

The Rearing Environment and Risk for Major Depression: A Swedish National High-Risk Home-Reared and Adopted-Away Co-Sibling Control Study

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Objective: The authors sought to clarify the role of rearing environment in the etiology of major depression.

Methods: Defining high risk as having at least one biological parent with major depression, the authors identified a Swedish National Sample of 666 high-risk full sibships and 2,596 high-risk half sibships containing at least one home-reared and one adopted-away sibling. Major depression was assessed from national medical registries.

Results: Controlling for sex, parental age at birth, and, for half siblings, history of major depression in the nonshared parent, the risk for major depression in the matched adopted compared with home-reared full and half siblings was reduced by 23% (95% CI=7–36) and by 19% (95% CI=10–38), respectively. This protective rearing effect was not influenced by the relative educational status of the biological and adoptive parents. However, in both full and half sibships, the

protective effect of adoption disappeared when an adoptive parent or stepsibling had major depression or the adoptive home was disrupted by parental death or divorce.

Conclusions: In matched full and half sibships at high risk for major depression, compared with individuals raised in their home environment, those reared in adoptive homes (homes selected in Sweden for their high-quality rearing environment) had a significantly reduced risk for major depression. This protective effect disappeared if an adoptive parent had major depression or if the adoptive home experienced parental death or divorce during childhood/adolescence. The rearing environment has a meaningful impact on risk for major depression, and this effect is likely mediated both by parental depression and the continuity or disruption of the home environment.

Am J Psychiatry 2020; 177:447–453; doi: 10.1176/appi.ajp.2019.19090911

Major depression has recently been the subject of an intensive search to find the specific DNA variants that underlie genetic risk (1, 2). It has often been claimed that the familiarity of major depression—which is substantial (3)—results largely from genetic factors. Although this is an accurate summary of the twin studies of major depression (3–5), these studies only examine sources of resemblance among siblings and cannot provide insight into the causes of the equally important cross-generational transmission.

The primary method in this area of psychiatric genetics has been adoption studies. Consistent with the twin findings, none of the four classic adoption studies of major depression (6–9) found evidence for the environmental transmission of risk for major depression from adoptive parents to adoptees. However, numerous studies have shown that growing up with depressed parents can have a range of adverse psychiatric effects (10–12). Contrary to these earlier adoption studies, Tully et al. showed that parental major depression

significantly increased risk for major depression in adopted adolescent offspring (13). Furthermore, in a recent full Swedish adoption study, we found that the resemblance in risk for major depression between adoptive parents and the adoptee was substantial and similar in magnitude to that found between the biological parents and the adoptee (14). A major advantage of that study was our ability, for the first time, to utilize, in national registry data, psychiatric diagnoses made not only from hospital admissions and specialist outpatient care but also from outpatient primary care, where the majority of cases of major depression are diagnosed and treated (15, 16).

Because of the potential importance of these findings and their implications for primary prevention, we sought in the present study to replicate them using the same ascertainment procedure but a different and especially powerful design. We examined different offspring of the same high-risk biological parent who were reared in distinct environments—either by

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their biological parents or by adoptive parents. We first compared the risk for major depression in high-risk full sibships, one of whom had been adopted and the other home-reared. We then attempted to replicate our findings in a parallel sample of half siblings.

The strength of this natural experiment derives from two design features. First, the siblings are genetically matched, allowing us to isolate the impact of their distinctive rearing environments. Second, the rearing exposures are likely to be divergent. Adoptive parents in Sweden are carefully selected for low levels of psychiatric and substance use disorders, high educational status, economic security, and the ability to provide a high-quality and stable rearing environment (17, 18). Compared with adoptive parents, however, biological parents of adoptees are at substantially higher risk for a wide range of psychopathology, are much younger, are more poorly educated, and have substantially higher divorce rates (18).

In addition to the primary comparison of risk between the home-reared and adopted-away offspring, this design permitted us to address a further important question. If the reduced risk for major depression in the siblings reared in the adoptive compared with the home environment results from the quality of the rearing environment in the adoptive home, then those differences in risk should decline when the environment is adversely affected by environmental exposures known to increase risk for subsequent depression. We examined two such exposures: being reared by a parent with a lifetime history of major depression (10) and the disruption of parent-child bonds and/or the family environment through parental divorce or death (19–22). A similar effect might be expected if the presence of a high-risk environment in the adoptive home is indexed by the development of major depression in a stepsibling of the adoptee.

METHODS

We used linked data from multiple Swedish nationwide registries and health care data, with linking achieved via the unique individual 10-digit personal ID number assigned at birth or immigration to all Swedish residents. This ID number was replaced by a serial number to preserve confidentiality. We secured ethical approval for the study from the Regional Ethical Review Board of Lund University (No. 2008/409).

Our database was created by entering all full and half sibling sets where one sibling in the set was adopted away, the other(s) was reared by their common biological parent(s) and at least one of their biological parents had a registration for major depression anytime in their life. To define major depression, we utilized the Swedish Hospital Discharge Register (national coverage, 1987–2015, and partial coverage, 1969–1986) and the Outpatient Care Register (national coverage, 2001–2015). We also used information from a primary care registry, a research data set including individual-level information such as diagnoses, based on visits to primary health care centers from the following Swedish counties: Blekinge (2009–2016), Värmland (2005–2015), Kalmar

(2007–2016), Sörmland (1997–2017), Uppsala (2005–2015), Västernorrland (2008–2015), Norrbotten (2009–2016), Gävleborg (2010–2016), Halland (2007–2014), Jönköping (2008–2014), Kronoberg (2006–2016), Skåne (1998–2013), Östergötland (1997–2014), Stockholm (2003–2016), and Västergötland (2000–2013). The time periods differ because of the timing of digitizing patient records. In 2016, these 15 counties (out of 21) contained 87% of the Swedish population. Major depression was identified by ICD-8 codes 296.2, 298.0, and 300.4; ICD-9 codes 296.2, 296.4, 298.0, and 300.4; and ICD-10 codes F32 and F33. The major depression diagnosis could be registered at any time. For half siblings, we required that the common biological parent be registered with major depression. Furthermore, we required that 1) all siblings were born between 1955 and 2000, 2) the adoptee had not been living with the biological parent for >5 years, and 3) the home-reared sibling had lived in the same household as the biological parent for a minimum of 10 of the first 15 years of his or her life. Siblings adopted by biological relatives or by an adoptive parent living with a biological parent were not included as adoptees in the analysis. The full sibling database included 666 adopted individuals who had 1,254 full siblings who were raised by the biological parent(s), and the half sibling database included 2,596 adopted individuals who had 5,511 half siblings who were raised by the biological parent. Two hundred sixty-seven adoptees were included in both the full sibling and half sibling analyses.

Follow-up time (in months) was measured from age 15 of the child until time of first registration for major depression, death, emigration, or end of follow-up (December 31, 2015), whichever came first. Thus, the offspring varied between the ages of 15 and 60 at the conclusion of our follow-up. Major depression in offspring was investigated in relation to the main predictor variable, adopted versus reared by biological parent(s), by stratified Cox proportional hazards models with a separate stratum for each sibling set. In the analysis, the resulting hazard ratio would reflect the relative difference in hazard for major depression in those adopted away compared with those residing with the biological parent(s). In the models, we controlled for parental age at birth, sex of the sibling, and, in the half sibling analyses, the major depression status of the nonshared parent.

In additional analyses, we examined four features of the adoptive environment: at least one adoptive parent with lifetime major depression, at least one stepsibling with lifetime major depression, disruption in the adoptive family by divorce or death among adoptive parents occurring before age 15 of the adoptee, and educational status (divided into two groups: adoptive parents with higher educational status than the biological parents and adoptive parents with the same or lower educational status). These analyses were performed by including in the full models an interaction term between the variable adopted versus home-reared and the variable of interest. All statistical analyses were performed in SAS, version 9.4 (23).

RESULTS

Full Siblings

The characteristics of the full and half sibling samples are summarized in Table 1. We identified 666 full sibships containing at least one sibling reared by his or her biological parents and one reared by adoptive parents. The age of the biological parents at the birth of the home-reared child (mean=24.5 years, SD=5.4) was, on average, slightly but significantly younger than their age at the birth of their adopted-away child (mean=25.5 years, SD=5.9) ($t=8.2$, $df=665$, $p<0.001$). The raw rates for major depression were higher (23.0%) among the home-reared than the adopted siblings (19.8%). As seen in Table 2, the raw hazard ratio and 95% confidence interval for major depression for being an adopted compared with a home-reared sibling was 0.84 (95% CI=0.70–1.00), and the effect became stronger after we controlled for gender and parental age at birth, with a hazard ratio of 0.77 (95% CI=0.64–0.93).

Half Siblings

We sought to replicate these results in 2,596 half sibships containing at least one sibling home-reared by biological parents and one adopted away. Of these half sibling pairs, 26% shared a common father and 74% a common mother. The shared biological parent was significantly older on average at the birth of the home-reared (mean=26.4 years, SD=5.7) than that of the adopted-away half sibling (mean=23.1 years, SD=5.7) ($t=24.2$, $df=2595$, $p<0.001$). A history of major depression in the nonshared parent was more than twice as common in the home-reared than in the adopted-away half siblings. Both of these variables, therefore, were controlled for in our final analysis.

The raw rate of major depression was modestly higher in the home-reared (22.9%) than the adopted-away half siblings (19.8%). As seen in Table 2, the raw hazard ratio for major depression for being an adopted compared with a home-reared half sibling was 0.58 (95% CI=0.52–0.64), an effect that became moderately weaker after we controlled for parental age at birth, gender, and major depression status of the non-shared parent, with a hazard ratio of 0.81 (95% CI=0.72–0.90).

Effects of the Adoptive Environment

We examined four features of the adoptive environment (Table 3). First, 20% of the adoptive parents of adopted full or half siblings had a lifetime diagnosis of major depression. In the full siblings, the risk for major depression was significantly lower in the adopted-away full siblings raised by unaffected parents compared with the risk in the home-reared siblings but did not differ when one of their adoptive parents had major depression. The same pattern of results was seen for the half siblings. The effect sizes were very similar in the full and half sibling groups and in that sense represented a replication. However, likely because of the differences in sample size, the interactions were statistically significant for the half sibships but not the full sibships.

TABLE 1. Descriptive statistics of the matched home-reared and adopted full and half sibling samples in a Swedish registry study of rearing environment and risk for major depression

Sibling Group and Characteristics	Home-Reared		Adopted	
	N	%	N	%
Full siblings	1,254		666	
Diagnosis of major depression	289	23.0	132	19.8
Male	660	52.6	345	51.8
	Mean	SD	Mean	SD
Parental age at birth (years)	24.5	5.4	25.5	5.9
Mean age at end of follow-up period (years)	47.3	11.9	47.2	9.9
	N	%	N	%
Half siblings	5,511		2,596	
Diagnosis of major depression	1,262	22.9	514	19.8
Male	2,871	52.1	1,350	52.0
	Mean	SD	Mean	SD
Parental age at birth (years)	26.4	5.7	23.1	5.7
Mean age at end of follow-up period (years)	43.2	11.7	47.3	10.3
		%		%
Major depression in nonshared parent	566	15.7	181	7.0

Second, 16% of the adoptive homes for both the full and half siblings contained one or more stepsiblings who developed major depression. In both sibling samples, the risk for major depression was significantly lower in the adopted-away than in the home-reared siblings in adoptive homes without an affected sibling but not in adoptive homes with such a sibling. The effect sizes were relatively similar in the two samples and so could broadly be considered a replication. However, given the larger sample of half siblings, the interaction effects were significant only in that sample.

Third, in 16% of the adoptive homes of the full and half siblings, the family was disrupted by parental death or divorce before the adoptee reached age 15. In both full and half sibships, the risk for major depression was significantly lower in the adopted-away member compared with in the home-reared sib when they were raised in adoptive homes without such disruptions. In both the full and half sibships, the hazard ratios between the home-reared and adopted members differed significantly when the adoptive home was disrupted by parental death or divorce compared with when it was not. In the full siblings, the disrupted adoptive home was actually associated with an increased risk compared with the home-reared siblings. In the half siblings, no difference in risk was seen in the home-reared and adopted-away siblings in the presence of a disrupted adoptive home.

Fourth, in 82% of full sibships and in 92% of half sibships, the educational status of the adoptive parents exceeded that of the biological parents. We examined whether differences in risk for major depression in the full and half sibships

TABLE 2. Hazard ratio for major depression in matched adopted-away versus home-reared full and half siblings in a Swedish registry study

Measure	Raw		Controlling for Parental Age		Controlling for Parental Age and Sex ^a	
	Hazard Ratio	95% CI	Hazard Ratio	95% CI	Hazard Ratio	95% CI
Full siblings						
Adopted versus home-reared	0.84	0.70–1.00	0.77	0.64–0.93	0.77	0.64–0.93
Parental age (years) at child's birth			1.09	1.06–1.12	1.09	1.06–1.12
Male					0.53	0.42–0.67
Half siblings						
Adopted versus home-reared	0.58	0.52–0.64	0.80	0.71–0.89	0.81	0.72–0.90
Parental age (years) at child's birth			1.11	1.10–1.13	1.12	1.10–1.13
Male					0.46	0.41–0.51
High risk status in nonshared parent					1.25	1.02–1.53

^a For half siblings, also controlling for high risk status of nonshared parent.

differed in these families compared with in the families where the educational status of the two families was the same or was higher in the biological parents. No consistent trends were seen across the two sibling groups, and the hazard ratios did not differ in either group in the two rearing conditions.

DISCUSSION

We sought to further clarify the role of the rearing environment in risk for major depression by utilizing a powerful natural experiment in which matched offspring of a high-risk biological parent were reared in different family environments. In full sibships, being raised by an adoptive family was associated with a significant 23% decrease (95% CI=7–36) in risk for treated major depression. In a largely independent sample of high-risk half sibships, we replicated these findings, showing that the adopted half sibling had a 19% decrease (95% CI=10–38) in risk for major depression.

This design has two methodological strengths. First, it can isolate the differences in rearing effects by controlling for many background factors shared among the sibling pairs. Second, the differences in average rearing environments is substantial because in Sweden, as in most Western countries, adoptive parents are carefully screened for their ability to provide a supportive and generally advantaged home for their adoptive child (17, 24–26). Because the number of children available for adoption is considerably smaller than the demand, the selection process in Sweden is rigorous. This process is designed to “assess the general health, personality, and mutual relationship of the presumptive adoptive parents” with the goal of forecasting “the durability of their marriage ... [and placing] the child in a harmonious, stable environment” (17, p. 87).

Our four additional follow-up analyses of the adoptive families clarified and expanded on our main findings. First, evidence that the difference in risk for major depression between home-reared and adopted-away siblings disappeared when one of the adoptive parents had major depression replicated our finding from both a standard

adoption and a stepparent design that being reared by a nonbiological parent with major depression increased risk for major depression in the child (14). These results are also consistent with a large literature demonstrating the adverse psychiatric effects of being reared by parents with depression (10–12).

Second, the presence in the adoptive home of a stepsibling who developed major depression may index high-risk features of that family environment. As predicted, adoptees raised in such homes had no reduction in risk for major depression compared with their home-reared siblings. Third, the protective effect of the adoptive rearing environment was reversed by family disruption, consistent with a range of previous studies showing that severance of parent-child bonds during childhood and adolescence or the disruption of the parental relationship increases risk for future major depression (20, 21, 27, 28).

Fourth, our findings of no effect of parental educational status on risk for major depression in the biological compared with adoptive families provide an informative negative result. We know that these effects can be potent, as they predict IQ differences between the home-reared and adoptive siblings in this sample (29). The absence of findings here indicates that the rearing effects we observed on risk for major depression are not driven by the effects of cognitive aptitude, which is of import given the documented association between low educational attainment or low income and risk for major depression (30, 31).

Our results are consistent with evidence for the impact of rearing on risk for major depression from a range of non-adoptive designs. These include “children of twins” studies (32–35), a novel “assisted conception design” (36, 37), and the sustained decrease in problem behaviors and symptoms in the children of mothers whose depression has improved in major depression treatment trials (38, 39).

These results should be interpreted in the context of six potentially important methodological limitations. First, we ascertained major depression from hospital, specialist, and primary care registries, which require neither subject

TABLE 3. Features of the adoptive family for the adopted-away full and half sibships and their impact on risk for major depression in a Swedish registry study

		Major Depression (%)				Risk for Major Depression	
Feature of Families and Sibling Type	Families (N)	Adopted	Home-Reared	Difference	Interaction p	Hazard Ratio	95% CI
One or more adoptive parents with major depression							
Full siblings							
No	541	19.4	22.5	3.1	0.348	0.74	0.59–0.91
Yes	125	21.6	25.8	4.2		0.93	0.60–1.43
Half siblings							
No	2,064	18.5	22.7	4.2	0.048	0.76	0.67–0.86
Yes	532	24.8	23.7	−0.9		0.99	0.79–1.25
One or more stepsiblings with major depression							
Full siblings							
No	564	20.0	23.4	3.4	0.497	0.75	0.61–0.92
Yes	102	18.6	21.2	2.5		0.92	0.54–1.56
Half siblings							
No	2,196	18.9	22.8	3.9	0.0162	0.76	0.68–0.87
Yes	400	24.5	23.4	−0.9		1.06	0.83–1.36
Disruption in the adoptive family due to parental death or divorce before adoptee age 15							
Full siblings							
No	562	18.5	23.9	5.4	<0.0001	0.65	0.52–0.80
Yes	104	26.9	18.1	−8.8		2.05	1.24–3.39
Half siblings							
No	2,178	19.0	23.0	4.0	0.018	0.76	0.67–0.86
Yes	418	24.3	22.1	−2.2		1.08	0.83–1.41
Parental educational status							
Full siblings							
Higher	544	19.1	22.9	3.8	0.351	0.74	0.60–0.92
Lower	122	22.9	24.0	1.1		0.93	0.60–1.44
Half siblings							
Higher	2,389	19.9	22.8	2.9	0.465	0.92	0.73–0.92
Lower	207	18.8	24.7	5.9		0.70	0.48–1.04

cooperation nor accurate recall. However, because of those who never seek treatment, cases are missed. While Sweden has no large-scale interview-based psychiatric epidemiological study, interview-based surveys in neighboring Norway and in Swedish twins produced lifetime estimates of major depression rates of 17.8% (40) and 19.5% (4), respectively. A population-based estimate for the prevalence of treated major depression in our age cohort equals 12.3%, suggesting a moderate proportion of unascertained cases. Since our adoptive siblings were usually raised in higher-socioeconomic-status homes than their nonadoptive siblings, and socioeconomic status is generally associated with higher treatment seeking for psychiatric conditions (41, 42), studying treated depression would likely bias downward rather than upward our evidence for the protective effect of the adoptive rearing environment. Of note, the prevalences of major depression in our full and half sibling samples—ranging from 19.8% to 23.0% (Table 1)—is substantially higher than that seen in the general population, consistent with the adoption literature (43).

Second, while the hospital discharge and specialist registries we used to ascertain cases of major depression were

nationwide in coverage, coverage by our primary care registry was less complete. Given the high percentage of major depression cases in Sweden coming only from primary care (16), we conducted analyses in which we controlled for years of residence in a county that contributed to the primary care registry. As seen in Table S1 in the online supplement, the protective effect of adoption on risk for major depression did not change appreciably in these models. We also examined only cases of major depression ascertained in hospital or specialist registries (Table S2 in the online supplement). With our standard covariates, the protective effect for what were likely to be more severe episodes of major depression was stronger than seen for all cases of treated major depression in both full siblings (hazard ratio=0.62, 95% CI=0.44–0.87) and half siblings (hazard ratio=0.73, 95% CI=0.60–0.88).

Third, the nonshared parents of the adopted-away half siblings had higher rates of major depression than did those of the home-reared half siblings. We controlled for this effect in our main analyses, but to be sure that some bias was not thereby introduced, we reran our analyses with the half sibships, including only those where the nonshared parents had no history of major depression (Table S3 in the online

supplement). With the other covariates in place, the protective effect (hazard ratio) of the adoptive home was 0.82 (95% CI=0.73–0.93), indistinguishable from that found for the entire sample.

Fourth, to maximize power in this rare sample, we included 267 adoptees with both a full sibling and a half sibling reared at home. If we eliminated those pairs from our half sibling analyses, the protective effect of the adoptive home did not change appreciably, with a hazard ratio of 0.80 (95% CI=0.72–0.91). Fifth, bias could arise when adopted-away siblings have substantial contact with their biological parents prior to adoption. In our sample, 91% of adopted-away full siblings and 94% of adopted-away half siblings were adopted before their second birthday. We repeated our analyses with standard covariates in this subsample and obtained results similar to those seen in the entire sample (full siblings: hazard ratio=0.77, 95% CI=0.63–0.94; half siblings: hazard ratio=0.77, 95% CI=0.79–0.87). Sixth, we had no direct measures of the quality of the rearing environment in the home-reared or adoptive families and relied instead on several indirect measures.

CONCLUSIONS

Using Swedish registry data, we attempted to replicate and extend previous evidence that rearing environment meaningfully contributes to risk for major depression. We did this with a natural experiment in which high-risk full and half sibling pairs were exposed to different rearing environments. We found, in both samples, that siblings reared in adoptive homes, which are chosen for the high quality of their rearing environment, had an appreciable reduction in risk for major depression compared with their nonadopted siblings. The protective effect of adoption on risk for major depression disappeared when the adoptive family environment was disrupted by death or divorce or contained an adoptive parent or stepsibling with major depression. Our results further strengthen the evidence that high-quality rearing environments can meaningfully reduce rates of major depression in individuals at high familial risk. This finding supports efforts to improve the rearing environment in high-risk families as an approach to the primary prevention of major depression.

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Supported by NIH grant R01AA023534, the Swedish Research Council, and ALF funding from Region Skåne.

The authors report no financial relationships with commercial interests.

Received September 4, 2019; revision received November 13, 2019; accepted December 19, 2019.

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