The economic burden of dissociative disorders: A qualitative systematic review of empirical studies

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Abstract

Objective: Dissociative disorders (DDs) are associated with intensive, long-term treatment, suicidality, recurrent hospitalizations, and high rates of disability. However, little is known about the specifics of the economic burden associated with DDs. This worldwide, systematic review examines the results of studies in adults on direct and indirect costs associated with DDs. **Method**: We searched six databases and the reference lists of articles. We also approached researchers to identify unpublished studies. No language restrictions were imposed. **Results**: A total of 1002 records met the search criteria, of which 29 papers were selected for full-text inspection. Ultimately, of these, we reviewed four empirical studies. We provide a narrative discussion of study findings. Our findings suggest that DDs are costly to society, and that there is a reduction in service utilization and associated costs over time with diagnosing of and specialized treatment for DDs. However, the overall quality of the economic evaluations was low, several types of DDs, comorbid conditions and costs were not included, and men were under-represented. Due to the heterogeneity among studies, we could not perform a meta-analysis. **Conclusions**: Due to the heterogeneity and low quality of the identified economic evaluations, no firm conclusions about the economic burden of DDs alone can be drawn. Higher quality research, including a detailed description of the study design, population and primary outcome measures used, utilizing appropriate clinical alternatives and including major comorbidities, is urgently needed to more rigorously assess the economic impact of DDs.

Clinical Impact Statement

This review suggests that dissociative disorders (DDs) are associated with substantial costs to the society, although conclusions are tentative due to few studies and methodological limitations. There was agreement in the studies about DDs having substantial direct mental health care costs. Considering that these disorders might often be undetected or misdiagnosed, clinicians and health care authorities should be aware of potential economic gains from earlier recognition and treatment. Appropriate diagnostic and treatment practice may result in financial savings as well as improved life quality for patients and their families.

Mental disorders account for more economic costs than many chronic somatic diseases such as cancer and diabetes (see Trautmann, Rehm, & Wittchen, 2016). The economic burden of many psychiatric disorders, such as schizophrenia and bipolar disorder, has been extensively examined, showing very high costs to society (e.g., Jin & McCrone, 2015; Chong et al., 2016). Despite higher lifetime prevalence rates (i.e. 9-13.5%) than schizophrenia or bipolar disorder (Şar, 2011), the economic burden of dissociative disorders (DDs) has received almost no systematic investigation. Given the evidence demonstrating that DDs are associated with significant psychiatric morbidity and impaired functioning (Brand, Classen, McNary, & Zaveri, 2009), it is important to examine the economic burden of DDs.

DDs are characterized by "a disruption of or discontinuity in the normal integration of consciousness, memory, identity, emotion, perception, body representation, motor control, and behavior" (American Psychiatric Association [APA], 2013). Individuals with DDs have impaired ability to purposefully control attention for memories, sensations, and movements (World Health Organization [WHO], 1992). Dissociative disorders include a variety of dissociative symptoms that manifest mentally as well as in the body, i.e., respectively psychoform and somatoform dissociative experiences. Psychoform dissociative experiences include amnesia and identity alteration, and depersonalization and derealization experiences. Somatoform dissociation includes dissociative convulsions (sometimes referred to as dissociative (psychogenic) non-epileptic seizures (DNES/PNES), non-organic paralyses, and loss of sensation (Nijenhuis, 2001).

Despite DDs being recognized in the Diagnostic and Statistical Manual of Mental Disorders (DSM) and the International Classification of Diseases (ICD), the validity of DDs, in particular DID, has been questioned by many clinicians and researchers, as has the etiology. Of the DDs, Dissociative Identity Disorder (DID) is the most disputed subtype. Although critics of the validity of this diagnosis claim that DID is fantasy-driven and assume

that dissociative symptoms can be simulated by normal healthy individuals (e.g., Lynn, Lillienfeld, Merckelbach, Giesbrecht, & van der Kloet, 2012), an increasing number of studies including neuroanatomical biomarkers support the validity of the DID-diagnosis (e.g., Reinders et al., 2019; Vissia, et al. 2016). According to supporters of the trauma-model, dissociation is often trauma-related and DID is a posttraumatic developmental disorder (Dalenberg et al., 2012). For example, across studies patients with DID report higher rates of childhood abuse and neglect (CAN) than any other diagnostic group (Spiegel et al., 2011). Further, DD patients may also be at higher risk than the general population for interpersonal violence and adult rape; phenomena that are associated with significant economic costs (Brown, Fang, & Florence, 2011; Letourneau, Brown, Fang, Hassan, & Mercy, 2018; Peterson, Degue, Florence, & Lokey, 2017; Rivara et al., 2007; Thielen et al., 2016). In addition, in general population studies, DD patients are often more severely ill and functionally impaired compared to other psychiatric populations, with DID showing the most impairment (Brand & Lanius, 2014; Spiegel et al., 2011). Specifically, DDs have been shown to have high rates of severe comorbidities, such as PTSD, depression, substance use disorders, personality disorders (particularly of the borderline type), and somatoform disorders (Şar, 2011; Spiegel et al., 2011). Likewise, DDs have been associated with other problematic outcomes, including non-suicidal self-destructive behavior and suicide attempts (Foote, Smolin, Neft, & Lipshitz, 2008; Webermann, Myrick, Taylor, Chasson, & Brand, 2015). It is therefore imperative for researchers conducting economic evaluations to take into account major comorbid psychiatric conditions.

DD patients are common in emergency care settings and more restrictive levels of psychiatric care, e.g., inpatient units, partial hospital programs, and residential facilities. In clinical settings, the prevalence of DDs ranges between 4.6% and 46%, depending on the treatment setting (see Loewenstein, 2018), however, some experts suggest that some DD-

patients are not recognized and receive other diagnoses. Studies report that patients diagnosed with a DD spend on average 5 to 12.4 years in treatment before accurate diagnosis, often with limited improvement with non-DD focused treatment (Spiegel et al., 2011). Due to somatoform dissociative symptoms, medical illnesses, addictions, and maladaptive behaviors associated with early life adverse childhood experiences (ACEs), DD patients frequently have high rates of medical health care and substance abuse treatment, as well as social service utilization. A subgroup likely has criminal justice involvement (Felitti & Anda, 2010; Loewenstein et al., 2017). Clinical experts assume that individuals with unrecognized DDs may become so symptomatic and demoralized that they develop a lifetime course of severe and persistent mental illness (Fritzsche, Baumann, Götz-Tabert, & Schulze-Bonhage, 2013; Loewenstein et al., 2017, Mueller-Pfeiffer et al., 2012). Therefore, cost of dissociative symptoms and disorders may not only be associated with direct health care costs arising from treatment, but may also include direct non-health care costs (e.g., disability pension, foster care in the child welfare system, adult criminality, investigation and prosecution in the judicial system) and indirect costs (e.g., fatality costs, lost productivity).

The economic effects of accurately diagnosing and treating DDs have not been studied in randomized controlled trials (RCTs). However, research shows that DD patients, particularly those with DID and related disorders, can improve with treatment models specifically designed to address the DD. Brand and colleagues (2009, 2013) undertook an international, longitudinal treatment outcome study of 280 DD patients, where treatment was consistent with expert treatment guidelines (International Society for the Study of Trauma & Dissociation [ISSTD], 2011). Over 30 months, patients showed significant reductions in PTSD and DD symptoms, suicide attempts, and non-suicidal self-destructive behavior, as well as reductions in inpatient hospitalization and drug abuse. There were decreased patient costs over time, as would be expected given reductions in treatment at more restrictive levels of

care, e.g., inpatient hospitalization, specialized substance abuse treatment, medical treatment

for substance use complications, and reductions in suicidal and self-destructive behavior.

Suicidal and self-destructive behavior may themselves have a variety of non-psychiatric costs:

medical care, absence from work, loss of productivity, income, and so on (see Kinchin &

Doran 2017; Myrick, Webermann, Langeland, Putnam, & Brand, 2017).

DDs characterized by somatoform symptoms have also been shown to improve with

specialized dissociation-focused treatment. For example, a pilot RCT (Goldstein et al., 2010)

showed that cognitive behavioral therapy - with a specific focus on gaining control of

dissociative seizures - was effective in reducing non-epileptic seizure frequency. Also,

patients showed improvement in psychological symptoms and psychosocial functioning.

The high prevalence, severe disability, chronicity, comorbidity, and high levels of

health care utilization among patients with DDs underscore the clinical and public health

significance of the economic burden associated with DDs. Previous literature reviews from

the 1990's on costs of DDs were focused on English-language papers describing direct

healthcare costs before and after correct diagnosis and treatment of DID, then known as

multiple personality disorder (MPD) (Kluft, 1993, 1999; Loewenstein, 1994). There has been

a lack of emphasis on methodological details and the type of cost estimations, which prompts

the need for a more exhaustive and updated review.

To our knowledge, no systematic review has been conducted to summarize the

economic burden of DDs. Current information about the costs associated with DDs may help

policy-makers understand the need for accurate diagnosis and treatment, encourage

development of efficient treatment methods, and lead to more research about the health care

costs of DDs. Therefore, the aim of the current work was to systematically identify, describe

data sources and methods, and summarize findings of studies on the economic burden of DDs

among adults worldwide.

Method

The research team identified search terms, databases to query, and eligibility criteria. Two reviewers (EJ and WL) independently evaluated the abstract of each citation identified by the initial search as potentially relevant against the formal inclusion criteria. Studies that appeared to meet criteria were read independently to inform reviewer's inclusion recommendation. When differences of opinion emerged, the reviewers discussed merits to arrive at consensus.

Search strategy

The search strategy was generated by a librarian of the University of Oslo Medical library, Norway, who also conducted the literature search.

The following databases were used to identify potential appropriate studies: MEDLINE / PubMed (Ovid), PsycINFO (Ovid), Cochrane Library, CINAHL (ESBCO), and Embase (Ovid). The search strategy combined terms for the following two concepts: costs and dissociative disorder. The search was not restricted to any particular cost estimation outcome, year of publication, or language of publication. Searches were conducted using synonyms and combinations of the following search terms: ("cost of illness" OR "health care cost" OR "cost-effectiveness" OR "societal cost" OR "economic burden") AND ("depersonalization disorder" OR "depersonalisation disorder" OR "dissociative fugue" OR "multiple personality disorder" OR "dual personality" OR "dual personalities" OR "multiple personality" OR "multiple personalities" OR "dissociative identity disorder" OR "dissociative disorder" OR "depersonalization/derealization disorder" OR "depersonalisation/derealisation disorder" OR "dissociative disorder not otherwise specified" OR "dissociative trance disorder" OR "other specified dissociative disorder" OR "dissociative amnesia" OR "dissociative stupor" OR "conversion disorder" OR "other dissociative and conversion disorders" OR "dissociative and conversion disorder, unspecified"). (See online Supplementary Appendix A for the search

strategy for each database.) In addition, we screened the reference lists of the selected studies and contacted experts in the DD field to solicit recommendations for potentially relevant papers. All records were exported to the reference management software EndNote X8 (Clarivate Analytics, Philadelphia, PA), undoubled and checked for the presence of withdrawn or corrected papers.

Inclusion and exclusion criteria

We identified the following criteria for formal inclusion in this review: (a) dissociative disorder diagnosed by the DSM from the Third edition (DSM-III; APA, 1980) through the Fifth edition (DSM-5; APA, 2013) or the ICD, specifically the Ninth and Tenth Edition (ICD-9/ICD-10; WHO, 1977, 1992) (see Online Supplemental Table S1 for the classification of DDs in the current classification systems used at the time of conducting this review); (b) adult participants (aged at least 18 years); (c) empirical studies of patients with DDs (controlled and uncontrolled), including retrospective and prospective cohort, cross-sectional, and case studies; and (d) outcomes aimed at estimating costs. We included studies of patients with DDs and comorbid psychiatric disorders. We excluded literature reviews and overviews, commentaries, conference abstracts, and study protocols.

Outcomes in terms of cost estimates

We endeavored to provide an overview of empirical studies evaluating direct and indirect costs of DDs across countries. Societal costs give an overview of the economic burden imposed by on a society. A cost-of-illness study should include all cost consequences of the disease, including direct healthcare costs, direct non-healthcare costs, and indirect costs. *Direct healthcare costs* are costs arising from treatment of the disease, and may include psychiatric hospitalization and non-psychiatric hospitalization, outpatient treatment, and community care (nursing home, rehabilitation, medications). *Direct non-healthcare costs* may include special education, disability pension, investigation of abuse cases, foster care in the

child welfare system, juvenile delinquency, adult criminality, investigation and prosecution in the judicial system, and transportation to treatment. *Indirect costs* may include fatality costs, morbidity costs (any disability incurred as a result of the disease) and lost productivity of the patients or their relatives who are providing care for patients. *Lost productivity costs* include lost wages and lost tax payments.

Data extraction and synthesis

Key features of each paper (i.e., author/s; year of publication; country; patient age, gender, ethnicity, and diagnosis; cost data) were extracted and summarized in tabular format. Studies' quality was assessed using reviewer-modified criteria from the Centre for Reviews and Dissemination (CRD, 2008). Cost estimates were not adjusted to a single reference year, nor was a quantitative synthesis (meta-analysis) of costs estimates performed due to the heterogeneity in DD populations, time periods of data collection, cost estimates reported, and other differences in methodology. Rather, a narrative synthesis of main study findings was generated.

Results

Study selection and inclusion

The systematic literature search identified 1245 records, which reduced to 999 after removing duplicates. Of the 999 records, 971 papers were excluded because they failed to meet one of the inclusion criteria (964 papers) or were withdrawn or corrected (7 papers). Three additional records (Fraser & Raine, 1992; Lloyd, 2011; Quimby, Andrei, & Putman, 1993) were identified by searching reference lists and requests to experts for relevant papers; Lloyd was eligible for inclusion, whereas the other two papers were not: Fraser & Raine could only be found in a conference proceeding, and Quimby et al. was not an empirical study. Of the remaining twenty-nine potentially eligible full-text papers, twenty-four (see Online Supplemental Table S2) were excluded for the following reasons: Not empirical studies (9

papers); did not specifically target DD's or only a subgroup had a DD and results were not

reported separately (8 papers); or did not report outcomes aimed at estimating costs (7

papers). (See Online Supplemental Figure S1 for a flowchart of the selection process.)

Characteristics of the included studies

Five papers describing four independent studies were ultimately found eligible for

inclusion in the present study: Study 1: Ross and Dua (1993); Study 2: Macy (2002); Study 3:

Lloyd (2011, 2016); and Study 4: Myrick et al. (2017). A summary of study characteristics is

shown in Table S3 (See Supplemental Materials). All studies presented data from Western

countries and included mostly or only female subjects. The sample size of included studies

ranged from a single patient (study 3) to 55,931 patients (study 2; including a subgroup of

1,438 MPD patients). Patients in studies 1 and 2 met criteria for MPD according to DSM-III-

R; studies 3 and 4 included patients with DID according to DSM-IV-TR (APA, 2000) and/or

DSM-5; and study 4 also included patients with DDNOS/OSDD. No study reported on costs

of other DDs diagnosed using either the DSM or ICD systems, e.g., the DSM

depersonalization/derealization disorder (DDD) or the ICD DDs of movement and sensation.

All studies relied on diagnoses made by clinicians and focused on DD alone, not accounting

for comorbid psychiatric and physical disorders, leaving unanswered what percentage of costs

was due to DD itself as opposed to comorbid conditions. Only one study (2) utilized

nationally representative data sets or control groups. All studies had a narrow scope of costs:

Only data related to direct treatment costs in specialized mental health care services (mainly

psychiatric hospitalization, outpatient treatment, emergency departments) were examined.

None of these studies addressed the direct non-healthcare costs of patients with DD, e.g.,

those associated with rehabilitation; medication; investigation or prosecution in the judicial

system; special education or child welfare; nor did they address indirect costs, e.g., those

associated with social security payments, work productivity loss, and loss of tax revenue.

The cost estimates found in these studies cannot be compared due to design and method differences: Two of the four studies (2 and 4) presented total costs over the study period; two studies (3 and 4) presented annual costs; and one study (1) presented average monthly costs. In two studies (1 and 2) cost estimates of mental health services for patients with DID/MPD were based on data from two decades ago. More up-to-date information about the costs associated with DDs was presented in the other studies (3 and 4). Study 4 was the only paper to evaluate the differences in costs between patients in different treatment stages. Time periods for economic outcomes varied, ranging from 30 months (study 4) to 10 years (study 1).

Finally, according to the reviewer-modified CRD-criteria, the overall quality of the economic evaluations was low. Only two studies (2 and 4) scored five out of a possible ten points on the quality measure used (see the online Supplementary Tables S4 and S5 for checklist items and quality assessment results).

Narrative summaries of the findings of the four studies

Ross and Dua (1993; study 1) reported the costs of care for fifteen female patients prior to and after MPD diagnosis in order to examine whether accurate diagnosis and treatment would lead to cost savings. The patients had been admitted to an inpatient service over a period of four years. The total psychiatric (inpatient and outpatient) health care costs before diagnosis for the group of fifteen patients were about $2.8 million Canadian dollars. Before diagnosis, patients had averaged 98.77 months in the mental health system and the average total cost per patient was $184,666.53. After diagnosis, patients had averaged 31.53 months in the system, and the average total cost per patient was $91,607.80. The authors calculated that diagnosing and treating MPD, according to their projections of costs, would result in a potential net saving of $84,899.44 per patient over a period of ten years. The formula that the authors used for the calculation of a net saving per patient after accurate diagnosis and treatment of the DD was based upon the following assumptions: a) treatment after a correct diagnosis of MPD averages four years, and b) the psychiatric health care costs for not

diagnosing the MPD would continue for another ten years.

Among 1,438 Medicaid-insured MPD patients (aged 15 to 64 years) from one state (Massachusetts), Macy (2002; study 2) reported the length of stay and costs of acute care (i.e., days of inpatient hospitalization and crisis stabilization) during a 42-month period. The MPD service recipients were a subgroup of a total of 55,931 Medicaid psychiatric service recipients that were included. The study compared the costs of MPD patients to patients with diagnoses including DSM-III-R posttraumatic stress disorder (PTSD), major depressive disorder (MDD), panic disorder (PD), and bipolar disorder (BD). Compared to recipients with the other diagnoses, the MPD service recipients had the highest utilization rates for both levels of acute care, namely 68.8 per 1,000 persons (95% Confidence Interval [*CI*] 55.8 - 81.9) for crisis stabilization and 643.9 per 1,000 persons (95% *CI* 619.2 - 668.7) for inpatient admissions. Moreover, on a per patient basis, a diagnosis of MPD was the costliest of all included mental health conditions, with $2,300 per recipient for acute care during the study period compared to $306, $200, $191, or $25 per recipient for BD, PTSD, PD, and MDD, respectively. However, Macy did not test the statistical significance of these differences, and he did not separately report figures for adolescents and adults.

Findings of two studies (3 and 4) suggest the potential for healthcare savings for patients with DID and related DDs when provided with long-term outpatient treatment consistent with expert consensus or guidelines (ISSTD, 2011; Brand et al., 2012).

Lloyd (2011; study 3) showed that investing in specialized therapy for a female patient with DID reduced costs substantially compared to the patient's prior care using the traditional case management protocols of the United Kingdom National Health Service (NHS). Traditional case management included care coordination within the community mental health team, crisis intervention, medication and admission. Prior to diagnosis with DID, this middle-aged woman's average annual treatment cost was £29,492 for each of four years prior to DID treatment. Costs decreased to £10,695 a year after initiating DID treatment, representing a cost saving of

£18,797/year. In a second paper, Lloyd (2016; study 3) provided follow-up results for the patient in the 2011 study. The patient's service use and associated costs continued to decline during the four years following the start of her specialized DID treatment. Specifically, the annual cost of her treatment was £9,362 across four years of therapy, representing an average cost reduction of £20,130 per year in the costs of services following the start of treatment for DID. In the 2016 paper, Lloyd also reported on the change in service use and associated costs of care for another female patient with DID. This case also showed a reduction in utilized services. The costs decreased from an average annual cost of £38,805 in the three years prior to DID treatment to £29,234 in the year following initiation of DID treatment, representing an average annual cost savings of £9,571. However, Lloyd (2011, 2016) reported only on cost of psychiatric services, not on other costs, nor on the clinical effectiveness (e.g., reduction of psychological symptoms, increase of quality of life) of the specialized treatment. Limitations of these reports include small sample size, e.g., 2 single case studies, and having no controls with treatment as usual.

Myrick and colleagues (2017; study 4) estimated reductions in cost for DD treatment based on Brand et al.'s (2009, 2013) 30-month prospective naturalistic treatment outcome study. Myrick et al. (2017) estimated treatment cost reductions based on study findings that patients showed longitudinal and cross-sectional reductions in treatment utilization at higher levels of care. Cost estimates were significantly lower for patients who had stabilized and advanced to later stages of treatment, as compared to patients in early treatment stages. In the earlier treatment stages, DD patients commonly struggle more with safety issues, severe symptom dysregulation, and associated clinical instability – factors that typically drive treatment at more restrictive levels of care. In addition to the cost savings, separate analyses found that DD treatment was associated with reductions in a wide range of symptoms according to both patients' and therapists' reports, and improvements in functioning according to therapists' reports (Brand et al., 2009, 2013). However, attrition of patients by

the 30 month-follow up (>50%) is a limitation in this study. Nevertheless, this is a relatively low attrition rate for a study of this type and length of follow up, especially for patients with significant levels of symptoms, safety issues, and general instability (Myrick et al., 2017). Although information about the patients' comorbid Axis I and II diagnoses were available (Brand et al., 2009), the authors focused on DD alone not accounting for major comorbidities. As in the other studies, lack of a control group prevents definitive conclusions that the treatment was responsible for the patients' changes and hypothesized cost savings.

Discussion

To our knowledge, this is the first systematic review of empirical studies evaluating costs of DDs. Our study selection process was aimed at identifying studies with DD subjects diagnosed by either the DSM or ICD systems that investigated any of a wide range of costs. Due to the low number of studies that specifically evaluated costs for DDs, we included studies using various designs, incorporating non-randomized and/or non-controlled studies. Four studies met our inclusion criteria; three examined patients with MPD/DID, and one examined patients with either DID or DDNOS/OSDD.

The identified studies provided some empirical evidence about the psychiatric treatment costs associated with DDs. Regardless of the methodological heterogeneity of the reviewed studies, there was an agreement about DDs having substantial direct mental health care costs. In the Macy (2002) study, despite being only about 2.6% of the patient cohort, on a per-patient basis, the treatment costs for MPD were far higher than those for other psychiatric disorders. However, the DD-diagnoses in the included studies were not validated, and there is a risk for over- as well as under-diagnosing (ISSTD, 2011). In addition, the economic effects of accurately diagnosing and treating DDs have not been studied in RCTs. Therefore, we cannot deduce a causal relationship between accurate diagnosis and/or treatment of DDs and the decrease of the economic burden of DD patients on the health care system. However, the

studies suggest that correct diagnosis and specialized psychological interventions are potentially associated with substantial reductions in health care costs for MPD/DID and DDNOS/OSDD. Further research with greater methodological rigor is needed, particularly on the relative efficiency – in terms of clinical effectiveness and cost-effectiveness – of dissociation-focused treatment for DDs compared to other active treatments. Notably, studies evaluating the cost of DDD, often a particularly refractory DD (Loewenstein et al., 2017; Spiegel et al., 2011), have not been done, nor of the costs of the dissociative PTSD subtype (PTSD-DS).

We found several studies that examined health care utilization and costs before and after initial diagnosis of DNES/PNES (e.g., Ahmedani et al., 2013; Martin, Gilliam, Kilgore, Faught, & Kuzniecky, 1998). In the ICD-10, DNES/PNES is classified as a DD, more specifically, dissociative convulsions. However, in the DSM system, this and related disorders are included as conversion disorders under the somatoform disorders designation in DSM-IV-TR, and among the somatic symptom disorders in DSM-5. In our data extraction, the studies on DNES/PNES described above did not meet our inclusion criteria, since neither study used the DSM or ICD diagnostic classification. Other studies suggest that patients with DNES/PNES who do not receive treatment interventions continue to be high health care utilizers (Salinsky, Storzbach, Goy, Kellogg, & Boudreau, 2016). One review estimated the yearly costs associated with DNES/PNES as US $900 million for diagnostic tests, procedures, anti-epileptic medications, repeated labs, emergency department utilization, and inpatient costs (Gedzelman & LaRoche, 2014). Studies of DNES/PNES have shown that these patients report high rates of (childhood) trauma, have elevated dissociation scores, and high rates of co-morbid DDs such as DID, mood disorders, substance abuse, and PTSD (Bowman & Markand, 1996). This suggests that there is significant overlap between patients diagnosed with DDs, many of whom have significant somatoform dissociative symptoms, and patients

seen in neurology and epilepsy centers for DNES/PNES (Şar, 2011). It is possible that the etiology of subgroups of patients with PNES may differ, e.g., some may have more dissociative psychopathology than others. This could have an impact on outcome and cost of illness. Thus, more fine-grained diagnostics of these patients are needed to assess for possible sub-groups (see e.g., Demartini et al., 2016).

The studies that we assessed in this review have one or more important methodological limitations, including lack of a detailed description of the study population (exclusion criteria used, refusers, subjects, reliability of diagnosis given), small sample sizes, absence of control groups, under-representation of men, focusing on DD alone not accounting for major comorbidities, reporting outcomes only for those participants that were followed up or completed the study, presenting cost estimates without *CI* or *p*-value, and lack of evaluation of direct non-healthcare costs or indirect costs. They suffered from a relatively limited evaluation of health care costs before and after diagnosis or treatment of DDs. The two best studies scored only five out of possible ten points on the measure of quality used. It is unknown if the current findings generalize beyond Western samples. In addition, grey literature was not included in the present review. Due to the heterogeneity and methodological weaknesses of the identified studies, caution must be used when drawing conclusions about the economic burden of DDs.

Nevertheless, all reviewed studies indicate that DDs may be associated with substantial costs to the health care system. In clinical and treatment outcome studies, one can readily hypothesize that DD patients will have high health care and other societal costs due to having multiple comorbidities, high rates of reported adverse childhood and adult experiences, and suicidality and self-destructive behavior often requiring treatment at more intensive levels of care (Felitti & Anda, 2010). Furthermore, DDs have been shown to be associated with high rates of disability, and a subgroup meets criteria for chronic, persistent

serious mental illness (Mueller-Pfeifer et al., 2012). In addition, across diagnostic groups, higher levels of comorbid dissociation predict poorer outcome to standard treatments for other disorders, like mood and psychotic disorders – again indicating greater healthcare and human costs (Lyssenko et al., 2018).

Suggested research priorities for DDs, based on the limitations of the available evidence, include RCTs, clinical studies that gather real world data from registers, cost-of-illness studies, and studies including more men with DDs. Also, a broader perspective (societal versus health care) is recommended. The advantages of registry data are more accurate information on distinct aspects of treatment and resource use (both direct and indirect costs), the possibility to evaluate health care costs of DDs and their comorbid conditions, larger population data and the ability to follow patients over time. In economic studies of the cost of psychiatric disorders, the focus has generally been on direct costs, not indirect ones (Neumann, 2009). This is true of the study of DDs as well. Cost estimates are limited to those directly linked to a primary DD diagnosis. However, the high rates of ACEs among DD patients (Vonderlin et al., 2018) and their association with high-risk behaviors (e.g., smoking, heavy drinking) and medical conditions (e.g., Hughes et al., 2017) likely affect the total costs. Future examination of these additional components of economic burden will result in a better understanding of the overall impact of DDs on patients, their families, and the healthcare system, and of possible gender differences in the costs associated with DDs.

Critically, despite the paucity of research on treatment outcome and cost of the DDs, most data point to the positive impact that the current treatments based on expert consensus have on outcome and cost for the DDs. For example, a recently published 2-year follow up of a prospective study of an online intervention for DD patients and therapists showed marked reductions in self-destructive behavior, as well as reductions in PTSD and dissociative symptoms (Brand et al., 2019). However, little is known about the long-term impact of

treatments, pointing to the need to investigate the long term impact of DD-focused treatments on outcome and costs for the DDs. If beneficial effects of dissociation/DD-focused treatment go far beyond clinical improvement, this may encourage better recognition of dissociation and DDs as an avenue into reduction of the myriad costs associated with CAN/ACEs.

Our review found that the economic costs associated with DDs are under-recognized and under-studied. We lack information about the economics of treatment options for clinically important DDs such as DDD that is associated with significant, often treatment resistant, disabling symptoms (Michal et al., 2016), as well as on diagnostically classified dissociative convulsions. Another area of potential study is comparison of costs of treating the dissociative subtype of PTSD (PTSD-DS) compared to the costs of treating non-dissociative PTSD, albeit the prevalence of DDs has not been fully explicated in patients with PTSD-DS.

We are aware of several ongoing DD treatment studies that may yield important information about DD treatment costs, including a cost-utility study of an online educational intervention for patients with DDs conducted by a multidisciplinary research team including health economists, and several ongoing RCTs of the clinical effectiveness and cost-effectiveness of treatment interventions for DDs or DNES/PNES (study protocols: Nct, 2015; Robinson et al., 2017). Future reviews should synthesize the evidence on the clinical effectiveness and economic benefits from these diverse ongoing studies in order to guide practice and policy decisions. In summary, our results suggest there is an urgent need for rigorous study of the economic burden of, and changes in costs related to, accurate diagnosis and treatment of DDs. There are methodological issues that require being addressed in future studies, including for instance, describing in detail the study population (exclusion criteria used, refusers, attrition as a result of loss to follow-up, subjects, random or non-random allocation of participants, reliability of diagnosis given) and if applicable, the intervention given and the number of individuals who received the intended treatment, stating the type of

economic evaluation (e.g., cost-effectiveness or -benefit analysis, cost utility analysis), the study design (clinical study or decision-analytic model), and the primary outcome measure used and the number of individuals that were analyzed for this outcome (completers or intent-to-treat), and presenting uncertainty around costs by using for instance bootstrapped costs/effects *CI*'s. A detailed description of the study population is necessary to assess the generalizability of the results of economic evaluations. It is essential for researchers to use best-practice standards when planning and conducting economic evaluations, in order to build a reliable evidence base for decision-making in mental health care of DDs.

Conclusion

We provide the only systematic review of the literature on the economic burden of DDs. There are only data of low quality to support that early recognition and treatment of DDs – particularly the most severe DDs, DID and DDNOS/OSDD – may provide substantial cost savings over the course of treatment. There are no cost-efficacy studies for DDD or DDs of movement and sensation or PTSD-DS. Therefore, further research on this subject with improved methodological rigor is needed.

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