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Title

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Permalink

<https://escholarship.org/uc/item/0j6892mb>

Journal

Pediatrics, 136(5)

ISSN

0031-4005

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Publication Date

2015-11-01

DOI

10.1542/peds.2015-0498

Peer reviewed

Psychosocial Adjustment in School-age Girls With a Family History of Breast Cancer

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abstract

OBJECTIVE: Understanding how young girls respond to growing up with breast cancer family histories is critical given expansion of genetic testing and breast cancer messaging. We examined the impact of breast cancer family history on psychosocial adjustment and health behaviors among >800 girls in the multicenter LEGACY Girls Study.

METHODS: Girls aged 6 to 13 years with a family history of breast cancer or familial *BRCA1/2* mutation (BCFH+), peers without a family history (BCFH-), and their biological mothers completed assessments of psychosocial adjustment (maternal report for 6- to 13-year-olds, self-report for 10- to 13-year-olds), breast cancer-specific distress, perceived risk of breast cancer, and health behaviors (10- to 13-year-olds).

RESULTS: BCFH+ girls had better general psychosocial adjustment than BCFH- peers by maternal report. Psychosocial adjustment and health behaviors did not differ significantly by self-report among 10- to 13-year-old girls. BCFH+ girls reported higher breast cancer-specific distress ($P = .001$) and were more likely to report themselves at increased breast cancer risk than BCFH- peers (38.4% vs 13.7%, $P < .001$), although many girls were unsure of their risk. In multivariable analyses, higher daughter anxiety was associated with higher maternal anxiety and poorer family communication. Higher daughter breast cancer-specific distress was associated with higher maternal breast cancer-specific distress.

CONCLUSIONS: Although growing up in a family at risk for breast cancer does not negatively affect general psychosocial adjustment among preadolescent girls, those from breast cancer risk families experience greater breast cancer-specific distress. Interventions to address daughter and mother breast cancer concerns and responses to genetic or familial risk might improve psychosocial outcomes of teen daughters.

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WHAT'S KNOWN ON THIS SUBJECT: Many families share genetic cancer risk information with their children, and some parents and providers believe *BRCA1/2* testing should be permitted in adolescence. The psychosocial effects and impact on health and risk behaviors of this knowledge is unknown.

WHAT THIS STUDY ADDS: In our cohort of 869 mother-daughter pairs, we found no differences in general adjustment, but 10- to 13-year-old girls with breast cancer family histories reported higher breast cancer-specific distress and perceived breast cancer risk. Mother distress was associated with daughter distress.

Although studies have reported psychosocial adjustment in children of parents with cancer, few studies have evaluated outcomes in youth from families at familial or genetic risk for breast cancer. Understanding the impact of growing up in a family at risk for breast cancer is important for many reasons. Breast cancer risk is increased twofold to fourfold for females with a family history and 10-fold for females with a *BRCA1/2* mutation.¹ Although *BRCA1/2* testing is not recommended during childhood,^{2,3} there is increasing evidence to suggest that childhood is a key period of carcinogenic vulnerability^{4,5} and that childhood exposures are associated with breast cancer risk.^{4–11} Many parents discuss genetic and familial risk with their children, and some believe genetic testing should be permitted in adolescence.^{12–15} Furthermore, some adolescent providers would consider testing a daughter of a *BRCA1/2* mutation carrier.¹⁶ Additionally, there are new guidelines recommending return of incidental genomic findings (including *BRCA1/2* mutations) regardless of age.¹⁷

Studies suggest that children of parents with cancer might be at risk for internalizing and externalizing problems,^{18–20} distress,^{21–24} and somatic concerns.²⁵ However, these studies have been relatively small, often not quantitative, and rarely included a comparison group.^{18–20} Extending this research to girls growing up in a family at risk for breast cancer (with or without parental cancer) is critical to ensuring healthy adaptation of youth and the development of genetic testing policies and cancer prevention messaging. First, parental distress has been associated with negative psychosocial outcomes in children.^{19,26,27} Chronic psychosocial stressors affect psychological and physical health,^{28–31} and increased risk for breast cancer might constitute a chronic stressor for

parents and offspring.³² Furthermore, some data suggest that the chronic stress of growing up in a family at risk for breast cancer could have a negative impact on immunologic host responses that might prevent cancer.^{27,33} Equally important, psychosocial distress can be associated with greater risk behaviors (eg, tobacco, alcohol use). Health and risk behaviors in preadolescence relate to the adoption and maintenance of health and risk behaviors throughout life, which is of particular importance for individuals at increased risk for cancer.^{34–38}

The LEGACY Girls Study is the first to focus on preadolescent girls growing up in families with breast cancer risk, including girls whose mothers have not had breast cancer.³⁹ This study addresses limitations of previous studies by being theoretically informed and including sociodemographically diverse girls, an unrelated comparison group, and both parent and child report. We applied a novel conceptual model⁴⁰ grounded in the Self-Regulation Theory of Health Behavior⁴¹ and developmental theory.^{34,37} Our model posits that response to a health threat, including psychosocial adjustment and the performance of health and risk behaviors, is a product of one's perceptions of the threat.^{40–42} This model is ideal for the study of youths' maturation because it emphasizes "commonsense" representations, encompasses sociocultural factors, and is iterative and dynamic, providing a unique opportunity to examine changing perceptions and outcomes longitudinally.⁴²

The primary behavioral aim of the LEGACY Girls Study was to understand if girls with a family history of breast cancer have poorer psychosocial adjustment (internalizing and externalizing problems and breast cancer-specific stress), and higher risk taking and

lower preventive health behaviors than BCFH- peers. Second, we sought to evaluate how daughter outcomes are impacted by family history and maternal and daughter factors. Third, we wanted to understand familial, maternal and daughter factors associated with higher perceived risk of breast cancer.

METHODS

Participants and Procedures

The LEGACY Girls Study enrolled 1040 girls, primarily at ages 6 to 13 years, at 5 study sites in the United States (New York City, Philadelphia, Salt Lake City, San Francisco Bay Area) and Canada (Ontario) (www.legacygirlsstudy.org) between August 2011 and July 2013.³⁹ The age range was selected to address multiple study aims during the transition through puberty. Given data that parents communicate genetic test results to children as young as 7 years old,^{12,15} we elected to evaluate psychosocial adjustment across the cohort age range. We elected to collect self-reported data from girls aged 10 or older (including nutrition, physical activity, built environment and behavioral items), based on feasibility interviews with parents⁴³ and girls.⁴⁴ We recruited 1) girls from families with breast cancer, defined as having ≥ 1 first- or second-degree relative with breast cancer or a *BRCA1/2* mutation in the family (BCFH+) and 2) girls without a family history of breast cancer or a *BRCA1/2* mutation in the family (BCFH-). Recruitment included a parent (97% were mothers) or guardian. Recruitment strategies, sources, and study procedures are described in detail elsewhere.³⁹ Briefly, BCFH+ girls were identified through a parent enrolled in the Breast Cancer Family Registry, local cancer registries, or cancer genetics and oncology clinics. BCFH- girls were recruited through local pediatric practices, friend referrals, social media, and public

notices. After recruitment, daughters were classified as BCFH+ or BCFH- based on parent-reported family history and parent and family *BRCA1/2* status. Institutional review board approval was obtained at each site. Parents/guardians provided written informed consent and permission for daughter participation. Girls provided assent based on institutional standards.⁴⁵

Measures

Mothers and daughters (10–13 years old) independently completed self-administered behavioral surveys before other baseline study assessments.³⁹

Daughter psychosocial adjustment reported by mothers (for all girls) and self-reported by 10- to 13-year-old girls was assessed with the Internalizing and Externalizing Composite Scales of the Behavioral Assessment System for Children.⁴⁶ Parent-reported internalizing subscales include anxiety, depression, and somatization. Externalizing subscales (reported only by parents) include hyperactivity, aggression, and conduct problems. Child-reported internalizing subscales include atypicality, locus of control, social stress, anxiety, depression, inadequacy, and somatization. Established criteria for at risk and clinical status were used.⁴⁶

Daughter breast cancer-specific distress was evaluated with the 8-item Child Impact of Events Scale, a developmentally appropriate version of the Revised Impact of Event Scale.^{47–50} Both have been used to evaluate intrusion and avoidance, as indices of cancer-specific “distress.”^{51–53} Daughter performance of health and risk behaviors were assessed with items from the Youth Risk Behavior Survey,⁵³ which has been used to track health and risk behaviors of >10 000 youths.^{54,55}

Daughter perception of breast cancer risk was assessed with a single item adapted from a longitudinal study of families at hereditary risk for breast cancer.^{42,56} Girls aged 10 to 13 years were asked, “Do you think your chances of getting breast cancer

when you are an adult are the same or different than other girls your age when they become adults?” Response choices were a 5-point Likert scale, plus “I don’t know.”

General family function and communication were evaluated

TABLE 1 Characteristics of LEGACY Girls and Mothers (*n* = 869)

	BCFH+, <i>n</i> (%)	BCFH-, <i>n</i> (%)
	<i>n</i> = 441	<i>n</i> = 428
Average age, Mean (SD)	9.5 (2.3)	9.4 (2.1)
Age distribution		
6	53 (12)	41 (10)
7	58 (13)	50 (12)
8	47 (11)	66 (15)
9	64 (15)	65 (15)
10	59 (13)	66 (15)
11	57 (13)	60 (14)
12	49 (11)	48 (11)
13	54 (12)	32 (8)
Race/ethnicity ^a		
Non-Hispanic white	321 (73)	255 (60)
Hispanic	60 (14)	66 (15)
Black/African American	23 (5)	44 (10)
Asian	28 (6)	45 (11)
Native Hawaiian/Pacific Islander/multiple ethnicities	9 (2)	18 (4)
Mother education		
High school or less	28 (6)	20 (5)
Vocation/tech school/some college	89 (20)	84 (20)
Bachelor’s degree	158 (36)	170 (40)
Graduate degree	162 (37)	150 (35)
Missing	4	4
Site		
California	148 (33)	147 (34)
Philadelphia	86 (20)	61 (14)
New York	63 (14)	73 (17)
Ontario	75 (17)	77 (18)
Utah	69 (16)	70 (16)
Family history ^b		
Mother with breast cancer	168 (38)	0 (0)
FDR with any cancer	182 (41)	20 (5)
Has a <i>BRCA1/2</i> + mother	62 (14)	—
No FDR/SDR with breast cancer, mean (SD), range	1.2 (0.63), 0–4	0.05 (0.25), 0–3 ^c
Development		
Mother-reported Tanner breast (girls aged 6–13 y)		
Stage 1	216 (55)	237 (61)
Stage 2	69 (17)	63 (16)
Stage 3	77 (19)	50 (13)
Stage 4	29 (7)	28 (7)
Stage 5	5 (1)	8 (2)
Daughter-reported Tanner breast (girls aged 10–13 y only)		
Stage 1	29 (14)	39 (21)
Stage 2	71 (34)	59 (31)
Stage 3	74 (35)	48 (25)
Stage 4	31 (15)	38 (20)
Stage 5	6 (3)	6 (3)
Have had menses ^b	66 (15)	62 (15)

FDR = first-degree relative; SDR = second-degree relative.

^a *P* = .003.

^b Maternal report.

^c Relatives of true-negative parents.

independently by mothers and 10- to 13-year-old girls using the general function and communication subscales of the McMaster Family Assessment Device.^{57,58} Internal consistency was high for daughters (Cronbach's $\alpha = 0.70-0.87$) and mothers (Cronbach's $\alpha = 0.82-0.89$).

Maternal psychosocial adjustment was assessed with the Hospital Anxiety and Depression Scale.^{59,60} Internal consistency was high (Cronbach's $\alpha = 0.80$ and 0.71). Maternal breast cancer-specific distress was measured using 8 items of the Revised Impact of Event Scale, to parallel the Child Impact of Events Scale (Cronbach's $\alpha = 0.88$).⁴⁷⁻⁵³

Statistical Analyses

In primary analyses, we compared psychosocial adjustment and behavior outcomes between BCFH+ and BCFH- girls. We used linear or logistic regressions to investigate whether psychosocial adjustment and behavior variables differed by group. We controlled for race/ethnicity in the models because it was the only demographic variable to show meaningful imbalance between the groups. To account for families with >1 daughter, we used robust standard errors that accounted for within-family correlation.⁶¹ We used $P < .05$ as the nominal criterion for statistical significance. Analyses were conducted by using Stata versions 12 and 13 (Statacorp, College Station, TX). We designed the study with 80% power to detect differences using simple linear regressions for standardized effect sizes >0.19 , assuming 450 girls per group. For analyses with a subsample of 225 girls in each group (10-13 years old), we designed the study for 80% power to detect differences by group using simple linear regressions for effect sizes >0.26 , assuming 2-sided hypothesis tests with a 5% type I error rate. We used pairwise deletion to account for missing data.

RESULTS

Participant Characteristics

Of 973 girls offered behavioral surveys, 97% of mothers/guardians and 99% of daughters ≥ 10 years old completed baseline surveys. Planned secondary analyses evaluating the relationship between maternal factors and daughter outcomes were restricted to 869 biological mother-daughter (6-13 years old) pairs. Maternally reported psychosocial adjustment outcomes are presented for the entire sample. We also examined mother and daughter reported primary outcomes in the subset of 10- to 13-year old girls. We aimed to identify any risks associated with this time period and how maternal and daughter report of functioning differed. Characteristics of girls and their mothers are shown in Table 1. Mothers of BCFH+ girls had higher general anxiety (7.1 vs 6.4, $P = .018$) and breast cancer-specific distress (7.6 vs 3.2, $P < .001$) than BCFH- mothers. BCFH+ mothers with a history of breast cancer had higher breast cancer-specific distress

than BCFH+ mothers without a history of breast cancer (12.1 vs 4.6, $P < .001$). These outcomes did not differ significantly between *BRCA1/2+* BCFH+ mothers and other BCFH+ mothers.

Differences in Psychosocial Adjustment, Perceptions of Breast Cancer Risk, and Health Behaviors

As reported by mothers, 6- to 13-year-old BCFH+ girls had lower internalizing problems overall (Table 2). In secondary analyses, BCFH+ girls received lower somatization scores (42.9, SD 30.5 vs 49.2, SD 30.4, $P = .003$). There were no significant differences in externalizing problems. However, in secondary analyses, a higher percentage of 10- to 13-year-old BCFH+ girls met at-risk or clinical criteria for externalizing problems (15.2% vs 7.7%, $P = .02$) and hyperactivity (15.7% vs 12.8%, $P < .02$) and conduct (12.9% vs 7.1%, $P = .04$) subscales.

Among the 10- to 13-year-old girls, there were no significant differences

TABLE 2 Mother-Reported Daughter Psychosocial Adjustment (Girls Aged 6-13 Years)

Composite Scores	BCFH+, $n = 441$		BCFH-, $n = 428$	
	Mean (SD)	% At Risk/Clinical	Mean (SD)	% At Risk/Clinical
Internalizing				
All girls (6-13 y)	44.9 (29.6), ^a	13%	49.8 (29.1), ^a	15%
6-7 y	44.0 (29.6)	11%	50.0 (29.3)	15%
8-9 y	44.0 (28.9)	12%	47.2 (28.7)	12%
10-11 y	46.5 (31.2), ^b	17%	57.3 (28.5), ^b	20%
12-13 y	44.8 (28.9)	10%	41.8 (28.1)	9%
Daughters of <i>BRCA1/2+</i> mother	34.3 (30.7), ^{c,d}	10%	49.8 (29.1), ^c	15%
Daughters of mother with BC	45.9 (30.1)	13%	49.8 (29.1)	15%
Externalizing				
All girls (6-13 y)	46.7 (29.4)	14%	49.1 (27.1)	11%
6-7 y	45.5 (30.7)	11%	50.5 (28.8)	13%
8-9 y	48.7 (28.8)	16%	51.5 (27.8)	14%
10-11 y	46.6 (29.0)	16%	51.3 (24.4)	9%
12-13 y	45.9 (29.3)	13%	40.4 (26.9)	8%
Daughters of <i>BRCA1/2+</i> mother	35.4 (28.2), ^{e,f}	7%	49.1 (27.1), ^e	11%
Daughters of mother with BC	46.4 (30.1)	15%	49.1 (27.1)	11%

The models also controlled for race/ethnicity and accounted for within family clustering. t scores ≥ 60 are classified as at-risk for clinically significant problems. BC, breast cancer.

^a $P = .02$.

^b $P = .004$.

^c $P = .001$.

^d $P = .005$ compared with BCFH+ and *BRCA1/2* negative/unknown.

^e $P < .001$.

^f $P = .001$ compared with BCFH+ and *BRCA1/2* negative/unknown.

between groups in self-reported internalizing problems (Table 3). Breast cancer-specific distress was significantly higher in BCFH+ girls, although levels of distress were relatively low (Table 3). Of note, 12% of BCFH+ girls met criteria for clinical breast cancer-specific distress, which was higher than in BCFH- peers. BCFH+ girls were 2.8 times (95% confidence interval 1.9–4.2) more likely to report themselves at increased risk than peers, although in both groups, many girls were unsure of their risk. Consistent with normative data in this age group,⁶² risk behaviors (ie, alcohol and

tobacco use) were low and did not differ between the 2 groups (Table 4). Sunscreen use, exercise, and weight intentions also did not differ significantly between the groups.

Family History, Maternal, Family, and Daughter Factors Associated With Daughter Psychosocial Adjustment and Breast Cancer-Specific Distress

We conducted secondary exploratory analyses to evaluate family history (number of relatives with breast cancer, maternal history of breast cancer and maternal *BRCA1/2* status), maternal (psychosocial adjustment and breast cancer-specific distress),

family (general family function and communication) and daughter factors (age, breast development, and perceived risk) associated with daughter outcomes in studies of children exposed to parental cancer.^{19,63} In multivariable models evaluating select maternally reported daughter psychosocial outcomes among the entire cohort of 6- to 13-year-old girls, mother having a *BRCA1/2* mutation was associated with better mother report of internalizing and externalizing behaviors, anxiety, and depression (Table 5). Additionally, greater mother anxiety was associated with poorer maternally reported daughter internalizing problems and each of the internalizing subscales. Poorer general family functioning was associated with greater depression and externalizing problems (Table 5). We conducted parallel analyses with maternally reported daughter adjustment for the subset of 10- to 13-year-old girls (data not shown). These revealed similar relationships between mother anxiety and maternally reported daughter psychosocial adjustment, although among 10- to 13-year-old girls, there was no relationship with maternal *BRCA1/2* mutation status, which could have been due to the small numbers in this subset.

In multivariable models of daughter-reported outcomes among 10- to 13-year-old girls, higher daughter general anxiety was again associated with higher maternal general anxiety and poorer family communication. Higher daughter breast cancer-specific distress was associated with higher maternal breast cancer-specific distress (Table 6). Being unsure of one's risk for breast cancer was associated with lower daughter internalizing problems, general anxiety, and lower breast cancer-specific distress. In multivariable analyses (data not shown) in which perceived risk is dichotomized as higher versus same/lower/don't know, greater

TABLE 3 Daughter Psychosocial Adjustment Outcomes (Girls Aged 10–13 Years)

	BCFH+, n = 211		BCFH-, n = 197	
	Mean (SD), % At-Risk/Clinical or n (%)		Mean (SD), % At Risk/Clinical or n (%)	
Internalizing composite				
All girls (10–13 y)	31.8 (24.9), 4.4%		31.9 (25.6), 5.1%	
10–11 y	33.0 (23.1), 2.8%		34.7 (25.9), 4.8%	
12–13 y	30.6 (26.7), 6.2%		27.8 (24.7), 5.5%	
Daughters of <i>BRCA1/2</i> + mother	24.8 (23.9), 0.0%		31.9 (25.6), 5.1%	
Daughters of mother with BC	28.3 (23.4), 2.2%		31.9 (25.6), 5.1%	
BC-specific distress				
Intrusive BC—distress (range 0–18)	1.9 ^a (3.3), NA		1.1 ^a (2.2), NA	
Avoidant BC—distress (range 0–20)	3.6 ^b (5.7), NA		1.9 ^b (4.2), NA	
Total BC distress (range 0–38)	5.4 ^b (8.1), 12% ^c		3.0 ^b (5.4), 5% ^c	
10–11 y	5.9 ^c (8.8), 13%		3.1 ^c (6.2), 6%	
12–13 y	5.0 ^d (7.4), 11%		3.0 ^d (4.1), 3%	
Daughters of <i>BRCA1/2</i> + mother	4.8 (9.1), 17%		3.0 (5.4), 5%	
Daughters of mother with BC	6.4 (8.5), 16% ^d		3.0 (5.4), 5% ^d	
Perceived risk of BC				
Perceived risk higher than peers	76 (38.4) ^e		25 (13.7) ^e	
10–11 y	34 (32.7) ^e		11 (10.5) ^e	
12–13 y	42 (44.7) ^e		14 (17.9) ^e	
Daughters of <i>BRCA1/2</i> + mother	10 (45.5) ^f		25 (13.7) ^f	
Daughters of mother with BC	41 (48.0) ^{e,g}		25 (13.7) ^e	
Perceived risk: "I don't know"	53 (26.8) ^h		76 (41.5) ^h	
10–11 y	34 (32.7) ⁱ		52 (49.5) ⁱ	
12–13 y	19 (20.2)		24 (30.8)	
Daughters of <i>BRCA1/2</i> + mother	10 (45.5) ^j		76 (41.5)	
Daughters of mother with BC	18 (21.2) ^f		76 (41.5) ^f	

The models also controlled for race/ethnicity and accounted for within family clustering. Daughters with a *BRCA1/2*+ mother = 25; daughters with a mother with BC = 90. Percentages reflect the percentage with nonmissing data. Means represent Behavioral Assessment System for Children percentile scores. *t* scores >60 are classified as at risk for clinically significant problems. Impact of Event Scale total scores ≥17 are classified as at risk for clinically significant problems. BC, breast cancer.

^a *P* = .01.

^b *P* = .001.

^c *P* = .02.

^d *P* = .008.

^e *P* < .001.

^f *P* = .002.

^g *P* = .005 for comparison with BCFH+ girls of mothers without BC.

^h *P* = .004.

ⁱ *P* = .03.

^j *P* = .04 for comparison with BCFH+ girls whose mother is *BRCA1/2* negative/unknown.

TABLE 4 Daughter Health and Risk Behaviors (Girls Aged 10–13 Years)

	BCFH+, <i>n</i> (%)	BCFH–, <i>n</i> (%)
	<i>n</i> = 211	<i>n</i> = 197
Preventive health and risk behaviors		
Tried alcohol	9 (4.3)	12 (6.1)
10–11 y	1 (0.9)	6 (5.1)
12–13 y	8 (8.1)	6 (7.7)
Daughters of <i>BRCA1/2+</i> mother	0 (0)	12 (6.1)
Daughters of mother with BC	1 (1.1)	12 (6.1)
Tried cigarettes	0 (0)	0 (0)
Sunscreen use most of the time/always	116 (55.5)	97 (50.5)
10–11 y	64 (58.2)	58 (50.4)
12–13 y	52 (52.5)	39 (50.6)
Daughters of <i>BRCA1/2+</i> mother	12 (50.0)	97 (50.5)
Daughters of mother with BC	47 (51.6)	97 (50.5)
Physical activity, mean (SD), d/wk	4.5 (1.9)	4.5 (1.9)
10–11 y	4.7 (1.9)	4.5 (1.9)
12–13 y	4.2 (1.8)	4.6 (1.8)
Daughters of <i>BRCA1/2+</i> mother	4.7 (1.5)	4.5 (1.9)
Daughters of mother with BC	4.5 (1.9)	4.5 (1.9)
Weight concerns		
Trying to lose weight	53 (25.7)	60 (31.6)
10–11 y	27 (25.2)	33 (29.2)
12–13 y	26 (26.3)	27 (35.1)
Daughters of <i>BRCA1/2+</i> mother	3 (12.5)	60 (31.6)
Daughters of mother with BC	21 (23.1)	60 (31.6)
Trying to gain weight	13 (6.3)	8 (4.2)
10–11 y	6 (5.6)	6 (5.3)
12–13 y	7 (7.1)	2 (2.6)
Daughters of <i>BRCA1/2+</i> mother	2 (8.3)	8 (4.2)
Daughters of mother with BC	9 (9.9)	8 (4.2)
Trying to maintain weight	51 (24.8)	51 (26.8)
10–11 y	26 (24.3)	31 (27.4)
12–13 y	25 (25.3)	20 (26.0)
Daughters of <i>BRCA1/2+</i> mother	7 (29.2)	51 (26.8)
Daughters of mother with BC	22 (24.2)	51 (26.8)
No weight concerns	89 (43.2)	71 (37.4)
10–11 y	48 (44.9)	43 (38.1)
12–13 y	41 (41.4)	28 (36.4)
Daughters of <i>BRCA1/2+</i> mother	12 (50.0)	71 (37.4)
Daughters of mother with BC	39 (42.9)	71 (37.4)

The models also controlled for race/ethnicity and accounted for within family clustering. BC, breast cancer.

perceived risk was significantly associated with increased breast cancer-specific distress (coefficient 2.8, $P < .01$), although the association did not remain statistically significant after removing those who stated “don’t know” from the analysis.

Factors Associated With Higher Perceived Risk Among 10- to 13-Year-Old Girls

In additional multivariable analyses among 10- to 13-year-old girls, higher perceived risk for breast cancer was significantly associated only with the number of relatives with breast cancer (odds ratio 1.79, confidence interval 1.05–3.05, $P = .03$). There

were no significant relationships with other family history, mother psychosocial, daughter, or family factors.

DISCUSSION

This study represents the largest study of girls growing up in families affected by breast cancer and provides the first report of the impact of growing up in a family with a history of and/or known genetic risk of breast cancer on preadolescent girls. In this study, preadolescent girls with BCFH did not experience worse general psychosocial adjustment than peers, as reported by

either mothers or daughters. These findings are consistent with some smaller studies in children when a parent had cancer, although some studies have suggested poorer psychosocial adjustment.^{18–20} Equally important, our study identified no difference in daughter general psychosocial adjustment by maternal breast cancer history.

However, 10- to 13-year-old girls from families at risk for breast cancer had significantly higher breast cancer-specific distress than peers, with 12% of the BCFH+ girls meeting cutoffs for clinically significant breast cancer-specific distress. Although this percentage and overall levels of distress were relatively low, this is a young cohort, and perceived risk may increase as girls progress through adolescence.^{23,45} Additionally, higher perceived risk was associated with higher breast cancer-specific distress. This is particularly important because distress and externalizing problems have been associated with risk-taking behaviors among youth.^{64–66}

Although mean externalizing scores did not differ by family history group, a higher percentage of 10- to 13-year-old BCFH+ girls met clinical cutoffs. It will be important to understand the mediators of psychosocial adjustment and the impact on health and risk behaviors over time. This is particularly important given data suggesting that modifiable risk factors in adolescence affect the risk of breast cancer in adulthood^{4–11} and are likely even more important for girls who are at increased risk for breast cancer.

In our study, maternal breast cancer history was not strongly associated with daughter outcomes in multivariable models. However, consistent with our model, perceived risk, a strong predictor of health behaviors, was associated with the number of relatives with breast cancer. The relevance of breast cancer family history to daughter

TABLE 5 Secondary Analysis of Factors Associated With Mother-Reported Daughter Psychosocial Adjustment in Fully Adjusted Multiple Linear Regression Models (Girls Aged 6–13 y)

Covariates	Mother-Reported Daughter Outcomes				
	Internalizing Problems	General Anxiety	General Depression	Somatization	Externalizing Problems
Family history factors					
No. FDR/SDR with BC	$\beta = -2.1$ $P = .25$	$\beta = -1.0$ $P = .58$	$\beta = -0.6$ $P = .73$	$\beta = -2.3$ $P = .22$	$\beta = -0.2$ $P = .91$
Mother history of BC	$\beta = -2.4$ $P = .56$	$\beta = -0.9$ $P = .84$	$\beta = -0.8$ $P = .82$	$\beta = -6.9$ $P = .09$	$\beta = -0.9$ $P = .83$
<i>BRCA1/2</i> + mother	$\beta = -13.3$ $P = .004$	$\beta = -11.2$ $P = .02$	$\beta = -11.1$ $P = .007$	$\beta = -8.7$ $P = .06$	$\beta = -12.4$ $P = .005$
Maternal factors					
Mother depression	$\beta = 0.2$ $P = .67$	$\beta = -0.2$ $P = .68$	$\beta = 0.5$ $P = .31$	$\beta = 0.2$ $P = .72$	$\beta = 1.3$ $P = .02$
Mother anxiety	$\beta = 2.3$ $P < .001$	$\beta = 2.7$ $P < .001$	$\beta = 1.5$ $P < .001$	$\beta = 1.4$ $P = .001$	$\beta = 0.7$ $P = .08$
Mother BC-specific distress	$\beta = 0.1$ $P = .45$	$\beta = -0.02$ $P = .90$	$\beta = -0.009$ $P = .95$	$\beta = 0.4$ $P = .04$	$\beta = -0.05$ $P = .79$
Daughter factors					
Daughter age	$\beta = 0.5$ $P = .55$	$\beta = 1.4$ $P = .08$	$\beta = -0.1$ $P = .90$	$\beta = -0.3$ $P = .69$	$\beta = -0.04$ $P = .95$
Daughter breast development ^{a,b}					
Stage 1	Reference	Reference	Reference	Reference	Reference
Stage 2	$\beta = -0.2$ $P = .96$	$\beta = 0.7$ $P = .85$	$\beta = -1.1$ $P = .73$	$\beta = -1.3$ $P = .72$	$\beta = -3.1$ $P = .34$
Stage 3	$\beta = -3.0$ $P = .46$	$\beta = -3.2$ $P = .45$	$\beta = -1.7$ $P = .65$	$\beta = -2.8$ $P = .51$	$\beta = -4.4$ $P = .24$
Stage 4	$\beta = -6.2$ $P = .23$	$\beta = -7.6$ $P = .16$	$\beta = -5.5$ $P = .25$	$\beta = -2.3$ $P = .67$	$\beta = -4.4$ $P = .40$
Stage 5	$\beta = 13.3$ $P = .11$	$\beta = 8.7$ $P = .33$	$\beta = 5.6$ $P = .54$	$\beta = 11.9$ $P = .24$	$\beta = 1.6$ $P = .87$
Family factors					
Family communication ^b	$\beta = 1.8$ $P = .69$	$\beta = 10.1$ $P = .02$	$\beta = -0.4$ $P = .92$	$\beta = -6.5$ $P = .16$	$\beta = -2.5$ $P = .60$
General family functioning ^b	$\beta = 3.4$ $P = .45$	$\beta = -6.9$ $P = .11$	$\beta = 8.9$ $P = .03$	$\beta = 9.3$ $P = .053$	$\beta = 9.6$ $P = .04$

The models also controlled for race/ethnicity and accounted for within family clustering. BC, breast cancer.

^a Included as a categorical variable in analyses.

^b Maternal report.

psychosocial adjustment is of great importance given an increasing appreciation of the importance of obtaining family history in routine medical visits^{67,68} and the expansion of genetic susceptibility testing.⁶⁹ Thus, understanding the impact of being identified at familial or genetic increased risk for adult cancer during childhood or adolescence is critically important to developing genetic risk assessment policies that minimize negative psychosocial and behavioral impact across the age span.

Consistent with the literature, poorer daughter psychosocial adjustment and distress were strongly associated

with poorer family function and mother adjustment.^{19,20,55,70–72} Mothers from families at risk for breast cancer reported greater general anxiety and breast cancer-specific distress. These data suggest that when pediatric providers identify girls with a family history of breast cancer, inquiring about maternal and family adjustment and encouraging follow-up for maternal and family psychosocial support could foster optimal psychosocial and behavioral adaptation of their daughters.²⁰ These data also provide support to provider and program efforts to address the psychosocial issues of not just breast cancer

survivors but “pre-vivors.” This will become increasingly important as susceptibility testing for breast and other cancers expands, thereby increasing the population of “at-risk” mothers and families.

It is interesting that when reported by mother, being from a *BRCA1/2+* family was associated with better adjustment, but only in the younger 6- to 9-year-old cohort, suggesting that “genetic risk” might somehow introduce an early resiliency factor. Alternatively, these associations may be attributed to how *BRCA1/2+* mothers perceive daughter adjustment or that *BRCA1/2+* mothers are more likely to limit information shared with preadolescent daughters.¹² To our knowledge, there are no studies evaluating these outcomes in daughters of *BRCA1/2* carriers. Given a relatively small number of *BRCA1/2* carriers in our study, these findings need to be confirmed in studies with a larger sample of families at genetic risk. Thus, they support further inquiry for this clinically relevant and growing “at-risk” patient population.

We acknowledge limitations to this study. Participants might represent a biased sample, which might not be generalizable to all girls and mothers. Although some girls were recruited through friends, introducing a potential bias, there were no significant differences in outcomes between BCFH- girls recruited through friends versus other sources. We only focused on mother-daughter pairs. These data might not reflect outcomes for daughters whose mother is deceased, who are raised by others, or the impact of fathers. Some of the analyses also include single-source and single-method data (maternal report on questionnaires), thus potentially contributing common method variance.⁷³ Our population of *BRCA1/2+* families is relatively small, and the findings will need to be confirmed in larger studies of

TABLE 6 Factors Associated With Daughter-Reported Psychosocial Adjustment in Fully Adjusted Multiple Linear Regression Models (Girls Aged 10–13 Years)

Covariates	Daughter Reported Outcomes			
	Internalizing Problems	General Anxiety	General Depression	BC-Specific Distress
Family history factors				
No. of FDR/SDR with BC	$\beta = -0.1$ $P = .96$	$\beta = 0.2$ $P = .93$	$\beta = 0.5$ $P = .81$	$\beta = 0.8$ $P = .18$
Mother history of BC	$\beta = -4.4$ $P = .35$	$\beta = -7.7$ $P = .15$	$\beta = -1.6$ $P = .71$	$\beta = -0.1$ $P = .93$
<i>BRCA1/2</i> + mother	$\beta = -6.9$ $P = .26$	$\beta = -12.8$ $P = .07$	$\beta = -9.4$ $P = .11$	$\beta = 0.7$ $P = .68$
Maternal factors				
Mother depression	$\beta = -0.1$ $P = .83$	$\beta = -0.5$ $P = .48$	$\beta = 0.2$ $P = .79$	$\beta = -0.3$ $P = .18$
Mother anxiety	$\beta = 1.0$ $P = .03$	$\beta = 1.6$ $P = .004$	$\beta = 0.7$ $P = .15$	$\beta = 0.2$ $P = .10$
Mother BC-specific distress	$\beta = 0.02$ $P = .91$	$\beta = 0.2$ $P = .49$	$\beta = -0.1$ $P = .68$	$\beta = 0.2$ $P = .005$
Daughter factors				
Perceived risk: higher	Reference	Reference	Reference	Reference
Perceived risk: same/lower	$\beta = -6.8$ $P = .04$	$\beta = -5.5$ $P = .18$	$\beta = -4.2$ $P = .23$	$\beta = -0.8$ $P = .46$
Perceived risk: don't know or NA	$\beta = -10.4$ $P = .006$	$\beta = -15.2$ $P < .001$	$\beta = -6.4$ $P = .07$	$\beta = -3.7$ $P = .001$
Daughter age	$\beta = -3.5$ $P = .01$	$\beta = -3.4$ $P = .06$	$\beta = -3.6$ $P = .02$	$\beta = -0.3$ $P = .61$
Daughter breast development^{a,b}				
Stage 1	Reference	Reference	Reference	Reference
Stage 2	$\beta = -4.6$ $P = .23$	$\beta = -6.6$ $P = .21$	$\beta = -3.9$ $P = .35$	$\beta = -0.7$ $P = .66$
Stage 3	$\beta = -5.0$ $P = .23$	$\beta = -7.7$ $P = .17$	$\beta = -4.1$ $P = .36$	$\beta = -1.7$ $P = .29$
Stage 4	$\beta = -0.1$ $P = .99$	$\beta = -5.8$ $P = .42$	$\beta = 5.3$ $P = .36$	$\beta = -1.2$ $P = .53$
Stage 5	$\beta = 2.1$ $P = .83$	$\beta = -5.8$ $P = .57$	$\beta = 9.5$ $P = .32$	$\beta = -2.9$ $P = .14$
Family factors				
Family communication ^b	$\beta = 10.8$ $P = .05$	$\beta = 16.4$ $P = .009$	$\beta = 5.6$ $P = .31$	$\beta = 2.2$ $P = .18$
General family functioning ^b	$\beta = 17.4$ $P = .001$	$\beta = 4.5$ $P = .44$	$\beta = 21.8$ $P < .001$	$\beta = 0.4$ $P = .78$

The models also controlled for race/ethnicity and accounted for within family clustering. BC = breast cancer.

^a Included as a continuous variable in analyses.

^b Reported by 10- to 13-year-old girls.

BRCA1/2+ families. Although the majority of daughters reported knowledge of mother's cancer, we did not specifically query what mothers communicated to daughters. This is an important area of further research. Similarly, the impact of daughter exposure to mother's treatment was not assessed given overall study burden but might

be an important variable for the subset of girls experiencing maternal illness.

Preadolescent girls with BCFH do not experience worse general psychosocial adjustment than peers but have greater breast cancer-specific distress and perceived risk of breast cancer. Identifying girls with a family history

of breast cancer and providing referrals for maternal and familial psychosocial support might promote optimal psychosocial and behavioral adaptation of their daughters. Understanding how these outcomes change through adolescence into young adulthood, including the impact on health and risk behaviors, is necessary to inform interventions that optimize responses to growing up in families at familial and genetic risk for breast cancer.

ACKNOWLEDGMENTS

The authors thank the staff at each LEGACY study site, including Alex Blacker, Connie Cady, Jocelyn Koo, Lisa Moy, Jennifer Nguyen, Meera Sangaramoorthy, Gauri Samant, Enid Satariano, Maria Talosig-Garcia (California site); Ann Johnson, Melissa White (New York site); Danielle Hanna MS, SGC, Teresa Selander (Ontario site); Lisa Bealin, Lauren Brumley, Eliana Butler, Patrick Sicilia (Philadelphia site); and Briar Doi, Karen O'Toole (Utah site) for recruitment and data collection and analysis.

The authors also thank the members of the Scientific Advisory Board (Tim A. Ahles, PhD; Christopher K. Daugherty, MD; Marcia E. Herman-Giddens, PA, DrPH; Robert Hiatt, MD, PhD; Lawrence H. Kushi, ScD; Susan L. Teitelbaum, PhD; Mary S. Wolff, PhD; Martin J. Yaffe, PhD) and the Event Monitoring Committee (Drs. Jeffrey Botkin, MD, MPH; Christopher K. Daugherty, MD; Branlyn DeRosa, PhD; Malcolm Pike, PhD and Ms. Cheryl Schuman, MS, CGC).

ABBREVIATION

BCFH: breast cancer family history

Drs Bradbury, Patrick-Miller, Schwartz, and Daly conceptualized and designed the study, participated in data analysis and interpretation, and drafted the initial manuscript; Dr Egleston conducted the analyses and participated in manuscript writing; Ms Burke Sands, Drs Chung, Andrulis, Buys, Keegan, Knight, Terry, and John, and Mr Glendon participated in the collection and assembly of data, analysis and interpretation, and manuscript writing; Drs McDonald, Moore, Rauch, Tuchman, and Frost participated in the analysis and interpretation of data and manuscript writing and approved the final manuscript as submitted.

FINANCIAL DISCLOSURE: Dr Egleston consults for Teva and has research funding from Janssen Infectious Diseases, Diagnostics BVBA (salary support) and Verilogue (salary support); these disclosures are unrelated to this study. The other authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Supported by grants from the National Cancer Institute (R01 CA138819, R01 138822, R01 CA138638, R01 138844 and Core grants: P30CA042014, P30CA006927) and UL1TR000003 (NCATS) and UL1RR024134 grants to the Clinical & Translational Research Center, The Children's Hospital of Philadelphia. The Stanford Cancer Institute (Developmental Cancer Research Award to Dr Keegan) and the Canadian Breast Cancer Foundation (Dr Andrulis). Dr Andrulis holds the Anne and Max Tanenbaum Chair in Molecular Medicine at Mount Sinai Hospital and the University of Toronto.

POTENTIAL CONFLICT OF INTEREST: Myriad Genetics provides the cost of genetic testing for a study conducted by Dr Bradbury. The other authors have indicated they have no potential conflicts of interest relevant to this article to disclose.

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