

BMJ Open Multidimensional impact of severe mental illness on family members: systematic review

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ABSTRACT

Objective The impact of severe mental illnesses (SMIs) is not limited to the person with the illness but extends to their family members and the community where the patient comes from. In this review, we systematically analyse the available evidence of impacts of SMI on family members, including parents, grandparents, siblings, spouses and children.

Data sources PubMed, PsycINFO, Embase and Global Index Medicus were searched from the inception of each database up to 9 November 2019. We also did manual searches of grey literature.

Eligibility criteria We included studies that assessed the impacts of SMI on any family member. We excluded studies in admitted clinics and acute wards to rule out the acute effect of hospitalisation.

Data extraction Two reviewers extracted data independently using the Cochrane handbook guideline for systematic reviews and agreed on the final inclusion of identified studies.

Risk of bias The quality of the included studies was assessed using effective public health practice project quality assessment tool for quantitative studies.

The review protocol was registered in the PROSPERO database.

Results We screened a total of 12 107 duplicate free articles and included 39 articles in the review. The multidimensional impact of SMI included physical health problems (sleeplessness, headache and extreme tiredness), psychological difficulties (depression and other psychological problems) and socioeconomic drift (less likely to marry and higher divorce rate and greater food insecurity). Impacts on children included higher mortality, poor school performance and nutritional problems. However, the quality of one in five studies was considered weak.

Conclusions Our review indicated a high level of multidimensional impact across multiple generations. The serious nature of the impact calls for interventions to address the multidimensional and multigenerational impact of SMI, particularly in low/middle-income countries. Given the relatively high number of studies rated methodologically weak, more robust studies are indicated. **PROSPERO registration number** CRD42018064123.

INTRODUCTION

Severe mental illnesses (SMIs), mainly schizophrenia, bipolar disorder and major

Strength and limitations of this study

- Comprehensive search strategy.
- Screening, extraction and rating of articles carried out by two reviewers.
- Assessment of multidimensional impact across multiple generations.
- Meta-analysis was not possible because of the heterogeneity of studies.

depression, are conditions that tend to be chronic and relapsing in nature and may lead to serious impairment in one or more areas of functioning.¹ SMIs decrease productivity and are associated with high rates of physical illness comorbidity and excess mortality.^{2–6} The negative impacts of SMI are not limited to the person with the illness but extend to the family members and the community where the person comes from. These impacts may particularly pronounce in low/middle-income countries (LMICs), where the treatment gap for mental disorders is very high. In LMICs, family members or relatives take almost all the responsibility of caring for the patient and the impact transcends generations.^{7–10}

Caring for a person with mental illness takes a substantial toll on social relationships, employment and income and psychological well-being.¹¹ Most families fear for their future health in addition to the stress of caring for their ill family member.^{9 10} Families of people with SMI have worse physical health and seek more medical care than those families without SMI.^{12 13}

Children of people with SMI have higher risk of developing physical and mental illness for a variety of reasons, including stigma, financial difficulties, the burden of caring for ill parents and genetic vulnerability. The impact on children is long term and affects their adult health and relationships.^{14–18}

There is no agreement in the literature about the level of burden in relation to

amount of time spent on caregiving. Some studies relate the burden level with time spent for caregiving^{19–21} while others evaluate the burden at the household level.^{22–23} Some studies also measure the impact of the illness on extended families such as grandparents and family members living in separate households with no direct contact with the patient.^{24–25}

Although there are small-scale studies and some literature reviews on aspects of the impact of SMI on family members,^{26–28} there are no reviews looking at the multi-dimensional impact of different types of SMI across generations. This paper aims to systematically review the available evidence on the impacts (health, socioeconomic and schooling) of schizophrenia, bipolar disorder and major depression on family members.

METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.²⁹ We have registered the protocol on the PROSPERO international register of systematic reviews online.

Search strategy

Four databases were searched: PubMed, Embase, PsycINFO and Global Index Medicus. The databases were searched from the inception of each database up to 9 November 2019 with no language restriction. We did a forward and backward search on included studies and hand searching for grey literature from Google Scholar and university repositories.

The search terms consisted of key Medical Subject Heading (MeSH) and Emtree terms, and controlled vocabularies for illness, list of family members affected by the illness and impact dimensions. The terms were combined with the Boolean term AND:

- Terms for illness:** ‘Severe mental illness’ OR schizophrenia OR psychosis OR bipolar OR ‘major depressive disorder’ OR ‘major depression’
- Terms for list of family member affected by the illness:** Caregiver OR family OR parent* OR child OR offspring OR siblings OR spouse.
- Terms for impact dimensions:** Burden OR Impact health OR morbidity OR mortality OR disability OR Psychopathology OR poverty OR economy OR financial OR education OR school. A full search strategy and search terms for databases can be accessed in a supplementary file (online supplementary file 1).

Eligibility criteria

We have included peer-reviewed studies that met the following criteria:

Participant

Any family member(s) or informal caregiver(s) (biologically related or not) of people with clinically diagnosed SMI (schizophrenia, bipolar disorder and major depression).

Duration of illness

Duration of illness 1 year or longer. If the duration was not mentioned, we have excluded studies in acute inpatients and acute wards to rule out the acute effect of hospitalisation.

Exposure

SMI.

Outcome

Burden/impact (positive and negative) and its dimensions excluding family genetic studies.

Study design

All excluding qualitative studies, case report and case series.

Publication year

Not restricted.

Data extraction

Studies were first screened on title and abstracts by two reviewers (WF and AM) independently. The two reviewers extracted data independently using the Cochrane handbook guideline for systematic reviews.³⁰ Discrepancies were resolved with discussion. The excluded articles and the reasons for exclusion were documented. Author, publication year, country, aim, study design, population, sample size, type of illness, duration, key outcomes (including measures) were extracted. The proportion of agreement between the two reviewers during the title and abstract screening was 91% and 96% in the full-text screening.

Assessment of bias

Two reviewers assess the risk of biases independently and reconciled with effective public health practice project (EPHPP) quality assessment tool for quantitative studies.³¹ The tool consists of eight criteria of which six were rated: selection bias, allocation bias, control of confounders, blinding of outcome assessors, data collection methods, and withdrawals and dropouts. Each section was rated as ‘weak’, ‘moderate’ or ‘strong’. A global rating of each article was decided as weak, moderate and strong (online supplementary file 2).

RESULTS

Study selection

In total, 13 102 articles were identified in the initial search. A total of 12 107 articles were eligible for title and abstract screening after removing 1 143 duplicates. Four hundred

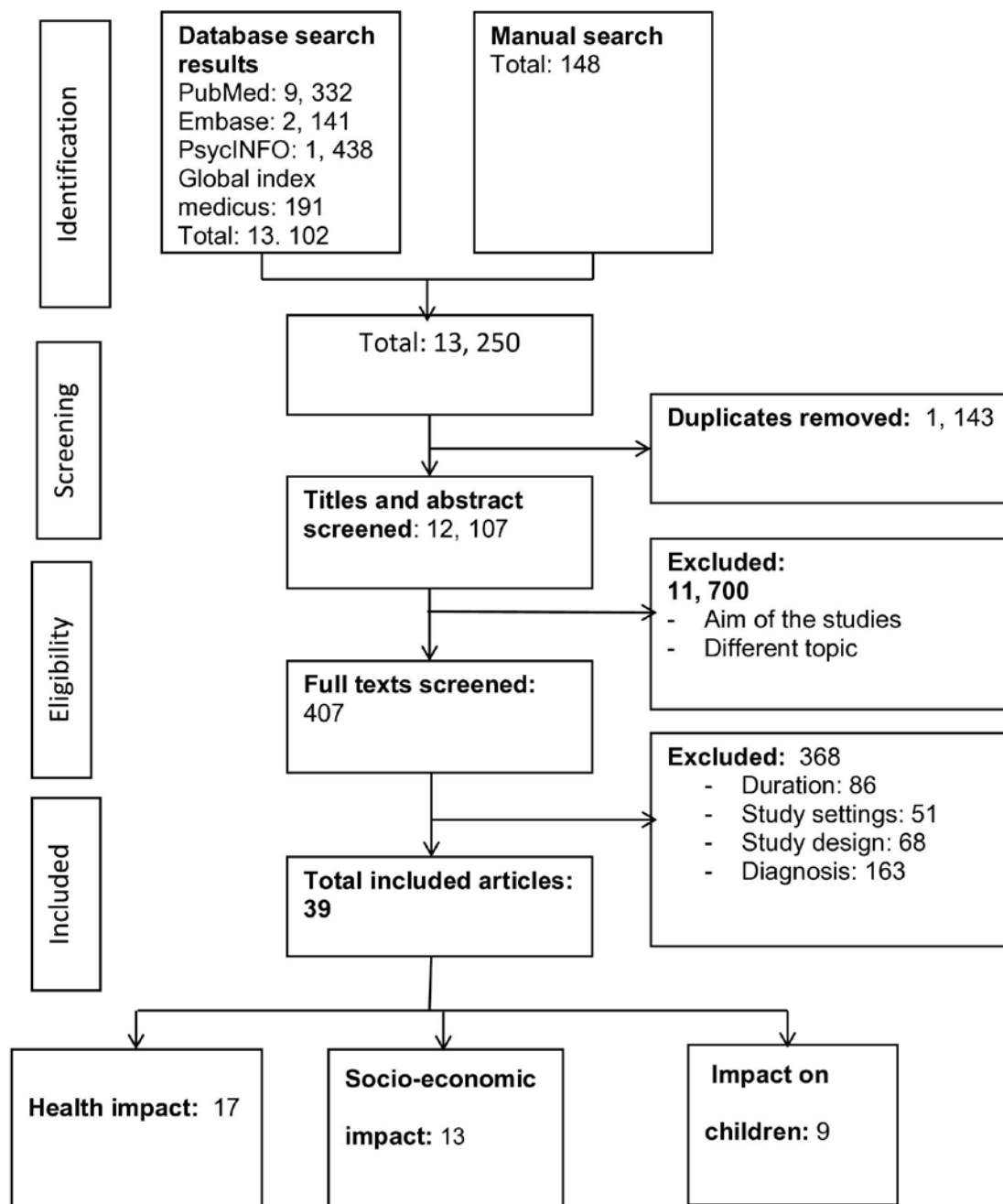


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of study selection process.

seven articles were eligible for whole paper review after removing 11 700 articles at the title and abstract screening stage, mainly because the study did not concern SMI. Three hundred sixty-eight articles were not eligible for the final manuscript because of short illness duration, lack of clinical diagnosis, study setting (in acute wards and inpatients), focus of the studies and study design (figure 1). We found six articles written in languages other than English. All had abstracts in English, but none fulfilled the inclusion criteria and so were not included in the final extraction. A total of 39 articles included in the review.

Study characteristics

Thirty-nine studies were included in the final review, which were conducted in 20 different countries, mostly

high-income countries (n=30, 76.9%). Most studies were conducted in Europe (n=14) and USA (n=9). The rest comes from Asia (n=6), Africa (n=6) and Latin America (n=4).

Sixteen (41%) studies were longitudinal, and the remaining were cross-sectional (with and without a comparison group) and case control studies. The publication year ranged from 2001 to 2018, while the durations of illness ranged from 1 year to 30 years. Eighteen of the studies focused on family members of people with schizophrenia, eight were done on bipolar disorder, four on major depressive disorder (MDD) while the remaining nine on SMIs. The impact dimensions included health (n=17), socioeconomic (n=13) and impact on children:

education, nutrition, mortality (n=9). The sample size of the studies ranged from 51 up to 5504. Two birth cohorts involved large sample sizes: one with 684 248 birth children and another study have 3654 cases and 1 439 215 controls (tables 1 and 2).

Risk of bias within studies

Nineteen studies were rated as strong, twelve moderate and the remaining eight were rated as weak in the global rating of the articles with EPHPP. Only six out of the thirty-nine studies were considered free from selection bias while the remaining studies had moderate to weak selection bias problems. Thirty-three studies failed to control for most of the confounders and nine out of thirty-nine were weak in controlling confounders. Twenty-seven studies were conducted with valid and reliable instruments.

Impacts

The main impact dimensions were related to health, economic and social domains, and impact on children's education and nutrition.

Impact on health and quality of life

Seventeen studies reported the health impact of having a family member with SMI; two studies reported overall health impact, three assessed physical health and the remaining reported on psychological impact.

Two studies report low mental and physical composite score measured with the Short-Form 36 compared with healthy controls.^{32,33} Family members have poor perceived physical health (65.5%), sleeplessness (53.1%), headache (44.2%) and extreme tiredness (56.2%). These physical problems were significantly higher in family members of people with SMI than the family members who did not have SMI: sleep problems (42.7% vs 28.5%), pain (39.7% vs 30.4%), headache (48% vs 42%) and heartburn (31.7% vs 22.9%).^{11 34 35}

The magnitude of psychological problems in family members was high³⁶⁻³⁹ including parents, siblings, children and grandchildren of people with SMI. One study reported higher depression score (Centre for Epidemiological Studies of Depression Scale) among parents of adult children with bipolar disorder compared with comparisons.³³ Another study report higher psychological distress in family members of people with schizophrenia than the controls (0.70 vs 0.34).⁴⁰

Two studies found 20%–50% of caregivers experience depressive symptoms.^{34 41} In one multicounty study, depressive symptoms were also reported by 29.4% of caregivers of people with schizophrenia compared with 19.4% in matched controls.³⁵

Families with a depressed grandparent experience more anxiety and other psychiatric disorders compared with non-depressed grandparents (24, 25, 33, 43).

Socioeconomic impact

Difficulties in social relationships and family finances were also reported by several studies. The social impacts

included higher divorce rate, fewer marriages, poor family cohesion and a strained family environment. Some studies report these impacts on a family member while others report across the entire household.

Family members with mental illness reported less chance of marriage (eg, 54.7% in children of parents with schizophrenia vs 66% in general population) and higher divorce rate (eg, 20% in parents of adult children with bipolar disorder vs 10.2% in controls).^{33 39} Family cohesion is lower and the environment in these families was also strained in these family members.^{23 41}

Financial impact was higher than other impact dimensions in three studies.⁴²⁻⁴⁴ These economic impacts were due to costs related to care (cost for treatment, cost of informal care giving), productivity (inability to work and time for care giving) and cost of treatment side effects, suicide and stigma. For example, in one study, out-of-pocket medical expense per year was higher in caregivers of people with bipolar disorder (US\$93.93) than caregivers of other medical conditions (US\$64.8) and general population comparisons (US\$56.18).⁴⁵ Family members ability to pursue regular activities was also affected.⁴⁶

The economic impact might result in long-term economic drift and food insecurity. One study found 32.5% of households of people with SMI experience severe food insecurity compared with 15.9% among the general population.²²

Impact on children

Four studies reported the level of psychopathology in children of parents with SMI. In one study the level of psychopathology differed by the specific type of illness. In this study 58.5% of the children of parents with a diagnosis of schizophrenia had lifetime axis I Diagnostic Statistical Manual IV (DSM-IV) psychiatric disorder compared with 36.7% of children of parents with bipolar disorder and 17.8% in children of healthy parents.⁴⁷

One longitudinal study reported 38.7%, 35.6% and 15.2% lifetime psychiatric disorders in children of parents with schizophrenia spectrum and other psychotic disorders, children of parents with bipolar disorder and children of parents without any mental disorder, respectively.⁴⁸

Psychopathology was compared by two matched studies. It was reported by 63% in offspring of parents with bipolar disorder and 33% in matched controls, while current axis I disorder was reported by 21.33% exposed offspring and 14% among controls.^{49 50} These children also receive more counselling (30.9% vs 13.5%), take medication (18.7% vs 5.3%) and experience more psychiatric hospitalisations.⁴⁹

Children's level of functioning was also affected.^{48 50} These children had poorer school performance and they were more likely to be placed in special rooms at school and face malnutrition.^{49 51-53} The impact of the parent's illness on children reported by one study to be long lasting. In this study, children of parents with MDD had higher

Table 1 Impact of SMI on family members in LMICs

Author (year) and country	Study design and illness duration	Participants (number and relationship)	Outcome	Result	Global quality rating
Ashaba <i>et al</i> 2015 Uganda ⁵²	Case control	<ul style="list-style-type: none"> ▶ 836 (mothers of children admitted with malnutrition) ▶ 83 (mothers of children admitted with other cases) 	Maternal depression and malnutrition	Maternal depression and malnutrition in children (AOR=2.4, 1.11–5.18)	Strong
Igberase <i>et al</i> 2012 Nigeria ⁴²	<ul style="list-style-type: none"> ▶ Cross-sectional ▶ 13.9 years 	200 caregivers of people with SCZ	Burden and correlates	Higher mean score on financial scale (1.94 (0.66)) Burden were associated with <ul style="list-style-type: none"> ▶ Unemployment (p<0.001) ▶ Educational status (p=0.01) ▶ Difficulty of coping (p<0.001) 	Weak
Petresco <i>et al</i> 2009 Brazil ⁶⁸	- Comparative cross-sectional	Children (6–18 years) of <ul style="list-style-type: none"> ▶ Women with BPD⁶⁴ ▶ Mild to moderate MI⁵¹ ▶ Control⁵¹ 	Psychopathology	Live with biological father <ul style="list-style-type: none"> ▶ Offspring of mothers with BPD (69.8%) ▶ Offspring from mothers with other psychiatric disorders (25.5%) and controls (28.8%) One or more axis I diagnosis Offspring of woman with bipolar d/o 2.8 higher risk (prevalence ratio=2.83)	Strong
Shibre <i>et al</i> 2012 Ethiopia ⁴⁴	Longitudinal	307 caregivers of people with SCZ	Burden	Burden reduces over time Burden associated with <ul style="list-style-type: none"> ▶ Negative score symptom (B=0.04) ▶ Positive symptom score (B=0.52) ▶ Full remission for over 75% of the follow (B=-0.51) 	Strong
Shibre <i>et al</i> 2003. Ethiopia ⁴³	Cross-sectional	301 caregivers of people with SCZ (spouse, parents, siblings, offspring, others)	<ul style="list-style-type: none"> ▶ Burden ▶ Coping 	Burden <ul style="list-style-type: none"> ▶ Financial difficulties (74.4%) ▶ Social problems (71%) ▶ Work-related burden (53.1%) ▶ Family related burden (50.5%) Coping <ul style="list-style-type: none"> ▶ Pray for guidance or strength (71.4%) ▶ Talk with someone (44.5%) ▶ Take pride in small successes (25.6%) 	Moderate
Terzian <i>et al</i> 2007 Brazil ³⁹	Comparative cross-sectional	431 adult offspring of parents with SCZ	Social adjustment	Reported mental disorder male (24.8%) versus female offspring (16.5%) Compared with general population <ul style="list-style-type: none"> ▶ Less frequently married (54.7% vs 66.0%) ▶ Poorer employment (66.7% vs 75.6%) 	Strong
Thunyadee <i>et al</i> 2015 Thailand ³⁴	Cross-sectional	200 caregivers of people with SCZ	Relationships and factors <ul style="list-style-type: none"> ▶ Caregiver burden ▶ Depressive symptoms ▶ Physical health 	<ul style="list-style-type: none"> ▶ Depressive symptoms (19.5%) ▶ Perceived poor physical health (65.5%) Predictors of depressive symptoms Burden, self-controlling coping strategies and physical health status Burden predicted physical health status.	Moderate
Tirfessa <i>et al</i> 2017 Ethiopia ²²	Comparative cross-sectional	<ul style="list-style-type: none"> ▶ 292 households with SMD ▶ 284 matched controls 	Household food insecurity	<ul style="list-style-type: none"> ▶ Severe household food insecurity (32.5% vs 15.9%) ▶ Median HFAS score: people with SMI (median 15, IQR 10), control households (median 12, IQR 7) 	Strong

Continued



Table 1 Continued

Author (year) and country	Study design and illness duration	Participants (number and relationship)	Outcome	Result	Global quality rating
Zergaw <i>et al</i> 2008 Ethiopia ⁴⁵	Longitudinal	<ul style="list-style-type: none"> ▶ 139 caregivers of people with BPD ▶ 36 diabetes, hypertension and asthma ▶ 401 controls 	<ul style="list-style-type: none"> ▶ Economic ▶ General burden 	Burden inducing event occur in 8–10 months/year versus may not occur Out-of-pocket medical expense/year <ul style="list-style-type: none"> ▶ 93.93US\$—bipolar ▶ 64.8US\$—DHA ▶ 56.18US\$—control (not statistically different) 	Strong

AOR, adjusted OR; BPD, bipolar disorder; DHA, diabetes hypertension asthma; d/o, disorder; HFIAS, household food insecurity assessment schedule; LMIC, low/middle-income countries; MI, myocardial infarction; SCZ, schizophrenia; SMD, severe mental disorder; SMI, severe mental illness.

mortality (5.5% vs 2.5%) with 8 years mean age difference after 30 years compared with healthy controls.²⁴

Predictors

The level of impact of the illness depends on patient-related factors, family member-related factors and factors related to health service delivery. The major patient-related factors were type of illness, severity and profile of symptoms. The other factors such as age of onset, duration of illness, number of hospitalisations and current functioning also predict the level of impact.^{36 40 41 44 54–56}

These factors are also seen in Ethiopia where the level of burden was associated with symptom severity, disability and remission.^{22 44}

Family member-related factors include relationship type, sex, economic and educational status, living in the same home and coping mechanisms.^{41 42 46 57 58} For example, in Chile, mothers developed higher burden than other family members⁵⁴ and in Taiwan parents experience higher burden than children.⁵⁸ The burden was also associated with unemployment, educational status and coping mechanisms of family members.⁴²

The impact may also depend on the healthcare system and financial investment for mental healthcare as evidenced by a difference in burden between two cities of China (Hong Kong and Guangzhou) and in Germany and Britain. For example, the level of caregivers burden in Britain was higher than in Germany (Involvement Evaluation Questionnaire Score: 46.1 vs 43.2) which has been attributed to the relatively lower financial investment on mental health in Britain^{59 60} (tables 1 and 2).

DISCUSSION

This is the first systematic review, which synthesises the global evidence on the impact of SMI on family members. Previous reviews have focused on primary caregivers, not the impact of the illness on other family members.^{26–28} These unrecognised impacts have effects on the person with the illness, the family and the community at large. The impact may be more pronounced in low-income

countries because the family relationship is more extended, social security is not available and higher level of stigma and discrimination.^{61–63}

Earlier studies focus mainly on schizophrenia and bipolar disorder,^{26–28} while our review includes the impact of severe depression on family members. This review also attempts to assess long-term, diverse impacts across the three specific illnesses and across multiple generations. These are essential inputs to develop family inclusive interventions.

It is of note that about one in five studies (8/39 studies) were rated as weak in global rating. While this constitutes an important limitation of this systematic review, we have presented the data irrespective of the methodological problems and quality. All the included studies had fulfilled the required inclusion criteria. Moreover, six of the eight studies rated weak had at least one strong rating and that all the studies have at least three of the six quality assessment items of the EPHPP criteria rated as strong or moderate. Moreover, we consider presenting the results of all studies fulfilling the inclusion criteria along with the quality of the studies will assist the readers to understand the reports and plan for further studies.

The health impact was common across the three specific illnesses, both in high/low-income countries^{11 34 39 47} and it is long-term and trans-generational.^{24 25 33 64} Psychological distress and physical complaints in family members can be explained by stressful family environment and high demand for care by the people with the illness.^{23 34 48} When this comes on top of other personal or economic difficulties, it has been suggested that the combination may result in psychological or physical ill health.^{65 66} However, it is not clear just how serious this can be. For example, the burden get so high as to lead to severe psychological problems such as suicidal behaviour or increased mortality. This has been suggested by Vitaliano *et al*⁶⁷ who showed how caregiving for Alzheimer's might even end up in death of the caregiver, an endpoint which might also apply to caring for SMI.⁶⁷

Table 2 Impact of SMI on family members in high-income countries

Author (year) and country	Study design and illness duration	Participants (number and relationship)	Outcome	Result	Global quality rating
Aschbrenner <i>et al</i> 2009 USA	Longitudinal Since 1957 19.2 years	▶ 145 parents of adult children with BPD ▶ control	▶ Physical functioning ▶ Mental functioning	Parents of children with BPD versus controls ▶ Self-acceptance (4.8 vs 4.9) ▶ CES-D score (8.5 vs 6.9) ▶ SF-12 mental functioning (53.6 vs 55.7) ▶ SF-12 physical functioning (45.8 vs 48.3)	Strong
Chessick <i>et al</i> 2009 USA ⁵⁵	One year longitudinal	500 caregivers of people with BPD	▶ Physical health ▶ Depression	▶ Increased suicidal behaviour in patients result in poor overall health ▶ Suicidal ideation in patients associated with high depression score in caregivers	Strong
De Andres Garcia <i>et al</i> 2016 Spain	▶ Longitudinal ▶ 15 years	▶ 41 parents of offspring with SCZ ▶ Community control	▶ Acute stress ▶ Salivary cortisol ▶ IgA	Caregivers with higher NA have ▶ Worse health ▶ Larger decreases in cortisol and IgA ▶ Cognitive coping high in low NA	Weak
Donatelli <i>et al</i> 2010 USA ⁵⁶	▶ Longitudinal ▶ 7 years and longer	▶ 281 children of parents with psychosis ▶ 185 controls	Childhood behaviour	▶ No significant difference of childhood behavioural problems at age 4 but more ▶ Externalising behaviour on female children (AOR=2.8) ▶ Internalised in male children AOR=3.6	Moderate
Ellersgaard <i>et al</i> 2018 Denmark ⁴⁸	Longitudinal	Children of 202 people with SSP ▶ 120 people with BPD ▶ 200 controls	Psychopathology	Lifetime psychiatric diagnoses ▶ SSP (38.7%) ▶ BPD (35.6%) ▶ Controls (15.2%) Level of functioning (CGAS) ▶ SSP (68.2) ▶ BPD (73.7) ▶ Controls (77.9)	Strong
Gupta <i>et al</i> 2015 France, Germany, Italy, Spain, UK ³⁵	▶ Comparative study ▶ 4 years and longer	▶ 398 caregivers of people with SCZ ▶ 158 to 989 matched controls ▶ 14 to 341 caregivers of other conditions	▶ HRQOL ▶ Health utility	Caregivers versus non-caregivers ▶ Sleep difficulties (42.7% vs 28.5 %) ▶ Insomnia (32.4% vs 18.5 %) ▶ Pain (39.7% vs 30.4 %) ▶ Headaches (48.0% vs 42.0 %) ▶ Heartburn (31.7% vs 22.9 %) ▶ Anxiety (37.9% vs 23.6 %) ▶ Depression (29.4% vs 19.4 %) Compared with other caregivers lower ▶ MCS (40.3 vs 42.7%) ▶ Health utilities scores (64 vs 67%)	Strong
Gutierrez Maldonado, 2005 Chile	Cross-sectional	▶ 65 caregivers of people with SCZ ▶ 5.6 years Average	▶ Burden score ▶ Caregiver general health	Burden score ▶ Mothers had higher score ▶ Younger patient more burden ▶ Number of hospitalisation and kinship associated with burden ▶ High burden lower SF-36 score	Weak
Hanzawa, 2008 Japan ⁵⁷	▶ Cross-sectional ▶ 1 year and longer	57 mothers of people with SCZ	Burden of care giving	Burden associated with ▶ General health status and difficulty in life ▶ Coping affect burden level	Weak

Continued



Table 2 Continued

Author (year) and country	Study design and illness duration	Participants (number and relationship)	Outcome	Result	Global quality rating
Henin <i>et al</i> 2005 USA ⁴⁹	Comparative cross-sectional	<ul style="list-style-type: none"> ▶ 117 offspring of parents with BPD ▶ 171 age and gender matched offspring 	<ul style="list-style-type: none"> ▶ Hospitalisation ▶ Placement in special classes ▶ Medication 	Offspring of parents with BPD <ul style="list-style-type: none"> ▶ Placed in special classes (OR=3.9) ▶ Received counselling (30.9% vs 13.5%) ▶ Took medication (18.7% vs 5.3%) ▶ Psychiatric hospitalisation (4.1% vs 0.6%) 	Strong
Hsiao, Tsai, 2014 Taiwan	<ul style="list-style-type: none"> ▶ Cross-sectional ▶ Average 12.67 years 	243 caregivers of people with SCZ	<ul style="list-style-type: none"> ▶ Caregiver burden ▶ Satisfaction 	<ul style="list-style-type: none"> ▶ Caregivers burden: 24.32% ▶ Satisfaction in caregiving: 57.21% 	Weak
Hsiao, Tsai, 2015. Taiwan ⁵⁸	<ul style="list-style-type: none"> ▶ Cross-sectional ▶ 14.74 years 	137 caregivers of people with SCZ	<ul style="list-style-type: none"> ▶ Caregiver burden ▶ Family functioning 	<ul style="list-style-type: none"> ▶ Lower burden in siblings than parents ▶ Burden and duration of illness had positive association ▶ Lower family SOC correlated with family hardiness ▶ Unaware of patient suicidality and high family functioning (ES=067) and educational level at or above college (ES=025), 	Moderate
Jundong <i>et al</i> 2012 Sweden ⁵¹	Birth cohort (since 1932)	<ul style="list-style-type: none"> ▶ 3654 parents with SCZ ▶ 1 439 215 controls 	School performance (9 years)	Influence of parental schizophrenia on offspring <ul style="list-style-type: none"> ▶ School performance (d=-0.31) ▶ After controlling covariates (d=-0.18) 	Strong
Mitsonis <i>et al</i> 2012 Greece ⁴⁰	<ul style="list-style-type: none"> ▶ Comparative cross-sectional ▶ 9 years 	<ul style="list-style-type: none"> ▶ 87 caregivers of people with SCZ ▶ 90 controls 	Psychological distress	Higher median symptom score in caregivers than controls (global severity index (0.70 vs 0.34))	Moderate
Parabiaghi <i>et al</i> 2007 Italy ³⁶	3 years longitudinal	51 caregivers of people with SCZ	<ul style="list-style-type: none"> ▶ Change in burden ▶ Emotional distress 	<ul style="list-style-type: none"> ▶ 51% emotional distress ▶ Family burden and distress reduce through time Predictors <ul style="list-style-type: none"> ▶ Symptom severity, functioning ▶ Lower QOL 	Moderate
Perlick <i>et al</i> 2016 USA	Longitudinal	500 caregivers' people with BPD	<ul style="list-style-type: none"> ▶ Caregiver burden ▶ Depression 	Baseline, 6 months and 12 months mean CES-D <p>10.0, 9.5 and 8.7</p> <p>Caregiver burden score 32.5, 27.4 and 24.4 level of burden at baseline predicted depression scores during the follow-up period (p<0.001).</p> <p>Level of depression at baseline was not associated with burden scores during follow-up (p=0.20)</p>	Strong

Continued

Table 2 Continued

Author (year) and country	Study design and illness duration	Participants (number and relationship)	Outcome	Result	Global quality rating
Ranning <i>et al</i> 2018 Denmark	Longitudinal	684 248 births between 1986 and 1996 ▶ 3806 offspring of parents with BPD ▶ 3895 offspring of parents with SCZ ▶ Controls	School completion and performance	No graduation ▶ Schizophrenia in mother (OR 2.32 (2.05–2.64)) ▶ Schizophrenia in father (OR 2.53 (2.24–2.86)) ▶ Bipolar in mother (OR 2.53 (2.24–2.86)) ▶ Bipolar in father (OR 1.16 (0.97–1.38)) High GPA ▶ Schizophrenia in mother (OR 0.73 (0.64–0.84)) ▶ Schizophrenia in father (OR 0.71 (0.63–0.81)) ▶ Bipolar in mother (OR 1.04 (0.93–1.15)) ▶ Bipolar in father (OR 1.02 (0.90–1.14))	Strong
Ritsher <i>et al</i> 2001 USA ⁷⁰	▶ Longitudinal study ▶ 17 years	756 families of people with MDD matched with age and sex	▶ Socioeconomic status ▶ MDD	▶ Parent socioeconomic status affects child psychological health ▶ Parent or offspring depression doesn't affect late socioeconomic status	Strong
Roick <i>et al</i> 2007 Germany and Britain ⁶⁰	Cross-sectional	333 relatives (parents and others) of people with SCZ in Germany and 170 in Britain	Family burden (IEQ-E)	Family burden was associated with ▶ Symptoms ▶ Male gender ▶ Unemployment ▶ Marital status ▶ Coping abilities patient contact British caregivers reported more burden than German IEQ=43.2 in Germany and 46.1 in Britain	Moderate
Romero <i>et al</i> 2005 USA ²³	Comparative cross-sectional	▶ 24 families with at least one parent with BPD ▶ 27 families without PD	Psychopathology Family environment	BPD families Had lower cohesion (p=0.009) and expressiveness scores (p=0.03) Compared with normative data BPD families reported lower cohesion and higher conflict	Weak
Sanchez <i>et al</i> 2015 Spain ⁴⁷	Longitudinal	▶ 47 children (7–17 years) of people with SCZ ▶ 90 BPD ▶ 107 controls	Psychopathology	Lifetime axis I DSM-IV psychiatric disorder ▶ 58.5% of SCZ offspring ▶ 36.7% of BP offspring ▶ 17.8% of control offspring Schizophrenia and control (AOR=3.96) Bipolar and control (AOR=2.36)	Strong
Sucksdorff <i>et al</i> 2014 Finland ³⁸	Nested-case control	▶ 1861 cases with BPD ▶ 3643 matched controls	Psychopathology	▶ AOR=2.79 for any psychiatric diagnosis in mothers ▶ AOR=2.5 BPD in father and ▶ AOR=BPD 5.36 in both parents BPD in offspring is associated with parental BPD, SCZ and related psychoses and other affective disorders	Moderate
Van Wijngaarden <i>et al</i> 2004 Netherlands ¹¹	Cross-sectional	260 caregivers of people with MDD	Consequence of living with a family member with MDD	▶ Depression (49.6%) ▶ Sleeplessness (53.1%) ▶ Headache (44.2%) ▶ Extreme tiredness (56.2%) ▶ 80% of caregivers reported distress	Moderate

Continued



Table 2 Continued

Author (year) and country	Study design and illness duration	Participants (number and relationship)	Outcome	Result	Global quality rating
Van Wijngaarden <i>et al</i> 2009 Netherlands Denmark and UK ⁴¹	Cross-sectional	▶ 260 caregivers of people with depression ▶ 151 caregivers of SCZ	Burden in SCZ and depression	Depression versus SCZ Worried about patient's future 44.8% versus 56.0% (p=0.020) Atmosphere was strained 27.4% versus 11.6% (p<0.001) Encouraged to take proper care 7.5% versus 24.8% (p<0.001)	Moderate
Weissman <i>et al</i> 2005 USA ²⁵	▶ Longitudinal ▶ 20 years and longer	161 grandchildren and their parents and grandparents with and without depression	Lifetime psychiatric disorder Functioning	59.2% psychiatric disorder in grandchildren with 2 generations of major depression Families with a depressed grandparent ▶ Anxiety (RR, 5.17 (1.4–18.7)) ▶ Any disorder (RR, 5.52 (2.0–15.4)) compared with non-depressed parents	Strong
Weissman <i>et al</i> 2016 USA ²⁴	▶ Longitudinal study ▶ 30 years	147 offsprings of moderately to severely depressed parents and healthy control	▶ Psychopathology ▶ Functioning	Offspring of depressed parent versus control ▶ Depression (73.8% vs 34.1%) (RR=3.18 (2.00–5.05)) ▶ Poorer functioning ▶ Mortality (5.5% vs 2.5%, 8 years mean age difference) ▶ Lower mean GAS (77.5 vs 83.3, p=<0.001)	Strong
Zahid 2010 Kuwait ⁴⁶	▶ Cross-sectional ▶ 1 year and longer	121 caregivers of people with SCZ	▶ Burden ▶ QOL	Inability to pursue activities regularly—always (60.4%) Burden level was associated with Education of caregiver, patient's general well-being	Moderate
Zendjidjian <i>et al</i> 2012 France ³²	▶ Matched cross-sectional ▶ 9.3 years	▶ 232 caregivers of people with BPD ▶ 246 people with SCZ ▶ 232 matched controls	QOL	Mental composite score of SF-36 ▶ Bipolar (40.2), MDD (36.4), SCZ (37.4) ▶ Matched controls (48.2) Physical composite score of SF-36 Bipolar=48.5, MDD=50.2, schizophrenia=46.9, matched controls=49.7	Strong

AOR, adjusted OR; BPD, bipolar disorder; CES-D, centre for epidemiological studies of depression scale; CGAS, children's global assessment scale; DSM-IV, diagnostic statistical manual-IV; ES, effect size; GAS, global assessemnt scale; GPA, grade point average; HRQOL, health related quality of life; IEQ, involvement evaluation questionnaire; IEQ-E, involvement evaluation questionnaire-european version; MCS, mental component score; MDD, major depressive disorder; NA, negative affect; QOL, quality of life; RR, relative risk; SCZ, schizophrenia; SF-12, short form-12; SF-36, short form-36; SMD, severe mental disorder; SMI, severe mental illness; SOC, sense of coherence; SSP, schizophrenia spectrum psychosis.

Studies with comparison group help us to ascertain the contribution of the illness for such high level of psychopathology among family members.^{24 33 40 48 68} Higher risk for psychological problems can also be attributed to genetic predispositions.⁶⁹

The social-economic impacts include temporary and short-term social and economic problems such as divorce, family cohesion problems and economic costs related to treatment and disability. It may also result in long-term socioeconomic drift, low marriage, less employment and greater food insecurity. This supports the previously established social causation (mental illness causes socioeconomic drift) and social selection (mental illness is common in people with low socioeconomic status) models in both low/high-income countries.^{70 71} However,

most of the impacts vary with setting and previous socio-economic status. So, any intervention should be done based on local longitudinal evidence.^{42–44}

Studies that explore the impacts of parental SMI on children largely focus on psychopathology and show this to be higher in children of parents with SMI than in other children. These problems are attributed both to preventable and unpreventable factors. The preventable factors include poor childcare including failing to fulfil basic needs as well as physical and emotional abuse on children by parents with the illness. Though it is reported by a single article, mortality was also higher in these children.²⁴ Further studies will be needed to ascertain this mortality report especially in low-income countries where there is high treatment gap for mental illness and

high child mortality rate.^{72 73} Problems with children's schooling and growth were reported in high-income countries while nutritional problems were reported in low-income setting.^{49 51–53} But as there is a lack of social security system in most LMICs, more studies and intervention programme are needed in children's schooling and nutrition.

The current family inclusive interventions mostly focused on solving psychological distresses in family members.^{74–77} But our review shows that the impact is multidimensional which may need designing of multidimensional interventions: economic, school, social and psychological.

STRENGTHS AND LIMITATIONS

The comprehensive nature of this review based on four databases and grey literature with detailed search strategies is the major strength. Limitations include the fact that most of the included reports were from high-income countries, which make it difficult to generalise for the global setting. About one in five studies was also rated methodologically weak.

CONCLUSIONS

The review shows that SMI had multidimensional, long-term and generational impacts on family members. The impact was distributed in grandparents, parents, siblings, offspring and spouses. This was true in schizophrenia, bipolar disorder and major depression. The review indicated a need for longitudinal research in community settings, and different population groups (eg, urban and rural), especially in low-income countries.

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