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Burden for Parents of Patients With Schizophrenia—A Nationwide Comparative Study of Parents of Offspring With Rheumatoid Arthritis, Multiple Sclerosis, Epilepsy, and Healthy Controls

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Background: **The study aimed to (1) compare the risk of health care use, adverse health status, and work productivity loss of parents of patients with schizophrenia to parents of patients with multiple sclerosis (MS), rheumatoid arthritis (RA), epilepsy, and healthy controls; and (2) evaluate such outcome measures while considering disease severity of schizophrenia.** ***Methods:*** **Based on linkage of Swedish registers, at least one parent was included (*n* = 18 215) of patients with schizophrenia (information 2006–2013, *n* = 10 883). Similarly, parental information was linked to patients with MS, RA, epilepsy, and matched healthy controls, comprising 11 292, 15 516, 34 715, and 18 408 parents, respectively. Disease severity of schizophrenia was analyzed. Different regression models yielding odds ratios (OR), hazard ratios (HR), or relative risks (RR) with 95% confidence intervals (CI) were run.** ***Results:*** **Psychiatric health care use, mainly due to anxiety and affective disorders, showed a strongly increasing trend for parents of patients with schizophrenia throughout the observation period. During the follow-up, these parents had an up to 2.7 times higher risk of specialized psychiatric health care and receipt of social welfare benefits than other parents. Parents of the moderately severely ill patients with schizophrenia had higher risk estimates for psychiatric health care (RR: 1.12; 95% CI: 1.07–1.17) compared with parents of least severely ill patients.** ***Conclusions:*** **Parents of patients with schizophrenia have a considerably higher risk of psychiatric health care and social welfare benefit receipt than other parents. Psychiatric health care use worsens over time and with increasing disease severity of the offspring.**

Key words: caregiver burden/schizophrenia/sickness absence/work productivity

Introduction

Schizophrenia is a severe psychiatric disorder with a chronic and relapsing course.[1,2] The lifetime prevalence of schizophrenia is around 1%,[2] with a geographical variation of up to 5 times.[3] Schizophrenia is a disabling disease[4] leading to approximately 80%–90% of the patients not being able to economically support themselves.[5,6]

Schizophrenia does not only have a strong influence on the affected patients, but also on their family members, particularly their parents.[7–9] This negative influence in parents might arise from worries about the offspring's future health and social situation, the stigma associated with schizophrenia, as well as from caring for a child with a chronic, severe disorders.[10–12] This situation is exacerbated by the parents' own morbidity. Schizophrenia is known to be a considerable degree heritable and therefore the parents themselves might suffer from the same disorder.[13,14] The burden of parents of patients with schizophrenia seems also to be intensified by the patient's symptom severity,[7,15–20] which is considered to be one of the main determinants of subjective or objective caregiver burden.[20,21] Moreover, low levels of functioning in patients with schizophrenia are associated with stress, anxiety, and depression in the patients' parents.[22,23]

For the mentioned reasons, a worse health-related quality of life with more use of health care resources among parents of patients with schizophrenia compared with parents of patents with other diseases (such as bipolar and depressive disorders) or parents of healthy children has been reported.[24,25] Moreover, the existing literature suggests that parents who are taking care of an offspring with schizophrenia have a greater loss of productivity

compared with parents of healthy children.[7,8,26] Research also suggests that having a child and particularly caring for a child with chronic conditions may negatively affect existing chronic conditions in the parents or even increase their risk of mortality.[27–30] The full range of health and social consequences of having a child with schizophrenia is, however, still unclear, especially when it comes to consequences like loss of productivity. These negative effects on health and social outcome measures for parents of patients with schizophrenia should, however, be balanced with reports on positive effects of being a caregiver, such as satisfaction and meaning derived from caregiving, greater sensitivity to people with disabilities, a greater sense of inner strength and a greater sense of clarity regarding priorities in life.[31,32]

Part of the burden for parents of patients with schizophrenia may include the effect the disorder has on cognition and behavior.[17,26,33] Additionally, stigma around schizophrenia can also contribute to higher burden.[10,12,15,34] Significant burden has also been reported in case of somatic diseases, eg, multiple sclerosis (MS),[35–37] rheumatoid arthritis (RA),[38,39] and epilepsy.[40,41] Studies, comparing health- and work-related factors between parents of patients with schizophrenia and parents of patients with chronic somatic diseases as well as with the general population, are, however, scarce.[7,25] These previous studies investigated caregivers and reported a higher caregiver burden for caregivers of patients with schizophrenia compared with other somatic disorders (cancer, Alzheimer's disease, and stroke) or depressive disorders. They were, however, based on small samples and self-reported survey data, with relatively short follow-up time and lack of analyses on newly diagnosed cases.[42] To the best of our knowledge, this is the first study that is based on nationwide registers, with a long observation period (from 5 years' prediagnosis to 7 years after diagnosis), covering a large number of parents of patients with schizophrenia, as well as parents of MS, RA, epilepsy, and healthy controls, and giving the possibility to take the disease severity of schizophrenia into account.

Aim

The study aimed to assess the risk of health care resource use, adverse health status, and work productivity loss in parents of patients with schizophrenia compared with parents of patients with MS, RA, epilepsy, and healthy controls. A further aim was to evaluate these outcome measures while taking the disease severity of schizophrenia into account.

Materials and Methods

Study Design and Population

This is a population-based cohort study based on the Insurance-Medicine-All-Sweden (IMAS) study with data derived from Swedish nationwide registers. Information regarding patients with schizophrenia and their parents was linked at individual level based on the personal id-number provided to all residents in Sweden. De-identified data on the patients were linked to data on their parents through the Multigeneration register. Additional information was gathered from the following nationwide registers:

1. Longitudinal integration database for health insurance and labour market studies (LISA) held by Statistics Sweden: gender, age, area of residence, family situation, annual disposable income, unemployment, and social welfare benefit.
2. National patient register (National Board of Health and Welfare, NBHW): diagnoses and dates for in- or specialized outpatient care.
3. Prescribed drug register (NBHW): type of medication, dispensing date, defined daily dose (DDD) and the Anatomical Therapeutic Chemical (ATC) Classification System code.
4. Cause of death register (NBHW): dates and causes of death.
5. Micro-data for analyses of social insurance (MiDAS) register, from the National Social Insurance Agency: date and diagnoses of sickness-absence (SA) and disability pension (DP).

Inclusion Criteria of Patients With Schizophrenia

Individuals living in Sweden, aged 16–45 years at cohort entry date (CED), diagnosed with schizophrenia from July 1, 2006 to December 31, 2013 (N = 10 883, prevalent population), with at least one identifiable parent with information on gender and age, were included. Cases of schizophrenia were identified by using the International Classification of Diseases version 10 (ICD-10) codes F20 or F25 as a main diagnosis in the following instances: either discharged from psychiatric inpatient care, or visit at specialized psychiatric outpatient care, sickness absence (SA), or DP. The CED was set as the earliest of any of these events since July 1, 2006. To perform sensitivity analyses, an incident (newly diagnosed) population of patients with schizophrenia (n = 3379) was formed. This incident population was identified by excluding those patients from the prevalent population who had a main or side diagnosis of F20–F29 (ICD-10), or 295 (ICD-9) recorded in either psychiatric health care, SA, or DP, or use of any antipsychotics (ATC code N05A) before July 1, 2006.

Definition of Parents

In total, 18 215 parents of patients with schizophrenia with a valid cohort entry date were selected. Parents of offspring with other chronic diseases comprised 11 292 parents of patients with MS (ICD 10 code G35; N = 6462);

15 516 parents of patients with RA (ICD 10 code M05, M06; $N = 8900$) and 34 715 parents of patients with epilepsy (ICD 10 code G40; $N = 19\,481$). For parents of control individuals with other diseases, CED was defined as the earliest date of any of the 4 events of the offspring: discharged from inpatient care, visit at specialized outpatient care or SA, DP due the disease in question, from July 1, 2006 to December 31, 2013. The proportions of single parents in the groups of "parents of patients with schizophrenia" and "healthy controls" were similar due to matching (ie, 45%). This proportion was lower in the control groups of parents of offspring with MS, RA, and epilepsy (ie, 34%). The numbers of offspring in each group were as follows: 10 883 with schizophrenia, 6462 with MS, 8900 with RA, 19 481 with epilepsy, and 10 963 healthy comparisons.

Healthy controls, referring to persons without schizophrenia, were matched 1:1 with patients with schizophrenia by gender, age (−3/+3 years) and inclusion year. In addition, parents of the patients with schizophrenia ($N = 19\,065$) were matched with parents of healthy controls (1:1, $N = 19\,065$) on gender, age (−5/+5 years), area of residence (3 categories), family situation (5 categories), and number of children (3 categories). For matched parents of healthy controls, CED was equal to the date of the corresponding matched parents of the patients with schizophrenia. Parents with multiple children matched in the process (multiple children with schizophrenia or multiple healthy children matched) were included only once, meaning that parents of children with specified chronic diseases were excluded if they were also parents of a s patient with schizophrenia (removal of duplicates of the same person, leaving 18 597 parents of patients with schizophrenia and 19 061 parents of healthy controls). Consequently, the cohort of parents of patients with schizophrenia was mutually exclusive with the cohorts of parents of offspring with RA, MS, or epilepsy. The parents of patients with RA, MS, or epilepsy were not mutually exclusive so, eg, a parent of a child with RA might have a child with MS. This overlap was marginal in most cases, however. In addition, matched parents not alive or resident in Sweden during the entire year of CED were excluded (leaving $N = 18\,215$ parents of the patients with schizophrenia and $N = 18\,408$ parents of healthy controls).

Outcome Measures

Health Care and Health Status. Health care use was assessed in terms of number of in- and specialized outpatient care visits due to psychiatric (ICD-10 codes: F00–F99) and somatic disorders (ie, diabetes mellitus type 2; diseases of the circulatory system; diseases of esophagus, stomach, and duodenum; liver disease; and dorsalgia: ICD-10 codes: E11–E14; I00–I99; K20–K31; K70–K77; and M54, respectively). Number of visits was used as a continuous outcome measure (Poisson regression), as mean annual number of visits and as a categorized variable (0, 1–2, 3–6, >6 visits; descriptive analyses). Outcomes variables related to the health status of parents comprised substance abuse (supplementary table 2), medication use for somatic and psychiatric disorders (supplementary table 3) and mortality.

Work Productivity. Long-term SA was defined as >90 annual gross days of SA (with benefits from the Social Insurance Agency). Information on granting of DP during follow-up was dichotomized. Annual income was based on yearly individualized disposable income derived from the family income (categorized based on quartiles as "no income" [yearly income is 0], "low" [first quartile], "medium low" [second quartile], "medium high" [third quartile], "high" [fouth quartile]). Long-term unemployment was measured as >180 annual days of unemployment. Social welfare benefits were calculated from the yearly individualized social welfare benefit derived from the family benefit (categorized as "yes" and "no").

Disease Severity

The number of psychiatric inpatient care visits due to "schizophrenia, schizotypal, delusional, and other nonmood psychotic disorders" (ICD-10: F20–F29) was used as a proxy for disease severity of schizophrenia. The severity variable was categorized by calculating the number of visits per year during follow-up for each patient with schizophrenia at the end of follow-up. The patients in the first quartile were defined as "least severe," those in the second–third quartiles as "moderately severe" and those in the fourth quartile as "most severe."

Covariates

Sociodemographic characteristics, including information on gender, age, educational level, area of residence, number of children, and family situation were obtained for all parental groups (supplementary table 1). All factors measured at start of follow-up except area of residence and family situation which are measured at the calendar year of the outcome measure. Family situation included information on single or cohabiting parents. This covariate was included in the analyses as the proportion of single parents differed in the parental groups. If a study variable included missing values, a missing-value category was added to that variable. In the analyses of disease severity, prescribed antipsychotics (ATC codes N05A) and treatment persistence of the patient were also used as covariates. Treatment persistence was measured annually and categorized as "no persistence" if there was no on-going antipsychotic use, "low persistence" if the longest annual antipsychotic treatment period lasted at

most 50% of the calendar days (excluding hospital days), "high persistence" if this treatment period was between 50% and 100%, and "total persistence" in case of 100% annual days of treatment period. Psychiatric morbidity at baseline was measured as diagnosis-specific psychiatric health care the year at cohort entry date. Four dichotomous diagnostic groups were formed: schizophrenia at baseline (ICD-10: F20–F29), mood disorders at baseline (ICD-10: F30–F39), anxiety disorders at baseline (F40–F49), and other psychiatric diagnoses at baseline (ICD-10: F00–F19, F50–F99).

Statistical Analyses

First, the mean number of diagnosis-specific specialized health care from 5 years before to 7 years after CED was plotted. Then, analyses in relation to comparison of parental groups, were performed for all outcome variables after CED during the entire 7-year follow-up period using pairwise comparisons: comparing parents of patients with schizophrenia to (1) parents of healthy controls (reference group); (2) parents of patients with MS, RA, epilepsy (reference groups). Yearly outcome variables were analyzed as dependent variables using logistic regression ("long-term sickness absence," "disability pension," "low or no income," "long-term unemployment," "social welfare benefit," "medication use," "substance abuse"), Cox regression (mortality), or Poisson regression (in- or specialized outpatient care due to psychiatric or somatic diagnoses). Related to these regression models, odds ratios (OR), hazard ratios (HR), and relative risks (RR) with 95% confidence intervals (CI) were calculated. Logistic regression analyses for longitudinal binary data yielding ORs were based on a model with repeated dichotomous measurements per individual. In these analyses, within-individual correlation between consecutive years was taken into account using generalized estimating equation modeling. Both unadjusted and adjusted analyses were conducted censoring for mortality. Analyses comparing parents of patients with schizophrenia and parents of healthy controls were controlled for gender, age, area of residence, family situation, number of children, and inclusion year by matching. Due to the small size of the population of parents of patients with other diseases (MS, RA, and epilepsy), matching was not possible. Instead, covariates (inclusion year, patient's gender and age, parents' gender and age, parents' family situation and area of residence) were dealt as confounders in the multivariate analyses. In analyses on disease severity, parents of patients with least (reference), moderate and highest disease severity were compared. Here, additional adjustments were made by controlling for medication use of the parents and for annually prescribed antipsychotics and treatment persistence of the patients. Moreover, all analyses reported in tables 1–3 were adjusted for psychiatric morbidity at CED in the final models. Parents with on-going DP at CED were excluded from the analyses with SA and DP as outcome measures. Moreover, in all analyses with outcome measures related to work productivity, a general exclusion criterion of age being 65 years or over at CED was applied. Sensitivity analyses with regard to psychiatric or somatic specialized health care use were carried out for the incident cases to ascertain the comparability between parents of prevalent and incident patient populations with schizophrenia.

Ethical Approval

The study was approved by the Regional Ethics Review Board of Stockholm, Sweden.

Results

Characteristics of the Schizophrenia Patients

The majority of the patients with schizophrenia were aged between 35 and 45 years (53%), of male gender (63%), with a medium level of education (50%), single and living alone (89%) and mostly living in big cities (39%) (data not shown). Almost two-thirds (64%) of the patients with schizophrenia had a disease with lowest clinical severity, whereas just above 11% were severely ill. Considerable differences in the sociodemographic characteristics compared with patients with schizophrenia were seen for gender: 71% and 77% were women among MS and RA patients, respectively (data not shown).

Characteristics of the Parents of Patients With Schizophrenia and Comparison Groups

Supplementary table 1 shows the distribution of sociodemographic characteristics for the different parental groups. The distribution of sociodemographic factors in the parents of the incident population with schizophrenia was similar to the prevalent population with one exception: individuals in the latter group were generally older (data not shown).

At start of follow-up, approximately twice as many parents of patients with schizophrenia consumed psychiatric specialized health care and 2–3 times as many received social welfare benefits compared with parents of other chronic diseases (MS, RA, and epilepsy) or parents of healthy controls (supplementary table 1). The proportion of parents of patients with schizophrenia with DP, low or no income, and long-term unemployment was also somewhat higher compared with the comparison groups, supplementary table 1. With regard to other measures of health care resource use, health status and work productivity, no major differences between the groups emerged.

Use of specialized health care due to psychiatric or somatic diagnoses showed an increasing trend for all parents throughout the observation period, ie, before and after CED (figures 1 and 2). For somatic in- or specialized outpatient care, the frequencies were highest in the

Table 1. Number of Events, Person Years During Follow-up (2006–2013), Adjusted and Unadjusted Risk Estimates for Comparison of Parents of Patients With Multiple Sclerosis (MS; *n* = 11 292), Rheumatoid Arthritis (RA; *n* = 15 516), Epilepsy (*n* = 34 715), and Healthy Control (*n* = 18 408) Against Parents of Patients With Schizophrenia (*n* = 18 215)

Outcome Measures	Events	Person Years	Unadjusted	*P*-Value	Adjusted[a]	*P*-Value
Psychiatric specialized health care use[a] (relative risk)						
Parents of patients with schizophrenia	14 528	102 366	—		—	
Compared with parents of MS	2977	57 458	2.74 (2.63–2.85)	<.0001	1.80 (1.73–1.88)	<.0001
Compared with parents of RA	3935	76 102	2.74 (2.65–2.84)	<.0001	1.76 (1.70–1.83)	<.0001
Compared with parents of epilepsy	12 097	182 160	2.14 (2.08–2.19)	<.0001	1.71 (1.66–1.75)	<.0001
Compared with parents of healthy controls	6214	102 659	2.34 (2.28–2.41)	<.0001	1.63 (1.58–1.68)	<.0001
Somatic specialized health care use[a] (relative risk)						
Parents of patients with schizophrenia	19 519	102 366	—		—	
Compared with parents of MS	11 503	57 458	0.95 (0.93–0.97)	<.0001	0.96 (0.94–0.98)	.00109
Compared with parents of RA	15 962	76 102	0.91 (0.89–0.93)	<.0001	0.93 (0.91–0.95)	<.0001
Compared with parents of epilepsy	31 357	182 160	1.11 (1.09–1.13)	<.0001	0.97 (0.96–0.99)	.00445
Compared with parents of healthy controls	19 874	102 659	0.98 (0.97–1.00)	.13231	1.00 (0.98–1.02)	.68587
Medication use[a] (odds ratios)						
Parents of patients with schizophrenia	73 891	102 366	—		—	
Compared with parents of MS	42 402	57 458	0.90 (0.78–1.03)	.13048	0.84 (0.73–0.97)	.01474
Compared with parents of RA	57 260	76 102	0.78 (0.68–0.88)	<.0001	0.66 (0.58–0.75)	<.0001
Compared with parents of epilepsy	125 805	182 160	1.51 (1.37–1.66)	<.0001	0.67 (0.61–0.73)	<.0001
Compared with parents of healthy controls	73 291	102 659	1.16 (1.03–1.31)	.01258	0.88 (0.79–0.98)	.0209
Substance abuse[a] (odds ratios)						
Parents of patients with schizophrenia (%)	990 (5.4)	102 366	—		—	
Compared with parents of MS (%)	345 (3.1)	57 458	1.46 (0.91–2.34)	.11408	1.14 (0.30–4.29)	.84489
Compared with parents of RA (%)	541 (3.5)	76 102	1.18 (0.79–1.76)	.41499	0.95 (0.30–2.97)	.92865
Compared with parents of epilepsy (%)	1585 (4.6)	182 160	1.03 (0.76–1.41)	.83738	0.82 (0.43–1.58)	.55071
Compared with parents of healthy controls (%)	715 (3.9)	102 659	1.30 (0.90–1.87)	.16277	0.86 (0.37–2.01)	.73480
Mortality[a] (hazard ratios)						
Parents of patients with schizophrenia (%)	1591 (8.7)	102 366	—		—	
Compared with parents of MS (%)	849 (7.5)	57 458	1.04 (0.96–1.13)	.35552	0.99 (0.91–1.08)	.80467
Compared with parents of RA (%)	1156 (7.5)	76 102	1.00 (0.93–1.08)	.90825	1.01 (0.91–1.08)	.91665
Compared with parents of epilepsy (%)	2128 (6.1)	182 160	1.32 (1.24–1.41)	<.0001	0.94 (0.88–1.00)	.05896
Compared with parents of healthy controls (%)	1534 (8.3)	102 659	1.04 (0.97–1.12)	.23965	1.05 (0.98–1.13)	.15779

[a]Adjusted for calendar year, patient's gender, parent's gender, patient's age, parent's age, number of children, parent's family situation, parent's area of residence, schizophrenia at baseline (F20–F29), mood disorders at baseline (ICD-10: F30–F39), anxiety disorders at baseline (ICD-10: F40–F49), and other psychiatric diagnoses at baseline (ICD-10: F00–F19, F50–F99).

parents of patients with RA and lowest in the parents of patients with epilepsy (figure 1). Concerning psychiatric in- or specialized outpatient care among parents of patients with schizophrenia a sharp rise was observed from 4 years before CED, which stabilized—despite some fluctuations—following the year of CED (figure 2). Similar patterns were seen for the other parents groups, but on a much lower level. Sensitivity analyses revealed similar patterns of psychiatric and somatic specialized health care use for the parents of the incident population with schizophrenia. The most frequent diagnostic groups of psychiatric diagnoses among parents of patients with schizophrenia were affective and anxiety disorders as well as schizophrenia (supplementary table 4).

Parents of patients with schizophrenia had a higher risk of psychiatric specialized health care use compared with the other parental groups (range of RRs: 1.63–1.80) during follow-up, however rather similar risk estimates were observed for specialized somatic health care use in similar comparisons (range of RRs: 0.93–1.00) (table 1). Parents of patients with schizophrenia had a lower risk of medication use compared with the parents of healthy controls and the other comparison groups. A lower risk of substance abuse among parents of patients with schizophrenia than parents of patients with RA was observed (table 1).

While the subsequent risk of long-term SA was somewhat higher in parents of patients with schizophrenia than that in parents of patients with RA and healthy controls, no differences in risk of DP, long-term unemployment or income loss were observed between the most of the groups during follow-up (table 2). Moreover, parents of patients with schizophrenia were considerably more likely to receive social welfare benefits than their peers of other parental groups (range of ORs 1.20 to 2.74). Finally, a slightly higher mortality risk of parents of patients with schizophrenia was seen only when compared with the parents of healthy controls (HR 1.05; 95% CI: 0.98–1.13).

Finally, parents of the moderately severely ill patients with schizophrenia had higher risk estimates for psychiatric specialized health care (RR: 1.12; 95% CI: 1.07–1.17) compared with the parents of least severely ill patients with schizophrenia (table 3). Higher risk estimates for

Table 2. Number of Events, Person Years During Follow-up (2006–2013), Adjusted and Unadjusted Risk Estimates for Comparison of Parents of Patients With Multiple Sclerosis (MS; *n* = 11 292), Rheumatoid Arthritis (RA; *n* = 15 516), Epilepsy (*n* = 34 715) and Healthy Control (*n* = 18 408) Against Parents of Patients With Schizophrenia (*n* = 18 215)

Outcome Measures	Events	Person Years	Unadjusted	*P*-Value	Adjusted	*P*-Value
Sickness absence (>90 days)[a] (odds ratios)						
Parents of patients with schizophrenia (%)	2158 (11.8)	82 943	—		—	
Compared with parents of MS (%)	1346 (11.9)	49 160	0.93 (0.74–1.17)	.52855	0.57 (0.39–0.82)	.00301
Compared with parents of RA (%)	1504 (9.7)	64 518	1.04 (0.83–1.29)	.75060	1.15 (1.15–1.16)	<.0001
Compared with parents of epilepsy (%)	5244 (15.1)	155 622	0.74 (0.62–0.87)	.00026	0.68 (0.67–0.68)	<.0001
Compared with parents of healthy controls (%)	1974 (10.7)	89 389	1.13 (0.93–1.38)	.21768	1.62 (1.16–2.26)	.00441
Disability pension[a] (odds ratios)						
Parents of patients with schizophrenia (%)	1298 (7.1)	82 943	—		—	
Compared with parents of MS (%)	691 (6.1)	49 160	1.09 (0.59–1.99)	.78773	1.13 (0.32–3.99)	.84954
Compared with parents of RA (%)	722 (4.7)	64 518	1.28 (1.28–1.28)	<.0001	0.71 (0.12–4.33)	.70877
Compared with parents of epilepsy (%)	2425 (7.0)	155 622	0.97 (0.62–1.53)	.90945	1.30 (0.37–4.56)	.68443
Compared with parents of healthy controls (%)	950 (5.2)	89 389	1.43 (0.84–2.45)	.19115	0.98 (0.41–2.30)	.95452
Low or no income[a] (odds ratios)						
Parents of patients with schizophrenia (%)	11942 (65.6)	45 147	—		—	
Compared with parents of MS (%)	5206 (46.1)	24 310	1.36 (1.12–1.66)	.00237	0.97 (0.69–1.37)	.85987
Compared with parents of RA (%)	6733 (43.4)	31 574	1.36 (1.13–1.64)	.00104	0.85 (0.68–1.05)	.13731
Compared with parents of epilepsy (%)	25232 (72.7)	106 405	1.26 (1.09–1.46)	.00179	1.03 (0.83–1.27)	.80195
Compared with parents of healthy controls (%)	9319 (50.6)	42 745	1.40 (1.18–1.67)	.00010	0.84 (0.61–1.15)	.27785
Unemployment (>180 days)[a] (odds ratios)						
Parents of patients with schizophrenia (%)	1150 (6.3)	102 366	—		—	
Compared with parents of MS (%)	514 (4.6)	57 458	1.18 (0.86–1.61)	.30891	1.03 (0.54–1.97)	.93449
Compared with parents of RA (%)	593 (3.8)	76 102	1.30 (0.96–1.75)	.08985	1.02 (0.52–2.02)	.95495
Compared with parents of epilepsy (%)	2208 (6.4)	182 160	0.90 (0.72–1.12)	.34179	1.59 (0.99–2.55)	.05413
Compared with parents of healthy controls (%)	943 (5.1)	102 659	1.16 (0.89–1.50)	.26534	1.77 (1.06–2.96)	.02781
Social welfare benefit[a] (odds ratios)						
Parents of patients with schizophrenia (%)	6231 (34.2)	102 366	—		—	
Compared with parents of MS (%)	849 (7.5)	57 458	3.86 (2.82–5.29)	<.0001	2.69 (1.20–6.02)	.01599
Compared with parents of RA (%)	1254 (8.1)	76 102	3.48 (2.67–4.53)	<.0001	2.74 (1.30–5.74)	.00783
Compared with parents of epilepsy (%)	6373 (18.4)	182 160	1.72 (1.45–2.04)	<.0001	1.20 (0.82–1.76)	.33786
Compared with parents of healthy controls (%)	2610 (14.2)	102 659	2.48 (2.00–3.07)	<.0001	2.30 (1.31–4.05)	.00379

[a]Adjusted for calendar year, patient's gender, parent's gender, patient's age, parent's age, number of children, parent's family situation, parent's area of residence, schizophrenia at baseline (ICD-10: F20–F29), mood disorders at baseline (ICD-10: F30–F39), anxiety disorders at baseline (ICD-10: F40–49), and other psychiatric diagnoses at baseline (ICD-10: F00–F19, F50–F99).

somatic specialized health care use was also observed among the parents of most severely ill patients (RR: 1.12; 95% CI: 1.06–1.18) (table 3).

Discussion

Strengths and Limitations

The prospective cohort design, the population-based and very large cohort of parents with annual and detailed data for all individuals and practically no drop-out rates are the main strengths of this study. Another strength is the high quality of data in the used administrative registers. Moreover, the wide range of different variables and the outcome measures were recorded independently from each other.

Limitations of the study include that knowledge about the validity of the SA or DP diagnoses is limited, although one study published on this reported an acceptable validity.[43] The register data contains only proxy information on disease severity, ie, number of inpatient care stays. This study could not elucidate the role of inherited frailty, ie, genetic factors or the environment during upbringing. Therefore, the current analyses point toward correlation and not causal mechanism. Nevertheless, this article primarily intended to assess the current burden of parents of patients with schizophrenia by assessing different associations rather than looking at causal inferences. Parents of patients with schizophrenia were matched with parents of healthy comparisons on several sociodemographic factors, among them family situation and the number of children. While the number of matching factors available is a clear advantage, matching on particularly family situation and number of children might have led to an underestimation of the expected differences between these groups (due to potential overrepresentation of over-burdened healthy control). Finally, given the nature of this study, we could not determine to which extent parents were actually providing care.

Health Care Use in Parents

Higher frequencies of psychiatric health care use were observed in parents of patients with schizophrenia

Table 3. Number of Events, Person Years (PY), Relative Risks (RR) of Health Care Use and Hazard Ratios (HR) of Mortality in Parents of Patients With Schizophrenia According to the Patients' Disease Severity

Outcome Measures	Events	PY	Unadjusted	*P*-Value	Model 1[a]	*P*-Value	Model 2[b]	*P*-Value
Psychiatric specialized health care use								
Least severe	6167	49 783	1		1		1	
Moderately severe	3225	18 786	1.39 (1.33–1.45)	<.0001	1.11 (1.06–1.16)	<.0001	1.12 (1.07–1.17)	<.0001
Most severe	1412	8362	1.36 (1.29–1.44)	<.0001	1.02 (0.96–1.09)	.43209	1.03 (0.97–1.10)	.27403
Somatic specialized health care use								
Least severe	9861	49 783	1		1		1	
Moderately severe	3789	18 786	1.02 (0.98–1.06)	.34383	1.05 (1.01–1.09)	.00092	1.05 (1.01–1.09)	.01123
Most severe	1769	8362	1.07 (1.02–1.12)	.01087	1.12 (1.06–1.18)	<.0001	1.12 (1.06–1.18)	<.0001
Mortality								
Least severe	914	49 783	1		1		1	
Moderately severe	339	18 786	0.98 (0.86–1.11)	.74079	1.07 (0.94–1.22)	.30738	1.06 (0.93–1.20)	.39184
Most severe	147	8362	0.95 (0.80–1.13)	.56745	1.05 (0.87–1.26)	.60804	1.03 (0.86–1.24)	.75205

[a]Adjusted for patient age and gender, parents' age and gender, parent's family situation, parent's area of residence, medication use (parent), number of different antipsychotics used (patient) within a year before start of follow-up, treatment persistence (patient), schizophrenia at baseline (ICD-10: F20–F29), mood disorders at baseline (ICD-10: F30–F39), anxiety disorders at baseline (F40–F49), and other psychiatric diagnoses at baseline (ICD-10: F00–F19, F50–F99).
[b]Adjusted for patient's age and gender, parent's age and gender, parent's family situation, parent's area of residence, medication use (parent), amount of antipsychotics used (patient) within the previous calendar year, number of different antipsychotics used (patient) within a year before start of follow-up, schizophrenia at baseline (ICD-10: F20-29), mood disorders at baseline (ICD-10: F30–F39), anxiety disorders at baseline (ICD-10: F40–F49), and other psychiatric diagnoses at baseline (ICD-10: F00–F19, F50–F99).

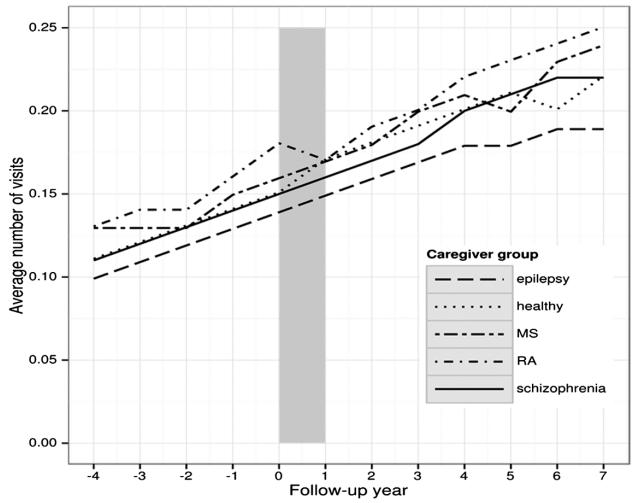

Fig. 1. Number of specialized somatic health care visits during the observation period in parents of patients with schizophrenia, multiple sclerosis (MS), rheumatoid arthritis (RA), epilepsy, and healthy controls. *Note*: observation period from −4 to +7 years after diagnosis of the offspring/cohort entry date, t0.

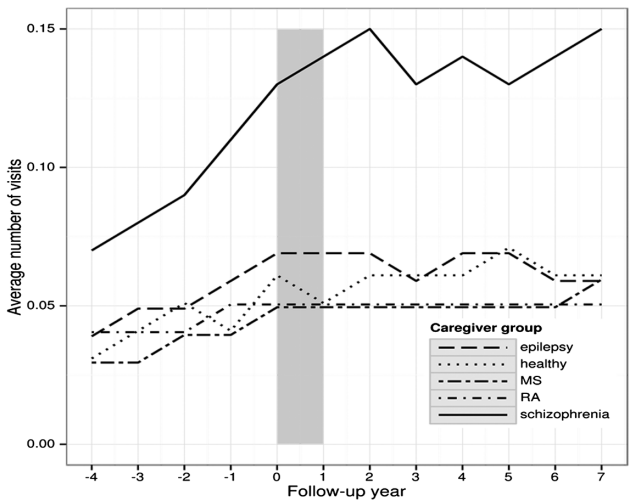

Fig. 2. Number of specialized psychiatric health care visits during the observation period in parents of patients with schizophrenia, multiple sclerosis (MS), rheumatoid arthritis (RA), epilepsy, and healthy controls. *Note*: observation period from −4 to +7 years after diagnosis of the offspring/cohort entry date, t0.

compared with parents of the different control groups. Such psychiatric health care rose sharply from 4 years before up to the year of inclusion, stabilizing thereafter. These findings suggest that mental health deteriorates strongly in parents of patients with schizophrenia up to the time point when the offspring gets the diagnosis and stays at a high level thereafter. It is possible that parents of patients with schizophrenia are strongly affected during the period when the offspring suffers from symptoms but gets no or nonspecifically treatment. Previous literature suggests that parents experience greater burden due to common mental disorders before a formal diagnosis of schizophrenia is made.[44] Such burden can be reflected in increasing health care use.

Additionally, adequate treatment is likely to be initiated following a newly diagnosed case, resulting in better compliance of the patients and thereby reducing the burden for the parents,[15,20,45] which ultimately may lead to stabilization of psychiatric health care use following diagnosis. There is also a possibility of a ceiling effect of psychiatric health care use for the parents following a diagnosis of schizophrenia of the offspring as the psychiatric health

care use was already at a high level. Different psychosocial interventions aiming at parents of patients with schizophrenia have been reported to be helpful to reduce stress,[15,46,47] which may also play a role in stabilizing mental health of such parents. Unfortunately, no data were available for this study regarding the proportion of parents attending such intervention. Another important issue in this aspect is heredity of the considered disorders.[48–51] Specifically for parents of offspring with schizophrenia, it is possible that the parent also has a psychiatric diagnosis,[48] which affects the use of health care and additionally may worsen with additional burden from caregiving.[24,52] This is also supported by the finding that specialized psychiatric health care use was already high among the parents of patients with schizophrenia at baseline. It is important to mention that affective and anxiety disorders were the most frequent diagnostic groups of specialized health care among the parents of patients with schizophrenia and that schizophrenia was much more common among these parents than in the comparison groups. Still, the proportions of parents with schizophrenia were very low: The annual proportion of parents having in- or specialized outpatient health care visit due to schizophrenia during the observation period was around 0.1%–1% among parents of patients with schizophrenia and 0%–0.1% among the other parent groups. Differences in the psychiatric health care use between different groups of parents can also be influenced by the disease-specific clinical differences and advancements of disease-specific management, eg, by newer and better drugs, etc.[53–56]

Health Status in Parents

About 70% of the parents of patients with schizophrenia used medication for psychiatric or somatic diseases at CED. The proportions of parents of patients with MS, RA, epilepsy, or healthy controls who used medication at CED were similar. Literature suggests that taking care of patients with chronic disease is associated with psychiatric disorders, like depression, anxiety, or stress in the parents and also may worsen pre-existing psychiatric or somatic morbidity in parents,[27,30,57,58] which may lead to increased medication use. Considering the higher risk for specialized psychiatric health care use of parents of patients with schizophrenia compared with parents of patients with other diseases, it is notable that their mortality risk was not increased. We found only a slightly higher (nonsignificant) risk for mortality among the parents of patients with schizophrenia compared with parents of healthy controls. This is in line with a previous study.[28]

Productivity Loss in Parents

The risk of DP, low or no income or unemployment did not differ between most of the comparison groups. Income loss, financial burden,[8,12,15,26,59] and labor market exit[60] have been reported for parents of patients with schizophrenia, partly because of spending a considerable amount of time taking care and thereby reducing productive working hours.[22] It is possible that the Swedish social insurance system can compensate for a potential income loss. Here, it should be noted that nearly one in every 5 parents of patients with schizophrenia was already on DP at baseline.

We found that parents of patients with schizophrenia were up to 2.7 times more likely to receive social welfare benefits during follow-up compared with other groups of parents. A possible explanation for this finding can be the specific social welfare system, maybe in a Swedish context, parents of patients with schizophrenia are more likely to fall through other social safety nets like unemployment and SA benefits. Future studies are required to investigate risk factors for social benefit dependence among parents of patients with schizophrenia.

Conclusions

Parents of patients with schizophrenia have considerably higher rates of psychiatric health care, mainly due to anxiety and affective disorders, and social welfare dependence than parents of patients with RA, MS, epilepsy, or healthy controls. The burden measured as psychiatric health care use worsens with increasing severity of the disease of the offspring with schizophrenia and over time. Such health care use increased continuously from 4 years before diagnosis of the offspring up to 7 years after diagnosis.

Supplementary Material

Supplementary data are available at *Schizophrenia Bulletin* online.

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Author Contributions

Ms M.M. and Dr J.M. had full access to all the data in the study and take responsible for the integrity of the data and the accuracy of the data analysis. J.T., E.M.-R., F.H., E.J., D.E., A.L., J.S., and A.T. were involved in study concept and design. E.M.-R., S.R., M.M., J.M., F.H., A.T., and H.T. were involved in acquisition, analysis, or interpretation of data. Drafting of the manuscript was done by E.M.-R. and S.R. Critical revision of the manuscript for important intellectual content was done by E.M.-R., S.R., J.T., M.M., J.M., F.H., E.J., D.E., A.L., J.S., A.T., and H.T. Statistical analysis has been carried out by M.M., J.M., F.H., A.T., and H.T.

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