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## Familial Liability for Eating Disorders and Suicide Attempts: Evidence From a Population Registry in Sweden.

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eFigure 1. Directed Acyclic Graph to determine whether familial factors exist that contribute to both eating disorders (ED) and suicide (SCD)

eTable 1. Odds ratio of suicide attempts and death by suicide in individuals with eating disorders, adjusted for different comorbid conditions

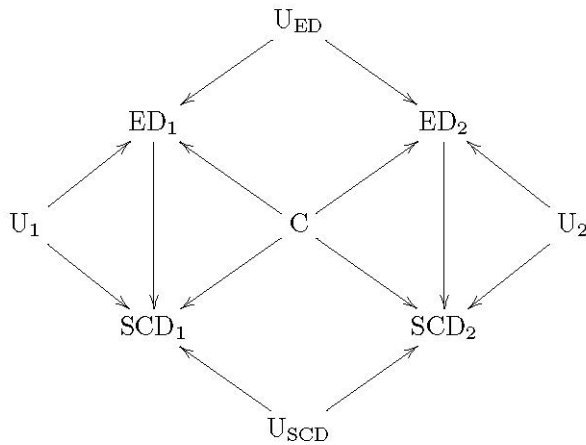
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**eFigure 1. Directed Acyclic Graph to determine whether familial factors exist that contribute to both eating disorders (ED) and suicide (SCD)**



eFigure1 illustrates the underlying mechanisms between eating disorders and suicide attempts in a Directed Acyclic Graph (DAG).<sup>1</sup> To simplify the exposition, here we restrict attention to pairs of relatives; the arguments carry over to familial clusters of arbitrary size. In eFigure1,  $ED_j$  and  $SCD_j$  represent eating disorders and suicide attempts, respectively, for individual  $j$  in a given pair;  $j = 1, 2$ .  $U_{ED}$  represents common causes for  $ED_1$  and  $ED_2$ , and  $U_{SCD}$  represents common causes for  $SCD_1$  and  $SCD_2$ .  $U_j$  represents common causes (confounders) for  $ED_j$  and  $SCD_j$  that may vary within the pair, and  $C$  represents common causes (confounders) for  $ED_j$  and  $SCD_j$  that are constant within the pair.

The (set of) variable(s)  $C$  can be thought of as representing familial liability to both eating disorders and suicide attempts. Thus, the research question is to what extent  $C$  exists. We addressed this question by exploring the association between  $SCD_1$  and  $ED_2$ , without and with adjusting for  $ED_1$  (analyses generating Table 3 and eTable 2, respectively). (Individual 1 is referred to as the “index individual” in the main manuscript). To motivate these analyses, consider the paths

$$\begin{aligned}
 &ED_2 \leftarrow C \rightarrow SCD_1 \\
 &ED_2 \leftarrow C \rightarrow ED_1 \rightarrow SCD_1 \text{ and} \\
 &ED_2 \leftarrow U_{ED} \rightarrow ED_1 \rightarrow SCD_1.
 \end{aligned}$$

In the analysis that does not adjust for  $ED_1$ , all these paths are open and may contribute to a statistical association between  $SCD_1$  and  $ED_2$ . Thus, the observed positive association between  $SCD_1$  and  $ED_2$  (Table 3) could, in principle, be explained by the path  $ED_2 \leftarrow U_{ED} \rightarrow ED_1 \rightarrow SCD_1$ , which does not presume the existence of  $C$ .

In the analysis that adjusts for  $ED_1$ , this path and the path  $ED_2 \leftarrow C \rightarrow ED_1 \rightarrow SCD_1$  are blocked; whereas path  $ED_2 \leftarrow C \rightarrow SCD_1$  is not influenced, if  $C$  exists. However, by adjusting for  $ED_1$  we additionally open the paths

$$\begin{aligned}
 &ED_2 \leftarrow C \rightarrow ED_1 \leftarrow U_1 \rightarrow SCD_1 \\
 &ED_2 \leftarrow U_{ED} \rightarrow ED_1 \leftarrow C \rightarrow SCD_1 \text{ and} \\
 &ED_2 \leftarrow U_{ED} \rightarrow ED_1 \leftarrow U_1 \rightarrow SCD_1.
 \end{aligned}$$

The first two of these paths presume the existence of  $C$ , whereas the third does not. Thus, in principle, the observed adjusted (for  $ED_1$ ) association between  $SCD_1$  and  $ED_2$  (eTable 2) could be explained by the path  $ED_2 \leftarrow U_{ED} \rightarrow ED_1 \leftarrow U_1 \rightarrow SCD_1$ . However, note that by symmetry  $U_{ED}$  is most likely to affect  $ED_1$  and  $ED_2$  in “the same direction”. That is, if high levels of  $U_{ED}$  are associated with high levels of  $ED_1$ , then high levels of  $U_{ED}$  are also associated with high levels of  $ED_2$ . Regarding  $U_1$ , it is easy to think of confounders that could affect  $ED_1$  and  $SCD_1$  in the same direction, e.g. a genetic “vulnerability” or a deplorable family environment. However, it is much more difficult to think of confounders that would affect  $ED_1$  and  $SCD_1$  in opposite directions. Thus, we allege that the “net effect” of  $U_1$  on  $ED_1$  and  $SCD_1$  is most likely in the same

direction. As a consequence, adjusting for  $ED_1$  is likely to induce a negative association between  $SCD_1$  and  $ED_2$ .<sup>2</sup> Thus, the fact that the positive association between  $SCD_1$  and  $ED_2$  remains when we adjust for  $ED_1$  is relatively strong evidence for the presence of path  $ED_2 \leftarrow C \rightarrow SCD_1$ , i.e., for the presence of  $C$ .

eTable 1. Odds ratio of suicide attempts and death by suicide in individuals with eating disorders, adjusted for different comorbid conditions

	Adjust for MDD		Adjust for ANX		Adjust for SUD	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Suicidal attempts						
Total population						
Any eating disorder	1.96 (1.85, 2.07)	<.001	2.82 (2.67, 2.98)	<.001	4.10 (3.89, 4.32)	<.001
Anorexia nervosa	1.75 (1.61, 1.90)	<.001	2.60 (2.41, 2.82)	<.001	3.55 (3.29, 3.84)	<.001
Bulimia nervosa	2.11 (1.90, 2.35)	<.001	3.14 (2.82, 3.48)	<.001	4.49 (4.04, 4.99)	<.001
Female						
Any eating disorder	1.85 (1.74, 1.96)	<.001	2.76 (2.61, 2.93)	<.001	4.06 (3.84, 4.30)	<.001
Anorexia nervosa	1.64 (1.50, 1.78)	<.001	2.52 (2.32, 2.74)	<.001	3.51 (3.24, 3.81)	<.001
Bulimia nervosa	1.96 (1.75, 2.19)	<.001	3.01 (2.70, 3.36)	<.001	4.35 (3.90, 4.87)	<.001
Male						
Any eating disorder	1.62 (1.25, 2.10)	<.001	2.00 (1.55, 2.58)	<.001	3.09 (2.39, 4.00)	<.001
Anorexia nervosa	1.43 (0.95, 2.16)	.09	1.98 (1.32, 2.95)	.001	2.65 (1.77, 3.99)	<.001
Bulimia nervosa	3.89 (1.97, 7.69)	<.001	4.49 (2.36, 8.51)	<.001	7.27 (3.84,13.78)	<.001
Death by suicide						
Total population						
Any eating disorder	2.13 (1.56, 2.91)	<.001	3.28 (2.39, 4.49)	<.001	3.52 (2.60, 4.77)	<.001
Anorexia nervosa	2.74 (1.83, 4.10)	<.001	4.23 (2.83, 6.32)	<.001	4.44 (2.99, 6.59)	<.001
Bulimia nervosa	1.63 (0.89, 2.98)	.12	2.52 (1.37, 4.63)	.003	2.60 (1.42, 4.77)	.002
Female						
Any eating disorder	2.01 (1.42, 2.85)	<.001	3.18 (2.24, 4.53)	<.001	3.21 (2.30, 4.49)	<.001
Anorexia nervosa	2.36 (1.50, 3.69)	<.001	3.71 (2.38, 5.79)	<.001	3.76 (2.43, 5.81)	<.001
Bulimia nervosa	1.48 (0.78, 2.82)	.23	2.35 (1.23, 4.49)	.01	2.29 (1.20, 4.37)	.01
Male						
Any eating disorder	2.19 (0.88, 5.44)	.09	3.26 (1.32, 8.07)	.01	3.85 (1.57, 9.46)	.003
Anorexia nervosa	4.37 (1.56,12.27)	.005	6.91 (2.49,19.22)	<.001	7.21 (2.58,20.11)	<.001
Bulimia nervosa	3.10 (0.41, 23.36)	.27	4.38 (0.59,32.70)	.15	4.82 (0.63,36.59)	.13

**eTable 2. Test if sex modifies the association between eating disorders and suicide attempts and death by suicide**

	Suicide attempts				Death by suicide			
	Crude model		Adjusted model		Crude model		Adjusted model	
	$\chi^2$	p	$\chi^2$	p	$\chi^2$	p	$\chi^2$	p
Any eating disorder	6.40	.01	0.15	.70	0.00	1.00	0.21	.65
Anorexia nervosa	2.14	.14	0.04	.84	0.89	.35	1.63	.20
Bulimia nervosa	3.82	.05	2.08	.15	0.53	.47	0.35	.56

**eTable 3. Odds ratio of suicide attempts among individuals with at least one relative with an eating disorder, adjusted for their own eating disorders**

	Any eating disorder		Anorexia nervosa		Bulimia nervosa		# Obs. used
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	
Full-sibling	<b>1.32 (1.21, 1.44)</b>	<.001	<b>1.16 (1.02, 1.32)</b>	.03	<b>1.52 (1.27, 1.81)</b>	<.001	1,680,658
Maternal half-sibling	1.09 (0.89, 1.33)	.41	1.09 (0.81, 1.47)	.57	1.12 (0.73, 1.72)	.61	253,172
Paternal half-sibling	1.20 (0.97, 1.48)	.09	1.25 (0.91, 1.73)	.16	1.32 (0.87, 1.99)	.19	248,939
Full-cousin	<b>1.11 (1.05, 1.17)</b>	<.001	<b>1.12 (1.03, 1.21)</b>	.005	<b>1.19 (1.07, 1.33)</b>	.002	1,753,065
Half-cousin	0.90 (0.78, 1.03)	.12	0.83 (0.68, 1.01)	.07	1.00 (0.77, 1.31)	.99	384,222

Note: OR: Odds Ratio; CI: Confidence Interval. The models adjusted for birth year, sex, number of the type of relatives, family cluster effect, and the eating disorders in the index individual (i.e., the individual from whom we acquired information on suicide attempts and relatives' eating disorders).

**eTable 4.1 Odds ratio of suicide attempts among individuals with at least one relative with eating disorders, adjusted for their own comorbidities**

	Adjust for MDD		Adjust for ANX		Adjust for SUD	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
<b>Any eating disorders</b>						
Full-sibling	<b>1.20 (1.10, 1.30)</b>	<.001	<b>1.30 (1.19, 1.42)</b>	<.001	<b>1.35 (1.23, 1.47)</b>	<.001
Maternal half-sibling	1.00 (0.81, 1.23)	.99	1.05 (0.85, 1.29)	.68	1.07 (0.87, 1.32)	.51
Paternal half-sibling	1.17 (0.95, 1.45)	.15	1.20 (0.97, 1.49)	.09	1.20 (0.96, 1.49)	.11
Full-cousin	<b>1.08 (1.02, 1.15)</b>	.005	<b>1.10 (1.04, 1.17)</b>	<.001	<b>1.12 (1.06, 1.19)</b>	<.001
Half-cousin	0.89 (0.78, 1.03)	.11	0.89 (0.77, 1.02)	.09	0.90 (0.78, 1.03)	.13
<b>Anorexia nervosa</b>						
Full-sibling	1.04 (0.91, 1.19)	.56	1.11 (0.98, 1.27)	.11	<b>1.17 (1.02, 1.33)</b>	.02
Maternal half-sibling	1.05 (0.76, 1.44)	.78	1.06 (0.77, 1.46)	.71	1.14 (0.83, 1.56)	.42
Paternal half-sibling	1.17 (0.85, 1.61)	.34	1.25 (0.91, 1.72)	.17	1.22 (0.87, 1.69)	.25
Full-cousin	<b>1.10 (1.01, 1.19)</b>	.02	<b>1.12 (1.04, 1.22)</b>	.004	<b>1.13 (1.04, 1.23)</b>	.003
Half-cousin	0.81 (0.66, 1.00)	.05	0.80 (0.65, 0.99)	.04	0.83 (0.68, 1.03)	.08
<b>Bulimia nervosa</b>						
Full-sibling	<b>1.34 (1.12, 1.61)</b>	.002	<b>1.48 (1.24, 1.77)</b>	<.001	<b>1.47 (1.23, 1.76)</b>	<.001
Maternal half-sibling	1.07 (0.68, 1.67)	.78	1.09 (0.70, 1.70)	.69	1.02 (0.65, 1.60)	.94
Paternal half-sibling	1.33 (0.86, 2.07)	.21	1.34 (0.88, 2.06)	.18	1.38 (0.89, 2.14)	.15
Full-cousin	<b>1.17 (1.05, 1.31)</b>	.006	<b>1.18 (1.05, 1.32)</b>	.005	<b>1.20 (1.07, 1.34)</b>	.002
Half-cousin	1.00 (0.75, 1.32)	.99	0.98 (0.74, 1.29)	.87	1.05 (0.80, 1.38)	.74



**eTable 4.2 Odds ratio of suicide attempts among individuals with at least one relative with eating disorders, adjusted for comorbidities in relatives**

	Adjust for MDD		Adjust for ANX		Adjust for SUD	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
<b>Any eating disorders</b>						
Full-sibling	1.06 (0.97, 1.16)	.18	<b>1.16 (1.07, 1.27)</b>	<.001	<b>1.30 (1.19, 1.41)</b>	<.001
Maternal half-sibling	0.98 (0.80, 1.20)	.82	0.98 (0.80, 1.20)	.84	1.04 (0.85, 1.27)	.70
Paternal half-sibling	1.08 (0.87, 1.33)	.48	1.12 (0.90, 1.38)	.31	1.15 (0.93, 1.41)	.20
Full-cousin	<b>1.05 (1.00, 1.11)</b>	.07	<b>1.07 (1.01, 1.14)</b>	.01	<b>1.10 (1.04, 1.16)</b>	.001
Half-cousin	0.87 (0.76, 1.00)	.05	0.88 (0.77, 1.01)	.08	0.89 (0.77, 1.02)	.09
<b>Anorexia nervosa</b>						
Full-sibling	0.93 (0.82, 1.06)	.30	1.03 (0.90, 1.17)	.71	1.13 (0.99, 1.28)	.07
Maternal half-sibling	0.98 (0.73, 1.33)	.92	0.99 (0.74, 1.34)	.97	1.05 (0.78, 1.42)	.74
Paternal half-sibling	1.14 (0.83, 1.56)	.43	1.17 (0.85, 1.62)	.33	1.21 (0.88, 1.66)	.25
Full-cousin	1.07 (0.99, 1.15)	.10	<b>1.09 (1.01, 1.18)</b>	.03	<b>1.11 (1.03, 1.20)</b>	.009
Half-cousin	0.80 (0.65, 0.98)	.03	0.81 (0.66, 0.99)	.04	0.81 (0.66, 0.99)	.04
<b>Bulimia nervosa</b>						
Full-sibling	1.11 (0.93, 1.33)	.23	<b>1.24 (1.04, 1.48)</b>	.02	<b>1.38 (1.16, 1.65)</b>	<.001
Maternal half-sibling	0.99 (0.64, 1.52)	.95	0.98 (0.64, 1.51)	.93	1.04 (0.68, 1.59)	.85
Paternal half-sibling	1.20 (0.79, 1.81)	.40	1.24 (0.82, 1.89)	.31	1.24 (0.82, 1.89)	.30
Full-cousin	<b>1.11 (1.00, 1.24)</b>	.06	<b>1.14 (1.02, 1.27)</b>	.02	<b>1.16 (1.04, 1.29)</b>	.009
Half-cousin	0.98 (0.75, 1.29)	.89	0.99 (0.76, 1.30)	.95	0.99 (0.76, 1.30)	.96

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