickramaratne P, Gameroff MJ, et al. Offspring of depressed parents: 30 years later. *Am J Psychiatry*. Published online 4/26/2016. doi: appi.ajp.2016.15101327

**eTable 1. Demographic Characteristics of Grandchildren (Generation 3) by Grandparental (Generation 1) and Parental (Generation 2) Depression Status**

	Neither Grandparent Had MDD (n = 18)		1 or More Grandparents Had MDD (n = 44)		Statistic
	Parental MDD		Parental MDD		
	No (n=33)	Yes (n=6)	No (n=65)	Yes (n=23)	
No. of grandchildren	74	14	125	38	
Sex, No. (%) female	45 (60.8)	5 (35.7)	64 (51.2)	17 (44.7)	$\chi^2_{(3)} = 3.60, P = .31$
Age at last interview, mean (SD)	18.5 (6.8)	18.5 (4.7)	17.8 (8.0)	18.8 (7.1)	$F_{1,186} = 0.12, P = .95$
Education, No. (%)					
Less than high school	20 (27.4)	4 (28.6)	47 (40.2)	11 (31.4)	$\chi^2_{(3)} = 0.21, P = .98$
High school	31 (42.5)	6 (42.9)	30 (25.6)	12 (34.3)	
College or higher	22 (30.1)	4 (28.6)	40 (34.2)	12 (34.3)	

**eTable 2-a. The Effect of Adjusting for Various Potential Confounders on the Association Between Parental MDD and Grandchild Outcomes**

	Parental MDD		Effect of Parental MDD					
	No	Yes	In Basic Model <sup>a</sup>			In Model Adjusted for <b>Parental Substance Abuse/Dependence</b> <sup>b</sup>		
No. of parents (G2)	88	29						
No. of grandchildren (G3)	199	52						
	%	%	Beta	Hazard Ratio (95% CI)	P	Beta	Change in Beta	Hazard Ratio (95% CI)
<b>Disorders in grandchildren<sup>c</sup></b>								
Any mood disorder (in low-risk G3's)	23.0	14.3	-	0.75 (0.44, 1.28)	.31	-0.117	+59%	0.89 (0.30, 2.63)
Any mood disorder (in high-risk G3's)	16.8	39.5	1.092	2.98 (1.61, 5.48)	<.001	1.014	-7%	2.76 (1.47, 5.18)
MDD (in low-risk G3's)	14.9	14.3	-	0.89 (0.50, 1.58)	.69	-0.359	-210%	0.70 (0.32, 1.54)
MDD (in high-risk G3's)	11.2	29.0	0.995	2.70 (1.30, 5.63)	.008	0.936	-6%	2.55 (1.22, 5.31)
DDNOS	2.5	1.9	-	0.67 (0.08, 5.11)	.71	-0.215	+46%	0.81 (0.10, 6.76)
Dysthymic disorder	5.0	9.6	0.801	2.23 (0.70, 7.11)	.18	0.538	-33%	1.71 (0.52, 5.63)
Any anxiety disorder	37.2	50.0	0.332	1.39 (0.89, 2.11)	.14	0.272	-18%	1.31 (0.79, 2.18)
Any disruptive disorder	14.1	25.0	0.531	1.70 (1.05, 2.74)	.03	0.447	-16%	1.56 (0.96, 2.56)
Substance abuse/dependence	14.1	30.8	0.983	2.67 (1.10, 6.03)	.03	0.882	-10%	2.42 (1.04, 5.64)
Substance abuse	6.7	12.2	0.580	1.79 (0.67, 4.74)	.24	0.468	-19%	1.60 (0.62, 4.11)
Substance dependence	11.8	28.6	1.087	2.96 (1.24, 6.58)	.01	0.948	-13%	2.58 (1.13, 5.88)
Any disorder	48.2	69.2	0.448	1.56 (1.15, 2.11)	.004	0.402	-10%	1.50 (1.04, 2.16)
Any suicidal ideation/gesture	20.1	38.5	0.710	2.44 (1.28, 4.64)	.007	0.684	-4%	2.16 (1.04, 4.48) <sup>d</sup>
	<b>M (SD)</b>	<b>M (SD)</b>	<b>Beta</b>	<b>Statistic</b>	<b>P</b>	<b>Beta</b>	<b>Δ in Beta</b>	<b>Statistic</b>
C-GAS Score	82.5 (7.4)	72.8 (10.8)	-	$F_{1,186} = 38.25$	<.001	-7.502	+11%	$F_{1,185} = 24.07$

<sup>a</sup>The basic model has the G3 disorder as outcome and parental MDD as the predictor, and is adjusted for age and gender of grandchild and for correlation within family.

<sup>b</sup>The adjusted model is identical to the basic model except that it also adjusts for parental substance abuse/dependence (yes/no).

<sup>c</sup>Unlike the other G3 disorders, any mood disorder and MDD were stratified by risk status (i.e., the presence vs. absence of MDD in G1) because for these outcomes, the effect of G2 MDD was found to significantly differ according to the presence vs. absence of MDD in G1 (see last column of **Table 3**).

<sup>d</sup>Estimate of relative risk (rather than hazard ratio), as age of onset was not available.

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**eTable 2-b. The Effect of Adjusting for Various Potential Confounders on the Association Between Parental MDD and Grandchild Outcomes (continued)**

	Parental MDD		Effect of Parental MDD					
	No	Yes	In Basic Model <sup>a</sup>			In Model Adjusted for Parental Separation or Divorce <sup>b</sup>		
			Beta	Hazard Ratio (95% CI)	P	Beta	Change in Beta	Hazard Ratio (95% CI)
No. of parents (G2)	88	29						
No. of grandchildren (G3)	199	52						
	%	%						
Disorders in grandchildren <sup>c</sup>								
Any mood disorder (in low-risk G3's)	23.0	14.3	-	0.75 (0.44, 1.31)	.31	-0.877	-209%	0.42 (0.12, 1.49)
Any mood disorder (in high-risk G3's)	16.8	39.5	1.09	2.98 (1.61, 5.48)	<.00	0.698	-36%	2.01 (0.99, 4.07)
MDD (in low-risk G3's)	14.9	14.3	-	0.89 (0.50, 1.57)	.69	-0.747	-545%	0.47 (0.14, 1.57)
MDD (in high-risk G3's)	11.2	29.0	0.99	2.70 (1.30, 5.24)	.008	0.914	-8%	2.50 (1.15, 5.40)
DDNOS	2.5	1.9	-	0.67 (0.08, 5.11)	.71	- <sup>d</sup>	- <sup>d</sup>	- <sup>d</sup>
Dysthymic disorder	5.0	9.6	0.80	2.23 (0.70, 7.11)	.18	-0.654	-182%	0.52 (0.10, 2.64)
Any anxiety disorder	37.2	50.0	0.33	1.39 (0.89, 2.14)	.14	0.062	-81%	1.06 (0.60, 1.89)
Any disruptive disorder	14.1	25.0	0.53	1.70 (1.05, 2.74)	.03	0.624	+17%	1.87 (1.08, 3.23)
Substance abuse/dependence	14.1	30.8	0.98	2.67 (1.10, 6.03)	.03	0.826	-16%	2.28 (0.79, 6.57)
Substance abuse	6.7	12.2	0.58	1.79 (0.67, 4.81)	.24	0.378	-35%	1.46 (0.35, 6.17)
Substance dependence	11.8	28.6	1.08	2.96 (1.24, 6.97)	.01	0.939	-14%	2.56 (0.81, 8.08)
Any disorder	48.2	69.2	0.44	1.56 (1.15, 2.11)	.004	0.316	-29%	1.37 (0.98, 1.92)
Any suicidal ideation/gesture	20.1	38.5	0.71	2.44 (1.28, 4.64)	.007	0.690	-3%	2.22 (1.14, 4.33) <sup>d</sup>
	M (SD)	M (SD)	Beta	Statistic	P	Beta	Δ in Beta	Statistic
C-GAS Score	82.5 (7.4)	72.8 (10.8)	-	F <sub>1,186</sub> =	<.00	-6.875	+18%	F <sub>1,165</sub> = 23.39

<sup>a</sup>The basic model has the G3 disorder as outcome and parental MDD as the predictor, and is adjusted for age and gender of grandchild and for correlation within family.

<sup>b</sup>The adjusted model is identical to the basic model except that it also adjusts for parental separation or divorce (yes/no) as reported by the grandchild.

<sup>c</sup>Unlike the other G3 disorders, any mood disorder and MDD were stratified by risk status (i.e., the presence vs. absence of MDD in G1) because for these outcomes, the effect of G2 MDD was found to significantly differ according to the presence vs. absence of MDD in G1 (see last column of **Table 3**).

<sup>d</sup>Could not be estimated.

<sup>e</sup>Estimate of relative risk (rather than hazard ratio), as age of onset was not available.