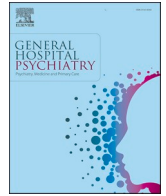


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Psychological and physical wellbeing in adults who grew up with a mentally ill parent: A systematic mixed-studies review

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ABSTRACT

Objective: Genetic vulnerability factors and adverse childhood experiences (ACE) are associated with an increased risk of psychopathology and other adverse health outcomes across the lifespan. However, less is known about how childhood experiences of parental mental illness affect psychological and physical wellbeing in adulthood. This review synthesizes research on the consequences of growing up as a child of a parent with mental illness (COPMI) for adult psychological and physical wellbeing.

Methods: A systematic review was conducted following PRISMA guidelines using a mixed-method-studies approach to enable evaluation of the broad array of research designs (Prospero registration #CRD420221983).

Results: Qualitative studies ($k = 10$; $N = 361$) revealed that a COPMI background is associated with substantial psychological challenges in adulthood. Quantitative studies ($k = 21$; $N = 865.402$) suggested that COPMI are at increased risk of adult psychopathology, including anxiety and depressive disorders, suicidality, somatoform disorders, substance abuse, but also general medical morbidity and mortality.

Conclusions: Growing up with a mentally ill parent is associated with adverse psychological and physical outcomes in adulthood, but the evidence-base is limited. Longitudinal studies are needed that go beyond establishing genetic and environmental risk factors to further evaluate how a COPMI background influences wellbeing in adulthood and which targeted clinical interventions could be developed.

1. Introduction

Children of parents with mental illness (COPMI) are at greater risk of developing psychological problems and other poor health outcomes [1–4]. The vast majority of studies in COPMI have focused on families with children who are younger than 25 years with the goal of optimizing quality of life of the ‘exposed’ children and reduce family burden. In addition to attention for these short-term challenges, there is increasing evidence that a COPMI background is associated with an increased risk of long-term adverse mental health outcomes [1] and physical health [5] in adulthood. These adverse risks can partially be explained by a combination of genetic vulnerability factors and adverse environmental exposures during childhood. However, relatively little is known about the experiences of adults with a COPMI background on how these childhood experiences affect their current mental and physical wellbeing.

Worldwide, millions of children grow up in a family in which one or both parents have a mental disorder. For example, 12.1% to 15.6% of Canadian children [6], 16% of Dutch children [7], and 21% to 23% of Australian children [8] are exposed to parental mental illness. It is plausible that a wide range of genetic and environmental factors play a role in the risk of poor health outcomes when COPMI reach adulthood [9]. Heredity estimates for mental disorders are typically above 50% and having a direct family member with mental illness is the largest known risk factor for an individual to have a mental disorder [1,9]. Another line of thought is that the experiences of COPMI can be considered as one specific type of adverse childhood experiences (ACE). Physical and emotional abuse, neglect, and other adverse circumstances are likely to be disproportionately prevalent in children who grow up in a family with mental illness [10–14]. Furthermore, COPMI often experience additional psychosocial challenges such as financial problems, parental divorce, low school attendance, and shorter parental life expectancy

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[12,15], which are also considered ACE. Thus, the genetic and environmental factors associated with growing up with a mentally ill parent are likely to increase the risk of several psychological and physical disorders.

Evidence indicates that individuals with a COPMI background are at a two- to four-fold higher risk of developing mental disorders before the age of 18 years [1,5,8,15–17]. After the age of 18, this risk increases to thirteen times higher than adult children of parents without a mental illness [1]. It is estimated that approximately two-thirds of COPMI experience psychosocial and/or mental disorders as an adult [18]. The long-term consequences of a COPMI background include anxiety disorders, major depression and substance use disorder [5,17]. In addition, adults with a COPMI background report a range of negative emotions connected with their parent's mental illness such as shame, loneliness, fear and loss [19–21]. A few studies also indicate that physical health problems are prevalent among adults with a COPMI background [5,22]. Given the important role of ACE in the development of Somatic Symptom Disorder (SSD) [12,23,24], COPMI may be at particularly high risk of developing high levels of somatic symptoms and clinical SSD in adulthood [1]. However, little is known about the individual childhood experiences and the pathways by which a COPMI background is related to subsequent mental and physical wellbeing and related experiences in adulthood.

This background indicates that a better understanding is needed of the experiences of adults as related to growing up with a mentally ill parent. The risks of parental psychopathology for the development of mental disorders in their offspring is well established, with an increasing knowledgebase regarding genetic and environmental risk factors. However, much less is known about how people with a COPMI background perceive this phase of their life as related to subsequent adult experiences relevant to mental and physical health. This information may guide clinical practice and future research on the long-term consequences of growing up with a mentally ill parent. The purpose of this systematic review is to synthesize the research on the long-term consequences of a COPMI background for the development of adverse psychological outcomes and somatic symptoms in adulthood.

2. Methods

This systematic review was conducted in accordance with the PRISMA guidelines [25] and the search strategy, study inclusion criteria and data-extraction procedures were registered with PROSPERO prior to conducting the review (#CRD42020221983). Given the broad array of research designs of studies that inform this literature, a systematic mixed-method-studies review was conducted to synthesize the literature. For studies to be eligible, the following inclusion criteria were applied:

- (1) Childhood experiences (before the age of 18 years) of growing up with a parent with a mental illness;
- (2) Assessments of (psychological or medical) outcomes obtained in adulthood (i.e., at the age of 25 years or older);
- (3) Journal research article published in the English language;
- (4) Original research articles (i.e., no abstracts, posters, review articles, meta-syntheses, dissertations, books and congress/seminar papers);
- (5) Publication in or after 2000.

The rationale for the inclusion criteria is as follows: Criterion 1 is inherent to the research question; criterion 2 used an age 25 years as cut-off to ensure that there was a clear difference between the exposure (COPMI before the age of 18) and the outcome (psychological problems in adulthood); criterion 3 was used to enable review of the full article as we had no possibilities to translate non-English articles; criterion 4 was used to include peer-reviewed papers as a general indicator of quality;

and criterion 5 was used to focus on relatively current research since the diagnosis and treatment of mental illness tends to vary over time.

Exclusion criteria for studies were:

- (1) No evaluation for mental disorder or psychological wellbeing during adulthood (based on self-report questionnaire, interview or clinician diagnosis);
- (2) Differentiation between COPMI assessments related to growing up with a sibling versus a parent not possible (i.e., this review focuses on parents, not other family members);
- (3) Case reports or case series with $N < 5$.

No restrictions were set on the study design: cross-sectional, longitudinal and intervention studies as well as qualitative studies meeting inclusion and exclusion criteria were all eligible).

2.1. Search strategy

Using the Medline/PubMed and PsycInfo databases, a systematic search was conducted using the following search terms: (('COPMI' OR 'children of parents with a mental illness' OR 'child of impaired parents' OR 'children of mentally ill parents' OR 'parental psychopathology') AND ('Adult' OR 'adulthood' OR 'adult offspring' OR 'longevity' OR 'lifespan' OR 'life span' OR 'life expectancy')). Because we were specifically interested in SSD and somatic symptoms as related to COPMI [5,22], we also further specified the search terms with: (AND ('Somatization' OR 'somatic symptom disorder' OR 'medically unexplained physical symptoms' OR 'MUS' OR 'medically unexplained somatic symptoms' OR 'MUSS' OR 'functional disorder' OR 'psychosomatic')). These search terms were selected after consultation with a library information specialist. As addition of the SSD-specific search terms resulted in only one article [26], the search in this review was focused on COPMI (and related terms) and 'adulthood' and related terms.

All titles and abstracts were screened for the above-mentioned inclusion and exclusion criteria using the Medline/PubMed and PsycInfo data-bases from 2000 to 2020. A total of 2386 papers were found in Medline/PubMed and 2471 articles were found in the search on PsycInfo. After screening for duplicates, a total of 2587 articles remained in this first step (Fig. 1). The search was conducted in June 2020. A follow-up search was conducted in December 2021 which revealed one additional paper published between June 2020 and December 2021 which is presented in the Discussion only because it falls outside the Prospero-registered date of completing this review.

The initial screening of titles and abstracts was done by IB, and in case of doubt double-checked by AV, and disagreements were settled by discussion between IB, AV and WK. Based on the review of titles and abstracts, the full text papers of 59 articles were evaluated for inclusion and exclusion criteria. A total of 28 out of these 59 articles met all inclusion criteria. The reasons for exclusion were: (1) did not evaluate mental disorder or psychological wellbeing during adulthood ($k = 13$); (2) it was not possible to differentiate COPMI from growing up with a sibling with a mental or physical disorder ($k = 13$); (3) the article was a case report/case series with $N < 5$ ($k = 3$); (4) the study focused on retrospective adult COPMI narratives on childhood experiences and not the long-term consequences of COPMI in adulthood ($k = 1$); and (5) mean age of the adult COPMI was younger than 25 years ($k = 1$). These 28 articles were reviewed for potential studies that could meet inclusion and exclusion criteria. Based on review of the reference lists, another 3 articles were found that met the inclusion criteria.

The 31 articles used in this systematic review are presented by study design in Tables 1, 2 and 3. One reviewer (IB) extracted the results of the article and the findings were discussed by the full team prior to summarizing the findings for each study as described in the Results section. Outcomes included a range of mental and physical health measures and psychological factors reported by adults who had COPMI experiences

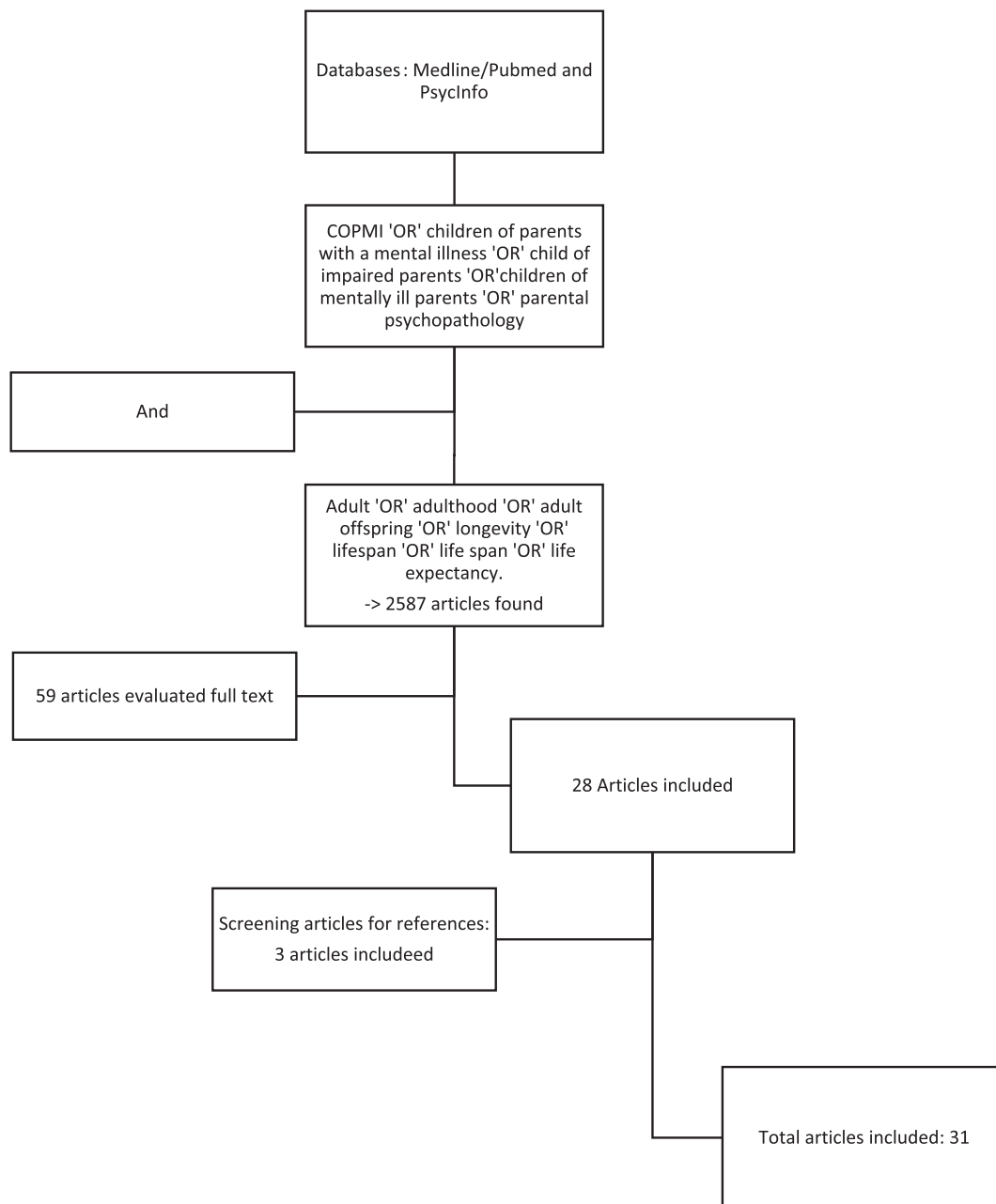


Fig. 1. Flowchart of literature search.

(also see supplemental Table S1 for themes derived from qualitative studies). For each outcome measure, the prevalence (frequency) and differences between COPMI vs. reference group (e.g., mean and standard deviation or odds ratios) are reported. In addition to the outcomes, for each study we report the study design, nature of COPMI background, the country where the study was conducted, sample size, age (mean and standard deviation), the sex distribution, and the main study findings.

2.2. Assessment of bias and quality of included studies

Two reviewers (IB and AV) assessed each article for potential bias and other factors relevant to the quality of individual articles using a scoring system appropriate for mixed-studies reviews. The inclusion of different study designs precluded use of a single quality appraisal instrument and separate tools were therefore used for quantitative and

qualitative studies. Both instruments include assessment of bias such as selection bias and reporting bias.

For articles reporting quantitative studies ($k = 21$) the Effective Public Health Practice Project (EPHP) tool was used [27], adapted for the papers included in the present review. Articles were graded on five dimensions (selection bias, design quality, assessment and analysis of confounding variables, blinding, and data collection methods/missing values or drop-outs) as strong, moderate, or weak using specific criteria. Based on these domain ratings, an overall quality assessment of each article was rated as: “strong,” “moderate” or “weak.”

For articles reporting qualitative studies [28] the criteria developed by the National Institute for Health and Care Excellence (NICE) were used [29]. This 14-item checklist was supplemented by additional items derived from reporting guidelines outlined by the EQUATOR network (COREQ) [30] and SRQR [31]. The 14 NICE-based items correspond

Table 1
Results from qualitative studies on the association between COPMI with psychological outcomes and somatic symptoms (k = 10).

Study	Design	Participants: N, age and sex	Nature of COPMI background	Experienced problems	Other findings
Duncan & Browning (2009)	Semi-structured, in-depth one-to-one interviews <u>Country: New Zealand</u>	Total N = 23 N COPMI = 23 Age range = 24–61 yrs. Age mean \pm SD = not reported Female = 19 (83%)	Raised by a parent with schizophrenia.	Difficulties with trust and vulnerability in intimate relationships. Feelings of fright, detachment or unpredictability experienced as a child were generalized into adulthood. What was 'abnormal' and 'unpredictable' has become normal for them, which makes it harder to develop a secure adult attachment based on trust.	Results suggest insecure attachment as a common theme.
Foster (2010)	Interpretive auto-ethnography Structured one-to-one interviews <u>Country: Australia</u>	Total N = 10 N COPMI = 10 Age range = 25–57 yrs. Age mean \pm SD = not reported Female = 8 (80%)	Raised by a parent with a range of mental illnesses	70% reported mental health problems being anxiety and depression. Furthermore a range of uncertainties, even as an adult they experience a lack of understanding about their parents' mental illness, a high level of parentification and a subjective and objective burden related to caretaking responsibilities towards the parent.	Need for support from others including health professionals may strengthen adult children's resilience and ability to cope with these challenges.
Knutsson-Medlin et al. (2007)	Structured one-to-one interviews and questionnaire constructed and adapted to the specific aim of the study including questions on retrospective socio-demographic data reported from childhood as well as current information <u>Country: Sweden</u>	Total N = 36 N COPMI = 36 Age range = 19–38 yrs. Age mean = 25.8 \pm 4.9 yrs. Female = 21 (58%)	Raised by a parent with a range of mental illnesses	25% of participants had been in contact with child and adolescent psychiatry and 19.4% with adult psychiatric services. Participants reported worry about the parent; having an increased responsibility for their families; felt negative emotions as shame, depressed mood, fear for different reasons, lack of confidence, anger and envy; and a changed parent/child relationship. Feelings of relief when someone else was responsible for the parent during a hospitalization, the experience of lack of support from health care staff.	They wished more contact with the staff, more information and more explanation about their parent's illness.
Metz & Jungbauer (2019/2021)	Semi-structured, in-depth one-to-one interviews <u>Country: Germany</u>	Total N = 18 N COPMI = 18 Age range = 18–64 yrs. Age mean = 40.8 yrs. \pm SD not reported Female = 15 (83%)	Raised by a parent with a range of mental illnesses	Physical problems mentioned were: migraine, sleep disturbances, chronic inflammatory bowel disease and facial paralysis. Most participants developed mistrust against others and attachment problems. Participants attributed this wide range of problems to their stressful childhood experiences.	Most participants expressed need to talk about their childhood experiences and long-term effects, and a need for professionals to consider that the current symptoms or difficulties can be related to childhood COPMI experiences, for validation when they discuss their burdensome experiences, and talking about their experiences was perceived as necessary to understand and treat their present problems.
Murphy et al. (2015)	Qualitative, narrative inquiry and analysis Semi-structured, in-depth one-to-one interviews All papers of Murphy et al. are based on one study ('Living in a Secret World study'). Each paper discusses a different theme identified from the findings of the 'Living in a Secret World Study' <u>Country: Australia</u>	Total N = 13 N COPMI = 13 Age range = 30–78 yrs. Age mean = 54 yrs. \pm SD not reported Female = 10 (77%)	Raised by parents with a range of mental illnesses	All participants reported childhood experiences of fear and mistrust of others. As a child, they felt lonely and isolated and were unable to obtain information about their parent's condition, leaving them unprepared and unskilled to handle the COPMI-related challenges, despite their desire to help their parent. For some, fear and mistrust continued into adulthood. This fear is highly associated with mistrust of the parents and others.	
Murphy et al. (2016)	As above	As above	As above	Participants felt unsure of their own emotions and felt they had lost a sense of who they were as individual people. They also felt confused about their sense of reality and their experiences of loss were closely associated with	

(continued on next page)

Table 1 (continued)

Study	Design	Participants: N, age and sex	Nature of COPMI background	Experienced problems	Other findings
Murphy et al. (2017)	As above	As above	As above	changing self-identity. Childhood experiences of fear and mistrust of others, particularly of the parent with mental illness, and of feeling lonely and isolated. Also feeling unable to disclose experiences of parental mental illness with others in adulthood. Participants were aware of social stigma during their childhood and reported behavioral changes to avoid disclosure of parental mental illness. This fear of disclosure to others fueled an atmosphere of familial secrecy, reinforcing the child's own sense of difference, which remained during adulthood. Participants reported anxiety as a child and anxiety in their parenting roles as adults. Anxiety during adulthood concerned the possibility that their own children may develop a mental illness. Participants noted that they lack an internal parenting framework. They also experienced an increased sense of self-worth from their parenting roles as adults.	
Murphy et al. (2018a)	As above	As above	As above	Participants reported 'dehumanizing' their parent with a mental illness: The humanistic characters of the parent was perceived as having less value in society. Feelings were expressed that the parent was 'reduced' to mental illness-related symptoms with loss of the experience of the parent as an individual person. Problems with parenting role in adulthood. The main challenge for adult COPMI is an absence of a reference point and lack of informal social support.	
Murphy et al. (2018b)	As above	As above	As above		
Patrick et al. (2019)	Semi-structured, in-depth one-to-one interviews <u>Country:</u> Australia	Total N = 10 N COPMI = 10 Age range = 27–51 yrs. Age mean = 40.3 ± 6.83 yrs. Female = 9 (90%)	Raised by a parent with a range of mental illnesses		

with the three domains of reporting qualitative research as described in the COREQ criteria: (i) research team and reflexivity; (ii) study design; and (iii) data analysis and reporting. Similar to the quantitative studies, the qualitative studies were rated as “strong”, “moderate” or “weak.” (see supplemental Appendix S-A1) for an overview of the checklists for quantitative and qualitative studies).

3. Results

3.1. Study characteristics

Fig. 1 displays the study selection flow chart resulting in the 31 studies included in this systematic review. A total of 10 qualitative studies and 21 quantitative studies were included. The qualitative studies involved a total of 361 participants and the quantitative studies presented data from a total of 865,402 participants. The studies were conducted in a wide range of countries and covered multiple endpoints. Table 1 summarizes the results of the qualitative studies, Table 2 the results from the cross-sectional cohort studies, and Table 3 results from between group design and prospective studies.

3.2. Results from qualitative studies

Qualitative studies (k = 10) found a wide range of mental and physical problems in adulthood associated with a COPMI background

(Table 1). Themes commonly experienced in childhood were lack of information and support from health professionals [22,32], a heightened level of responsibility and parentification and a sense of worry and burden during childhood [22], unpredictability at home and shame as a result of the times when the parents behaved differently [33,34].

Adult COPMI reported that the emotions they had as a child/adolescent (e.g., shame, loneliness, fear, insecurity, lack of safety, sadness and anger) continued in their adulthood [20,22,35–37]. COPMI also mentioned that more information and explanation about their parent's illness and professional support during childhood could have reduced problems in adulthood. Anxiety was reported to influence adult COPMI's own parenting role because of lack of an internal parenting framework and concerns that their own children may develop a mental illness [38]. Adults with a COPMI background also experienced problems in relationships with peers, family, friends and parents [22,32]. They reported stigma and behavioral changes to avoid disclosure of the parental mental illness to others [39]. Adults with a COPMI background also reported a range of somatic symptoms, including migraine, sleep disturbances, chronic inflammatory bowel disease and facial paralysis [22].

These qualitative studies reveal that adults with a COPMI background face a range of physical and psychological problems, but specific psychiatric disorders or abuse-related adversities were not mentioned as a primary concern. Somatic symptoms were mentioned [22] but did not emerge as a central theme in qualitative studies. The overall themes in

Table 2

Results from descriptive studies examining the association between COPMI with psychological outcomes and somatic symptoms (k = 8).

Study	Design	Participants: Total N/N COPMI, age and number of females	Nature of COPMI background	Main findings
Aazh et al. (2019)	Descriptive cohort study: retrospective, cross-sectional study among patients who sought help for tinnitus and/or hyperacusis from a specialist clinic <u>Country:</u> United Kingdom	Total N = 292 N COPMI = 113 Age range = 18–87 yrs. Mean age = 52.4 ± 15.6 yrs. Female = 149 (51%)	Raised by parents with depression	38.7% (113/292) was raised (before age 18 yrs) by parent(s) who suffered from a mental illness. 63% (174/275) had no hearing loss; 34.3% (99/289) experienced hyperacusis; 98% had tinnitus; 40% (116/291) experienced depressive symptoms; and 45% (130/289) experienced anxiety. Parental mental illness was associated with an increased risk of suicidal and self-harm ideations. Almost 16% of participants reported a level of suicidal or self-harm ideations.
Atwoli et al. (2014)	Stratified multi-stage sample design with structured interviews <u>Country:</u> South Africa	Total N = 4315 N COPMI = not reported ¹ Age range = divided in four categories (18–20, 30–44, 45–59, 60 or older), range not reported Age mean ± SD = not reported Female = 2529 (58.6%)	Raised by a parent with a range of mental illnesses	Parental psychopathology was associated with increased risk of suicidal ideation and attempts in offspring. Parental panic disorder was associated with the onset and persistence of suicidal ideation in offspring. Parental panic disorder, generalized anxiety disorder and suicide were significantly associated with suicide attempts in offspring. Results showed a strong relationship (17 times more likely) between maternal internalizing disorders and anxious-preoccupied attachment. Paternal externalizing disorders were associated with insecure attachment styles, especially with an anxious-preoccupied attachment. Both anxious preoccupied attachment and fearful avoidant attachment were associated with suicidal ideation and plans, whereby fearful attachment had the highest risk for 12-month suicidal plans.
Boyda et al. (2018)	Secondary data analysis of the national comorbidity survey-replication (NCS-R) <u>Country:</u> United States of America	Total N = 5692 N COPMI = 5692 Age range = ≥18 yrs., divided in four categories, not reported Age mean ± SD = not reported Female = 3017 (53%)	Raised by a parent with a range of mental illnesses Differentiation between parents with internalizing and externalizing problems	Parental disorders were associated with increased risk of suicidal ideation among offspring. Generalized anxiety and depression in the parent were the only predictors of the onset and persistence of suicide plans and antisocial personality. Anxiety disorders were the only predictors of the onset and persistence of suicide attempts. Neither the sex of the parent nor whether one or both parents had the disorder showed a consistent relationship with suicidal behavior in the (adult) child. Paternal suicide was associated with increased odds of suicidal behavior in male offspring and maternal suicide was associated with increased odds suicidal behavior in female offspring.
Gureje et al. (2011)	Descriptive cross-national study with national representative samples in 21 countries, from the world mental health surveys (WMHS) <u>Country:</u> 21 countries: Belgium, Brazil, Bulgaria, France, Germany, India, Israel, Italy, Japan, Lebanon, Mexico, New Zealand, Nigeria, Romania, South Africa, Spain, The Netherlands, Ukraine, United States of America	Total N = 55,302 N COPMI = not reported ¹ Age range = ≥18 yrs. Age mean ± SD = not reported Female = not reported	Raised by parents with major depression, panic disorder, generalized anxiety disorder, substance dependence, and antisocial behavior.	Participants' childhood COPMI-related experiences were disruptive, and sometimes abusive and neglectful. Many were still feeling pain related to their childhood's experiences, and 52% reported diagnosis of depression in adulthood. Most participants identified their mother as having the most importance (positive or negative) to them in childhood and the most impact (positive and negative) on them as adults. Female participants reported significantly more family problems/conflicts than males. There were no differences in wellbeing by participants' sex. When mothers were diagnosed at or before the age of 31, family problems increased and there was also a trend for less attachment. Those participants who were age 15 or less when they realized their mother's diagnosis were more likely to be currently clinically
O'Connell (2008).	Cross sectional, descriptive design with quantitative and qualitative data from a nonrandomized voluntary sample of adult COPMI <u>Country:</u> United States of America	Total N = 40 COPMI N 40 Age range = 23–66 yrs. Age mean = 40.29 ± 9.57 yrs. Female = 35 (88%)	Raised by a mother with serious mental illness	Participants' childhood COPMI-related experiences were disruptive, and sometimes abusive and neglectful. Many were still feeling pain related to their childhood's experiences, and 52% reported diagnosis of depression in adulthood. Most participants identified their mother as having the most importance (positive or negative) to them in childhood and the most impact (positive and negative) on them as adults. Female participants reported significantly more family problems/conflicts than males. There were no differences in wellbeing by participants' sex. When mothers were diagnosed at or before the age of 31, family problems increased and there was also a trend for less attachment. Those participants who were age 15 or less when they realized their mother's diagnosis were more likely to be currently clinically

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Table 2 (continued)

Study	Design	Participants: Total N/N COPMI, age and number of females	Nature of COPMI background	Main findings
Pilowsky et al. (2006)	Descriptive, cross-sectional, interview-based study. Parents and offspring were interviewed independently, and the interviews of offspring were blind to the clinical status of the parents. This is the same cohort as Weissman et al. (2006; 2016; see Table 3) and involves the 4th wave of interviews of the overall study, a 20-year longitudinal study.	Total N = 182 COPMI N = 125 ² Age range = not reported Age mean = 34.1 ± 5.6 yrs. Female = 96 (53%)	Raised by a parent with depression and a range of other mental illnesses	depressed then those participants who were age 16 or more. Most participants were doing well in adulthood and the ability to function well was seen as resulting from their own initiative. Among children of depressed parents, family discord had no statistically significant association with offspring major depressive disorder or anxiety disorders. Among children of nondepressed parents, parental affectionless control was associated with increased risk of substance abuse.
Santana et al. (2015)	<u>Country:</u> United States of America Descriptive cross-sectional household study with a representative sample of the adult population living in the Sao Paulo Metropolitan Area Data are from the SPMHS study (Sao Paulo Mental Health Survey). <u>Country:</u> Brazil	Total N = 2942 COPMI N = not reported Age range = divided in four categories, is not reported Age mean ± SD = not reported Female = not reported	Raised by a parent with a range of mental illnesses	Parental psychopathology was significantly associated with suicidal behaviors. Parental disorders defined by impulsive aggression and anxiety-agitation were the main predictors of offspring lifespan suicidality. Parental generalized anxiety disorder (GAD) and antisocial personality disorder were associated with offspring suicidal ideation. Parental panic and GAD were associated with offspring suicidal attempts, and panic was related to the transition from ideation to attempts. The association between parental mental illness with problems in offspring continues from childhood until young adulthood with the most evident influence during adolescence.
Singh et al. (2010)	Descriptive, cross-sectional study with semi-structured interviews. <u>Country:</u> Australia	Total N = 2555 COPMI N = 945 Age range = 14–39 yrs. Age mean = 25.1 ± 5.7 yrs. Female = 1303 (51%)	Raised by a parent with a range of mental illnesses.	Offspring exposed to parental depression had more major depressive disorders than their cousins without an exposure to parental depression in a way that an environmental process underlies the intergenerational association of depression. Furthermore, common genetic factors seem to account for the association of parental depression and offspring conduct disorder.

¹ No total number of COPMI reported, only percentages of disorders in parents, some of whom may have comorbid disorders, therefore these percentages are reported in the table.

² No total number of COPMI reported, of the 182 participants; 125 were offspring from high-risk families and 57 offspring from low-risk families.

adult COPMI involved concerns about own parenting roles, risks related to one's own mental health, emotional problems, and difficulties with relationships (see supplemental Appendix S-A2).

3.3. Results from descriptive cross-sectional quantitative studies

The results from quantitative research ($k = 21$) are presented separately for descriptive (one sample, cross-sectional) studies (Table 2) and studies with a between-groups or prospective design (Table 3).

Results of descriptive studies ($k = 8$) indicate that a COPMI background was associated with problems related to secure attachment and suicidal ideation and also self-harm behaviors, whereas no associations with somatic symptoms were found (Table 2).

Specifically, parental affectionless control was associated with an increased risk of substance abuse among adult children of non-depressed parents, but not in children of depressed parents [40]. Singh et al. [9] found that parental depression was associated with depression and conduct disorders in adult COPMI. Regarding attachment, Boyda and colleagues [41] differentiated between parents with internalizing and externalizing mental health problems. Results showed a strong relationship (17 times more likely) between maternal internalizing

disorders and anxious-preoccupied attachment. Paternal externalizing disorders were associated with insecure attachment styles, especially with an anxious-preoccupied attachment. Both anxious-preoccupied attachment and fearful-avoidant attachment were associated with suicidal ideation and plans. The connection between parental psychopathology and suicidal and self-harm behavior in the adult offspring was also found in multiple other cross-sectional studies [26,41–43].

O'Connell [44] described that participants' COPMI-related experiences were disruptive, and sometimes abusive and neglectful. Many were, as adults, still feeling pain related to their childhood experiences, and 52% reported a diagnosis of depression in adulthood. Participants who were aged 15 or less when they realized their mother's diagnosis, were more likely to be currently clinically depressed than participants who were aged 16 or older. Most participants identified their mother as having the most importance in childhood and the most impact (positive and negative) on them as adults. However, most participants were doing well in adulthood and the ability to function well was seen as resulting from their own initiative. No differences between adult women versus men were reported with regard to psychological wellbeing.

These descriptive cross-sectional studies indicate that insecure and fearful attachment are among the main consequences of a COPMI

Table 3

Results from between group design, case-control studies and prospective studies examining the association between COPMI with psychological outcomes and somatic symptoms ($k = 13$).

Study	Design, included participants, instruments, follow-up duration, country of study	Participants: N, age (range and mean \pm SD), and number of females	Main findings
Between groups and case-control studies ($k = 3$)			
Alkan et al. (2016)	<p>Between-groups design</p> <p><u>Included participants:</u> COPMI group: Raised by a parent with schizophrenia; Controls: No COPMI background</p> <p>Instruments: Questionnaires on (1) demographic information; (2) conservation of psychological resource scale; (3) multidimensional quality of life (MQOL).</p> <p><u>Country:</u> Israel</p>	<p>N COPMI = 31 Age range = 20–50 yrs. Age mean = 42,57 \pm 9.38 yrs. Female = 31 (100%)</p> <p>N Controls = 30 Age range = 20–50 yrs. Age mean = 40,52 \pm 10.07 yrs. Female = 30 (100%)</p>	<p>Quality of life was markedly lower in adult women with COPMI background compared to controls. They also had lower levels of functionality in the family environment and high levels of negative emotions and loss of resources.</p> <p>The daughters had some resource gains in developing resilience in the presence of supportive relationships with other family members, but these gains were less than in controls. Resource loss was more strongly associated with quality of life than resource gain.</p>
Peisah et al. (2004)	<p>Between group comparison</p> <p><u>Included participants:</u> COPMI group: Raised by a parent with clinical depression, who were admitted 25 years prior Controls: no COPMI background, children of a surgical group</p> <p><u>Instruments:</u> Self-report questionnaire measures of socioeconomic background using the Daniel prestige scale; psychiatric diagnoses; current psychological distress with the 30 item general health questionnaire (GHQ-30); personality using DSM-III-R nosology; family and intimate relationships using (1) the parenting bonding scale (PBI), the parent-adult child relationship questionnaire (PACQ) (2) quantitative and qualitative data from semi structured interviews; and (3) self-report on intimate relationships with the intimate bonding measure (IBM).</p> <p>Statistical model: Logistic regression with a forward stepwise method of entry.</p>	<p>N COPMI = 125 Age range = not reported Age mean = 36.1 \pm 13.0 yrs. Female = 53 (42%)</p> <p>N Controls = 94 Age range = not reported Age mean = 35.8 \pm 10.5 yrs. Female = 18 (19%)</p>	<p>Parental depression was associated with non-phobic anxiety, and lifetime substance and alcohol use disorders in adult offspring.</p> <p>No association was found for overall psychological morbidity nor for affective disorders.</p> <p>COPMI had more problematic relationships with their fathers. COPMI reported more caring in current relationships compared to the control group.</p>
Peisah et al. (2005)	<p>Between group comparison</p> <p><u>Included participants:</u> As above</p> <p><u>Instruments:</u> As above</p> <p><u>Country:</u> As above</p>	As above	<p>Parental disorders were associated with increased risk of suicidal ideation among offspring.</p> <p>Generalized anxiety and depression in the parent were the only predictors of the onset and persistence of suicide plans and antisocial personality.</p> <p>Anxiety disorders were the only predictors of the onset and persistence of suicide attempts.</p> <p>Neither the sex of the parent nor whether one or both parents had the disorder showed a consistent relationship with suicidal behavior in the (adult) child.</p> <p>Paternal suicide was associated with increased odds of suicidal behavior in male offspring and maternal suicide was associated with increased odds suicidal behavior in female offspring.</p>
Prospective studies ($k = 10$)			
Dean et al. (2010)	<p>Longitudinal study: Population based cohort study between 1980 and 2008</p> <p><u>Included participants:</u> All offspring born in Denmark between 1980 and 1994 who were 14 years or older at the start of the study in 1980.</p> <p><u>Instruments:</u> (1) Participants and their parents were linked with their Central Person registration number to the Psychiatric Central Register; (2) the International Classification of diseases: ICD-8; between April 1969–December 1993 and the ICD-10 from January 1994, only parental diagnosis given prior to the child's age of 14 yrs. were considered.</p> <p><u>Follow-up duration:</u> a range between 15 and 29 yrs.</p>	<p>Total $N = 865,078$ N COPMI = not reported Age range ≥ 14 yrs. in 1980 Age mean \pm SD = not reported Female = not reported</p>	<p>Having a parent with serious mental disorder is positively associated with an increased risk for the offspring to developing a range of mental disorders. Of the offspring, 5% ($N = 49,682$) had at least one contact with either inpatient or outpatient psychiatric services in Denmark after their 14th birthday and before the end of the follow-up period in 2008. The most common psychiatric diagnosis categories in offspring were anxiety and somatoform disorders ($N = 25,552$, 2.95%). Almost 1/5 (9.6%) of the offspring who made contact with psychiatric services had a parental history of mental disorder.</p>

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Table 3 (continued)

Study	Design, included participants, instruments, follow-up duration, country of study	Participants: N, age (range and mean \pm SD), and number of females	Main findings
Diaz (2019)	<p><u>Country:</u> Denmark Data are derived from the same cohort as Weissman et al. (2006; 2016).</p> <p><u>Included participants:</u> Children and adolescents of parents with moderate to severe and impairing major depressive disorder (MDD) who were outpatients receiving medication for depression as part of research; and children of non-depressed parents from an epidemiological sample in the same community who had no lifetime history of psychiatric illness. Associations between disruptive disorder (DD) and psychiatric and functional outcomes were tested.</p> <p><u>Instruments:</u> (1) the Diagnostic Interview Schedule for Affective Disorders and Schizophrenia-Lifetime (SADS-L) for adults (across all waves). (2) the Kiddie-SADS child version modified for DSM-IV for age 6-17 yrs.; (3) the Kiddie-SADS-E was used at wave 3; (4) the Kiddie-SADS-PL version was used in waves 4 through 6; final diagnoses were made by an experienced M.D. of Ph.D. level clinician using integrated sources of information; (5) the Global assessment Scale (GAS and the GAS-child version rated participants at each wave; (6) the Social Adjustment Inventory for Children and adolescents was used to obtain school performance; and (7) the childhood or adolescence section of the DSM-III.</p> <p><u>Follow-up duration</u> 33 yrs.</p>	<p>N COPMI = 70 (of 89 participants with disruptive behavior disorder) Age range = not reported Age mean = 19.8 \pm 6.8 yrs. Female = 19 (21%)</p> <p>N Controls = 178 (participants without disruptive behavioral disorder; no details about absence of COPMI in that group) Age range = not reported Age mean = 18.3 \pm 6.7 yrs. Female = not reported</p>	<p>Child and adult outcomes of disruptive disorders (DD) in offspring whose biological parents did not have a history of antisocial personality disorder, bipolar disorder or substance use disorder, were examined. At wave 1 and 2, 33.3% of the participants (children of parents with or without MDD but without an antisocial personality disorder or a bipolar disorder) were diagnosed with DD. Of these children, 70 were COPMI and more likely to be male (59.6%). The children diagnosed with DD had worse outcomes in both child- and adulthood, even in the absence of parental risk factors (lifetime history of substance abuse, bipolar disorder, ASPT) children with DD had distinctly poorer outcomes that persisted into adulthood</p>
Gluschkoff et al. (2017)	<p><u>Country:</u> United States of America Longitudinal population-based cohort study with participants from the Young Finns study between 1980 and 2012 with five measures in 1992 (age 15) -1997-2001-2007-2012</p> <p><u>Included participants:</u> Participants from the prospective Cardiovascular Risk in Young Finns Study, at age 3-18 yrs. at baseline in 1980.</p> <p><u>Instruments:</u> (1) Self report by the participants parents at baseline using a scale derived from the Operation Family Study; (2) self-report of parents on mental health problems and use of prescription medicines for psychiatric disorders; (3) a modified version of the Beck Depression Inventory to measure self-reported depressive symptoms; (4) Parental socioeconomic status (SES) was assessed at baseline using two indicators: 1. Mean of mothers and father's years of education and 2. The annual income of the household.</p> <p><u>Follow-up duration:</u> 32 yrs.</p> <p>Multilevel modeling for repeated measurements was used to examine the association of hostile parenting and parental history of psychopathology with trajectories of depressive symptoms across five study phases</p>	<p>Total N = 3596; longitudinal data used of 2122 participants</p> <p>Total N = 2122 (in 1980) Age range = not reported Age mean = 9.63 \pm 4.84 yrs. Female = 1155 (54.43%)</p> <p>Total N = 2122 (in 2012) Age range 35–50 yrs. Age mean \pm SD = not reported Female 1155 (54,4%)</p>	<p>Parental psychopathology was the strongest predictor of depressive symptoms in the COPMI and hostile parenting predicted higher levels of depressive symptoms. The combination of parental history of psychopathology and exposure to high parental intolerance was associated with the highest level of depressive symptoms in the adult children. COPMI exposed to more tolerant parenting showed a relatively stronger decline in depressive symptoms from adolescence to adulthood. COPMI exposed to hostile parenting showed, after an initial decrease until the age of 30, a rise of depressive symptoms.</p>

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Table 3 (continued)

Study	Design, included participants, instruments, follow-up duration, country of study	Participants: N, age (range and mean \pm SD), and number of females	Main findings
Gonçalves et al. (2016)	<p><u>Country:</u> Finland</p> <p>Longitudinal population-based birth cohort study (cross-sequential design) with two measures of maternal mental disorder.</p> <p><u>Included participants:</u> Offspring of mothers who were interviewed (in 1982) after given birth in the maternity hospital.</p> <p><u>Instruments:</u> (1) Interview done by nurse with mothers after given birth in maternity hospital; and (2) SRQ-20 The SRQ-20 was completed by mothers when (1) mean age of their children was 3.6 yrs. and again (2) at child's age 18–19. The SRQ-20 was answered by the offspring at age 18–19; (3) at age 23–24; and (4) at age 30 yrs.</p> <p><u>Follow-up duration:</u> 30 yrs. (between 1982 and 2012)</p>	<p>Total N = 3156 (follow-up 1) Age range = 18–19 yrs. Age mean \pm SD = not reported Female = not reported</p> <p>Total N = 4265 (follow-up 2) Age range = 23–24 yrs. Age mean \pm SD = not reported Female = not reported</p> <p>Total N = 3156 (follow-up 3) Age of participant assessments at 30 yrs. Age range = not reported Age mean \pm SD = not reported Female = not reported</p>	Maternal mental disorder during adolescence, was associated with an increased prevalence of depression and anxiety at 18–19, 23–24 and 30; and is associated with persistence of episodes in female offspring. In male offspring there was no convincing evidence for associations.
Kasen et al. (2014)	<p><u>Country:</u> Brazil</p> <p>Longitudinal case-control study with interviews at baseline (T1), 2 (T2), 10 (T10) and 20 (T20) yrs. later</p> <p><u>Included participants:</u> Participants were children of depressed and nondepressed parents. Depressed parents received an outpatient treatment in 1982. Nondepressed parents and their children were drawn from a longitudinal survey conducted in the same community in 1975.</p> <p><u>Instruments:</u> Assessment of: 1. psychosocial functioning in past week (GAS); 2. lifetime MDD (SADS-L or K-SADS-E, for <17 yrs. at T1 and T2) and diagnostic interview; 3. three questions about religiosity</p> <p><u>Follow-up duration:</u> 20 yrs.</p>	<p>Total N = 222 (follow-up T10) N COPMI = not reported Age range = 17–38 yrs. Age mean = 29.0 \pm SD not reported Female = not reported 109 (58.9%)</p> <p>Total N = 185 (follow-up T20) N COPMI = 126 Age range = not reported Age mean \pm SD = not reported Female = 109 (58.9%)</p>	Having had a depressed parent during childhood was associated with lifetime prevalence of depression in both daughters and sons At T20, 57.8% of daughters and 40.8% of sons were diagnosed with depression. There was a relationship between lifetime MDD and poorer psychosocial functioning among daughters at T10 and T20, and in sons a significantly poorer psychosocial functioning at T10 but a marginally poorer functioning at T20. Both daughters and sons with lifetime MDD or a depressed parent or both, improved with higher levels of religiosity compared with the participants without lifetime MDD and/or a depressed parent regarding their psychosocial functioning. A higher level of service attendance at T10 in daughters with lifetime MDD and a higher level of religious/spiritual importance at T10 in sons with lifetime MDD was related to improved psychosocial functioning based on higher GAS scores. That association was not significant in daughters and sons without lifetime MDD.
Taka-Eilola et al. (2019)	<p><u>Country:</u> United States of America</p> <p>Longitudinal general population-based cohort study (NFBS 1966 study).</p> <p><u>Included participants:</u> Children born between January 1 and December 31, 1966. Information was used from the Care Register for health care.</p> <p><u>Instruments:</u> (1) Interviews by a nurse at the antenatal clinic; (2) data from the Care Register for Healthcare (CRHC) on parents with inpatient treatment for severe mental disorders</p> <p><u>Follow-up duration:</u> 43 yrs.</p>	<p>Total N = 10,521 Age range 16–43 yrs. Age mean \pm SD = not reported Female = 5124 (48.7%)</p> <p>N COPMI = 1462 (maternal mood during pregnancy)</p> <p>N COPMI = 838 (with paternal severe mental disorder)</p> <p>COPMI N = 231 (with both maternal mood during pregnancy + severe paternal mental disorder)</p>	In this sample, 13.9% of the offspring had a mother with antenatal depression (AD); 10.2% had a parent diagnosed (between 1972 and 1984) with a severe mental disorder; and 2% had both. Offspring with an AD mother had a higher risk for depression compared with offspring without Ad mothers. The offspring with an AD mother + parental severe mental disorder had especially higher risk for depression and schizophrenia compared to offspring with only one or none of these risk factors.
Valenstein et al. (2012)	<p><u>Country:</u> Finland</p> <p>Longitudinal study: Parents assessed at baseline and offspring assessed 23 yrs. later</p> <p><u>Included participants:</u> Parents participated in a study of depression (baseline) and their adult children were assessed 23 years later.</p> <p><u>Instruments:</u> Respondents completed (1) The Health and Daily Living Form (HDL); (2) the Family Environment Scale (FES)</p> <p><u>Follow-up duration:</u> 23 years</p>	<p>Total N = 340 N COPMI = 340 Age range = not reported Age mean = 34.1 \pm 11.5 yrs. Female = 180 (53%)</p>	Having a parent who displayed a combination of suicidal ideation, an inflexible parenting style and had a more avoidant coping, was predictive of suicidal ideation in offspring 23 yrs. later.

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Table 3 (continued)

Study	Design, included participants, instruments, follow-up duration, country of study	Participants: N, age (range and mean \pm SD), and number of females	Main findings
Van Eck van der Sluijs et al. (2018)	<p><u>Country:</u> United States of America</p> <p>Follow-up study with data derived from the Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2).</p> <p><u>Included participants:</u> Patients with medically unexplained symptoms (MUS) at baseline, and examined predictive value of COPMI for persistent MUS at 3-yr follow-up with participants who did not have persistent MUS</p> <p><u>Instruments:</u> Using the data NEMESIS-2, a multistage, stratified random sampling of households with one respondents aged 18-64 yrs. randomly selected in each household for a face-to-face interview.</p> <p><u>Follow-up duration:</u> 3 yrs. At T0 data were used from November 2007 to July 2009 and at T1 data were used from November 2010 to June 2012.</p> <p>Logistic regression analyses were used to determine risk factors for persistency of MUS.</p>	<p>Total N = 324</p> <p>N COPMI = not reported</p> <p>Age: in four groups: 18–34 yrs.: N = 13.3% 35–44 yrs.: N = 21.6% 45–54 yrs.: N = 30.2% 55–64 yrs.: N = 34.9%</p> <p>Age mean \pm SD = not reported</p> <p>Female = not reported</p>	<p>In the adult general population, persistence of MUS was significantly associated with parental psychopathology, number of comorbid medical disorders, and physical functioning.</p>
Weissman et al. (2006)	<p><u>Country:</u> The Netherlands</p> <p>Longitudinal study (cross-sequential design) with interviews and diagnostic assessments</p> <p><u>Included participants:</u> Individuals with COPMI-depression and participants without COPMI background.</p> <p><u>Instruments:</u> Diagnostic interviews at baseline and 2, 10, and 20 yrs., blind to the medical status of the parent. Information from medical records was available.</p> <p><u>Follow-up duration:</u> 20 yrs.</p> <p><u>Country:</u> United States of America</p>	<p>Total N = 151</p> <p>Age range 26–43 yrs. Age mean = 35 yrs., SD = not reported (SD = 19.4 yrs. at 1e interview Female 88 (58%)</p> <p>N COPMI = 101 Age range = not reported Age mean \pm SD = not reported Female = 58 (57%)</p> <p>N Controls = 50 Age range = not reported Age mean \pm SD = not reported Female = not reported</p>	<p>This study reported the data from the 20-year follow-up (4th wave).</p> <p>Offspring of depressed parents had a threefold higher risk of mood and anxiety disorders than offspring with non-depressed parents (control group). This consisted mainly of major depressive disorders and phobia and the mean age of onset was lower than with offspring of non-depressed parents (16 vs 19 yrs).</p> <p>Furthermore, the offspring of depressed parents had a twofold higher risk of alcohol dependency, a sixfold higher risk of drug dependence.</p> <p>At the age of 35 offspring of depressed parents reported more medical problems, especially cardiovascular problems (more than five times as likely), neuromuscular problems (more than twice as likely); they had a two times higher probability of any physical health problem; and they had a higher mortality rate (3% of the risk group died and 0% of the controls).</p>
Weissman et al. (2016)	<p>As above</p> <p>In the whole study there were six waves of interviews, at baseline and 2, 10, 20, 25 and 30 yrs. later.</p> <p><u>Included participants:</u> Individuals with COPMI-depression and participants without COPMI background.</p> <p><u>Instruments:</u> At 25 yrs. a small sample had a MRI</p> <p><u>Follow-up duration:</u> 33 yrs. (mean duration 28.1 yrs., range of 20.0–32.3 yrs)</p> <p><u>Country:</u> As above</p>	<p>Total N = 147</p> <p>N COPMI = 103 Age range = not reported Age mean = 47.9 \pm 7.3 yrs. Female = 61 (59.2%)</p> <p>CONTROL N = 44 Age range = not reported Age mean = 46.3 \pm 6.4 yrs. Female = 23 (52.3%)</p>	<p>At the 30-year follow-up, the offspring of depressed parents had a twofold higher risk of mood and anxiety disorders compared to the control group. These disorders consisted mainly of major depression (a threefold risk) and phobia. Although the cumulative risk of major depression for offspring of a depressed parent was threefold, the relative risk of prepubertal onset of major depression was nearly tenfold. The results showed a small increase in onsets of major depression in women around the age of 45 yrs.</p> <p>The offspring with depressed parents had an overall poorer functioning, they had more divorces, had significant fewer children, they had more and longer treatment for emotional problems, more continuous treatment, and they had more medication for emotional problems.</p> <p>Although a higher risk for medical problems was found at 20 yrs. follow-up, the 30-year follow-up showed no difference between the groups (possibly explained by the control group developing more illnesses as they grew older). The offspring of depressed parents, compared to the control group, had a higher mortality rate because of unnatural causes (suicide, car accident, and overdose): 2.8% of the offspring of depressed parents died and none of the control group.</p>

background with potential impact on substance abuse, anxiety, depression, suicidality and self-harm. Family discord during childhood was not significantly associated with major depressive disorder or anxiety disorders in adulthood [40]. The descriptive studies did not provide evidence for a relationship between a COPMI background with somatic symptoms in adulthood.

3.4. Results from between-groups quantitative studies

Table 3 provides an overview of the between-groups and prospective studies in adults with a COPMI background.

Between-group studies (i.e., comparing adults with vs. without a COPMI background) are presented first. A COPMI background was associated with several psychological problems in adulthood. Peisah et al. [45] found that parental depression was associated with non-phobic anxiety and lifetime substance use disorders in their offspring when they became adults; but no association was found for affective disorders. Furthermore, adult children of depressed mothers had more problematic relationships with their fathers. Adults with COPMI experiences repeated in their current relationships what they experienced in their parents with the result that they reported more care giving behaviors in relationships compared to the reference group. In addition, Peisah et al. [46] showed that younger age of the child at the time of the parent's illness and the children's perception of the parent as being more controlling, were also associated with psychopathology in adulthood.

Similar findings as O'Connell and colleagues [44], were found by Alkan et al. [47] such that quality of life was markedly lower in adult female COPMI compared to controls without a COPMI background. They also had lower levels of functionality in the current family environment and higher levels of negative emotions and loss of resources. Adult women with COPMI experiences had some resource gains as indicated by resilience in the presence of supportive relationships with other family members, but these gains were less than in the non-COPMI comparison group. Resources loss was more strongly associated with quality of life than resource gain.

Regarding SSD and somatic symptoms, Peisah et al. [46] found that the duration of exposure to parental depression was associated with clinical diagnoses of medically unexplained symptoms. None of the other between-groups studies reported differences in somatic symptoms between adults with a COPMI background vs. controls.

The between-group studies indicate that a COPMI background is associated with more general psychological dysfunction and psychopathology and poorer quality of life, whereas less evidence was found for an association with somatic symptom disorder or poor physical health. A few studies also found that COPMI experiences could result in higher resilience to adversity.

3.5. Results from prospective quantitative studies

The prospective studies listed in the lower part of Table 3 indicate elevated risks for the development of several mental disorders among adults with a COPMI background. Weissman et al. [5,48] documented that COPMI was associated with a threefold increased risk of anxiety disorders, major depressive disorder (MDD) and substance abuse, and the increased risk of depression was also found at 30 years follow-up. Gluschkoff et al. [49] found that adults who grew up with hostile parenting or parental psychopathology showed higher levels of depressive symptoms. These increases followed a higher prevalence of depressive symptoms in childhood and an initial decline in early adulthood. Consistent findings are reported by Kasen et al. [50] based on a 2, 10 and 20 years follow-up study. At 20 years follow-up, 57.8% of daughters and 40.8% of sons had a lifetime diagnosis of MDD, which was accompanied by poorer psychosocial functioning. Evidence from this study also indicated that spirituality and/or attendance to religious services might play a role in adjusting to a COPMI background. As in the cross-sectional studies mentioned above, psychopathology was

predictive of suicidality in adulthood when investigated prospectively [51].

Gonçalves et al. [52] also focused on maternal depression and anxiety disorders and the risk for the children. They found that female (but not male) offspring showed an increased prevalence of depression and anxiety in adulthood when the mother had a depression or anxiety disorder during their adolescence.

Regarding parental depression, specific attention has been given to pregnancy-related depression. Taka-Eilola et al. [53] found that children of mothers with an antenatal depression had an elevated risk for depression compared to cohort members without maternal antenatal depression. When these mothers also had a severe mental disorder after birth, the children had an elevated risk for depression and schizophrenia [52].

It is possible that mental disorders in individuals with a COPMI background are related to disruptive behavioral disorders; Diaz et al. [54] found that in a group of 267 participants, 89 displayed disruptive behavioral disorders at the age of 18, of whom 70 (86%) had a parent with a mental illness. These disruptive behavioral disorders were associated with an increased risk of substance abuse, bipolar disorder and antisocial personality disorder in adulthood, independent of COPMI experiences.

Regarding SSD and physical symptoms in adulthood, three prospective studies documented significant associations of a COPMI background with somatoform disorders or physical symptoms. In a large cohort study from Denmark, Dean et al. [1] found that the most common categories of adult mental disorders of individuals with a COPMI background were anxiety disorders and somatoform disorders. Weissman et al. [5] compared the longitudinal changes in physical and mental health in individuals with a COPMI background (i.e., with a depressed parent) to individuals with non-depressed parents. At the 20-year follow-up, a higher incidence of medical problems and mortality was found in adults with a COPMI background, with medical problems beginning at middle age. At the age of 35, more medical problems emerged among individuals with a COPMI background with a twofold higher likelihood of any medical disorder compared to the reference group. At the age of 45 the differences in cardiovascular and neuromuscular disorders were no longer observed [48]. Van Eck et al. [55] found that parental psychopathology was the main predictor for persistence of medically unexplained symptoms.

These prospective studies indicate that COPMI are at increased risk of major mental disorders in adulthood, including depression, anxiety disorders, suicidality and somatic symptom disorder. However substantial individual differences exist in these adverse outcomes and many COPMI do not develop major adverse or physical health outcomes in adulthood.

3.6. Study quality and estimates of bias

The quality rating for the qualitative studies was moderate ($k = 1$) or strong ($k = 9$). None of the studies reported potential bias of the investigator nor whether the relationship between investigator and participant was taken into account. Furthermore, none of the qualitative studies reported whether data saturation was reached. All five articles by the research group of Murphy and colleagues [33,36–39] were based on one interview in one group of 13 participants. 50% of the qualitative studies were performed in Australia.

The quality rating for the quantitative studies was weak ($k = 1$); moderate ($k = 9$) or strong ($k = 11$). In most studies, the diagnosis of the parents of adult COPMI was based on retrospective reports of adult COPMI or not reported. In general, the studies had a sufficient number of participants, although sample sizes were not justified based on a priori power analyses. All studies measured confounders and most studies adjusted statistically for these cofounders. Missing values were described in approximately half of the studies but not tracked or analyzed in most studies. The studies of Weissman [5,48] and Pilowsky

[40] were based on the same group of participants, as were the two studies of Peisah and colleagues [45,46]. See supplemental Appendix S-A3 for Study quality evaluation.

3.7. Synthesis of results

A dialectical and complementary approach was used to synthesize results from the quantitative and qualitative studies (see Discussion for details and interpretation). The qualitative studies were used to describe the adult experiences of having had a childhood with a mentally ill parent and the quantitative studies were used to describe the prevalence and associations of COPMI experiences with psychological and physical outcomes. The overall quality of the qualitative studies was strong but five articles were based on one interview in one group of (13) participants [33,36–39], and of the quantitative studies moderate to strong.

The quantitative studies indicated that a COPMI background might increase the risk of anxiety and depressive disorders in adulthood, with a prevalence estimate of up to 70% [5,9,20,32,44,48–50,53]. A COPMI background was also associated with other types of psychopathology, including substance abuse [5,45,48], schizophrenia [53], and suicidality [26,41–43,46,56]. We were specifically interested in the association between COPMI with persistent somatic symptoms and SSD in adulthood because ACE are disproportionately common in COPMI and ACE are also a major risk factor for persistent somatic symptoms and SSD. Significant associations were indeed found, but only 4 out of 21 quantitative studies investigated this association [1,5,46,55].

4. Discussion

This systematic review of 31 studies indicates that a COPMI background is associated with substantial psychosocial and physical health challenges in adulthood. The main findings of the qualitative studies revealed substantial psychological problems during adulthood, whereas issues related to childhood abuse and current somatic symptoms were not raised as common themes. The quantitative studies found evidence that a COPMI background was associated with a higher incidence of anxiety disorders, depression, suicidality, substance abuse and somatic symptom and related disorders. These findings suggest that addressing a patient's COPMI background may be a relevant treatment target, irrespective of abuse or other childhood adversities.

The qualitative studies revealed different but intermingled themes, namely: quality of life during childhood, safety, lack of information, parentification during childhood, and loneliness. These themes emerged during childhood but continued to be present in adulthood. Four additional themes during adulthood were: concerns about own parenting role, risks related to one's own mental health, emotional problems, and difficulties with relationships (see supplemental Appendix S-A2 for additional details). Specific diagnoses or severe ACE did not predominate the results of the qualitative studies. The themes observed in the qualitative studies may be important topics to address during counseling and clinical interventions of adult COPMI.

The quantitative studies indicated that MDD, anxiety disorders and suicidality are common long-term outcomes for COPMI in adulthood. These findings are consistent with a recent study showing that emotional maltreatment is associated with onset of mood disorders in offspring of a parent with a bipolar disorder [57]. Furthermore, we found that seven studies documented a relationship between a COPMI background with suicidal ideation or behaviors [26,41–43,46,51,56]. These studies each had their own focus resulting in a wide variety of study characteristics, such as specific parental mental disorders, sociodemographic characteristics and parenting styles. Despite this diversity, parental psychopathology is an important factor in the onset and persistence of suicidal plans, self-harm ideations or suicidal behaviors in adult COPMI. The quantitative studies rarely explicitly inquired about how adults perceived their COPMI background as related to their current mental or physical wellbeing. Longitudinal studies examining gene-environment

interactions are needed to determine the relative contributions of these factors and whether interventions can reduce the risk of mental disorders and suicidality, as well as sub-clinical psychological problems interfering with mental and physical wellbeing, in children growing up with a mentally ill parent.

Adult COPMI seem to have difficulties with (long-term) interpersonal relationships, including their family, relating to shame and fear of being judged and/or left alone. These feelings may arise from the family tradition of keeping the parental mental illness a secret, and the idea that, as a child, they were and still are responsible for the wellbeing and behavior of the parent. These factors are further complicated by the coexistence of stigma related to mental illness. The habit of 'not telling others' heightens the feeling of loneliness and the idea of not being understood by others what growing up as a COPMI means, which in turn could influence relationships in adulthood. Weissman et al. [48] found in their 30-year follow-up that COPMI of depressed parents were more often separated or divorced and had fewer children. It is possible that interventions that improve social skills, building trust and solid attachments may prevent adverse long-term consequences for COPMI as they become adults.

This review found limited support for the adverse consequences of COPMI for SSD during adulthood. For example, Dean et al. [1] found that somatoform disorders and anxiety are the most common psychiatric diagnoses of adult COPMI, and Van Eck van der Sluijs et al. [55] documented that persistence of medically unexplained symptoms was significantly more common in adult COPMI. This finding is consistent with the high prevalence of childhood adversities in COPMI and the documented risk of ACE for somatic symptom and related disorders. However, the qualitative studies rarely found adult COPMI to report abuse and/or physical health problems [22]. It is therefore important that the potential role of COPMI is addressed in patients with SSD as it is likely that they will not spontaneously bring up issues related to parental mental illness.

The findings of this review need to be considered in the context of several limitations. One limitation is the quality of the studies and the risk of bias, especially in the qualitative studies where the relationship between researcher and participants was not taken into account and suboptimal efforts were made to reach optimal data richness and saturation. Furthermore, the search terms of the present systematic review were based on our interest in adult experiences as related to their COPMI background. This approach may have resulted in the non-inclusion of papers in which this issue was not the primary focus, for example articles with a main emphasis on genetic factors, rather than the "adult COPMI" experiences as vantage point. There are still multiple opportunities to expand our knowledge about how the adult participants of (genetic or other follow-up) studies reflect back on their childhood experiences and how these experiences influence their current mental and physical wellbeing. The cut-off of only including adults 25 years and older was used to ensure a clear distinction between exposure to parental illness during childhood and the outcomes during adulthood. However, this cut-off resulted in the non-inclusion of articles reporting on young adults in the transition phase from living at home to living independently which is an important topic for future research. Articles published before 2000 CE were not included, which may have resulted in some loss of information, but this limitation is potentially outweighed by the advantages of more consistent assessments of mental illness and improved methodological rigor of more recent studies. Non-inclusion of articles that were not published in the English language may have resulted in selection bias of samples from industrialized countries. Another problem is that the diagnosis of parents of adult COPMI is typically not reported or based on retrospective reports of adult COPMI. Future longitudinal studies with large samples and valid assessment tools are needed to further address this issue.

In conclusion, the lived experiences of COPMI and the effects of these experiences in their adult lives is well documented in the qualitative studies included in this review. Recent qualitative research indicates

that these factors are particularly important in life's transition phases, particularly in early adulthood [58]. Quantitative research indicates that adults with a COPMI background are at elevated risk of depressive mood disorders, anxiety, suicidality, and somatic symptom and related disorders. More information is needed about potentially protective factors and identification of COPMI who are at high risk of adverse mental health outcomes during adulthood. The complexity in variables and diversity in problems can be seen as an incentive for professionals to consider that physical and psychological symptoms in their patients can be related to childhood experiences as a COPMI. Discussing these experiences can help understand, and improve treatment of, psychological problems in adulthood. In some instances, it may be helpful to include a multi-generational approach to help adult COPMI interpret their family environment [59]. These investigations could be integrated with research on genetic vulnerability factors [1,9,60,61] and long-term consequences of adverse experiences during childhood for the development of mental disorders [10–15]. Interventions may involve providing information about parental mental illness during childhood, training in social skills and insight into secure attachment, and identification of high-risk individuals during adolescence and (early) adulthood.

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Access to the data

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Author statement

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AV: Conceptualization, Investigation, Methodology, Supervision, Writing – review & editing

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