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The high price of depression: Family members' health conditions and health care costs

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ABSTRACT

Objective: To compare the health conditions and health care costs of family members of patients diagnosed with a Major Depressive Disorder (MDD) to family members of patients without an MDD diagnosis.
Methods: Using electronic health record data, we identified family members (n = 201,914) of adult index patients (n = 92,399) diagnosed with MDD between 2009 and 2014 and family members (n = 187,011) of matched patients without MDD. Diagnoses, health care utilization and costs were extracted for each family member. Logistic regression and multivariate models were used to compare diagnosed health conditions, health services cost, and utilization of MDD and non-MDD family members. Analyses covered the 5 years before and after the index patient's MDD diagnosis.
Results: MDD family members were more likely than non-MDD family members to be diagnosed with mood disorders, anxiety, substance use disorder, and numerous other conditions. MDD family members had higher health care costs than non-MDD family members in every period analyzed, with the highest difference being in the year before the index patient's MDD diagnosis.
Conclusions: Family members of patients with MDD are more likely to have a number of health conditions compared to non-MDD family members, and to have higher health care cost and utilization.

1. Introduction

At least 15 million children annually live with a depressed parent [1]; the number is much higher when considering the entire span of childhood [2]. A study using the 1997 national Medical Expenditure Panel Survey found that children of depressed parents were twice as likely as children of parents without depression to have health problems [3]. A 23 year study found that the adult children of depressed parents had “poorer personal functioning” than children of non-depressed parents and more health conditions [4]. A 1990 review found that children of depressed parents had higher risk of adjustment problems, and had similar risk as children of schizophrenic parents [5].

This earlier literature finds that having a family member with depression affects family functioning and dynamics [6,7], which may lead to increased prevalence of medical and psychiatric conditions and medical utilization [3,8]. Our study builds on this research and addresses gaps by using more recent data from a large, heterogeneous health system that is increasingly representative of many public and private care models [9]. We compare the prevalence of health conditions, and the utilization and cost of health services of adult and child family members of patients diagnosed with Major Depressive Disorder (MDD) (without another such diagnosis in the prior year) to family members of matched patients without an MDD diagnosis. We hypothesized that MDD family members would have more health conditions compared to non-MDD family members, and that MDD family members would use more health care resources over time compared to non-MDD family members.

Identifying health care conditions and resource use of family members of depressed individuals can inform health policy on the need to screen for these conditions, and may support the case for early-treatment of adults with MDD to minimize the potential impact on the health of family members.

2. Methods

2.1. Setting

Kaiser Permanente Northern California (KPNC) is a nonprofit, integrated health care delivery system providing comprehensive health services to 4 million members. The membership overall reflects the

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general population in northern California and is racially and socioeconomically diverse: > 40% of adult members are non-white or Hispanic, nearly 30% have a high school or lower level of education, and 44% earn less than $65,000 annually [10].

2.2. Data sources

Membership, health services, and cost data are archived in electronic health record (EHR) and administrative databases, which contain individual patient records linked using the patient's medical record number [11].

2.3. Analytic approach

We first identified an index MDD patient and a matched index patient without MDD. We then compared the cost and diagnosed health conditions of the family members of these two sets of index patients – but did not include the index patients themselves. The matched sample ensured that non-MDD family members each had at least one family member who was similar to the corresponding MDD index patient with respect to demographics and propensity to use health services, but did not have MDD.

2.4. Identification of index patients

Using the KPNC databases, we identified persons with, and without, an MDD diagnosis; their respective family members were the study subjects (Fig. 1). We focus on MDD since there is concurrence that treatment for MDD is important and the diagnosis has better precision (vs. subsyndromal depression) [12,13].

To identify the potential index MDD patients, we selected the first outpatient MDD diagnosis (ICD-9 codes 2962.x and 2963.x) recorded for any adult between January 1, 2009 and December 31, 2014 without an MDD diagnosis in the year prior. This diagnosis date was the patient's index date. Individuals were retained if they: 1) were KPNC members in the entire year prior to the index date, 2) were ≥ 18 years old on the index date, and 3) had at least one other eligible family member during the month of the index date. Patients without self-reported race/ethnicity (about 4%) were excluded. If more than one member of the same family was identified as a potential index patient, we randomly selected the index patient.

Non-MDD index patients were identified by randomly selecting one primary care visit between 2009 and 2014. We retained visits where the person met the following criteria: 1) was a KPNC member the entire year before the visit; 2) had no MDD diagnosis in the prior year; 3) was ≥ 18 years old; 4) had at least one eligible family member; 5) had known race/ethnicity; and 6) was not in the pool of MDD index patients. We required non-MDD index patients to have a primary care visit in order to include only members with demonstrated service use, and to provide index dates analogous to MDD index patients.

2.5. Matching process

For all potential index patients, we collected: 1) year of index visit; 2) birthdate; 3) gender; 4) race/ethnicity; 5) membership role (subscriber, spouse, or dependent); 6) number of primary care visits, and number of specialty care visits, in the 30, 180 and 360 days, before the index visit; 7) number of hospitalizations and hospital days in the 360 days before the index visit; and, 9) DxCG risk score (derived using DxCG Intelligence software produced by Verisk Health [14]) based on data in the year prior to the index date.

Potential MDD and non-MDD index patients were separated into subgroups based on year of index date, age (within 10-year intervals), and gender. For each subgroup, we ran a logistic regression model in which the outcome indicated whether or not the patient was a potential MDD index member; independent variables were the above character-

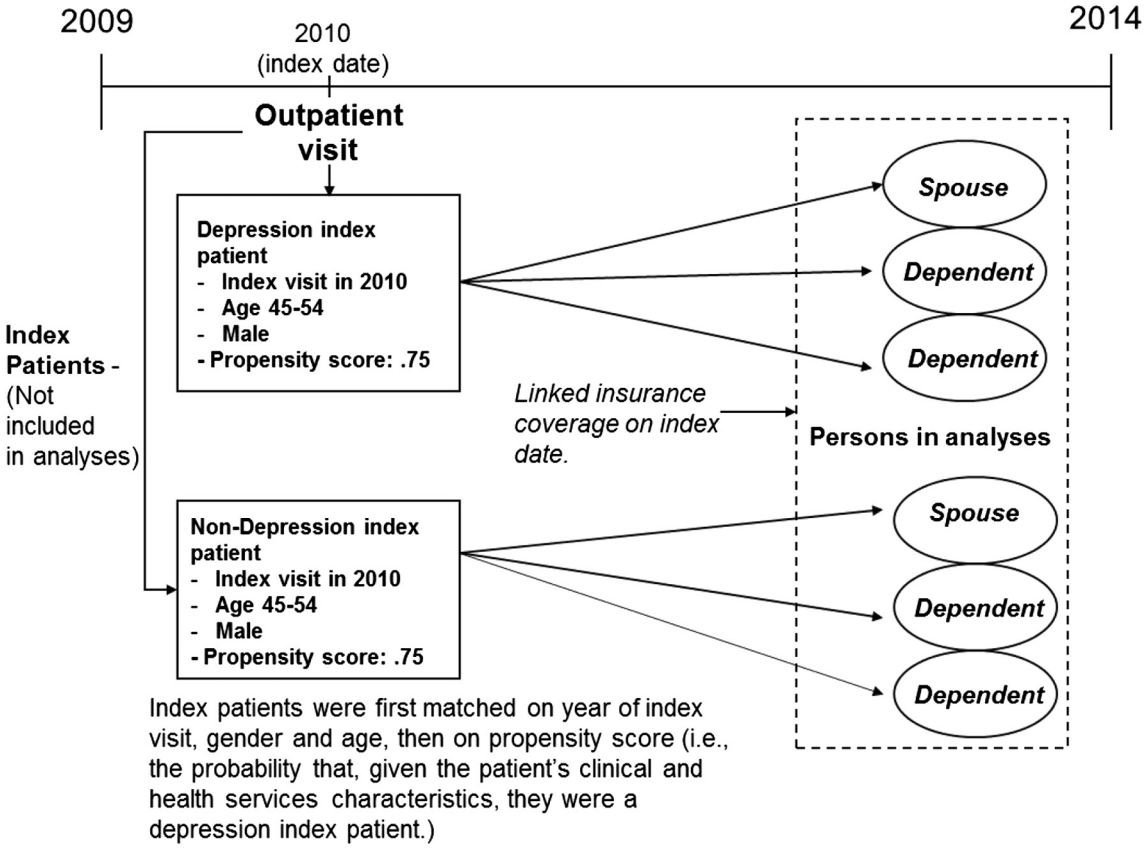

Fig. 1. Example of selection of family members.

istics. The predicted probability that the patient was a potential MDD index member was the propensity score. We then matched the two groups of potential index patients using the Mahalanobis metric matching within calipers defined as one quarter of the standard deviation of the logit of the propensity score [15]. Thus, index patients were matched directly on year of index date, age and gender, and then on propensity score. The final cohort included 92,399 MDD index patients and 92,399 matched non-MDD index patients.

2.6. Identification of family members

We identified KPNC members who were family members of the MDD and non-MDD index patients on the index date (referred to as "MDD family members" and "non-MDD family members"). As in recent studies [16–18], we defined the family from the health plan perspective: persons who shared a membership account number with the index patient. This number links the subscriber to any person who has KPNC coverage through the subscriber. Whether the index patient was the subscriber, spouse, or dependent, this method identified the other members to whom their coverage was connected. The final cohort included 201,914 MDD, and 187,011, non-MDD family members. Due to annual inclusion requirements, not all family members contributed to every analysis.

2.7. Demographic, membership and neighborhood characteristics

For each index patient and family member, we had month-by-month membership status, sex, age, race/ethnicity, and census block of their address. A neighborhood deprivation index (NDI) was created from the 2006–2010 American Community Survey (ACS) collected by the US Census Bureau, and assigned to each family member. The NDI is a composite measure of socio-economic deprivation [19,20]. Family members with addresses mapping to the same census block at the time of the index date were considered living together.

2.8. Health conditions

We extracted all family members' diagnoses in the year before their index date. We used the Agency for Healthcare Research and Quality's Clinical Classification Software (CCS) to group diagnoses into clinically meaningful "health condition" categories [21]. For mental health diagnoses, we used the more specific level 2 multi-level CCS categories, but separated out Major Depressive Disorder from the CCS category "mood disorders"; otherwise, the more general level 1 CCS categories were used. Family members were identified with the condition if they had at least one diagnosis in the CCS diagnostic category. We report results for conditions diagnosed in at least 3% of members.

2.9. Cost and utilization data

As in prior KPNC studies [16,17,22], costs for services provided by KPNC were obtained from the Cost Management Information System, an automated system that integrates utilization and financial databases. Pharmacy costs were obtained from KPNC's Pharmacy Information Management System, which records acquisition cost of outpatient medications dispensed at KPNC pharmacies. For covered services provided by non-KPNC vendors, we used payments made to those vendors. The Consumer Price Index was used to adjust costs to 2015 dollars.

Health care utilization and costs were estimated for each family member for each year from five years prior to five years post their index date. We estimated costs relating to: 1) hospitalizations; 2) Emergency Department (ED) visits; 3) primary care related visits (those to the Departments of Medicine, Family Practice, and Obstetrics/Gynecology – which includes some specialties such as cardiology); 4) Addiction Treatment Program (ATP) visits; 5) Psychiatry Department visits; 6) other clinic visits (e.g., the Departments of Urology, Neurology); 7) outpatient pharmacy. The following utilization measures were also analyzed: 1) hospital days; 2) ED visits; 3) primary care related visits; 4) ATP visits; 5) Psychiatry Department visits; 6) other clinic visits.

2.10. Analyses

We used logistic regression to test if health conditions were more common in MDD versus non-MDD family members in the year before their index date. Only family members who were continuously linked to the index patient's insurance account each month of the entire year were included. (See Supplemental Table 1 for counts of family members eligible in each year.) Analyses controlled for family member gender and age at index date (an 18 level categorical variable, in five-year increments, by gender), race/ethnicity, NDI (quartiles), and family size. We also controlled for the following index patient characteristics: gender, age (continuous), age-squared, membership role, and DxCG risk score. Models were run separately for adults and children.

To analyze cost and utilization, we ran generalized linear regression models (Gaussian distribution assumption and identity link function) for each cost and utilization type. In preliminary analyses using 10-fold cross-validation [23], we found this approach predicted costs and utilization as well or better than models involving two-part log-transformed costs, or gamma or Poisson distribution assumptions with log-link functions – findings consistent with other prior studies [22,24]. Cost and utilization models adjusted for the same independent variables as the health conditions models. After reviewing the models assessing cost by year-in-relation-to-index-date, we classified each year as being in one of four time periods: 1) years 2 to 5 before the index date; 2) the year before the index date; 3) the year after the index date, and 4) years 2 to 5 after the index date. Models included all years and the interaction of family member type (MDD or non-MDD) with time period indicated the difference between MDD and non-MDD family members by time period. Each family member identifier was treated as a random effect to account for within-person correlation. All differences reported use non-MDD family members as the reference group; thus, positive differences indicate that MDD family members had higher cost or utilization than non-MDD family members.

We performed two sets of post-hoc analyses: 1) difference in total cost by relationship of the family member to the index patient (dependent, spouse, parent/guardian, sibling); 2) difference in total cost, and total non-hospital cost, by whether or not the family member was living with the index patient on the index date. (Due to the high variability of hospital costs, estimates of non-hospital costs are more stable than estimates of total cost). The last of these post-hoc analyses was also run separately for family members who were spouses, and family members who were dependents, of the index patient. Statistical analyses were performed using SAS software (Version 9.3, Cary, NC).

3. Results

3.1. Subject and index patient characteristics

Compared to non-MDD family members, MDD family members were slightly younger, less likely to be living with the index patient on the index date, more likely to be in larger families, and had higher health care costs in the year before their index date ($3911 vs. $3247 (Table 1). MDD index patients and non-MDD index patients were similar in age, gender, and DxCG risk score.

3.2. Health conditions

Three mental health conditions, and thirteen non-mental health conditions, were diagnosed in ≥ 3% of adults in either family group (Table 2). Adult MDD family members were more likely than adult non-MDD family members to be diagnosed with each condition, with the

Table 1
Demographic characteristics of MDD family members and non-MDD family members[a].

Characteristics	MDD family members (n = 201,914)	Non-MDD family members (n = 187,011)
Gender		
Female	89,779 (44)	82,761 (44)
Male	112,135 (56)	104,250 (56)
Mean (median) age of family members at index date*	30 (21)	31 (21)
Age group, years (%)*		
< 5	17,461 (9)	17,117 (9)
5– < 18	60,764 (30)	54,838 (29)
18– < 50	77,051 (38)	68,418 (37)
50– < 65	37,471 (19)	37,421 (20)
65 +	9167 (5)	9217 (5)
Race/ethnicity*		
Asian	21,293 (11)	21,433 (11)
Black	17,532 (9)	15,517 (8)
Hispanic	47,979 (24)	42,461 (23)
Native American	1096 (1)	877 (< 1)
Multiracial	7422 (4)	6605 (4)
Unknown	73 (< 1)	118 (< 1)
White	106,519 (53)	100,000 (53)
Neighborhood deprivation, n (%)*		
Quartile 1, least deprived	47,613 (24)	47,066 (25)
Quartile 2	52,365 (26)	48,645 (26)
Quartile 3	53,696 (27)	47,578 (25)
Quartile 4, most deprived	47,834 (24)	43,302 (23)
Missing	406 (< 1)	420 (< 1)
Living with index patient on index date[b]	158,128 (78)	152,210 (81)
Family size at index date*		
2	37,703 (19)	42,611 (23)
3	39,358 (19)	38,669 (21)
4	62,934 (31)	58,010 (31)
5 +	61,919 (31)	47,721 (26)
Relationship to index patient*		
Dependent	96,226 (48)	83,863 (45)
Spouse	65,537 (32)	65,806 (35)
Parent/guardian	22,087 (11)	21,214 (11)
Sibling	15,312 (8)	13,887 (7)
Unknown	2752 (1)	2241 (1)
Unadjusted mean total cost of health services in year before index date, US$ (median)*	3911 (1114)	3247 (986)
Mean follow-up years per person[c,*]	6.70 (7.00)	6.33 (6.00)
Characteristics of index patients		
Number of index patients	81,943	81,943
Number (%) of index patients that were female	62,614 (67.76)	62,614 (67.76)
Mean (median) age of index patients at index date	44.76 (45.17)	44.77 (45.14)
DxCG Risk Score (median) in year before index date[d]	2.37 (1.37)	2.40 (1.20)

[a] Includes family members of MDD and non-MDD index patients who were 1) KPNC members on the index date, 2) linked to the index patient by insurance account, and 3) were continuous KPNC members, and continuously linked to the index patient, for at least one entire year in the 5 years prior to 5 years after index date.

[b] Based on whether the family member's address (as it was recorded in administrative databases) was in the same census block as the index patient's at the time of the index date. We considered this a proxy for living together at the time of the index date. However, we note that: 1) family members may have lived with the index patient at any time before or after the index date; 2) there may be delays between address changes and changes recorded in the health plan's databases, and 3) addresses may not record the actual residences of persons (for example, children of separated parents).

[c] Includes years from 5 years prior to 5 years after index date.

[d] Derived by employing the DxCG Intelligence software produced by Verisk Health. The DxCG score is typically used to predict an individual's health expenditures in the following year.

* MDD family members were significantly different from non-MDD family members at $p \leq 0.05$.

highest odds ratio for mood disorders (OR: 1.32; CI: 1.28–1.37), anxiety disorders (OR: 1.25, CI: 1.22–1.29) and substance use disorders (OR: 1.17; CI: 1.12–1.22). Four mental health conditions, and eleven non-mental health conditions, were diagnosed in ≥ 3% of children in either group. Child MDD family members were more likely to be diagnosed with each condition, with the highest odds ratio for mood disorders (OR: 1.77; CI: 1.65–1.91), anxiety disorders (OR: 1.67; CI: 1.57–1.77), and attention deficit/conduct disorders (OR: 1.57; CI: 1.65–1.91). MDD was more common among child MDD family members (OR: 2.01; CI: 1.77–2.29), although the percent of children with MDD was small (1.12% of child MDD family members and 0.52% of child non-MDD family members.)

3.3. Cost and utilization

In adjusted models, MDD family members had higher health care costs and utilization per person than non-MDD family members in each time period and in most categories measured (Table 3). The difference in total cost was $294 (CI: $225–$364) per year in the 2 to 5 years before the index date; $697 (CI: $595–$798) in the year before the index date; $491 (CI: $384–$598) in the year after the index date, and; $493 (CI: $412–$573) in the 2 to 5 years after the index date. Cost differences relating to psychiatry visits peaked in the year after the index date ($82, CI: $76–$88), while differences relating to hospitalizations peaked in the year before the index date ($375; CI: $290–$459). In adjusted models that compared differences between time periods, all differences in costs in the later three time periods were significantly higher than differences in the 2 to 5 years before the index date, except for ATP visit costs in the year before, and the 2 to 5 years after the index date, and hospital costs in the year after and the 2 to 5 years after the index date. After excluding family members with mean annual costs over $100,000, differences in annual total cost decreased between $5 and $90 (depending on the period), but the relationship in the cost differences among the periods remained similar.

In the post-hoc model stratified by relationship of the family member to the index patient, differences in total costs were higher in every period for spouses compared to dependents, parents/guardians, or siblings (Supplemental Table 2). In the year before the index date, total annual cost differences for spouses and dependents were $1243 (CI: $1048–$1439) and $542 (CI: $409–$675), respectively, and in the year after the index date they were $921 (CI: $716–$1127), and $360 (CI: $221–$499), respectively.

In the second post-hoc analysis, MDD family members had higher annual total costs than non-MDD family members, regardless of whether they were living with the index patient on the index date (Table 4, panel 1). In the year before the index date, MDD family members who were not living with the index patient cost $378 (CI: $139–$617) more than non-MDD family members not living with the index patient; MDD family members who were living with the index patient cost $802 (CI: $688–$916) more than non-MDD family members living with the index patient. The difference between these two differences (the “difference-in-differences”) was positive and significant in both the year before ($424; CI: $159–$690) and the year after ($558; CI: $271–$846) the index date.

Among family members who were dependents of the index patient, the difference-in-differences was positive in each period, and was significant in the year after the index date ($492; CI: $862–$123). Among spouses, difference-in-differences were not significant, but confidence intervals were wide. In order to assess costs with less variability, we repeated the above analyses for all non-hospital costs (Table 4, panel 2). Among dependents, living with the index patient was consistently associated with larger positive differences in total non-hospital costs. Among spouses, MDD family members had equally higher non-hospital costs compared to non-MDD family members whether they lived with the index patient or not.

Table 2
Health conditions diagnosed in the year before the index date, defined by Multi-Level Clinical Classification Software Diagnostic Category.

Health conditions defined by Clinical Classification Software Multi-Level Diagnostic Category[a]	Number (%) of persons receiving diagnosis during year before index date					
	Adults			Children		
	MDD family members (n = 118,721)	Non-MDD family members (n = 110,320)	Odds ratio (95% CI)[d]	MDD family members (n = 71,958)	Non-MDD family members (n = 65,808)	Odds ratio (95% CI)[d]
Mental health: Major Depressive Disorder[b]	6367 (5.36)	5933 (5.38)	1.03 (0.99 to 1.07)	804 (1.12)	341 (0.52)	2.01 (1.77 to 2.29)*
Mental health: anxiety disorders (CCS 5.2)	10,865 (9.15)	8302 (7.53)	1.25 (1.22 to 1.29)*	2997 (4.16)	1649 (2.51)	1.67 (1.57 to 1.77)*
Mental health: attention deficit, conduct, and disruptive behavior disorders (CCS 5.3)	[e]	[e]	[e]	4467 (6.21)	2677 (4.07)	1.57 (1.49 to 1.65)*
Mental health: mood disorders (CCS 5.8)[c]	7178 (6.05)	5164 (4.68)	1.32 (1.28 to 1.37)*	2384 (3.31)	1190 (1.81)	1.77 (1.65 to 1.91)*
Mental health: Substance-related disorders (CCS 5.12)	4643 (3.91)	3548 (3.22)	1.17 (1.12 to 1.22)*	5275 (7.33)	4141 (6.29)	1.10 (1.05 to 1.15)*
Infectious and parasitic diseases (CCS 1)	33,274 (28.03)	29,111 (26.39)	1.08 (1.06 to 1.10)*	32,697 (45.44)	30,136 (45.79)	1.03 (1.00 to 1.05)*
Neoplasms (CCS 2)	13,608 (11.46)	12,638 (11.46)	1.07 (1.04 to 1.10)*	[e]	[e]	[e]
Endocrine; nutritional; and metabolic diseases and immunity disorders (CCS 3)	39,252 (33.06)	36,232 (32.84)	1.10 (1.08 to 1.12)*	13,503 (18.77)	11,348 (17.24)	1.11 (1.08 to 1.14)*
Diseases of the blood and blood-forming organs (CCS 4)	5223 (4.40)	4466 (4.05)	1.13 (1.09 to 1.18)*	[e]	[e]	[e]
Diseases of the nervous system and sense organs (CCS 6)	45,187 (38.06)	41,081 (37.24)	1.08 (1.06 to 1.10)*	23,426 (32.56)	21,215 (32.24)	1.04 (1.01 to 1.06)*
Diseases of the circulatory system (CCS 7)	32,704 (27.55)	30,511 (27.66)	1.09 (1.06 to 1.11)*	[e]	[e]	[e]
Diseases of the respiratory system (CCS 8)	35,659 (30.04)	31,065 (28.16)	1.11 (1.09 to 1.13)*	28,432 (39.51)	24,446 (37.15)	1.15 (1.12 to 1.17)*
Diseases of the digestive system (CCS 9)	26,331 (22.18)	23,196 (21.03)	1.12 (1.10 to 1.14)*	8664 (12.04)	7046 (10.71)	1.18 (1.14 to 1.22)*
Diseases of the genitourinary system (CCS 10)	28,889 (24.33)	25,677 (23.28)	1.10 (1.08 to 1.12)*	6176 (8.58)	4998 (7.59)	1.14 (1.10 to 1.19)*
Complications of pregnancy, childbirth and the puerperium (CCS 11)	9611 (8.10)	8470 (7.68)	0.99 (0.96 to 1.03)	3543 (4.92)	2561 (3.89)	1.19 (1.13 to 1.26)*
Diseases of the skin and subcutaneous system (CCS 12)	25,600 (21.56)	22,826 (20.69)	1.08 (1.06 to 1.10)*	11,298 (15.70)	9521 (14.47)	1.09 (1.06 to 1.13)*
Diseases of the musculoskeletal system and connective tissue (CCS 13)	39,200 (33.02)	35,198 (31.91)	1.11 (1.09 to 1.13)*	8865 (12.32)	7425 (11.28)	1.08 (1.04 to 1.12)*
Congenital anomalies (CCS 14)	[e]	[e]	[e]	2401 (3.34)	2113 (3.21)	1.08 (1.02 to 1.15)*
Injury and poisoning (CCS 16)	26,039 (21.93)	22,185 (20.11)	1.12 (1.10 to 1.14)*	16,907 (23.50)	13,942 (21.19)	1.14 (1.11 to 1.16)*

[a] Diagnostic categories were derived using the Agency for Healthcare Research and Quality's Clinical Classification Software (CCS). Diagnosis codes for family members in the study were extracted from the Electronic Health Record in the year before the index date and run through the CCS software. Mental health diagnoses were grouped using the more specific level 2 multi-level CCS categories. All other diagnoses were grouped using the level 1 multi-level CCS categories. With the exception of Major Depressive Disorder (MDD), only those diagnostic categories into which at least 3% of either the MDD family members or non-MDD family members were classified are included. Conditions not meeting the 3% inclusion rule were: Adjustment disorders (CCS 5.1), dementia (CCS 5.4), developmental disorders (CCS 5.5), disorders usually diagnosed in infancy, childhood or adolescence (CCS 5.6), impulse control disorders not otherwise specified (CCS 5.7), personality disorders (CCS 5.9), schizophrenia (CCS 5.10), alcohol disorders (CCS 5.11), suicide and self-inflicted injury (CCS 5.13), miscellaneous mental health disorders (CCS 5.15), and certain conditions originating in the perinatal period (CCS 15).

[b] The CCS includes Major Depressive Disorder (MDD, ICD-9 codes 2962.x and 2963.x) in the level 2 category "mood disorders" (CCS 5.8). However, MDD is here reported separately and is not included in the mood disorders category.

[e] Less than 3% of persons in both the MDD and non-MDD families received diagnoses in this CCS.

[c] We excluded Major Depressive Disorder from CCS 5.8. However, non-MDD depression is included.

[d] Odds ratio from logistic regression. All models adjusted for the following: gender, age at index date, race/ethnicity, Neighborhood Deprivation Index, family size, index patient gender, index patient age, index patient age-squared, index patient insurance account role (subscriber, spouse, or dependent), and index patient DxCG risk score in the year before index date.

* Difference between MDD family members and non-MDD family members was significant at $p \leq 0.05$, after adjusting for covariables.

Table 3
Mean adjusted per person annual difference in cost and utilization of MDD family members compared to non-MDD family members, by time period in relation to index date.[a]

Cost/utilization type	Time period in relation to index date			
	2 to 5 years prior to index date	Year before index date	Year after index date	2 to 5 years after index date
All hospital-related costs	119 (65 to 173)*	375 (290 to 459)*	153 (64 to 242)*	179 (115 to 243)*
ED-related costs	17 (15 to 20)*	35 (31 to 39)*	38 (34 to 42)*	34 (31 to 37)*
Outpatient primary care-related visit costs	33 (28 to 38)*	47 (40 to 54)*	54 (46 to 61)*	57 (51 to 63)*
Outpatient Addiction Treatment Program visit costs	5 (3 to 7)*	2 (−1 to 6)	11 (7 to 14)*	6 (3 to 8)*
Outpatient psychiatry dept visit costs	34 (30 to 38)*	58 (52 to 63)*	82 (76 to 88)*	44 (40 to 49)*
Other outpatient visit costs	36 (16 to 56)*	104 (76 to 132)*	71 (41 to 100)*	88 (66 to 111)*
Outpatient pharmacy costs	33 (17 to 49)*	56 (36 to 76)*	62 (41 to 83)*	60 (42 to 77)*
Total costs	294 (225 to 364)*	697 (595 to 798)*	491 (384 to 598)*	493 (412 to 573)*
Number of inpatient hospital days	0.02 (0.01 to 0.03)*	0.06 (0.05 to 0.08)*	0.03 (0.02 to 0.05)*	0.04 (0.03 to 0.05)*
Number of ED visits	0.02 (0.01 to 0.02)*	0.04 (0.03 to 0.04)*	0.04 (0.04 to 0.04)*	0.04 (0.03 to 0.04)*
Number of primary care visits	0.12 (0.10 to 0.13)*	0.15 (0.13 to 0.18)*	0.17 (0.14 to 0.19)*	0.18 (0.16 to 0.20)*
Number of psychiatry dept visits	0.10 (0.09 to 0.11)*	0.17 (0.16 to 0.19)*	0.25 (0.23 to 0.27)*	0.13 (0.12 to 0.15)*
Number of other outpatient visits	0.07 (0.05 to 0.09)*	0.07 (0.05 to 0.09)*	0.06 (0.04 to 0.09)*	0.05 (0.03 to 0.07)*

[a] Positive values indicate MDD family members had higher cost or utilization than non-MDD family members. Differences were estimated using a generalized linear model in which the cost or utilization statistic was the dependent variable. All time periods were included in the same model and the coefficient of the interaction of the time period indicator and the indicator for family type provided the estimate of the difference in cost between MDD and non-MDD family members. A member identification variable was treated as a random effect to account for within-person correlation. Numbers in parentheses represent lower and upper bounds of 95% confidence interval. All models adjusted for the following: gender, age at index date, race/ethnicity, Neighborhood Deprivation Index, family size, index patient gender, index patient age, index patient age-squared, index patient role (subscriber, spouse, or dependent), and index patient DxCG risk score in the year before index date. All costs are in 2015 $US.

* Difference between MDD family members and non-MDD family members was significant at $p \leq 0.05$, after adjusting for covariables.

4. Discussion

Findings suggest that both child and adult family members of patients with MDD were diagnosed with more health conditions than family members of similar patients not diagnosed with MDD, and this was particularly true for mental health conditions (mood disorders, anxiety, attention-deficit, and substance use disorders). Health care costs and utilization were higher in MDD family members in all periods in relation to the index date, but especially from the year before the index date forward.

We found that MDD family members were more costly than non-MDD family members in periods before the index date (as well as after), and this was especially true in the year before the index date. The index date for the MDD patient was the date of their first MDD diagnosis, without another such diagnosis in the prior year. It is likely that the depression disorder existed or had been developing for some time in the index patient prior to its diagnosis [25]. This in turn may be associated with increased pre-diagnosis utilization among family members, as we found in a study of family members of persons with alcohol and drug diagnoses [16]. The criteria for identifying index patients was such that they may have either had undiagnosed MDD, or diagnosed MDD in years 2 to 5 before the index date. Nevertheless, that there was an increase in cost differences starting the year before the index date suggests that something changed in that time period, and the effect of this change continued for several years afterward.

Although this study could not assess biologic or genetic relationships of family members to index patients, we found higher costs among both spouses (who likely have no biological relationship) and dependents (who likely do have a biological relationship) of MDD patients, with the absolute difference for spouses being more than for dependents. However, the “baseline” cost for dependents (largely due to younger age) was about half of that for spouses; thus, the relative cost difference between dependents and spouses was similar, with the cost for MDD family members of both groups being about 10% higher than similar non-MDD family members.

Although MDD family members had higher costs than similar non-MDD family members whether or not they lived with the index patient, the difference was greater among family members who lived with the index patient. This was true even though our designation of cohabitation is likely imperfect, given that family members may have lived with the index patient at any time before, or after, the index date, that there may be delays between a change in address and that address being updated in the health plan's membership databases, and the possibility that children may frequently move between the residences of separated parents. The implication is that there is an added effect of living with an MDD patient, possibly due to an effect of MDD on family dynamics and functioning, and through that on health services utilization. Also interesting is that we found that this differential effect of living with the index MDD patient was almost entirely associated with dependents rather than spouses. Dependents who did not live with the index MDD patient were only slightly more costly than similar non-MDD dependents; but dependents who lived with the index MDD patient were much more costly. For spouses, the additional cost of being in a family with an MDD patient was similar whether or not they lived with the index patient.

We hypothesized that MDD in the family could lead to increased prevalence of medical and psychiatric conditions in other family members, and to increased medical utilization. We expected that patients diagnosed with MDD would likely be experiencing problems and have increased utilization prior to being diagnosed. The matching of MDD and non-MDD index patients was designed, in part, to isolate the effect of MDD on the family rather than that of simply having a high-utilizing person in the family. However, identifying causal mechanisms for correlations in health conditions and utilization among families is very challenging. In addition to our main hypothesis, other factors to consider include: (1) characteristics of the shared environment; (2) shared genetics; (3) that persons with similar pre-existing risks and propensity to use health services choose each other as partners (“assortative mating”); (4) that health events in family members may cause a family member to develop and/or be diagnosed with MDD. Although the goal of this study was not to disentangle these various mechanisms, our methodology and analyses attempted to address most of them, at least in part. Thus, we included neighborhood deprivation in our modeling and performed analyses of family members who live, and do not live, with the index patient (Item 1); we performed analyses that separated out spouses and dependents (Item 2); and we matched MDD and non-MDD index patients on health services utilization and DxCG risk score in the year before the index date (Item 3). Although we did not specifically address Item 4, our finding that the difference in hospital-related costs in the year before the index date was especially high lends some support to the possibility that serious health episodes in the family members caused the index patient to develop or be

Table 4
Mean adjusted per person annual difference in cost of MDD family members compared to non-MDD family members by whether family member was cohabitating with index patient.

Cost type	Relationship of family member to index patient	Was family member living with index patient on index date?[b]	Difference in cost (MDD minus Non-MDD), $ (95% CI)[a]			
			2 to 5 years prior to index date	Year before index date	Year after index date	2 to 5 years after index date
Total costs	All persons	No	193 (27 to 359)*	378 (139 to 617)*	29 (−232 to 290)	340 (135 to 545)*
		Yes	323 (245 to 401)*	802 (688 to 916)*	588 (468 to 707)*	533 (443 to 622)*
		Difference (in differences)[c]	130 (−54 to 314)	424 (159 to 690)*	558 (271 to 846)*	193 (−32 to 417)
	Dependents	No	122 (−94 to 338)	372 (63 to 681)*	−35 (−370 to 300)	411 (154 to 668)*
		Yes	227 (122 to 332)*	587 (437 to 738)*	458 (302 to 613)*	497 (382 to 612)*
		Difference (in differences)[c]	105 (−136 to 346)	215 (−129 to 559)	492 (123 to 862)*	86 (−196 to 368)
	Spouses	No	679 (275 to 1084)*	1047 (483 to 1611)*	1306 (692 to 1920)*	731 (256 to 1206)*
		Yes	559 (410 to 708)*	1329 (1114 to 1544)*	893 (668 to 1118)*	749 (581 to 918)*
		Difference (in differences)[c]	−120 (−542 to 302)	282 (−309 to 873)	−413 (−1053 to 228)	18 (−476 to 512)
All non-hospital costs	All persons	No	98 (27 to 170)*	157 (65 to 249)*	151 (52 to 250)*	116 (33 to 199)*
		Yes	161 (127 to 195)*	329 (285 to 373)*	352 (306 to 398)*	318 (281 to 355)*
		Difference (in differences)[c]	62 (−17 to 142)	172 (69 to 275)*	201 (91 to 311)*	202 (110 to 293)*
	Dependents	No	109 (33 to 185)*	94 (−5 to 193)	123 (17 to 229)*	175 (88 to 261)*
		Yes	127 (90 to 164)*	275 (227 to 323)*	318 (269 to 368)*	298 (259 to 337)*
		Difference (in differences)[c]	18 (−67 to 103)	180 (70 to 291)*	196 (78 to 313)*	123 (28 to 219)*
	Spouses	No	350 (148 to 553)*	610 (365 to 854)*	670 (410 to 931)*	393 (170 to 616)*
		Yes	328 (252 to 405)*	596 (502 to 689)*	561 (464 to 658)*	489 (408 to 571)*
		Difference (in differences)[c]	−22 (−234 to 190)	−14 (−270 to 243)	−109 (−382 to 163)	96 (−136 to 328)

[a] Positive values indicate MDD family members had higher total cost per year than non-MDD family members. Differences were estimated using a generalized linear model in which the cost or utilization statistic was the dependent variable. Separate models were run for all persons, dependents, and spouses. Due to small numbers outside these age ranges, “dependents” were restricted to persons under 27 years of age and “spouses” were restricted to persons over 18 years of age. All time periods were included in the same model and the coefficients of the interaction of the time period indicator, the indicator for family type, and the indicator of cohabitation provided the estimate of the difference in cost between MDD and non-MDD family members. A member identification variable was treated as a random effect to account for within-person correlation. Numbers in parentheses represent lower and upper bounds of 95% confidence interval. All models adjusted for the following: All models adjusted for the following: gender, age at index date, race/ethnicity, Neighborhood Deprivation Index, family size, index patient gender, index patient age, index patient age-squared, index patient role (subscriber, spouse, or dependent), and index patient DxCG risk score in the year before index date.

[b] Persons were considered to be living with the index patient if their address in the health plan's administrative data mapped to the same census block as the index patient's address at the time of the index date.

[c] Positive values indicate that the difference between the total annual cost of MDD family members compared to non-MDD family members was higher among family members who cohabitated with their index patient than among family members who did not cohabitate with their index patient. “Difference-in-differences” were estimated by parameterizing the interaction of time period, family member relationship and cohabitation so as to provide the contrast desired.

* Difference between MDD family members and non-MDD family members was significant at $p \leq 0.05$, after adjusting for covariables.

diagnosed with MDD. However, in the year before the index date, only 3.5% of MDD family members, and 3.0% of non-MDD family members, had a hospitalization.

This study is timely in informing policy and clinical care. The passage of mental health parity legislation increased treatment access [25]. The adoption of EHRs, incentivized by health reform policies and used by over 80% of primary care physicians in the U.S. in 2014, improves the capability of health systems to collaborate and communicate among departments and across systems, with the potential to improve care coordination [26]. HEDIS performance measurement on antidepressant medication management and mental health utilization [27] brings more accountability to health plans to address depression, and reimbursement mechanisms increasingly encourage health plans to do so. This new climate improves the environment for addressing depression in families as a basic part of health care. Tied to these opportunities, evidence of how individuals with depression impact the health and health resource use of their family members, may make expanded services for family members more feasible. Services might include outreach to children and spouses of persons with MDD for prevention and treatment of potential medical and mental health problems.

Several limitations warrant consideration. Family members were identified by linked health plan coverage to index patients. Family members without KPNC coverage, or covered under a different account, were not included. While this might affect estimates of family size, it seems unlikely it would affect estimates of per-person differential costs between the two family groups. The direction of causality is also not clear; the medical conditions of the family members could exacerbate depression potential in adults. Though not precisely limitations, index MDD patients may have received an MDD diagnosis any time during follow-up other than the year before the index date; and index patients were matched using data from the year before the index date and not earlier years. The study population may not be representative of other populations. However, it is representative of the larger Northern California population and is a health system designated as a benchmark for the small group plans on the California health insurance exchange [28]. It would be difficult, if not impossible, to examine the full medical utilization and cost of family members in a different type of system.

In conclusion, family members of patients diagnosed with MDD are more likely to be diagnosed with a number of health conditions compared to family members of otherwise similar patients without an MDD diagnosis. They also have higher health care costs and utilization. Identifying depression in adults earlier, as well as providing medical and mental health services to their family members may have important benefits.

Disclosures

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Contributors statements

G. Thomas Ray contributed to the design of the study, made substantial contributions to the data acquisition, data analysis, and interpretation of data, was primarily responsible for drafting the manuscript, and approved the final manuscript.

Constance Weisner, Cosette Taillac, and Cynthia Campbell conceived the study, contributed to the design of the study, obtained funding, made substantial contributions to the interpretation of data, helped to draft the manuscript and revise it for important intellectual content, and approved the final manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.genhosppsych.2017.04.004.

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