Association Between Children With Life-Threatening Conditions and Their Parents’ and Siblings’ Mental and Physical Health

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Abstract

IMPORTANCE Despite concerns regarding the potential deleterious physical and mental health outcomes among family members of a child with a life-threatening condition (LTC), few studies have examined empirical measures of health outcomes among these family members.

OBJECTIVES To examine whether mothers, fathers, sisters, and brothers of children with 1 of 4 types of pediatric LTCs have higher rates of health care encounters, diagnoses, and prescriptions compared with families of children without these conditions.

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study included US families with commercial insurance coverage from a single carrier. Children who had 1 of 4 LTCs (substantial prematurity, critical congenital heart disease, cancer, or a condition resulting in severe neurologic impairment) were identified by a diagnosis in their insurance claim data between July 1, 2015, and June 30, 2016. Each case child and their family was matched with up to 4 control children and their families based on the age of the case and control children. Data were analyzed between August 2020 and March 2021.

EXPOSURES Having a child or sibling with substantial prematurity, critical congenital heart disease, cancer, or a condition resulting in severe and progressive neurologic impairment.

MAIN OUTCOMES Rates of occurrence of health care encounters, physical and mental health diagnoses, and physical and mental health medication prescriptions, identified from insurance claims data, were compared between case and control families using a multivariable negative binomial regression model. The statistical analysis adjusted for observed differences between case and control families and accounted for clustering at the family level.

RESULTS The study included 25 528 children (6909 case children [27.1%] and 18 619 control children [72.9%]; median age, 6.0 years [IQR, 1-13 years]; 13 294 [52.1%] male), 43 357 parents (11 586 case parents [26.7%] and 31 771 control parents [73.3%]; mean [SD] age, 40.4 [8.1] years; 22 318 [51.5%] female), and 25 706 siblings (7664 case siblings [29.8%] and 18 042 control siblings [70.2%]; mean [SD] age, 12.1 [6.5] years; 13 114 [51.0%] male). Overall, case mothers had higher rates of the composite outcome of health care encounters, diagnoses, and prescriptions compared with control mothers (incident rate ratio [IRR], 1.61; 95% CI, 1.54-1.68), as did case fathers compared with control fathers (IRR, 1.55; 95% CI, 1.46-1.64). Sisters of children with LTCs had higher rates of the composite outcome compared with sisters of children without LTCs (IRR, 1.68; 95% CI, 1.55-1.82), as did brothers of children with LTCs compared with brothers of children without LTCs (IRR, 1.70; 95% CI, 1.56-1.85).

Key Points

Question Do family members of children with a serious pediatric illness have higher rates of health care encounters, diagnoses, and prescriptions?

Findings In this cohort study of family members of 6909 children with 1 of 4 types of serious pediatric illness and 18 619 control children without illness, mothers, fathers, sisters, and brothers each had higher overall rates of health care encounters, diagnoses, and prescriptions compared with family members of control children.

Meaning The findings suggest that family members of children with a serious pediatric illness may have increased physical and mental health care needs.

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CONCLUSIONS AND RELEVANCE  In this cohort study, mothers, fathers, sisters, and brothers who had a child or sibling with 1 of 4 types of LTCs had higher rates of health care encounters, diagnoses, and medication prescriptions compared with families who did not have a child with that condition. The findings suggest that family members of children with LTCs may experience poorer mental and physical health outcomes. Interventions for parents and siblings of children with LTCs that aim to safeguard their mental and physical well-being appear to be warranted.
Study Design and Eligibility and Identification of Case Children

The study included 4 retrospective cohorts. Each was assembled on the basis of 1 of 4 conditions: substantial prematurity (prematurity cohort, defined as infants born at ≤30 weeks' gestational age or with a birth weight <1500 g), critical congenital heart disease (cardiac cohort, defined as newborns with critical congenital heart defects who typically underwent surgery by 1 year of age), oncologic disease (oncologic cohort, defined as children aged 0-18 years with new-onset pediatric oncologic diagnoses, including liquid, solid, and brain cancer), and severe and progressive neurologic impairment (neurologic cohort, defined as children aged 0-18 years with conditions that resulted in severe neurologic impairments associated with substantial functional impairment and with prognosis of progressive deterioration with a substantially shortened life span).

Case children were identified based on the occurrence of an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) or International Statistical Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis code in their claim data between July 1, 2015, and June 30, 2016. A full list of the specific codes is provided in eTable 1 in the Supplement. The cohort observational data were health insurance claims observed from July 1, 2015, to December 31, 2017.

Matching of Case Children to Control Children

Each case child was matched with up to 4 control children based on the case child's date of birth (matched children had a birth date within 1 month of the case child's). For each cohort, the set of potential control children included all children who did not have any of the diagnoses for that specific cohort (but could have other diagnoses); individual control children were selected only once.

Specification of Family Members of Case and Control Children

Family members were operationally defined as individuals with insurance coverage through the policy holder. The policy holder was the parent of either the case or the control child and lived at the same residential address. Family members of case or control children were identified as parents (any age) and siblings (0 to 19 years of age) of the child. For both case and control family members, their initial study day was inherited from the originating case child's initial study date.

Specification of Diagnoses, Prescriptions, and Health Care Encounters

Claims files included information regarding diagnoses, prescriptions, and health care encounters. All diagnoses were recorded as ICD-10-CM codes. Codes from F10 to F59 and from F50 to F98 (for siblings only) were classified as mental health diagnoses, codes from S00 to T79 and from V00 to Y38 were classified as physical trauma diagnoses, and all other codes were classified as physical health diagnoses.

Prescription information included generic drug names, which were matched to the Anatomical Therapeutic Category coding system via the application program interface using RxMix, version 2.1.16.34 Drugs with Anatomical Therapeutic Category codes with prefixes of N05A, N05B (excluding N05BB), N05C, N06A, NO6C (excluding N05CM), and N03AE were specified as mental health prescriptions, whereas the remainder were specified as all other prescriptions. Health care encounters in the claims data included categories for hospitalizations, emergency department visits, and urgent care visits.

The composite outcomes of interest were the sums of the number of occurrences of each outcome event type for each individual during the observation period. Similar to the health care utilization data, demographic data, including age, sex, and race and ethnicity, were derived from the insurance database.

Statistical Analysis

To characterize cohort members, we used descriptive statistics with a 2-tailed t test and χ² test to screen for demographic differences between case and control individuals. We specified 4 main
overall hypotheses with regard to whether mothers, fathers, sisters, and brothers of case patients, compared with control patients’ family members, experienced increased rates of a composite measure of health care use, diagnoses, and prescriptions, implementing separate models for each of the 4 types of family members. In planned subanalyses, we also analyzed each of the 3 outcome types (health care use, diagnoses, and prescriptions) separately, with further subanalyses within each of these outcome types. In addition, we examined differences between bereaved case parents (identified by noting the death of their child as recorded in the child’s claims file) and control parents based on diagnosis. A multivariable negative binomial regression model with a logarithm link function was used to estimate the incidence rate ratios (IRRs) with 95% CIs for case individuals compared with control individuals on the person-level count data for each of the 4 cohorts. All implementations of this model adjusted for individuals’ duration of time observed, age, and the race and ethnicity category specified in the data source (which included a combined category for other race or ethnicity or data missing for race and ethnicity) and accounted for any within-family clustering of sibling observations. Two-sided \( P = .01 \) was designated as the threshold of statistical significance of the 4 overall hypotheses, and 2-sided \( P = .05 \) was designated as the threshold of statistical significance for the subanalysis comparisons. Data were analyzed between August 2020 and March 2021. All statistical analyses were performed with Stata, version 16.1 (StataCorp LLC).

A more complete description of the methods is shown in the eAppendix in the Supplement. Discrepancies between the original study protocol and how the study was conducted are reported in eTable 2 in the Supplement.

## Results

Of the 25,528 total children in the 4 cohorts of pediatric LTCs (eTable 3 in the Supplement), 6909 (27.1%) were case children and 18,619 (72.9%) were control children. Ages ranged from birth to 19 years, with a median age of 6.0 years (IQR, 1-13 years); 13,294 children (52.1%) were male, 13,57 (5.3%) were Asian, 15,98 (6.3%) were Black, 24,48 (9.6%) were Hispanic, 16,893 (66.2%) were White, and 3,323 (13.0%) identified as other race or ethnicity or had missing data on race and ethnicity.

Among the 43,357 total parents (Table 1), of whom 11,586 (26.7%) were case parents and 31,771 (73.3%) were control parents, the mean (SD) age was 40.4 (8.1) years; 22,318 (51.5%) were female, 2633 (6.1%) were Asian, 2729 (6.3%) were Black, 4397 (10.1%) were Hispanic, 31,285 (72.2%) were White, and 2,213 (5.3%) identified as other race or ethnicity or had missing data on race and ethnicity.

Among the 25,706 total siblings (Table 2), of whom 7,664 (29.8%) were case siblings and 18,042 (70.2%) were control siblings, the mean (SD) age was 12.1 (6.5) years; 13,114 (51.0%) were male, 10,694 (42.2%) were Asian, 16,262 (6.3%) were Black, 26,90 (10.5%) were Hispanic, 17,681 (68.8%) were White, and 2,640 (10.3%) identified as other race or ethnicity or had missing data on race and ethnicity.

In all cohorts, the mean (SD) follow-up time was 612.9 (228.2) days (range, 31-914 days). In total, 491 case children died during the study: 139 of 1176 (11.8%) in the prematurity cohort, 135 of 1520 (8.9%) in the oncologic cohort, 71 of 911 (7.8%) in the cardiac cohort, and 146 of 3302 (4.4%) in the neurologic cohort. Among the parents and the siblings (Table 1 and Table 2), statistically significant differences between case and control families were noted across the 4 cohorts with regard to sex, age, and race and ethnicity categories.

### Parents

Overall, case mothers, compared with control mothers, had 61% higher rates of the combined 3 outcome measures (health care use, diagnoses, and prescriptions) (IRR, 1.61; 95% CI, 1.54-1.68; \( P < .001 \)) after stratifying each of the outcome measures and adjusting for the mothers’ ages, duration of observation, race, and ethnicity. Overall, in the same analysis, case fathers, compared with control family fathers, had 55% higher rates of the combined 3 outcome measures (IRR, 1.55; 95% CI, 1.46-1.64; \( P < .001 \)).
### Table 1. Demographic Characteristics of Case and Control Parents by Cohort

| Characteristics        | Parents, No. (%)                   | P value |
|------------------------|-----------------------------------|---------|
|                        | Case cohort | Control cohort |         |
| **Prematurity cohort** | 2093 (0.1) | 6062 (0.0)    | NA      |
| Age, y                 |            |                |         |
| <19                    | 2 (0.1)    | 0              |         |
| 19 to <29              | 204 (9.8)  | 667 (11.0)     | .01     |
| 29 to <39              | 1407 (67.3)| 4178 (68.9)    |         |
| 39 to <49              | 435 (20.8) | 1140 (18.8)    |         |
| ≥49                    | 44 (2.1)   | 77 (1.3)       |         |
| Sex                    |            |                |         |
| Female                 | 1158 (55.3)| 3151 (52.0)    | .009    |
| Male                   | 935 (44.7) | 2911 (48.0)    |         |
| Race and ethnicity     |            |                |         |
| Asian                  | 115 (5.5)  | 391 (6.5)      |         |
| Black                  | 243 (11.6) | 397 (6.6)      | <.001   |
| Hispanic               | 248 (11.9) | 564 (9.3)      |         |
| White                  | 1345 (64.3)| 4269 (70.4)    |         |
| Missing or other       | 142 (6.8)  | 441 (7.3)      |         |
| **Cardiac cohort**     | 1610 (0.1) | 4773 (0.0)     | NA      |
| Age, y                 |            |                |         |
| <19                    | 2 (0.1)    | 0              |         |
| 19 to <29              | 165 (10.3) | 535 (11.2)     | .01     |
| 29 to <39              | 1072 (66.6)| 3266 (68.6)    |         |
| 39 to <49              | 339 (21.1) | 907 (19.0)     |         |
| ≥49                    | 31 (1.9)   | 65 (1.4)       |         |
| Sex                    |            |                | .41     |
| Female                 | 860 (53.5) | 2943 (52.3)    |         |
| Male                   | 749 (46.6) | 2279 (47.8)    |         |
| Race and ethnicity     |            |                | .005    |
| Asian                  | 98 (6.1)   | 307 (6.4)      |         |
| Black                  | 153 (9.5)  | 325 (6.8)      |         |
| Hispanic               | 152 (9.5)  | 421 (8.8)      |         |
| White                  | 1109 (68.9)| 3386 (70.9)    |         |
| Missing or other       | 98 (6.1)   | 334 (7.0)      |         |
| **Oncologic cohort**   | 2655 (0.1) | 6502 (0.0)     | NA      |
| Age, y                 |            |                |         |
| <19                    | 10 (0.4)   | 0              |         |
| 19 to <29              | 30 (1.1)   | 114 (1.8)      | <.001   |
| 29 to <39              | 698 (26.3) | 1513 (23.3)    |         |
| 39 to <49              | 1297 (48.9)| 3154 (48.5)    |         |
| ≥49                    | 620 (23.4) | 1721 (26.5)    |         |
| Sex                    |            |                | .96     |
| Female                 | 1344 (50.6)| 3295 (50.7)    |         |
| Male                   | 1311 (49.4)| 3207 (49.3)    |         |

(continued)
To better understand the origins of the overall outcomes for parents in case families compared with control families, we examined each of the 3 major outcome types separately, with further distinctions between subtypes of health care encounters (hospitalizations, emergency department visits, and urgent care visits), diagnoses (mental health, physical health, and physical trauma), and prescriptions (mental health and all other) (Figure 1 and eTable 4 in the Supplement).

With regard to the 3 subtypes of health care encounters, most point estimates (20 of 24 [83.3%]) of the rate ratio of use for case parents compared with control parents indicated that case parents had greater use, and 6 point estimates (25.0%) showed significantly increased use. An exception to this pattern was hospitalizations, for which the point estimates were evenly split between an increase and reduction in use.

With regard to the subtypes of diagnoses, when comparing rate ratio point estimates for case parents with those for control parents, most (19 of 24 [79.2%]) were greater for case parents, and 12 (50.0%) were significantly greater. Increased levels of diagnoses were more consistently seen for the oncologic and neurologic cohorts (12 of 12 [100%]) compared with the prematurity and cardiac cohorts (7 of 12 [58.3%]).

With regard to the subtypes of prescriptions, most of the rate ratio estimates (14 of 16 [87.5%]) were greater for case parents than for control parents, and 11 estimates (68.8%) were significantly greater. Again, the oncologic and neurologic cohorts had a more consistent pattern of increased rate ratio estimates among case parents (8 of 8 [100%], all statistically significant) compared with the prematurity and cardiac cohorts (6 of 8 [75.0%], of which 3 [37.5%] were significantly different).
Table 2. Demographic Characteristics of Case and Control Siblings by Cohort

| Characteristics | Case cohort | Control cohort | P value |
|-----------------|-------------|----------------|---------|
| **Prematurity cohort** | | | |
| Siblings, No. | 784 | 2807 | NA |
| Age, y | | | |
| 0 to <3 | 30 (3.8) | 73 (2.6) | |
| 3 to <5 | 164 (20.9) | 887 (31.6) | <.001 |
| ≥5 | 590 (75.3) | 1847 (65.8) | |
| Sex | | | |
| Female | 373 (47.6) | 1383 (49.3) | .40 |
| Male | 411 (52.4) | 1424 (50.7) | |
| Race and ethnicity | | | |
| Asian | 24 (3.1) | 131 (4.7) | |
| Black | 88 (11.2) | 167 (6.0) | |
| Hispanic | 93 (11.9) | 281 (10.0) | <.001 |
| White | 456 (58.2) | 1845 (65.7) | |
| Missing or other | 123 (15.7) | 383 (13.6) | |
| **Cardiac cohort** | | | |
| Siblings, No. | 770 | 2292 | NA |
| Age, y | | | |
| <19 | 25 (3.3) | 51 (2.2) | |
| 19 to <29 | 207 (26.9) | 776 (33.9) | <.001 |
| ≥29 | 538 (69.9) | 1465 (63.9) | |
| Sex | | | |
| Female | 413 (53.6) | 1135 (49.5) | .048 |
| Male | 357 (46.4) | 1157 (50.5) | |
| Race and ethnicity | | | |
| Asian | 30 (3.9) | 95 (4.1) | |
| Black | 72 (9.4) | 153 (6.7) | |
| Hispanic | 76 (9.9) | 226 (9.9) | |
| White | 496 (64.4) | 1536 (67.0) | |
| Missing or other | 96 (12.5) | 282 (12.3) | |
| **Oncologic cohort** | | | |
| Siblings, No. | 2072 | 4058 | NA |
| Age, y | | | |
| 0 to <3 | 75 (3.6) | 35 (0.9) | |
| 3 to <5 | 98 (4.7) | 147 (3.6) | <.001 |
| ≥5 | 1899 (91.7) | 3876 (95.5) | |
| Sex | | | |
| Female | 1020 (49.2) | 1915 (47.2) | .13 |
| Male | 1052 (50.8) | 2143 (52.8) | |
| Race and ethnicity | | | |
| Asian | 64 (3.1) | 161 (4.0) | |
| Black | 103 (5.0) | 219 (5.4) | |
| Hispanic | 231 (11.2) | 413 (10.2) | .30 |
| White | 1467 (70.8) | 2860 (9.9) | |
| Missing or other | 207 (10.0) | 401 (9.9) | |
| **Neurologic cohort** | | | |
| Siblings, No. | 4292 | 8885 | NA |
| Age, y | | | |
| 0 to <3 | 171 (4.0) | 117 (1.3) | |
| 3 to <5 | 293 (6.8) | 408 (4.6) | <.001 |
| ≥5 | 3828 (89.2) | 8360 (94.1) | |

(continued)
Siblings

Overall, sisters of children with LTCs, compared with sisters of children without LTCs, had 68% higher rates of the combined 3 outcome measures (IRR, 1.68; 95% CI, 1.55-1.82; \(P < .001\)) after adjusting for the sisters’ ages, duration of observation, race, and ethnicity and stratifying each of the outcome measures. In the same analysis, brothers of children with LTCs had 70% higher rates than brothers of children without LTCs (IRR, 1.70; 95% CI, 1.56-1.85; \(P < .001\)).

Patterns similar to those observed among parents were observed among siblings (Figure 2 and eTable 5 in the Supplement). With regard to health care encounters, most of the rate ratio point estimates (16 of 24 [66.7%]) were greater among case siblings than among control siblings, with 5 (20.8%) being significantly different. With regard to diagnoses, 17 of the 24 point estimates (70.8%) were greater among case siblings, with 8 (33.3%) being significantly different. With regard to prescriptions, 14 of the 16 (87.5%) point estimates were greater among case siblings, with 9 (56.3%) being significantly different. The pattern of greater point estimates among case siblings was more consistently observed in the oncologic and neurologic cohorts than in the prematurity and cardiac cohorts.

Additional Cross-Cohort, Sex, and Race and Ethnicity Comparisons

We examined the cross-cohort comparative observations in more quantitative detail using a multivariable regression model that stratified the 3 outcomes; controlled for family members’ age, sex, race and ethnicity, and duration of observation; and accounted for family-level clustering of observations (Table 3). The cardiac cohort had the smallest increase among case family members in the composite outcome rate at 29% (IRR, 1.29; 95% CI, 1.15-1.36), followed by the prematurity cohort at 39% (IRR, 1.39; 95% CI, 1.29-1.51), whereas the neurologic cohort had the greatest increase at 76% (IRR, 1.76; 95% CI, 1.68-1.84), followed by the oncologic cohort at 62% (IRR, 1.62; 95% CI, 1.53-1.73).

Although the case family mothers, fathers, sisters, and brothers had similar degrees of increase in outcome rates compared with their control family counterparts, in all 4 cohorts, case mothers had composite outcome rates that were 44% greater than those for case fathers (IRR, 1.44; 95% CI, 1.39-1.49), whereas case sisters’ composite outcome rates were 11% higher than those for case brothers (IRR, 1.11; 95% CI, 1.05-1.17).

The models adjusted for differences observed in the distribution of the 5 different categories of race and ethnicity among case and control families. In the overall outcomes model including all 4 cohorts, compared with family members classified as White, family members classified as Black had similar composite outcome rates (IRR, 0.98; 95% CI, 0.92-1.05); those classified as Hispanic had lower rates (IRR, 0.90; 95% CI, 0.85-0.95), as did those classified as other race and ethnicity or who had missing data on race and ethnicity (IRR, 0.89; 95% CI, 0.84-0.95). Those classified as Asian had the lowest rates (IRR, 0.66; 95% CI, 0.62-0.71).

Table 2. Demographic Characteristics of Case and Control Siblings by Cohort (continued)

| Characteristics | Siblings, No. (%) | P value |
|----------------|------------------|--------|
|                | Case cohort      | Control cohort |
| Sex            |                  |        |
| Female         | 2145 (50.0)      | 4330 (48.7) | .18 |
| Male           | 2147 (50.0)      | 4555 (51.3) |
| Race and ethnicity |              |        |
| Asian          | 136 (3.2)        | 436 (4.9)   |
| Black          | 265 (6.2)        | 590 (6.6)   |
| Hispanic       | 477 (11.1)       | 922 (10.4)  | <.001 |
| White          | 3024 (70.5)      | 6150 (69.2) |
| Missing or other | 390 (9.1)      | 787 (8.9)   |

Abbreviation: NA, not applicable.
The analysis was adjusted for parent age, race and ethnicity, and duration of medical coverage. ED indicates emergency department.
Figure 2. Diagnoses, Prescriptions, and Health Care Encounter Types for Case Siblings Compared With Control Siblings

The analysis was adjusted for sibling age, race and ethnicity, and duration of medical coverage. ED indicates emergency department.
Additional Analysis Restricted to Case Families of Children Who Died

We performed the aforementioned analyses but limited them to the 434 case mothers, 350 case fathers, 263 case sisters, and 223 case brothers of children who died, comparing their health care use during the entire observation period (including before and after the death of the child) with that of the matched control family members (eTable 6 in the Supplement). Overall, the composite rate of health care utilization among case families of children who died was increased 83% (IRR, 1.83; 95% CI, 1.66-2.03) compared with that of control families.

Discussion

In this large sample of families with children who were born substantially prematurely, were born with critical congenital heart conditions, developed cancer, or had progressive neurologic conditions, we found that parents and siblings of children with these serious illnesses were 55% to 70% more likely to use health care and to receive diagnoses and prescriptions than were family members of control children. This degree of increase among case families compared with control families was similar for mothers and fathers and for sisters and brothers; however, case mothers experienced 44% higher composite outcome rates than did case fathers. Among the 4 different sets of medical conditions, the increases were greatest for neurologic and oncologic case families (range, 62%-76%) and were lower for cardiac and prematurity case families (range, 29%-39%). The degree of increase was greater in families of children who died.

Our findings are consistent with those of previous research. Literature based mostly on self-reported health ratings and health-related quality of life measures has documented increases in emotional distress, physical health problems, and sleep disturbances and a lower quality of life among parents of children with LTCs. This study’s findings are also consistent with those of prior studies showing that siblings of children with LTCs may experience increased stress, depression, anxiety, and behavioral problems and a lower quality of life.

More recently, studies have examined health care encounters, diagnoses, and prescriptions. One study found that parents of children who had been recently discharged from a pediatric intensive care unit were more than twice as likely to receive a mental health diagnosis during the subsequent 6 months compared with during the prior 6 months, and 3% to 4% of these parents received new prescriptions for antidepressant or anxiolytic medications, with mothers twice as likely as fathers to receive new prescriptions. A study of mothers of children with debilitating conditions residing in England identified an increased risk among these mothers (compared with control mothers) for depression, cardiovascular disease, and death.

Three aspects of the current study’s findings warrant discussion. First, health care encounters, diagnoses, and prescriptions are predicated on health care use and practices, and thus the association between the study’s results and the actual physical and mental health of these family members is indirect. If the case families of children with LTCs were less likely to use health care than were control families (as has been observed for families of children who have cancer), then this...

| Type of family member | Cardiac cohort | P value | Prematurity cohort | P value | Oncologic cohort | P value | Neurologic cohort | P value |
|-----------------------|----------------|---------|---------------------|---------|------------------|---------|-------------------|---------|
| All                   | 1.29 (1.15-1.36) | <.001   | 1.39 (1.29-1.51)   | <.001   | 1.62 (1.53-1.73) | <.001   | 1.76 (1.68-1.84)  | <.001   |
| Mothers               | 1.40 (1.24-1.59) | <.001   | 1.62 (1.47-1.80)   | <.001   | 1.60 (1.45-1.76) | <.001   | 1.68 (1.57-1.80)  | <.001   |
| Fathers               | 1.13 (0.98-1.29) | .09     | 1.30 (1.14-1.47)   | <.001   | 1.58 (1.42-1.76) | <.001   | 1.63 (1.51-1.76)  | <.001   |
| Sisters               | 1.22 (1.02-1.45) | .03     | 1.05 (0.85-1.31)   | .64     | 1.72 (1.49-1.99) | <.001   | 2.05 (1.84-2.29)  | <.001   |
| Brothers              | 1.30 (0.96-1.77) | .09     | 1.27 (0.95-1.70)   | .11     | 1.77 (1.52-2.07) | <.001   | 1.89 (1.68-2.13)  | <.001   |

Abbreviation: IRR, incident rate ratio.

* Negative binomial regression models were stratified by outcome type (encounters, diagnoses, and prescriptions) and adjusted for the family member’s age, race and ethnicity category, and duration of observation; they also accounted for family-level clustering of observations. In addition, the overall model was adjusted for the type of family member.
study's findings likely underestimate the degree of increase of physical and mental health conditions in the case families. In contrast, parents of children with LTCs may be more likely to use health care, for instance, because parents often worry that the siblings will have health problems because of the ill child's LTC. This pattern of behavior would result in our having overestimated the true degree of increased health care use. Of these 2 possibilities, the findings that case families also showed greater increases in diagnoses and prescriptions than did control families and that the increases in diagnoses and prescriptions were greater than for health care encounters suggest that case families may have had more health problems but may have been less likely to seek health care when needed compared with control families.

Second, comparisons of the study's findings among the 4 cohorts may provide insights regarding specific theories about how having a child with an LTC in the family could adversely affect the physical and mental health of parents and siblings. Despite findings in the cohort of families of children who died that suggested an association between a child's death and increased rates of the study outcomes, the greater degree of increases in outcome rates in the oncologic and neurologic cohorts cannot be explained by this factor because the mortality was significantly higher in the prematurity cohort. An alternative explanation focuses on the onset, duration, and prognostic uncertainty of serious illness as well as the parental workload. Compared with case newborn infants in the cardiac and prematurity cohorts, most of whose conditions likely substantially improved after several months (thereby resolving prognostic uncertainty), children in the neurologic and oncologic cohorts were most likely previously healthy and more likely to experience long-duration illnesses with sustained prognostic uncertainty and substantial ongoing parental workload, such that these family members likely experienced the stress and other negative effects associated with a child's LTC for longer periods. These observations would be consistent with at least 3 theories of how having an ill family member may affect other family members. One theory is that the emotional, financial, and other forms of stress of having an ill family member impose a deleterious allosteric load on other family members in the short and long term. The second theory is that over time, maladaptation to this load would result in poor health habits. The third theory is that coping with the extra tasks and constraints (including financial hardship) imposed by the care needs of the ill family member may lead other family members to defer preventive care.

Third, if this study's findings, in conjunction with previous findings, are accepted as indicating higher levels of physical and mental health conditions among parents and siblings of children with LTCs, questions arise regarding whether this adverse health effect can be prevented or mitigated by effective physical and mental health care. Care for these at-risk families should also provide both instrumental support (eg, assistance with transportation, insurance, navigation, financial hardship, health promotion, and school) and emotional support (eg, psychotherapy, support groups, and stress reduction) aimed to minimize financial hardship and distress.

Limitations
This study has limitations. First, the study used data generated from health care encounters and did not directly measure differences in physical and mental health. Second, the sample consisted entirely of families who had private insurance coverage, limiting generalizability to individuals without private insurance coverage. Third, because only children with 1 of 4 LTCs were included, the details of these findings cannot be generalized to all families who have children with any form of LTC.

Conclusions
The findings of this cohort study, limited to families of children with 1 of 4 LTCs, are consistent with increasing evidence that family members of children with LTCs may have increased health care use and poorer mental and physical health. Although more research is warranted to better understand the mechanisms underlying these findings, interventions for parents and siblings of children with LTCs that aim to safeguard their mental and physical well-being appear to be warranted.
ARTICLE INFORMATION

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SUPPLEMENT.

eAppendix. Expanded Description of Study Methods

eTable 1. International Classification of Disease Codes Used to Define Cohorts and Identify Case Patients With Specified Conditions

eTable 2. Discrepancies From Proposed Analysis Registered on ClinicalTrials.gov

eTable 3. Demographic Characteristics of Case and Matched Control Children by Cohort

eTable 4. Comparison of Mothers and Fathers Regarding Health Care Encounters, Diagnoses, and Prescriptions

eTable 5. Comparison of Sisters and Brothers Regarding Health Care Encounters, Diagnoses, and Prescriptions

eTable 6. Comparison of Bereaved Mothers and Fathers Regarding Health Care Encounters, Diagnoses, and Prescriptions