

INTERVENTIONS FOR INFORMAL CAREGIVERS

Demonstrated and perceived benefits and factors that influence the ability to establish and maintain services for informal caregivers of people with rare diseases: a scoping review

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1 **ABSTRACT**

2 **Background:** Little is known about benefits and barriers and facilitators to providing
3 psychosocial support to caregivers to a loved one with a rare disease. The objective of our
4 scoping review was to map evidence on (1) perceived benefits and (2) barriers and facilitators of
5 establishing and maintaining services.

6 **Methods:** CINAHL and PubMed were searched in December 2018. Qualitative and quantitative
7 studies in any language that described perceived or tested benefits of participating in
8 psychosocial interventions for caregivers or the barriers and facilitators of providing these
9 interventions were eligible.

10 **Results:** Thirty-four studies were included. Interventions were behavioural or psychological,
11 supportive, educational, or multi-component. All included studies reported on benefits of
12 participating in psychosocial interventions; 14 (41%) also reported on facilitators and 19 (56%)
13 on barriers. Benefits that were most commonly found included statistically significant
14 improvements in emotional states (e.g., stress) and caregiver burden and narrative reports of
15 intervention helpfulness. Statistically significant improvements in mental health outcomes (e.g.,
16 depression symptoms) were rarely detected. Four themes for facilitators were identified,
17 including intervention characteristics, intervention delivery characteristics, provision of
18 necessary resources, support provided outside of intervention. Four barrier themes were also
19 identified: misalignment of intervention to caregiver needs, inability to make time for
20 intervention, practical barriers, emotional barriers).

21 **Conclusions:** Psychosocial interventions for caregivers to a loved one with a rare disease may be
22 helpful in reducing stress, burden, and feelings of isolation among caregivers. Future research

should design interventions for caregivers that take into account facilitators and barriers to establishing and maintaining such interventions.

Keywords: Rare Diseases; Psychosocial Interventions; Scoping Review; Caregivers

Key Points

- Current evidence suggests that psychosocial interventions are perceived as an important resource for caregivers to a loved one with a rare disorder.
- Psychosocial interventions delivered to caregivers may help to reduce stress, caregiver burden, and feelings of isolation; however, establishing and maintaining these interventions may be challenging over time, given the rarity of the disorders.
- Considering the facilitators of establishing and maintaining interventions for caregivers to a loved one with a rare disease in the design of these interventions (e.g., tailoring sessions to caregiver needs) while reducing identified barriers (e.g., accessibility issues of the intervention) may enhance the sustainability of psychosocial interventions for caregivers.

1 INTRODUCTION

Informal caregivers are people who provide ongoing support for a family member or friend (referred to as a ‘a loved one’) in need of care due to a health condition [1]. They are caregivers who are not compensated monetarily for providing care, and most do not receive formal training [1]. Nonetheless, the level of care that they provide can be substantial [1] and may include physical, practical and emotional aspects of care [2]. Tasks involved vary across situations, but may include assisting with transportation, activities of daily living (e.g., feeding, dressing), managing medication and household activities (e.g., chores, meal preparation, paying bills), negotiating work and school environments, and emotional support [3, 4].

Significant burden on informal caregivers is common. A survey of over 1200 informal caregivers from the United States found that 58% reported moderate to high levels of burden, defined by the amount of time spent providing care and the degree of dependency of care recipients [5]. On average, caregivers reported that they provide 24 hours of care per week with approximately one in four providing 41 hours or more [5]. A systematic review of burden among informal caregivers of a loved one with cancer found that greater reported burden was associated with a higher likelihood of caregivers reporting physical health problems (e.g., pain, headache, muscle tension), social problems (e.g., difficulties paying bills, balancing multiple roles, feelings of being unappreciated), and emotional problems (e.g. anxiety, worry, fear of leaving the patient alone) [3].

Little is known about the experiences and challenges faced by informal caregivers of a loved one with a rare disease [6]. It would be expected that they experience the same challenges faced by carers of a loved one with more common diseases. Additionally, they may need to navigate challenges related to gaps in knowledge about the rare disease of the care recipient, as

well as more limited support resources than are available for people with more common diseases [7-11]. Caregivers regularly attend medical appointments and provide transportation for a loved one, which can involve travelling long distances for some people with rare diseases. Obtaining an accurate diagnosis and making treatment decisions often involves multiple consultations with different doctors [12, 3]. Unlike common medical disorders, many caregivers of a loved one with a rare disease have never met another individual caring for the same disease [13]. This can result in significant isolation for informal caregivers supporting a family member or friend diagnosed with a rare disease [8].

Many informal caregivers of a loved one with common medical disorders rely upon informational and emotional support interventions offered by professionals, volunteers, or peers. Psychoeducational and supportive interventions have been developed with the goal of improving caregiver well-being [14]. Psychoeducational interventions may offer information about a loved one's diagnosis, implications of an illness, caregiving skills, and support networks [15]. Psychosocial interventions may include professionally provided services or peer support options, such as support groups, which can provide emotional connection by bringing together individuals facing similar disease-related or caregiving challenges to empower one another through social contact and support [16, 14]. A meta-analysis found that professionally led support groups for informal caregivers of a care recipient with dementia led to improvements in psychological well-being, caregiver burden, and social consequences (e.g., social support, relationship with the patient) [17].

In common medical conditions, psychosocial services to support caregivers may be available through the health care system or advocacy groups and are organized and delivered by knowledgeable professionals [18, 17]. In rare diseases, on the other hand, where professionally

1 organized resources are not typically available, care recipients and caregivers sometimes
2 organize their own informational and emotional sources of support [19, 7]. Establishing and
3 maintaining these types of interventions, however, pose challenges related to the small number
4 of care recipients or caregivers affected by any rare disease and their wide geographical
5 distribution.

6 The establishment and maintenance of effective services for informal caregivers of a loved
7 one with a rare disease requires an understanding of the reasons why people may use these
8 services and what they hope to obtain from them, as well as factors that influence the ability to
9 establish and maintain informational and emotional support services in a rare disease context.
10 Thus, the objective of this scoping review was to identify and map evidence on the (1)
11 demonstrated and perceived benefits of psychosocial interventions for caregivers to a loved one
12 with a rare disease and (2) the barriers and facilitators to initiating and maintaining these
13 interventions.

14 **2 METHODS**

15 A scoping review is a “form of knowledge synthesis that addresses an exploratory research
16 question aimed at mapping key concepts, types of evidence, and gaps in research related to a
17 defined area or field by systematically searching, selecting, and synthesizing existing
18 knowledge” [20]. A scoping review is rigorous like a systematic review but addresses broader
19 topics and includes relevant studies regardless of their study design [21]. A protocol for the
20 methods for this scoping review was drafted prior to beginning the review. The methods were
21 not published or posted online. The methods applied drew upon recommendations by Arksey and
22 O’Malley [21], as well as subsequent refinements by Levac, Colquhoun, and O’Brien [22] and
23 Colquhoun et al. [20]. As recommended in these publications, we utilized a five-stage

methodological framework: (1) Identifying the research question, (2) Identifying relevant studies, (3) Selecting studies, (4) Charting the data, and (5) Collating, summarizing, and reporting results [21, 22, 20]. The reporting of this review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) reporting guidelines.[23]

2.1 Identifying the research question

Rare disease organizations have identified supporting caregivers as an important priority. In a national Canadian survey of caregivers to individuals with a rare disease, 66% of respondents reported feeling unsupported by the healthcare system [24]. To guide this scoping review and the development and implementation of services for caregivers, we defined the following research question: What are the (1) demonstrated and perceived benefits of psychosocial interventions for caregivers of patients with rare diseases and 2) barriers and facilitators to initiating and maintaining these interventions.

2.2 Identifying relevant studies

Articles published in any language that described tested or perceived benefits of an intervention intended to support caregivers of a loved one with a rare disease or the facilitators and barriers of establishing and maintaining these interventions were eligible for inclusion. We did not set any methodological or study design restrictions in our eligibility criteria in order to avoid missing important or significant data, which is consistent with standard scoping review methods [21, 20, 22]. Both qualitative, quantitative, and mixed-methods studies were eligible for inclusion. Articles were eligible if they included informal caregivers of a loved one diagnosed with a rare disease based on Orphanet's "List of rare diseases and synonyms in alphabetical order" (March 2016, available at

https://osf.io/2cd7w/?view_only=d5b686b288ab46e081db815ff39f8512), which includes diseases with prevalence rates of one person in 2,000 or less in European countries. The only exception to this was when an article was conducted in a non-European setting where the disease may or may not be rare (e.g., tuberculosis in Ethiopia); in these instances, we determined the disease's prevalence rate in the country in question based on data available on the World Health Organization's website (<https://www.who.int/health-topics/>) [25]. If the intervention was conducted in a country where the disease's prevalence rate is one person in 2,000 or less, then the article was included; however, if it was conducted in a country where the disease's prevalence rate is greater than one person in 2,000, then the article was excluded. Articles about interventions intended for caregivers to a loved one without a rare disease were excluded, even if some participants in the studies described may have cared for a loved one with a rare disease.

For the purpose of this study, any intervention intended to support informal caregivers of a loved one with a rare disease was included. Informal caregivers were defined as a family member or friend helping to care for a loved one (e.g., a family member or friend) diagnosed with a rare disease. Examples of eligible interventions included strategies for reducing emotional distress, decreasing burden, or providing education to caregivers. Eligible interventions could be delivered in any format, including in-person interventions, written materials, or the use of the telephone or internet and could be delivered in groups (e.g., support groups), or individually (e.g., individual psychotherapy). Interventions that were delivered to informal caregivers but that were intended to impact outcomes only of the care recipient, but not the caregiver, were excluded. Interventions delivered to informal caregivers and that involved outcomes for both the care recipient and for the informal caregiver were included. Studies that did not include an

intervention were excluded. When studies reported a duplicate sample, the study that included the greatest number of results and outcomes was retained.

In order to identify potentially relevant publications that described relatively current versions of interventions for caregivers of a loved one with a rare disease, we searched PubMed and CINAHL through the EBSCOhost platform from January 2000 through December 2018. A medical librarian developed the search strategy and performed the search. To develop the search strategy, we extracted the names of rare diseases listed in Orphanet's March 2015 "Rare Disorders and Cross-References" dataset (available at https://osf.io/2cd7w/?view_only=d5b686b288ab46e081db815ff39f8512). The list included names of disorders, groups of disorders, subtypes, and synonyms and totalled 20,169 unique terms. To manage the size of the search, we excluded names of groups of disorders and synonyms, leaving 6,999 unique rare disorders and subtypes. We then combined these disorder names with terms relevant to caregiving ("caregiv*", "carer", "home nursing") and informational and psychosocial interventions (e.g., "intervention", "counselling", "support")[14]. The complete search strategy can be found in Online Resource 1.

2.3 Selecting studies

The results of the search were downloaded into the citation management database RefWorks (RefWorks, RefWorks-COS, Bethesda, MD, USA), and duplicate references were identified and removed. Following this, references were transferred into the systematic review software DistillerSR (Evidence Partners, Ottawa, Canada). Using this software, we assessed the eligibility of each reference through a two-stage process. First, two investigators independently reviewed the titles and abstracts of all articles identified through the search strategy. If either investigator deemed an article potentially eligible based on the inclusion criteria, then two

investigators completed a full-text review, independently. Disagreements after full-text review were resolved by consensus, with a third investigator consulted when necessary.

2.4 Charting the data, and collating, summarizing, and reporting results

Two investigators independently extracted data from each included study and entered it into a standardized Excel spreadsheet. For each publication, we extracted the following information: (1) first author; (2) publication year; (3) study design (4) country where the intervention took place; (5) disease; (6) number, mean age, and gender or sex of caregivers; (7) intervention description; (8) control group intervention description, if applicable; (9) type of intervention; (10) participants included in the study (i.e., caregiver only, caregiver and care-recipient, or caregiver, care-recipient and family); (11) intervention delivery format (e.g., group, individual); (12) individual that delivered the intervention (e.g., peer); (13) mode of intervention delivery (i.e., in person, online, telephone, multi-delivery); (14) whether the intervention was rare disease-specific; (15) actual or perceived benefits of the intervention; (16) facilitators of the intervention; and (17) barriers of the intervention. For articles on interventions that included both care recipient and informal caregivers, only data from informal caregivers was extracted. Disagreements were resolved by consensus, and a third investigator was consulted when necessary. In line with the purpose of scoping reviews and consistent with their methodology, we did not appraise the quality of included studies.

To capture all study designs of interest, we synthesized quantitative and qualitative findings. Quantitative findings related to benefits, barriers, or facilitators to establishing and maintaining rare disease interventions for caregivers were extracted, including any results from statistical tests or aggregate data that were reported. All reported results in each eligible study, including significant and non-significant findings were extracted and included in results tables.

Only statistically significant findings, however, were categorized as “tested benefits” for mapping perceived and tested benefits. Evaluation of benefits included between group comparisons where available (e.g., any study that compared an intervention to a control group) or within group differences if the study only compared pre and post scores. If effect sizes were not reported, standardized mean differences (SMDs) were calculated using study data (i.e., sample sizes, means, standard deviations, t-values, degrees of freedom) when necessary data were provided [26, 27]. Baseline and first post-intervention follow-up points were used to calculate pre-post changes. In the case that only baseline and a later follow-up time point were available, this information was used.

Qualitative results of perceived benefits, barriers, and facilitators to establishing and maintaining rare disease support services for caregivers were extracted and included any reports in results presented in narrative format or solely descriptive results that did not include comparative statistical tests. These findings were categorized using conventional content analysis [28]. Two investigators independently identified key themes in the qualitative findings without using preconceived categories. Themes generated were discussed between reviewers until consensus was achieved. Subthemes were generated by one investigator and reviewed by a second investigator. Content analysis was also used to identify key themes for quantitative findings, such as classifying the type of outcomes reported. All results were collated and grouped based on the type of intervention studied. Results were presented in tabular format.

3 RESULTS

The database search yielded 2257 unique titles and abstracts. Of these, 2163 were excluded after title and abstract review, leaving 94 publications for full-text review. A total of 34 publications [29-62] met the inclusion criteria and were included in the scoping review (see

Figure 1). A list of studies excluded at full-text level, with reasons, is provided in Online Resource 2.

3.1. Publication Characteristics

All 34 included publications were primary research studies, 17 (50%) of which were trials of interventions that included a control group [29, 36, 38, 39, 42, 43, 45, 46, 48-50, 53, 54, 56, 58, 62, 59]. The sample size in studies ranged from four to 475 caregivers (median = 28). Twenty-one publications (62%) were from North America [32, 33, 35-39, 42-46, 49-53, 55, 58, 62, 60] nine (26%) were from Europe [29, 30, 34, 40, 41, 47, 56, 57, 61], two (6%) were from Australia [31, 48], and two (6%) were from Asia [54, 59]. Six publications included caregivers to a loved one with hematopoietic stem cell transplantation [50, 32, 33, 42, 43, 46], four included caregivers to a loved one with amyotrophic lateral sclerosis [30, 47, 56, 61], four included caregivers to a loved one with spinal cord injury [38, 39, 53, 54], three included caregivers to a loved one with cystic fibrosis [40, 41, 60], three included caregivers to a loved one with traumatic brain injury [49, 52, 58], two included caregivers to a loved one with frontotemporal dementia [36, 48], two publications included caregivers to a loved one with HIV/AIDS [59, 55], and one publication reported on a sample that combined caregivers to a loved one with either traumatic brain injury or spinal cord injury [51]. The remaining nine publications involved caregiving to a loved one with a rare disease that was not reported on in any other included study [31, 34, 35, 37, 44, 45, 57, 62, 29]. Characteristics of included publications and all extracted study findings are summarized in Tables 1-4.

3.2 Characteristics of Interventions

Sixteen publications described behavioural or psychological interventions [31-33, 35, 36, 40, 42, 43, 45-48, 50, 56, 60, 39], three publications described support focused

interventions [54, 55, 61], two publications described an educational intervention [30, 41], and 13 publications described interventions that involved more than one component [29, 34, 37, 38, 44, 49, 51-53, 57-59, 62]. Twenty-six interventions (76%) were either adapted (n=17, 50%) [29, 32, 33, 35, 38, 40, 42, 43, 46, 47, 51, 53, 55-58, 60] or were specifically developed for the rare disease (n=9, 26%) [30, 34, 37, 41, 44, 45, 49, 52, 59]. The remaining eight studies (24%) [31, 36, 39, 48, 50, 54, 61, 62] delivered generic interventions not adapted for the needs of rare disease caregivers.

Sixteen interventions (47%) were for caregivers only [55, 46, 48-50, 52, 54, 34, 36, 38-43, 61], 14 (41%) were for both caregivers and care recipients [29, 30, 32, 33, 35, 37, 45, 51, 53, 56, 57, 47, 62, 60], and 4 (12%) were for families, caregivers, and care recipients [31, 44, 58, 59]. Twenty-two interventions (65%) were delivered in person [29-34, 41-48, 50, 51, 54, 56, 57, 61, 60, 59], four interventions (12%) were delivered online [40, 49, 52, 58], three interventions (9%) were delivered by telephone [35, 37, 55], and five interventions (15%) were delivered in with more than one modality [36, 38, 39, 53, 62]. All interventions were delivered by a professional.

3.3 Perceived benefits of rare disease support services for caregivers

All 34 included publications (100%) reported on tested or perceived benefits of caregiving interventions [29-58, 62, 60, 61, 59]. Possible benefits that were described most often were related to statistically significant improvements in emotional states (e.g., reduced symptoms of stress) and reductions in caregiver burden and qualitative descriptions of helpfulness of the delivered interventions.

Thirteen unique themes of tested (statistically significant) and perceived (narratively described) benefits were identified from quantitative and qualitative study results (see Table 5).

Seven themes were identified through both qualitative descriptions of perceived benefits and quantitative tests of benefits (i.e., improvements in: physical health, dyadic relationship, existential concerns, emotional states, general skills, self-efficacy, knowledge), while two were only reported via quantitative findings (i.e., burden, quality of life and well-being) and four via qualitative descriptions (i.e., resources, social relationships, support, financial stability) (see Table 5 and Table 6).

Behavioural or Psychological Interventions (Table 1). Sixteen studies described behavioural or psychological interventions (e.g., problem solving therapy, emotional expression interventions) [36, 31-33, 35, 39, 40, 42, 43, 45-48, 60, 50, 56]. Nine studies included a control group (RCTs = 7; quasi-experimental studies = 2) [36, 42, 43, 45, 46, 56, 39, 48, 50], five studies were pre-post designs without a control group [31-33, 35, 40], and two studies sought qualitative information about perceived benefits of an intervention [47, 60].

Among RCTs, sample sizes ranged from 15 to 218 total participants (median = 57). Significant between-group reductions in perceived stress ($n = 3/3$ studies) [36, 43, 45] were found favoring the intervention groups among all RCTs that reported this outcome. Interventions resulting in reductions in stress included aspects of psychoeducation and were delivered weekly either individually or in a group, and focused on (1) improving positive emotion through practicing gratitude, mindfulness, and altruistic behaviours, among other positive psychology techniques; (2) teaching coping skills, stress management, and relaxation techniques; and (3) improving lifestyle and disease management through educating caregivers and patient about the disease, end of life care, and cognitive behavioural techniques. In most cases, the seven RCTs that tested group differences on health outcomes or mental health symptoms did not generate statistically significant differences, including for general mental health ($n = 4/5$ studies non-

significant) [39, 43, 45, 46, 56], symptoms of anxiety ($n = 3/3$ non-significant) [45, 46, 56], symptoms of depression ($n = 5/6$ studies non-significant) [36, 39, 43, 45, 46, 56], and general health ($n = 3/3$ studies non-significant) [39, 43, 45].

Two quasi-experimental studies that did not assign participants to comparison groups randomly included sample sizes of 21 and 36 participants, respectively [48, 50]. The tested interventions included providing massage therapy or a healing touch intervention [50] and a cognitive appraisal intervention [48]. The study that assessed massage therapy and healing touch reported between group differences, where reductions in negative mental health outcomes (i.e., symptoms of anxiety, depression and fatigue) were found favoring the massage therapy group. No significant differences were found for caregiver burden. In the study that delivered a cognitive appraisal intervention, within group differences were reported separately for the experimental and control groups. Only caregivers in the intervention group demonstrated statistically significant reductions in caregiver burden, improved reactions to care recipient behavior, and increased coping skills. Neither the intervention nor the control group improved significantly on measures of mental health (i.e., stress, depression, anxiety).

Five pre-post studies included sample sizes ranging from eight to 72 total participants and reported within group differences [31-33, 35, 40]. Interventions included therapeutic writing [40], problem-solving therapy [32, 33], coping skills training [35], and general counselling [31]. Results for within group differences differed across studies, with no mental health outcomes (e.g., symptoms of depression, anxiety, self-efficacy, quality of life) demonstrating significant or non-significant results in more than two studies (see Tables 1 and 5). The two qualitative studies described perceptions of outcomes of weekly meditation ($n = 18$) [47] and four sessions of counselling ($n=8$) [60], respectively. These studies described caregiver reported improvements in

1 mental health outcomes such as emotional self-regulation, ability to relax, acceptance, and
2 increased support, among other outcomes. They also reported that participants indicated that they
3 obtained practical skills (i.e., coping skills and time management skills).

4 Support Focused Interventions (Table 2). Three studies delivered support focused
5 interventions (i.e., in-person or telephone support groups). One study included a control group
6 (RCTs = 1) [54], and two studies sought qualitative information about perceived intervention
7 benefits [61, 55]. In the RCT (N = 36), statistical tests were conducted to compare outcomes
8 between those assigned to an in-person support group and to no support group [54]. Seven
9 support groups sessions were delivered by professionals over a two-week period and included
10 role-play and relaxation techniques. Statistically significant effects were found for all outcomes
11 measured, including general health, symptoms of depression and anxiety, and quality of life, all
12 favouring the intervention group. The two qualitative studies included a support group delivered
13 in person (10 sessions total, frequency of sessions not reported) [61] and one delivered by
14 telephone (weekly for 12 weeks) [55]. Caregivers that received both interventions reported being
15 satisfied with the support groups and noted that they found the groups helpful to decrease
16 feelings of loneliness and isolation. Caregivers receiving the in-person support group also
17 indicated that they benefitted from sharing fears and concerns and listening to other caregivers'
18 experiences. Caregivers that received the telephone support group reported improved
19 communication, relationships, and confidence. They also noted that the intervention provided
20 affirmational, informational, and emotional support (see Tables 2 and 5).

21 Educational Interventions (Table 3). Two studies delivered educational interventions
22 which incorporated didactic learning [30, 41]. One was a pre-post study without a control group
23 and 1 study sought qualitative information about the benefits of an intervention. The pre-post

1 study included 30 caregivers while the qualitative study included 50 caregivers. The pre-post
2 study provided individualized education in the form of power-point sessions and a booklet based
3 on caregiver identified needs [30]. A significant improvement was found between pre and post
4 scores for caregiver burden but not caregiver reported general health. The qualitative study
5 delivered an educational event at an annual meeting, which included presentations, small group
6 discussions, and question and answer sessions with clinicians [41]. All caregivers in the study
7 reported being satisfied or very satisfied with the topics covered, the presentation, and the
8 location of the event. More than 80% of caregivers also reported being satisfied or very satisfied
9 with the duration and day of the event. Caregivers described feeling less isolated due to
10 interacting with other caregivers (see Tables 3 and 5).

11 Multi-Component Interventions (Table 4). Thirteen studies delivered multi-component
12 interventions (e.g., interventions that included both psychoeducation and behavioural
13 components) [38, 59, 62, 49, 53, 58, 29, 34, 37, 44, 51, 52, 57]. Six studies, all RCTs [38, 59, 62,
14 49, 53, 58], included a control group, and the remaining seven studies were pre-post designs
15 without a control group [29, 34, 37, 44, 51, 52, 57]. Among RCTs, sample sizes ranged from 12
16 to 475 total participants (median = 51). Few statistically significant between-group
17 improvements were found for any outcomes measured in the RCTs. Symptoms of depression
18 were measured most frequently, and the majority of studies found no significant difference
19 between groups (n=5/6 studies non-significant) [38, 59, 62, 49, 53, 58], when comparing
20 intervention groups that incorporated problem solving, interactive groups, psychoeducation and
21 exercise, stress management, and/or cognitive behavioral therapy components to control groups.
22 Other commonly reported measures for comparing the intervention and control groups found few
23 statistically significant differences for general health (n= 4/5 studies non-significant) [53, 49, 62,

38, 58], perceived burden (n=2/2 non-significant) [53, 59], problem solving (n=1/2 studies non-significant) [58, 38], and symptoms of anxiety (n=1/1 non-significant) [62]. The pre-post studies had sample sizes ranging from four to 186 caregivers. Results for pre-post analyses demonstrated a significant improvement in caregiver burden (n = 3/4 studies statistically significant) [51, 34, 37, 29] after receiving interventions that involved group psychoeducation and emotional or social support. No other patterns were found among pre-post within group findings, as the remaining outcomes collected (e.g., caregiver strain, quality of life, perceived stress) were measured in just one study. Narrative benefits were also described in nine of the 13 studies testing a multicomponent intervention and included feeling less isolated, improved mood, and enhanced caregiver knowledge, (see Tables 4 and 5).

3.4 Facilitators and barriers of establishing and maintaining rare disease support services for caregivers

Fourteen publications (41%) described facilitators of establishing and maintaining the interventions [35, 36, 43, 49-56, 58, 62, 61], and 19 (56%) described barriers [29, 31, 32, 63, 40-48, 50, 55, 58, 62, 61, 60] (see Tables 1-6). No studies conducted statistical tests on facilitators or barriers. Four themes of facilitators were identified through qualitative results of studies, including, (1) characteristics of the intervention, (2) characteristics of intervention delivery, (3) providing resources, (4) support provided outside of intervention. Examples of facilitators within each theme included, (1) tailoring sessions to caregiver needs (characteristics of the intervention), (2) telephone or online delivery of intervention (characteristics of intervention delivery), (3) providing equipment (e.g., computers) to caregiver (providing resources), (4) receiving support between sessions (support provided outside of intervention). Facilitators were reported within behavioural or psychological, support-focused, and multi-component

interventions and were found to be similar between the types of interventions (Table 2). Studies testing educational interventions did not report any facilitators to establishing and maintaining support services.

Four themes of barriers were identified through analysis of qualitative results, including, (1) interventions being misaligned to caregiver needs, (2) the inability to make time for participation in an intervention, (3) practical barriers (e.g., cost, continuity, accessibility, technical problems with intervention), (4) emotional barriers (see Tables 1-6). Examples of barriers within each theme included, (1) the intervention being perceived as being too tiresome/long/burdensome (intervention misaligned to caregiver needs), (2) limited time to attend an intervention (inability to make time for intervention), (3) accessibility issues, such as intervention being too far away (practical barriers), (4) talking about caregiving causes distress (emotional barriers). Barriers were reported within all intervention types, including, behavioural or psychological, support-focused, educational, and multi-component interventions and were similar between the types of interventions (Table 2).

4 DISCUSSION

4.1 Overview of Findings

A total of 34 publications, including 17 studies (50%) with a control group, examined behavioural or psychological, support-focused, educational, or multi-component interventions for caregivers of a loved one with a rare disease. The majority of interventions were behavioural or psychological, were delivered in person and by a professional. Most studies included caregivers to a loved one with a rare acquired condition as opposed to a rare chronic genetic disorder. All interventions were delivered by a professional. Commonly tested benefits that resulted in statistically significant improvements were reductions in self-reported stress and

caregiver burden. These improvements were found after receiving behavioural or psychological interventions (e.g., teaching stress management and coping skills, cognitive behavioural therapy) and support-focused interventions (i.e., support groups). Health and mental health symptom outcomes were rarely found to significantly improve among caregivers after receiving any of the interventions reviewed. Qualitative studies reported many perceived benefits including decreased feelings of isolation, benefits from listening to other caregivers' experiences, and an increase in coping skills.

Facilitators and barriers to establishing and maintaining these interventions were reported in close to half of all included studies (41% and 56%, respectively). Commonly reported facilitators included characteristics of the intervention (i.e., sessions tailored to the needs of caregivers) and its delivery (e.g., delivering the intervention online or by telephone). Commonly reported barriers included interventions being misaligned to caregiver needs (e.g., lack of understanding from professional leading the intervention) and practical barriers of the intervention (e.g., accessibility issues such as the intervention being too far away).

4.2 Findings in Context

Many studies have reported on benefits from interventions among caregivers to a loved one with a common disease. For example, a recent Cochrane review and meta-analysis assessed the effectiveness of psychosocial interventions delivered by health professionals to caregivers to a loved one living with cancer [64]. Similar interventions (e.g., psychoeducational) were tested in 19 studies included in the review and in line with our findings; little to no improvements were found for outcomes of depression, anxiety, and caregiver health. Minimal improvements of quality of life were found post-intervention (standardized mean difference = 0.29), however, all included trials were rated as having a high risk of bias, and the authors concluded that there is an

1 immediate need for rigorous trials in order to draw firm conclusions on the effectiveness of
2 psychosocial interventions delivered by health professionals for caregivers of a loved one living
3 with cancer. The Cochrane review did not find any RCTs that measured caregiver satisfaction
4 with the intervention, and the review did not assess outcomes such as stress or caregiver burden,
5 which were the outcomes most often found to significantly improve in studies included in our
6 review.

7 **4.3 Clinical Implications of Findings**

8 Reduced isolation was also a common theme among studies in our review. This finding
9 aligns with regional and disease-specific recommendations for rare diseases [65, 66]. For
10 example, psychosocial recommendations were recently developed for individuals caring for a
11 loved one with a rare disorder, epidermolysis bullosa, where the complexity of the disease was
12 highlighted, as was the need to stimulate social participation to prevent patients and caregivers
13 from feeling isolated [65]. These guidelines recommend that care recipients and their families
14 have access to a supportive network (e.g., a support group) to optimize social wellbeing and
15 provide a sense of feeling understood. Consistent with these goals, three studies which delivered
16 support-focused interventions in our scoping review found benefits including statistically
17 significant improvements in health, symptoms of depression and anxiety, and quality of life as
18 compared to a control group, while perceived benefits included decreased feelings of loneliness
19 and isolation and the receipt of affirmational, informational, and emotional support. Receiving
20 social support may be a key construct needed for caregivers to those with a rare disorder to
21 provide a sense of being understood, alongside educational resources.

22 The findings of this scoping review suggest that psychosocial interventions may be an
23 important resource for caregivers to a loved one with a rare disorder, and that they have been

1 tested most often among those caring to a loved one with an acquired condition. Establishing and
2 sustaining these interventions, however, may be challenging over the long-term, given the rarity
3 of the disorders and the unique needs described by caregivers to those with a rare disease [67].
4 Rare disease organizations may be able to increase the feasibility and accessibility of
5 interventions by considering peer-led interventions, including those available online. There is
6 currently no evidence from trials on the effectiveness of such interventions for caregivers to a
7 loved one with a rare disease, but, the facilitators of establishing and maintaining psychosocial
8 interventions highlighted in our current review may allow for the informed development and
9 testing of such novel interventions in close collaboration with caregivers with lived experience
10 and rare disease organizations.

11 **4.4 Limitations**

12 There are several limitations that should be considered when interpreting the results of
13 this study. First, our search was restricted to publications in PubMed and CINAHL and we did
14 not conduct supplemental searches by hand; therefore, relevant information from grey literature,
15 such as rare disease websites, could have been missed. Our search strategy captured literature
16 published until December 2018 and any article published after this were not identified or
17 presented in this review. Second, most of the publications reviewed included small sample sizes,
18 which can result in high levels of imprecision and overestimate possible intervention
19 effectiveness. Third, although rare diseases share many commonalities, there are important
20 differences that must be considered, such as prevalence, age of onset, and disease severity [8].
21 Given the wide range of rare diseases present in this review, specific rare disease characteristics
22 must be considered when interpreting the results of this study. Fourth, as this is a scoping review,
23 we did not appraise the quality of included studies or assess the risk of bias for individual

1 studies. Similarly, we did not assess the potential risk of publication bias among included studies
2 or attempt to synthesize effect estimates.

3 **5 Conclusions**

4 Psychosocial interventions may be a helpful resource for individual's caregiving for a
5 loved one with a rare condition, specifically acquired rare diseases. Available studies have found
6 that psychosocial interventions may result in statistically significant reductions in stress and
7 caregiver burden while decreasing feelings of isolation, based on qualitative findings. There is a
8 limited understanding of the facilitators and barriers that can help to establish and maintain these
9 interventions, especially among caregivers to a loved one with chronic genetic disorders;
10 however, providing interventions that addresses caregivers' unique needs through accessible
11 platforms (e.g., online) may decrease the barriers that exist for establishing and maintaining these
12 interventions. The findings of this scoping review present an overview of the various
13 interventions that have been tested among caregivers to a loved one with a rare condition and
14 provide a preliminary understanding of interventions that may help support caregivers, especially
15 within the many rare diseases where no research has been conducted.

16

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