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## The needs of informal caregivers of people with a rare disease: a rapid review of the literature.

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# The needs of informal caregivers of people with a rare disease: a rapid review of the literature.

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## Abstract

*Objectives:* Many people living with a rare disease are cared for by a family member. Due to a frequent lack of individual rare disease (RD) knowledge from healthcare professionals, the patient and their informal caregiver are frequently obliged to become 'experts' in their specific condition. This puts huge strain on family life and results in caregivers juggling multiple roles in addition to unique caring roles including as advocate, case manager, and medical navigator. We conducted a rapid review of literature reporting on the unmet needs of informal caregivers for people living with a RD.

*Setting:* Searches were conducted in Medline, Embase, Web of Science, GreyLit and OpenGrey.

*Results:* Thirty-five papers were included in the final review & data extracted. This rapid review presents several unmet needs identified by informal caregivers of persons with a RD. The related literature was organised thematically: caregiver burden, support through the diagnosis process, social needs, financial needs, psychological needs, information needs and acknowledgement from healthcare professionals.

*Conclusions:* This review provides evidence that increased meaningful support is required for caregivers. Active engagement should be encouraged from this cohort in future research and awareness raised of the support available to improving the quality of life for families living with an RD.

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3 The unmet needs identified through this review will benefit people living with a RD, caregivers,  
4 healthcare professionals and policy makers.  
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9 **Key words:** burden, informal caregiver, needs, rare disease, review.  
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### 13 **Introduction**

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15 Rare diseases (RDs) are those which affect less than 1 in 2000 people in a specified population <sup>1</sup>.  
16 Although each RD occurs infrequently, collectively RDs are a major public health issue affecting  
17 approximately 300 million people globally <sup>2 3</sup>. RDs result in a wide variety of healthcare needs  
18 stemming from the involvement of multi-organ systems and cognitive and/or developmental issues.  
19 Many RDs are chronic, complex and associated with physical, intellectual, or neurological disabilities  
20 that significantly affect patients and their families. In addition, many families living with a RD lack peer  
21 and community support services <sup>4-7</sup>.  
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28 The family often plays a pivotal role in a person's adjustment to chronic disease and is influenced by  
29 behavioural, social factors <sup>8</sup>. Caring for someone with an RD affects many areas of life including  
30 psychologically, economically, physically and logistically <sup>9</sup>. The importance of good mental and  
31 physical health for the informal caregiver is therefore vital for their own wellbeing and to ensure they  
32 can sustain the essential role of assisting the person with an RD <sup>10 11 11</sup>. Individuals with RDs and their  
33 families often have limited evidence-based information to guide decisions about disease management  
34 and symptom relief <sup>12 13</sup>. Further, the inherent uncertainty that comes with having a RD, including  
35 delays in diagnosis and a lack of knowledge about current and future care needs <sup>14 15</sup>, impact access  
36 to services and management of the RD <sup>16</sup>. Research on the experience of having an RD indicates that  
37 care and service needs are often not identified based on the severity of the health condition, but  
38 rather are associated with poor quality of care and barriers to access <sup>15 17</sup>.  
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48 Given the few people with a specific RD, healthcare providers often are not knowledgeable about the  
49 condition. Therefore people living with a RD and their carers have to become their own experts <sup>18</sup>.  
50 This causes a change to the usual patient-doctor relationship, which can bring challenges <sup>19 20</sup>. Caring  
51 for someone with a RD can be highly demanding often requiring intense and unique care specific to  
52 the individuals needs <sup>21</sup>. Delayed diagnosis, lifelong caring, limited capacity for independent living,  
53 lack of treatment options and large health service needs have severe impacts on parent's physical and  
54 psychosocial wellbeing <sup>22</sup>.  
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5 Rapid reviews are an emerging type of knowledge synthesis used to inform health-related policy  
6 decisions and discussions, especially when information needs are immediate<sup>23-26</sup>. Rapid reviews  
7 streamline systematic review methods – for example, by focusing the literature search<sup>23</sup> while still  
8 aiming to produce valid conclusions. The requirements of the review, which was undertaken with a  
9 short deadline, were for a short but in-depth synthesis of the current state of the issues facing  
10 caregivers for those with a rare disease.  
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16 The purpose of this study was to identify literature reporting on the unmet needs of informal  
17 caregivers for people living with a RD.  
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## 20 21 **Methodology**

### 22 *Search strategy and inclusion criteria*

23 Three electronic databases were searched -- Medline, Embase and Web of Science -- using the  
24 combined terms 'informal caregiver\*' and 'rare disease\*'. All searches were conducted on 14  
25 September 2021. Reference lists of included papers were screened for further sources. A search was  
26 also conducted of grey literature using the databases GreyLit and OpenGrey. Duplicates and non-  
27 English language articles were excluded.  
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### 33 *Study selection and data extraction*

34 Database searches were last conducted on 14 September 2021 by JM. Titles and abstracts of the  
35 identified articles were downloaded onto Endnote. Duplicate articles were removed and the  
36 remaining papers were screened through analysing their titles and abstracts. If relevant, the papers  
37 were then further screened by reading the full text. Data were extracted by JM who recorded the  
38 follow data for each study:  
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- 45 • Author & year of publication
  - 46 • Country in which the study was conducted
  - 47 • Data collection method(s)
  - 48 • Participants
  - 49 • Identified caregiver needs
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The criteria for inclusion were articles that address caregiving for people living with an RD. Articles on caregiving alone or RD alone were excluded. Primary research studies and systematic review were considered for inclusion as shown in Table 1.

**Table 1: Literature search results**

| Database       | No. of articles retrieved | No. of articles included in review |
|----------------|---------------------------|------------------------------------|
| Medline        | 6                         | 5                                  |
| Embase         | 6                         | 5                                  |
| Web of Science | 62                        | 13                                 |
| GreyLit        | 0                         | 0                                  |
| OpenGrey       | 0                         | 0                                  |

This table shows the number of articles identified from each database before reference lists were checked.

An illustration of the search strategy including databases searched and screening methods is displayed in Figure 1, modelled on the PRISMA flow diagram.

### *Patient and Public Involvement*

The need for this review was highlighted by a priorities workshop in 2020, which considered contributions from >2,000 individuals living with rare disease. The review was also shared with representatives from a local rare disease charity in Northern Ireland (the Northern Ireland Rare Disease Partnership).

## **Results**

### *General description of the literature*

Sources initially identified from each database were as follows: MEDLINE  $n=6$ , Embase  $n=6$ , Web of Science  $n=62$ , OpenGrey  $n=0$  and GreyLit  $n=0$ . The screening process resulted in 30 documents which were reviewed based on their titles and abstracts. Following the screening 5 duplicate papers were removed and 25 papers were identified for full text screening. Further studies were identified from search the reference lists. Finally, 35 texts were included in the full review, with characteristics of each source summarised from the completed data extraction table (Supplementary file 1).

Of the texts included, publication dates were from 2006 to 2021 and the studies were conducted in Australia, Canada, Germany, Ireland, Italy, Netherlands, Spain, United Kingdom and the United States.

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3 A narrative review is presented below, highlighting the main needs of caregivers of people living with  
4 an RD. The related literature has been organised thematically under the following headings:  
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- 7 • Caregiver burden
- 8 • Support through the diagnosis process
- 9 • Social needs
- 10 • Financial needs
- 11 • Psychological needs
- 12 • Information needs
- 13 • Acknowledgement from healthcare professionals

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22 Findings from these studies were organised thematically under the following headings as shown  
23 visually in Figure 2.  
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### 26 27 28 *Caregiver burden*

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31 Caring for someone with an RD presents a range of challenges<sup>27 28</sup> that are affected by the severity of  
32 the illness and its duration, knowledge about the condition and its changes over time, and one's ability  
33 to address the emotional toll involved with long-term care<sup>29</sup>. Despite the stress and difficulties  
34 associated with being a family caregiver<sup>30</sup>, often they acknowledge the positive aspects of caring for  
35 their loved ones<sup>30</sup>.  
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41 The quality of life of caregivers is often compromised by their placing others' needs before their own  
42<sup>31</sup>. Previous research has shown that family caregivers do not have enough time for themselves,<sup>32</sup>  
43 and that caring for someone with an RD can negatively impact on all dimensions of family life<sup>33</sup>.  
44 Caregivers are often forced to miss work or school days due to the demands of their role, frequently  
45 address unpleasant events and watch a loved one suffer<sup>28</sup>. Consequently, they would benefit greatly  
46 from support to reduce the burden of caring<sup>34</sup>. This includes both supports for informal carers of  
47 people with a variety of health issues, as well as for RD-related issues<sup>34</sup>.  
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### 54 *Support through the diagnosis process*

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56 In spite of marked medical progress over the past several decades in identifying an RD, there are  
57 substantial delays in diagnosing these conditions<sup>35</sup>. This can have adverse impacts on families<sup>12</sup>.  
58 Little attention is given to parent concern in the diagnostic process with previous research reporting  
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3 concerns regarding how the diagnosis was delivered to parents, lack of guidance and poor follow-up  
4 post diagnosis<sup>35</sup>. Previous research has shown that families are often dissatisfied by the way in which  
5 a diagnosis is given, including an insensitive style of communication, not offering support or  
6 counselling, and inadequate provision of information about the disease. This can cause emotional  
7 stress for caregivers who have not yet learned about the condition and how it will affect them and  
8 their families. Therefore, interventions to support the following a diagnosis would be useful, delivered  
9 either in hardcopy or online<sup>36</sup>.

### 16 *Social needs*

17  
18 Social isolation is common among caregivers with the impact on personal relationships being a  
19 reoccurring theme<sup>45</sup>. All too often, caregivers have little time to themselves and rely heavily on family  
20 members for support and respite. This in turn causes further emotional stress and in the case of  
21 parents, uncertainty about their child's future<sup>37</sup>. Parents of children with an RD often feel isolated  
22 from mainstream society and struggle to stay socially connected<sup>4</sup>. It was suggested that the insights  
23 gained through research studies regarding the impact on caregivers' social lives should be considered  
24 in future clinical service planning. Additionally holistic, empathic, and person-centred medical and  
25 psychosocial care is urgently needed for this cohort<sup>6</sup>. Support is needed as family relationships are  
26 often impacted due to demands of caring<sup>4</sup>. There is a need for improved parental supportive care as  
27 many common unmet needs exist across RDs<sup>38</sup>.

### 36 *Financial needs*

37  
38 Previous research has indicated that financial issues are a top concern of caregivers of persons with  
39 RD<sup>30 6 39 27</sup>. The high economic costs that families must cover means that financial burden is common  
40 among caregivers of those with an RD, many of whom are forced to exhaust their financial savings<sup>40</sup>.  
41 Purchasing equipment, hiring professionals, and the additional financial burden the illness has on  
42 families poses immense stress on family life<sup>41</sup>. Often financial issues impact on the ability of the  
43 caregiver to meet the individual's healthcare needs, increasing the strain on their lives<sup>42</sup>. Substantial  
44 social/economic burden is mostly attributable to high direct non-healthcare costs<sup>43</sup>. Previous  
45 research has shown that caregivers' financial burden might be conditioned by the clinical condition of  
46 the patient<sup>44</sup>. In addition to the direct healthcare costs, caregivers of those with an RD report that  
47 their career choices are influenced due to their caring role. Furthermore, caring duties can result in  
48 missed working days due to emergency caring demands<sup>37</sup> making it difficult for many caregivers to  
49 maintain their job and advance in their careers<sup>41</sup>. Financial hardship adversely effects the mental  
50 health of caregivers<sup>42</sup>.

### *Psychological needs*

There is a lack of psychological support for families caring for children with a RD, and many report that accessing appropriate psychological care is difficult<sup>6,12</sup>. Previous research has suggested that this form of support should be offered at the time of diagnosis<sup>12,10</sup>. Depressive symptoms are often associated with caregiving burden and therefore there is a need to develop interventions for caregivers considering their special needs<sup>10</sup>. Caregivers often express concerns about the future<sup>32</sup>, experiencing emotional distress that can compromise the well-being of family carers, who attempt to maintain multiple roles<sup>11</sup>. Psychological interventions can help reduce stress, a sense of being burdened and feelings of isolation that many RD caregivers feel<sup>45</sup>. Research has suggested that screening for depression is needed and emphasises the need for a holistic approach to family mental health in the context of chronic childhood disease<sup>46</sup>. Peer support is a key resource in terms of information and emotional support for parents who often begin their journey feeling isolated and alone<sup>21</sup>.

### *Information needs*

Suggestions were made that information about the condition should be given to caregivers at the time of diagnosis as well as signposting them to groups connecting families who share common experiences<sup>21</sup>. Caregivers require access to accurate information, appropriate services and improved communication between patients, families, and a range of both health and social care and other public services<sup>2</sup>. Families require easily accessible services that include the family in the unit of care, provide support and information, and understand the process of family adjustment and adaptation in the long term<sup>47</sup>. Policies and structures are needed to support social and economic needs<sup>48</sup>. Engaging caregivers in future avenues of research is vital to ensure resources and funding are targeted in the best way<sup>49</sup>.

### *Acknowledgement from healthcare professionals*

Out of necessity, informal carers often know more about a particular RD than healthcare providers do. This often leads to poor communication and collaboration. Furthermore a lack of coordination of care force carers to fill the gap by juggling multiple roles including that of advocate, case manager, and medical navigator<sup>50</sup>. Caregivers often experience silencing or being silenced when interacting with health-care and social care systems and providers<sup>51</sup>. This has been attributed to the lack of knowledge about RDs by health-care providers who also are unaware of the impact that caring for someone with RD<sup>50</sup>. This points to the need to improve the knowledge of health care providers on the medical, social and financial impact these informal carers experience<sup>4</sup>. Health care providers

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3 should also acknowledge the vital role that informal caregivers play in promoting the health and  
4 quality of life of persons with an RD <sup>52</sup>. Caregivers, especially parents caring for someone with an RD,  
5 work hard to be heard and acquire services within health and social systems <sup>50</sup>. Another way that  
6 informal caregivers are silenced is due to how they are overlooked in the world of research despite  
7 growing emphasis on ensuring 'patient and public involvement' (PPI). It is vital that this pattern is  
8 changed so that they have an opportunity to be heard <sup>53 27</sup>.  
9

## 15 Discussion

16 The purpose of this rapid review was to synthesise and describe what is currently known about the  
17 needs of informal caregivers for people living with an RD. Based on the findings, several  
18 recommendations for future healthcare practices and policies, as well as for research are evident.  
19 First, it is important to consider the extreme burden often experienced by these caregivers, many of  
20 whom place the need of others ahead of their own while navigating this journey with little or no  
21 support <sup>s 31</sup>. Support is needed to help caregivers with many aspects of their caring duties from the  
22 initial diagnosis process which has been a difficult time for many families <sup>35</sup>.  
23

24 Social support would be welcomed to enable caregivers to have much needed time away from their  
25 caring duties to recharge and also to relieve them of the emotional strain which impacts on not only  
26 themselves but their wider family <sup>4</sup>. The mental strain of caregiving is evident from previous research,  
27 psychological interventions are required that consider the family as a whole to reduce the emotional  
28 strain and depression too often experienced by caregivers <sup>21 45</sup>. Many caregivers have also reported  
29 struggling financially not only due to the high costs of the practical side of caring but as a result of the  
30 impact caring can have on their ability to maintain a career <sup>41</sup>, financial support therefore a priority.  
31

32 Clear information should be provided for caregivers from diagnosis through to their rare disease  
33 journey <sup>2</sup> to replace the current situation of confusion and uncertainty due to unclear and incomplete  
34 or conflicting messages. Lastly, caregivers must be recognised by healthcare professionals for the  
35 integral part they have in caring for someone with a rare disease. This relationship often changes the  
36 dynamic between health professional and patient and so caregivers must be listened to and viewed  
37 as an 'expert' <sup>52</sup>. All of the above-mentioned issues should be taken into consideration when planning  
38 future research, it is vital that informal caregivers views are valued.  
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## 57 Strengths and limitations

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3 This study explored a cohort of individuals who frequently go unnoticed and unreported in the  
4 literature – informal caregivers of individuals diagnosed with a rare disease. The rapid review followed  
5 the guidelines for conducting a rapid review of the literature<sup>23 24 25 26</sup>. The review was conducted by  
6 experienced researchers in the area of RD carer needs who have a wealth of relevant experience.  
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8 Additionally, manual searches of reference lists were conducted to identify any papers not found by  
9 the initial search strategy.  
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15 However, it is important to acknowledge limitations of this review. Due to resource constraints, only  
16 one author (JM) initially screened the titles and abstracts from the total set of documents retrieved.  
17 This could lead to bias. However, conducting a rapid review produced results quickly, including  
18 identifying the main self-identified needs of caregivers of people living with an RD. This is particularly  
19 important given the key role that informal caregivers play, and the fact that earlier research has  
20 focused on the person with an RD and not the caregiver. The authors of this paper consider the needs  
21 of RD caregivers a priority and recognises the value they bring to the unique caring needs.  
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## 28 **Conclusion**

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30 This rapid review presents several unmet needs identified by informal caregivers of persons with a RD.  
31 It is hoped that the findings contribute to increasing the amount of meaningful support for caregivers  
32 as well as encourage their active participation in improving the quality of life for families living with  
33 an RD. It is important that this cohort are engaged in future research to ensure their needs are being  
34 addressed. Better meeting needs of informal caregivers for people living with a RD is in the best  
35 interests of people with a RD, healthcare professionals and policy makers, as well as caregivers. It is  
36 important that awareness is raised about the range of support options are available for informal  
37 caregivers of people with an RD from health and social care providers, charities and/or support groups  
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## 52 **Abbreviations**

53 RD Rare disease

## 54 **Declarations**

- 55 • Ethics approval and consent to participate: Not applicable
- 56 • Consent for publication: Not applicable
- 57 • Availability of data and materials: Not applicable
- 58 • Competing interests: The authors declare that they have no competing interests.

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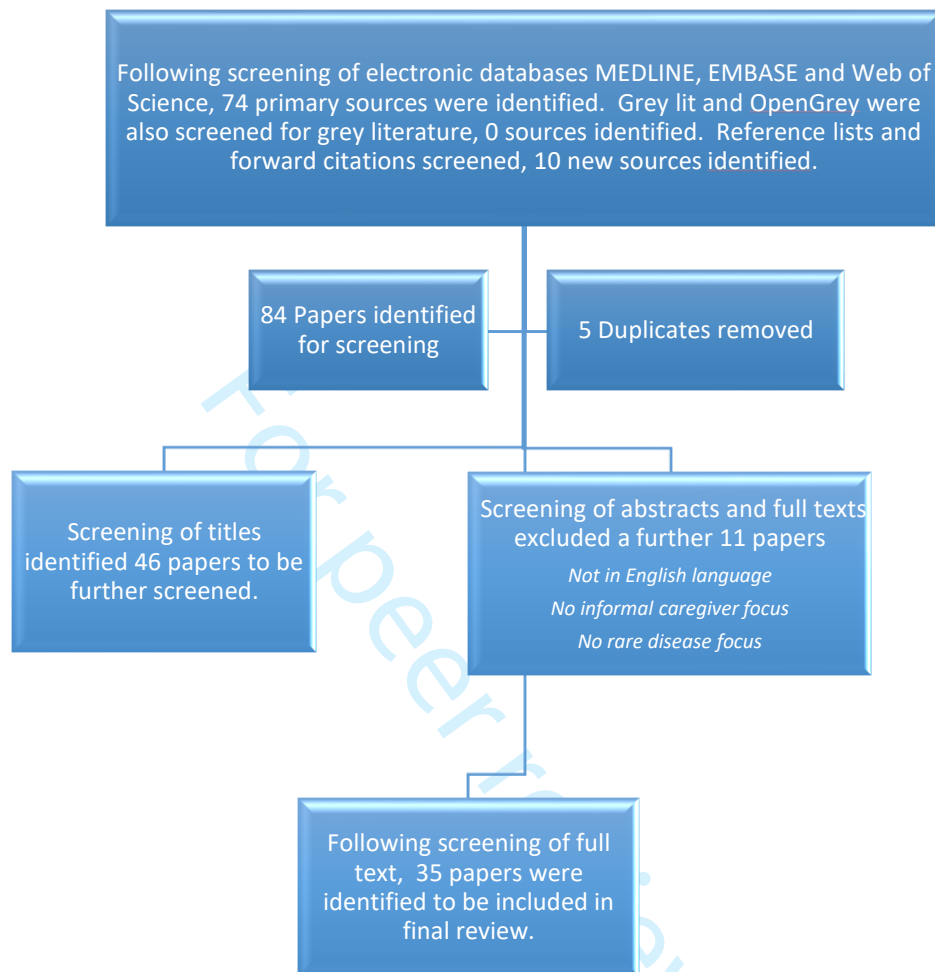


Figure 1 PRISMA flowchart

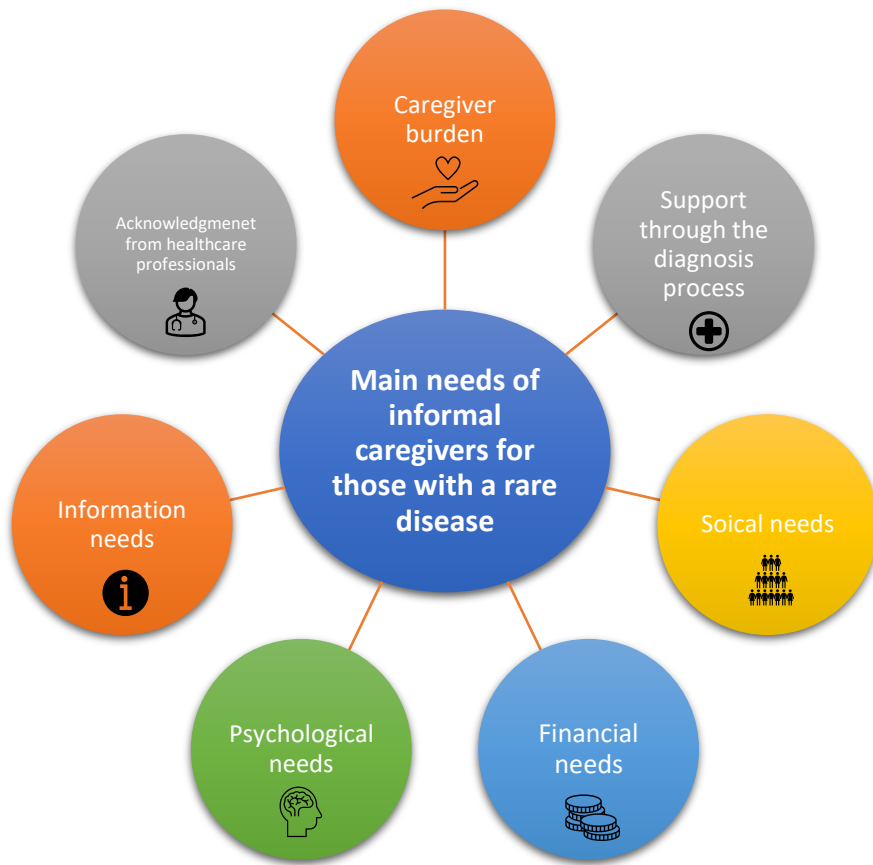


Figure 2 Main needs of caregivers for those with a rare disease

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| Supplementary file 1: Data extraction table                  |  |                                      |  |  |
|--|--|--------------------------------------|--|--|
| Author & year of publication                                 | Country in which the study was conducted | Data collection method(s)            | Participants   | Identified caregiver needs   |
| Anderson, M., Elliott EJ, Zuryski YA.<br>2009                | Australia                                | Survey                               | Parents/carers   | <ul style="list-style-type: none"> <li>• Support around diagnosis.</li> <li>• Access to peer support groups.</li> <li>• Psychological support.</li> </ul>  |
| Applebaum A.J., Polacek L.C., Walsh L. <i>et al.</i><br>2020 | USA                                      | Survey and semi-structured interview | Caregivers of patients with Erdheim-Chester disease              | <ul style="list-style-type: none"> <li>• Social connections to prevent extreme isolation</li> </ul>  |
| Aubeeluck A.V. Buchanan H.E., Stupple E.J.N.<br>2011         | England                                  | Focus groups                         | Caregivers of those with Huntington's Disease                    | <ul style="list-style-type: none"> <li>• More time to focus on themselves.</li> </ul>  |
| Craig T.J., Banjerji A., Riedl M.A., <i>et al.</i><br>2021   | USA                                      | Online survey                        | Adults caring for an individual with Hereditary angioedema (HAE) | <ul style="list-style-type: none"> <li>• Recognition for the important role they have.</li> <li>• Inclusion in treatment discussions.</li> </ul>   |
| Hanbury A, Smith AB & Buesch K<br>2021                       | England                                  | Vignettes were developed             | Caregivers   | <ul style="list-style-type: none"> <li>• Engagement with research</li> </ul>   |
| Baumbusch, J., Mayer, S., & Sloan-Yip, I.<br>2018            | Canada                                   | Semi-structured interviews           | Parents of children with a RD                                    | <ul style="list-style-type: none"> <li>• Acknowledgment from healthcare providers</li> <li>• Support coordinating care</li> <li>• Peer support – information and emotional</li> <li>• Policies and programs to validate their role</li> <li>• Support from genetic counsellor to connect them to others</li> </ul> |

|  |             |                            |   |   |
|--|-------------|----------------------------|---|---|
| Bendixen, R. M., & Houtrow, A.<br>2017                             | USA         | Interviews                 | Parents of children with Duchenne muscular dystrophy          | <ul style="list-style-type: none"> <li>Listened to by healthcare providers</li> <li>Inclusion in the diagnostic process</li> <li>Improved delivery of the diagnosis</li> <li>Improved follow up after diagnosis</li> </ul>  |
| Cañedo-Ayala, M., Rice, D. B., Levis, B., et al.<br>2020           | USA         | Questionnaire              | Informal caregivers   | <ul style="list-style-type: none"> <li>Mental health support</li> </ul>   |
| Currie, G., & Szabo, J.<br>2019                                    | Canada      | Semi-structured interviews | Parents of children with RDs                                  | <ul style="list-style-type: none"> <li>Communication issues need addressed as parents often know more about the disease than healthcare providers.</li> <li>Improved coordination of care between providers and services caring for children with rare diseases.</li> <li>Gap in accessibility to government supports needs addressed.</li> </ul> |
| Currie, G., & Szabo, J.<br>2019                                    | Canada      | Semi-structured interviews | Parents of children with rare neurodevelopmental diseases     | <ul style="list-style-type: none"> <li>Health-care providers need more understanding of rare conditions.</li> <li>More support needed, parents often 'lose themselves' in this demanding caring role.</li> </ul>  |
| Flores D., Ribate M.P., Montolio M., et al.<br>2020                | Spain       | Questionnaires             | Caregivers to patients with Duchenne muscular dystrophy       | <ul style="list-style-type: none"> <li>Financial support.</li> </ul>  |
| Kanters T.A., van der Ploeg Ans. T, Brouwer W.B.F., et al.<br>2013 | Netherlands | Questionnaire              | Caregivers for those with Pompe disease.                      | <ul style="list-style-type: none"> <li>Support needed for informal caregivers.</li> </ul>   |
| Kasparian, N. A., Rutstein, A., Sansom-Daly, et al.                | Australia   | Telephone interviews       | Patients and caregivers affected by Von Hippel-Lindau disease | <ul style="list-style-type: none"> <li>More supportive care services requested.</li> </ul>  |

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|---|-------------------------|--|--|---|
| 2015  |                         |  |  |   |
| Landfelt E., Lindgren P., Bell C.F., <i>et al.</i>                    | Germany, Italy, UK, USA | Visual analogue scale, survey, interview | Caregivers to patients with Duchenne muscular dystrophy        | <ul style="list-style-type: none"> <li>• Screening for depression.</li> <li>• Holistic approach to family mental health needed.</li> </ul>  |
| 2016  |                         |  |  |   |
| Lagae, L., Irwin, J., Gibson, E., <i>et al.</i>                       | Europe                  | Survey                                   | Caregivers for those with Dravet syndrome (DS)                 | <ul style="list-style-type: none"> <li>• Time needed to escape caring duties.</li> <li>• Formal support and respite required.</li> <li>• Stress is common – support needed.</li> </ul>  |
| 2019  |                         |  |  |   |
| Lopez-Bastida J., Pena-Longobardo L.M., Aranda-Reneo I, <i>et al.</i> | Spain                   | Questionnaire                            | Patients and caregivers with Spinal Muscular Atrophy           | <ul style="list-style-type: none"> <li>• Financial support</li> <li>• QoL must be addressed</li> </ul>  |
| 2017  |                         |  |  |   |
| Lyon, M. E., Thompkins, J. D., Fratantoni, K., <i>et al.</i>          | USA                     | Semi-structured interviews               | Caregiving families  | <ul style="list-style-type: none"> <li>• Worries about the future need to be addressed.</li> <li>• More time for themselves needed.</li> <li>• Financial concerns must be addressed.</li> </ul>   |
| 2019  |                         |  |  |   |
| McKnight, A. J. M., Walker, R., Collins, C. (2020).                   | Northern Ireland        | Report                                   | N/A  | <ul style="list-style-type: none"> <li>• Access to accurate information</li> <li>• Access to appropriate services</li> <li>• Improved communication</li> </ul>  |
| 2020  |                         |  |  |   |
| McMullan, J., Crowe, A. L., Bailie, C. <i>et al.</i>                  | Northern Ireland        | Survey and semi-structured interviews    | Rare disease collaborative groups                              | <ul style="list-style-type: none"> <li>• Caregivers often overlooked in RD research – their opinions and experiences must be valued.</li> </ul>   |
| 2021  |                         |  |  |   |
| McMullan J, Crowe A.L., Downes K., <i>et al.</i>                      | Northern Ireland        | Survey and workshop                      | Caregivers of those with a rare disease                        | <ul style="list-style-type: none"> <li>• Improved interactions with healthcare professionals.</li> <li>• Improved emotional, psychological and social support.</li> <li>• Assistance with finances.</li> <li>• Better awareness of support services.</li> </ul> |
| 2015  |                         |  |  |   |
| Mooney J., Graham K. & Watts R.A.                                     | England                 | Semi-structured interviews               | Patients with ANCA-associated vasculitis and their caregivers. | <ul style="list-style-type: none"> <li>• Emotional support is needed.</li> <li>• Reassurance about the future.</li> </ul>   |

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| 2019   |           |  |   |   |
| Mori, Y., Downs, J., Wong, K., <i>et al.</i>                               | Australia | Survey   | Families with a child with CDKL5 disorder | <ul style="list-style-type: none"> <li>Burden of daily caregiving requires support, particularly in relation to emotional wellbeing, sleep problems, financial difficulties, QoL.</li> </ul>  |
| 2017   |           |  |   |   |
| Mutch, K., Methley, A., Hamid, S., <i>et al.</i>                           | England   | Semi-structured interviews   | Partners of people with NMO               | <ul style="list-style-type: none"> <li>Acknowledgement from HCP regarding the vital role they play in caring.</li> </ul>  |
| 2017   |           |  |   |   |
| Palacios-Cena, D., Famoso-Perez, P., Salom-Moreno, J., <i>et al.</i>       | Spain     | Interviews, focus groups, researcher's field notes, caregiver's personal documents | Caregivers of children with Rett Syndrome | <ul style="list-style-type: none"> <li>Answers needed regarding 'the first symptoms' and 'the need for a diagnosis'.</li> <li>Help with managing day to day life.</li> <li>Financial support.</li> </ul>  |
| 2018   |           |  |   |   |
| Pelentsov, L. J., Fielder, A. L., & Esterman, A. J.                        | Australia | Semi-structured focus group interviews   | Parents of a child with a RD              | <ul style="list-style-type: none"> <li>Social isolation must be addressed.</li> <li>Knowledge of HCP needs to be improved.</li> <li>Support needed as family relationship often impacted due to demands of caring.</li> </ul>                                     |
| 2016   |           |  |   |   |
| Pelentsov, L. J., Laws, T. A., & Esterman, A. J.                           | Australia | Scoping Review   | Parents of child with a RD                | <ul style="list-style-type: none"> <li>Improve parental supportive care – common unmet needs between RDs.</li> </ul>  |
| 2015   |           |  |   |   |
| Rice D.B., Canedo-Ayala M., Carboni-Jimenez A., Carrier M-E, <i>et al.</i> | USA       | Online questionnaire   | Caregivers of people with SSc             | <ul style="list-style-type: none"> <li>Emotional support is required.</li> <li>Help with physical needs.</li> <li>Interventions needed delivered through hardcopy or online resources, including those delivered after the care recipient's diagnosis.</li> </ul> |
| 2020   |           |  |   |   |
| Rice D.B., Carbino-Jimenez A., Canedo-Ayala M. <i>et al.</i>               | USA       | Scoping review   | N/A                                       | <ul style="list-style-type: none"> <li>Psychosocial interventions needed to reduce caregiver's stress, burden and feelings of isolation among caregivers.</li> </ul>  |
| 2020   |           |  |   |   |

|   |             |  |  |   |
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|   |             |  |  | <ul style="list-style-type: none"> <li>• Future research should design interventions for caregivers.</li> </ul>   |
| Rodriguez A.A., Martinez O., Amayra I, <i>et al.</i><br><br>2021        | Spain       | Questionnaire  | Carers of children with neuromuscular disease                        | <ul style="list-style-type: none"> <li>• Financial assistance.</li> <li>• Employment support.</li> <li>• Physical and psychological support.</li> </ul>   |
| Selman L.E., Beynon T., Radcliffe S., <i>et al.</i><br><br>2014         | London      | Semi-structured qualitative interviews                       | Adult informal caregivers of patients with Cutaneous T-cell lymphoma | <ul style="list-style-type: none"> <li>• Easily accessible services are needed that include the family in the unit of care, provide support and information, and understand the process of family adjustment and adaptation.</li> </ul> |
| Sloper, T., & Beresford, B.<br><br>2006                                 | UK          | Report   | Families of disabled children  | <ul style="list-style-type: none"> <li>• Policies and structures to support social and economic needs.</li> </ul>   |
| Somanadhan, S., & Larkin, P. J.<br><br>2016                             | Ireland     | In-depth interviews  | Parents of those with Mucopolysaccharidosis                          | <ul style="list-style-type: none"> <li>• Reassurance and certainty needed about the future.</li> </ul>  |
| Wiblin, L., Durcan, R., Lee, M., <i>et al.</i><br><br>2017              | England     | Qualitative in depth interviews                              | Patients and caregivers living with MSA and PSP                      | <ul style="list-style-type: none"> <li>• Better connections to others to reduce social isolation.</li> <li>• Improved communication.</li> </ul>   |
| Williams, J. K., Skirton, H., Paulsen, J. S., <i>et al.</i><br><br>2009 | USA, Canada | Focus groups   | Adult caregivers of people with Huntington's disease                 | <ul style="list-style-type: none"> <li>• Emotional distress support should be provided.</li> <li>• Assistance in managing several roles.</li> <li>• Mental health monitoring.</li> </ul>  |
| Wu, Y., Al-Janabi, H., Mallett, A., <i>et al.</i><br><br>2020           | Australia   | Clinical data was used from Mitochondrial Disease, Epileptic | Parents of those with rare genetic conditions                        | <ul style="list-style-type: none"> <li>• Health effects on family members need to be considered.</li> </ul>   |

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|  |  | Encephalopathy and Brain Malformation projects |  |  |
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# BMJ Open

## The needs of informal caregivers of people with a rare disease: a rapid review of the literature.

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| <b>Primary Subject Heading</b>: | Public health  |
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| Keywords:                       | Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PUBLIC HEALTH   |
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# 1 **The needs of informal caregivers of people with a rare disease: a rapid review** 2 **of the literature.**

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## 13 14 **Abstract**

15 *Objectives:* Many people living with a rare disease are cared for by a family member. Due to a frequent  
16 lack of individual rare disease (RD) knowledge from healthcare professionals, the patient and their  
17 informal caregiver are frequently obliged to become 'experts' in their specific condition. This puts  
18 huge strain on family life and results in caregivers juggling multiple roles in addition to unique caring  
19 roles including as advocate, case manager, and medical navigator. We conducted a rapid review of  
20 literature reporting on the unmet needs of informal caregivers for people living with a RD.

21  
22 *Setting:* Searches were conducted in Medline, Embase, Web of Science, GreyLit and OpenGrey.

23  
24 *Results:* Thirty-five papers were included in the final review & data extracted. This rapid review  
25 presents several unmet needs identified by informal caregivers of persons with a RD. The related  
26 literature was organised thematically: caregiver burden, support through the diagnosis process, social  
27 needs, financial needs, psychological needs, information and communication needs and  
28 acknowledgement from healthcare professionals.

29  
30 *Conclusions:* This review provides evidence that increased meaningful support is required for  
31 caregivers. Active engagement should be encouraged from this cohort in future research and  
32 awareness raised of the support available to improving the quality of life for families living with an RD.

2

33 The unmet needs identified through this review will benefit people living with a RD, caregivers,  
34 healthcare professionals and policy makers.

35

36 **Key words:** burden, informal caregiver, needs, rare disease, review.

37

### 38 **Strengths and limitations**

- 39 • This study explored a cohort of individuals who frequently go unnoticed and unreported in  
40 the literature – informal caregivers of individuals diagnosed with a rare disease.
- 41 • The rapid review followed the guidelines for conducting a rapid review of the literature.
- 42 • The review was conducted by experienced researchers in the area of RD carer needs who have  
43 a wealth of relevant experience. Additionally, manual searches of reference lists were  
44 conducted to identify any papers not found by the initial search strategy.
- 45 • It is important to acknowledge limitations of this review. Due to resource constraints, only  
46 one author (JM) initially screened the titles and abstracts from the total set of documents  
47 retrieved. This could lead to bias.
- 48 • Conducting a rapid review produced results quickly, including identifying the main self-  
49 identified needs of caregivers of people living with an RD. This is particularly important given  
50 the key role that informal caregivers play, and the fact that earlier research has focused on  
51 the person with an RD and not the caregiver.

52

53 The authors of this paper consider the needs of RD caregivers a priority and recognises the value they  
54 bring to the unique caring needs.

55

### 56 **Introduction**

57 In Europe, rare diseases (RDs) are those which affect less than 1 in 2000 people in a specified  
58 population<sup>1</sup>. Although each RD occurs infrequently, collectively RDs are a major public health issue  
59 affecting more than 450 million people globally<sup>2 3</sup>. RDs result in a wide variety of healthcare needs  
60 stemming from the involvement of multiple organ systems, such as respiratory complications, the  
61 circulatory system. Muscular system, digestive system, and central nervous system. Many RDs are  
62 chronic, complex and associated with physical, intellectual, or neurological disabilities that  
63 significantly affect patients and their families. In addition, many families living with a RD lack peer and  
64 community support services<sup>4-7</sup>

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3 66 Although not always the case, family often plays a pivotal role in a person's adjustment to chronic  
4 67 disease and is influenced by behavioural and social factors<sup>8</sup>. A family member frequently takes on  
5 68 the role as caregiver or a person with a close relationship as an informal caregiver. Caring for  
6 69 someone with an RD affects many areas of life including psychologically, economically, physically  
7 70 and logistically<sup>9</sup>. The importance of good mental and physical health for the informal caregiver is  
8 71 therefore vital for their own wellbeing and to ensure they can sustain the essential role of assisting  
9 72 the person with an RD<sup>10 11</sup>. Individuals with RDs and their families often have limited evidence-  
10 73 based information to guide decisions about disease management and symptom relief<sup>12 13</sup>. Further,  
11 74 the inherent uncertainty that comes with having a RD, including delays in diagnosis (the average  
12 75 time for a diagnosis of a rare disease in Northern Ireland is 5 years) and a lack of knowledge about  
13 76 current and future care needs<sup>14 15</sup>, impact access to services and management of the RD<sup>16</sup>.  
14 77 Research on the experience of having an RD indicates that care and service needs are often not  
15 78 identified based on the severity of the health condition, but rather are associated with poor quality  
16 79 of care and barriers to access, for example lower satisfaction with healthcare services and care  
17 80 coordination<sup>15 17</sup>.

18 81  
19 82 Given the few people with a specific RD, healthcare providers often are not knowledgeable about  
20 83 the condition. Therefore people living with a RD and their carers have to become their own experts  
21 84<sup>18</sup>. This causes a change to the usual patient-doctor relationship, which can bring challenges such as  
22 85 difficulties in communication and patients struggling to get sufficient accurate information to make  
23 86 informed choices<sup>19 20</sup>.

24 87  
25 88 Caring for someone with a RD can be highly demanding often requiring intense and unique care  
26 89 specific to the individuals needs<sup>21</sup>. Delayed diagnosis, lifelong caring, limited capacity for  
27 90 independent living, lack of treatment options and large health service needs have severe impacts on  
28 91 parent's physical and psychosocial wellbeing<sup>22</sup>.

29 92  
30 93 Rapid reviews are an emerging type of knowledge synthesis used to inform health-related policy  
31 94 decisions and discussions, especially when information needs are immediate<sup>23-26</sup>. Rapid reviews  
32 95 streamline systematic review methods – for example, by focusing the literature search<sup>23</sup> while still  
33 96 aiming to produce valid conclusions. The requirements of the review, which was undertaken with a  
34 97 short deadline, were for a short but in-depth synthesis of the current state of the issues facing  
35 98 caregivers for those with a rare disease.

99

4

1  
2  
3 100 This review focuses on informal caregivers for people living with a RD. We were particularly interested  
4  
5 101 in their holistic needs when caring for this unique population and how these may differ from other  
6  
7 102 caring populations where there is often more support available e.g. carers of people with dementia or  
8  
9 103 cancer.

10 104

## 11 105 **Methodology**

### 12 106 *Search strategy and inclusion criteria*

13  
14  
15 107 Three electronic databases were searched -- Medline, Embase and Web of Science -- using the  
16  
17 108 combined terms 'informal caregiver\*' and 'rare disease\*'. All searches were conducted on 14  
18  
19 109 September 2021, with no date restrictions. Reference lists of included papers were screened for  
20  
21 110 further sources. A search was also conducted of grey literature using the databases GreyLit and  
22  
23 111 OpenGrey. Duplicates and non-English language articles were excluded. The criteria for inclusion  
24  
25 112 were articles that address caregiving for people living with an RD. Articles on caregiving alone or RD  
26  
27 113 alone were excluded. Primary research studies and systematic review were considered for inclusion  
28  
29 114 as shown in Table 1.

115

116

117

### 118 118 *Study selection and data extraction*

119 Database searches were last conducted on 14 September 2021 by JM. Titles and abstracts of the  
120  
121 identified articles were downloaded onto Endnote. Duplicate articles were removed and the  
122  
123 remaining papers were screened through analysing their titles and abstracts. Additionally, manual  
124  
125 searches of reference lists were conducted on 21 September 2021 to identify any papers not found by  
126  
127 the initial search strategy. If relevant, the papers were then further screened by reading the full text.  
128  
129 Data were extracted by JM who recorded the follow data for each study:

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134

- Author & year of publication
- Country in which the study was conducted
- Data collection method(s)
- Participants
- Identified caregiver needs

The identified caregiver needs were extracted from the included papers [JM] and presented the data  
extraction table [AMcK, JM & LL] (Supplementary file 1). From this, common needs were grouped

5

134 together under headings which became the themes for this review. The themes and content for the  
 135 themes was agreed between the research team [AMcK, JM & LL].

136

137 **Table 1: Literature search results**

| Database       | No. of articles retrieved | No. of articles included in review |
|----------------|---------------------------|------------------------------------|
| Medline        | 6                         | 5                                  |
| Embase         | 6                         | 5                                  |
| Web of Science | 62                        | 13                                 |
| GreyLit        | 0                         | 0                                  |
| OpenGrey       | 0                         | 0                                  |

138 This table shows the number of articles identified from each database before reference lists were checked.

139

140 An illustration of the search strategy including databases searched and screening methods is  
 141 displayed in Figure 1, modelled on the PRISMA flow diagram.

142

### 143 *Patient and Public Involvement*

144 The need for this review was highlighted by a priorities workshop in 2020, which considered  
 145 contributions from >2,000 individuals living with rare disease. The review was also shared with  
 146 representatives from a local rare disease charity in Northern Ireland (the Northern Ireland Rare  
 147 Disease Partnership).

148

## 149 **Results**

### 150 *General description of the literature*

151 Sources initially identified from each database were as follows: MEDLINE  $n=6$ , Embase  $n=6$ , Web of  
 152 Science  $n=62$ , OpenGrey  $n=0$  and GreyLit  $n=0$ . The screening process resulted in 30 documents which  
 153 were reviewed based on their titles and abstracts. Following the screening 5 duplicate papers were  
 154 removed and 25 papers were identified for full text screening. Further studies were identified from  
 155 searching the reference lists. Finally, 35 texts were included in the full review, with characteristics of  
 156 each source summarised from the completed data extraction table (Supplementary file 1).

157 Of the texts included, publication dates were from 2006 to 2021 and the studies were conducted in  
 158 Australia, Canada, Germany, Ireland, Italy, Netherlands, Spain, United Kingdom and the United States.  
 159 The identified studies focus on many rare diseases including Hereditary angioedema, Huntington's  
 160 Disease, Duchenne muscular dystrophy and Von Hippel-Lindau disease.

6

161

162 A narrative review is presented below, highlighting the main needs of caregivers of people living with  
163 an RD. The related literature has been organised thematically under the following headings:

- 164 • Caregiver burden
- 165 • Support through the diagnosis process
- 166 • Social needs
- 167 • Financial needs
- 168 • Psychological needs
- 169 • Information and communication needs
- 170 • Acknowledgement from healthcare professionals

171

172 Findings from these studies were organised thematically under the following headings as shown  
173 visually in Figure 2.

174

### 175 *Caregiver burden*

176 Caring for someone with an RD presents a range of challenges<sup>27 28</sup> that are affected by the severity of  
177 the illness and its duration, knowledge about the condition and its changes over time, and one's ability  
178 to address the emotional toll involved with long-term care<sup>29</sup>. Despite the stress and difficulties  
179 associated with being a family caregiver<sup>30</sup>, often they acknowledge the positive aspects of caring for  
180 their loved ones<sup>30</sup>.

181

182 The quality of life of caregivers is often compromised by their placing others' needs before their own  
183<sup>31</sup>. Previous research has shown that informal caregivers do not have enough time for themselves,<sup>32</sup>  
184 and that caring for someone with an RD can negatively impact on all dimensions of family life<sup>33</sup>.  
185 Caregivers are often forced to miss work or school days due to the demands of their role, frequently  
186 address unpleasant events and watch a loved one suffer<sup>28</sup>. Consequently, they would benefit greatly  
187 from support to reduce the burden of caring for example from support groups, respite care and  
188 employment arrangements<sup>34</sup>. This includes both supports for informal carers of people with a variety  
189 of health issues, as well as for RD-related issues<sup>34</sup>.

190

### 191 *Support through the diagnosis process*



1  
2  
3 192 In spite of marked medical progress over the past several decades in identifying an RD, there are  
4  
5 193 substantial delays in diagnosing these conditions<sup>35</sup>. This can have adverse impacts on families, for  
6  
7 194 example, financial and mental health<sup>12</sup>. Little attention is given to parent concern in the diagnostic  
8  
9 195 process with previous research reporting concerns regarding how the diagnosis was delivered to  
10  
11 196 parents, lack of guidance and poor follow-up post diagnosis<sup>35</sup>. Previous research has shown that  
12  
13 197 families are often dissatisfied by the way in which a diagnosis is given, including an insensitive style of  
14  
15 198 communication, not offering support or counselling, and inadequate provision of information about  
16  
17 199 the disease. This can cause emotional stress for caregivers who have not yet learned about the  
18  
19 200 condition and how it will affect them and their families. Therefore, interventions to support the  
20  
21 201 following a diagnosis would be useful, delivered either in hardcopy or online<sup>36</sup>.

202

### 203 *Social needs*

204 Social isolation is common among caregivers with the impact on personal relationships being a  
205 reoccurring theme<sup>4 5</sup>. All too often, caregivers have little time to themselves and lack appropriate  
206 support and time for respite. This in turn causes further emotional stress and in the case of parents,  
207 uncertainty about their child's future<sup>37</sup>. Parents of children with an RD often feel isolated from  
208 mainstream society and struggle to stay socially connected<sup>4</sup>. It was suggested that the insights gained  
209 through research studies regarding the impact on caregivers' social lives should be considered in  
210 future clinical service planning. Additionally holistic, empathic, and person-centred medical and  
211 psychosocial care is urgently needed for this cohort<sup>6</sup>. Support is needed as relationships among  
212 family members are often impacted due to demands of caring<sup>4</sup>. There is a need for improved parental  
213 supportive care as many common unmet needs exist across RDs<sup>38</sup>.

214

### 215 *Financial needs*

216 Previous research has indicated that financial issues are a top concern of caregivers of persons with  
217 RD<sup>30 6 39 27</sup>. The high economic costs that families must cover means that financial burden is common  
218 among caregivers of those with an RD, many of whom are forced to exhaust their financial savings<sup>40</sup>.  
219 Purchasing equipment, hiring professionals, and the additional financial burden the illness has on  
220 families poses immense stress on family life<sup>41</sup>. Often financial issues impact on the ability of the  
221 caregiver to meet the individual's healthcare needs, increasing the strain on their lives<sup>42</sup>. Substantial  
222 social/economic burden is mostly attributable to high direct non-healthcare costs<sup>43</sup>. Previous  
223 research has shown that caregivers' financial burden might be conditioned by the clinical condition of  
224 the patient<sup>44</sup>. In addition to the direct healthcare costs, caregivers of those with an RD report that  
225 their career choices are influenced due to their caring role. Furthermore, caring duties can result in

8

226 missed working days due to emergency caring demands<sup>37</sup> making it difficult for many caregivers to  
227 maintain their job and advance in their careers<sup>41</sup>. Financial hardship adversely effects the mental  
228 health of caregivers<sup>42</sup>.

229

### 230 *Psychological needs*

231 There is a lack of psychological support for families caring for children with a RD, and many report that  
232 accessing appropriate psychological care is difficult<sup>6,12</sup>. Previous research has suggested that this form  
233 of support should be offered at the time of diagnosis<sup>12,10</sup>. Depressive symptoms are often associated  
234 with caregiving burden and therefore there is a need to develop interventions in addition to  
235 promoting the existing validated tools for caregivers considering their special needs<sup>10</sup>. Caregivers  
236 often express concerns about the future<sup>32</sup>, experiencing emotional distress that can compromise the  
237 well-being of family carers, who attempt to maintain multiple roles<sup>11</sup>. Psychological interventions can  
238 help reduce stress, a sense of being burdened and feelings of isolation that many RD caregivers feel  
239<sup>45</sup>. Research has suggested that screening for depression is needed and emphasises the need for a  
240 holistic approach to family mental health in the context of chronic childhood disease<sup>46</sup>. Peer support  
241 is a key resource in terms of information and emotional support for parents who often begin their  
242 journey feeling isolated and alone<sup>21</sup>.

243

### 244 *Information and communication needs*

245 Suggestions were made that information about the condition should be given to caregivers at the time  
246 of diagnosis as well as signposting them to groups connecting families who share common experiences  
247<sup>21</sup>. Caregivers require access to accurate information, appropriate services and improved  
248 communication between patients, families, and a range of both health and social care and other public  
249 services<sup>2</sup>. Families require easily accessible services that include the family in the unit of care, provide  
250 support and information, and understand the process of family adjustment and adaptation in the long  
251 term<sup>47</sup>. Policies and structures are needed to support social and economic needs<sup>48</sup>. Engaging  
252 caregivers in future avenues of research is vital to ensure resources and funding are targeted in the  
253 best way<sup>49</sup>.

254

### 255 *Acknowledgement from healthcare professionals*

256 Out of necessity, informal carers often know more about a particular RD than healthcare providers  
257 do. This often leads to poor communication and collaboration. Furthermore a lack of coordination of  
258 care force carers to fill the gap by juggling multiple roles including that of advocate, case manager,  
259 and medical navigator<sup>50</sup>. Caregivers often experience silencing or being silenced when interacting

with health-care and social care systems and providers<sup>51</sup>. This has been attributed to the lack of knowledge about RDs by health-care providers who also are unaware of the impact that caring for someone with RD<sup>50</sup>. This points to the need to improve the knowledge of health care providers on the medical, social and financial impact these informal carers experience<sup>4</sup>. Health care providers should also acknowledge the vital role that informal caregivers play in promoting the health and quality of life of persons with an RD<sup>52</sup>. Caregivers, especially parents caring for someone with an RD, work hard to be heard and acquire services within health and social systems<sup>50</sup>. Another way that informal caregivers are silenced is due to how they are overlooked in the world of research despite growing emphasis on ensuring 'patient and public involvement'. It is vital that this pattern is changed so that they have an opportunity to be heard<sup>53 27</sup>.

270

## 271 Discussion

272 The purpose of this rapid review was to synthesise and describe what is currently known about the  
273 needs of informal caregivers for people living with an RD. Based on the findings, several  
274 recommendations for future healthcare practices and policies, as well as for research are evident.  
275 First, it is important to consider the extreme burden often experienced by these caregivers, many of  
276 whom place the need of others ahead of their own while navigating this journey with little or no  
277 support<sup>31</sup>. Support is needed to help caregivers with many aspects of their caring duties from the  
278 initial diagnosis process which has been a difficult time for many families<sup>35</sup>.

279

280 Social support would be welcomed to enable caregivers to have much needed time away from their  
281 caring duties to recharge and also to relieve them of the emotional strain which impacts on not only  
282 themselves but their wider family<sup>4</sup>. The mental strain of caregiving is evident from previous research,  
283 psychological interventions are required that consider the family as a whole to reduce the emotional  
284 strain and depression too often experienced by caregivers<sup>21 45</sup>. Many caregivers have also reported  
285 struggling financially not only due to the high costs of the practical side of caring but as a result of the  
286 impact caring can have on their ability to maintain a career<sup>41</sup>, financial support therefore a priority.

287

288 Clear information should be provided for caregivers from diagnosis through to their rare disease  
289 journey<sup>2</sup> to replace the current situation of confusion and uncertainty due to unclear and incomplete  
290 or conflicting messages. Lastly, caregivers must be recognised by healthcare professionals for the  
291 integral part they have in caring for someone with a rare disease. This relationship often changes the  
292 dynamic between health professional and patient and so caregivers must be listened to and viewed

10

293 as an 'expert'<sup>52</sup>. All of the above-mentioned issues should be taken into consideration when planning  
294 future research, it is vital that informal caregivers views are valued.

295

## 296 **Conclusion**

297 This rapid review presents several unmet needs identified by informal caregivers of persons with a RD.  
298 It is hoped that the findings contribute to increasing the amount of meaningful support for caregivers  
299 as well as encourage their active participation in improving the quality of life for families living with  
300 an RD. It is important that this cohort are engaged in future research to ensure their needs are being  
301 addressed. The insights that are gained through future research in relation to the impact on  
302 caregivers' social lives should be considered in the priorities and strategic directions for clinical  
303 services. Interventions to support them following a diagnosis would be useful, delivered either in  
304 hardcopy or online. Better meeting needs of informal caregivers for people living with a RD is in the  
305 best interests of people with a RD, healthcare professionals and policy makers, as well as caregivers.  
306 It is important that awareness is raised about the range of support options are available for informal  
307 caregivers of people with an RD from health and social care providers, charities and/or support groups  
308 <sup>27</sup>.

309

## 310 **Abbreviations**

311 RD Rare disease

312

## 313 **Declarations**

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- 315 • Consent for publication: Not applicable
- 316 • Availability of data and materials: Not applicable
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322 drafting and reviewing the original manuscript. LL & AJM contributed to study conception  
323 and design, data interpretation, project administration, supervision and reviewing  
324 manuscript drafts. All authors approved the final version of the manuscript for submission.
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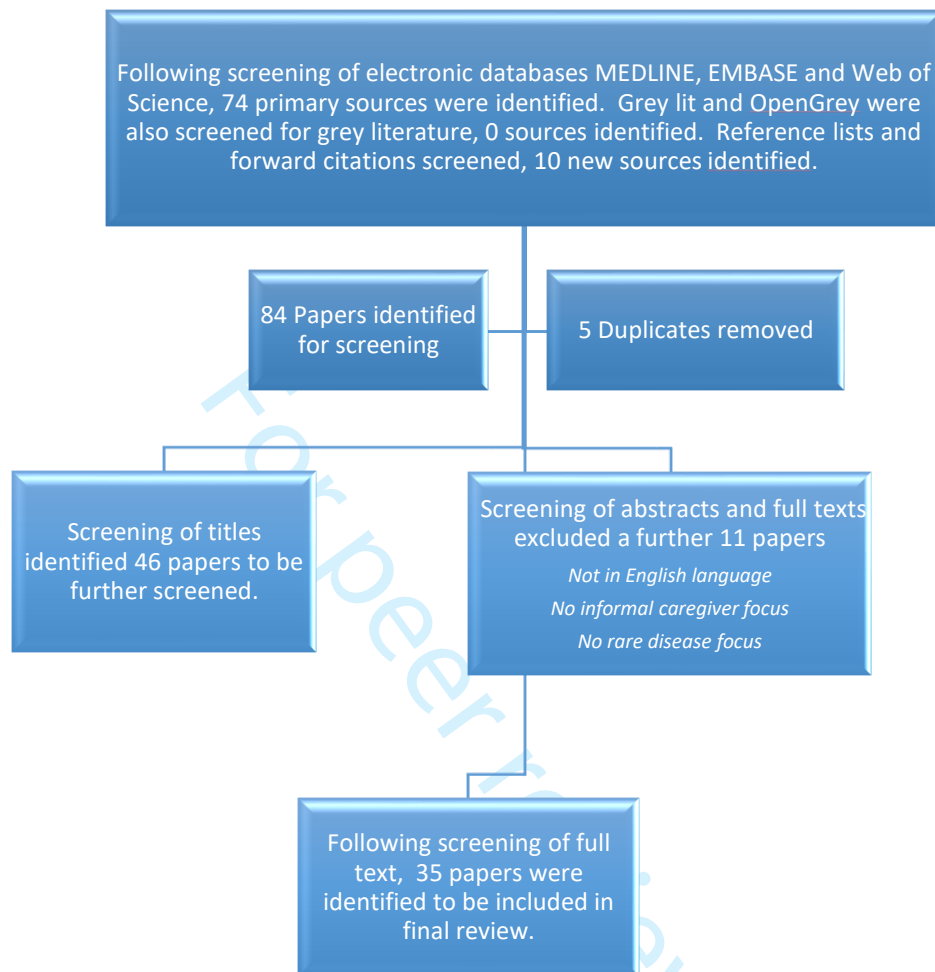


Figure 1 PRISMA flowchart



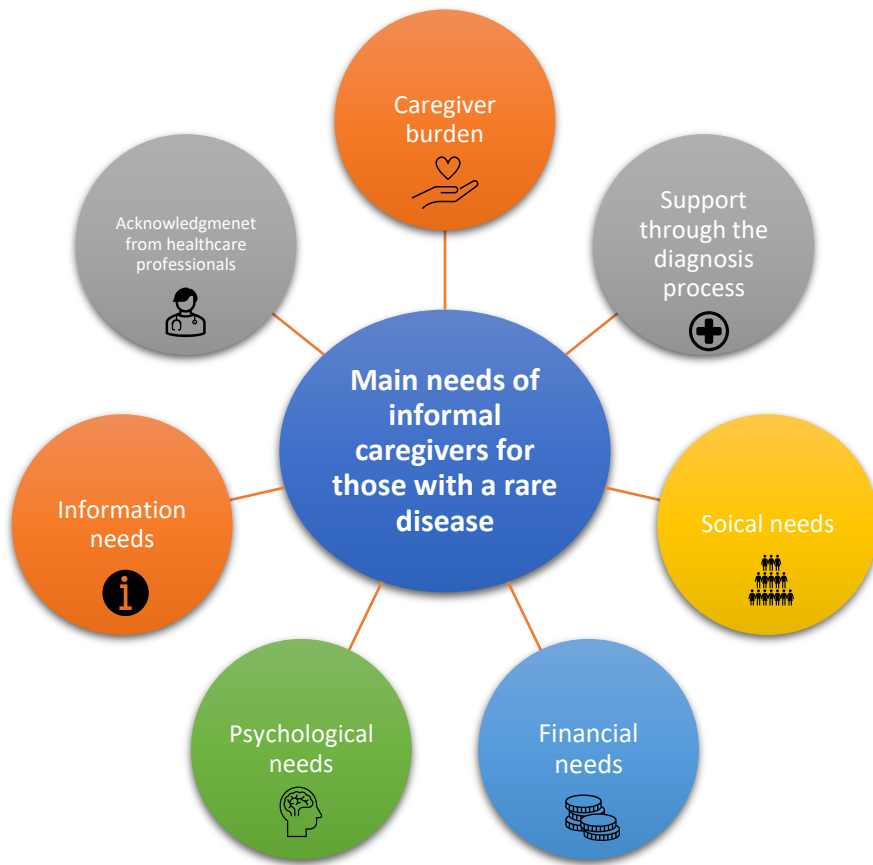


Figure 2 Main needs of caregivers for those with a rare disease

| Supplementary file 1: Data extraction table                  |  |                                      |  |  |
|--|--|--------------------------------------|--|--|
| Author & year of publication                                 | Country in which the study was conducted | Data collection method(s)            | Participants   | Identified caregiver needs   |
| Anderson, M., Elliott EJ, Zuryski YA.<br>2009                | Australia                                | Survey                               | Parents/carers   | <ul style="list-style-type: none"> <li>• Support around diagnosis.</li> <li>• Access to peer support groups.</li> <li>• Psychological support.</li> </ul>  |
| Applebaum A.J., Polacek L.C., Walsh L. <i>et al.</i><br>2020 | USA                                      | Survey and semi-structured interview | Caregivers of patients with Erdheim-Chester disease              | <ul style="list-style-type: none"> <li>• Social connections to prevent extreme isolation</li> </ul>  |
| Aubeeluck A.V. Buchanan H.E., Stupple E.J.N.<br>2011         | England                                  | Focus groups                         | Caregivers of those with Huntington's Disease                    | <ul style="list-style-type: none"> <li>• More time to focus on themselves.</li> </ul>  |
| Craig T.J., Banjerji A., Riedl M.A., <i>et al.</i><br>2021   | USA                                      | Online survey                        | Adults caring for an individual with Hereditary angioedema (HAE) | <ul style="list-style-type: none"> <li>• Recognition for the important role they have.</li> <li>• Inclusion in treatment discussions.</li> </ul>   |
| Hanbury A, Smith AB & Buesch K<br>2021                       | England                                  | Vignettes were developed             | Caregivers   | <ul style="list-style-type: none"> <li>• Engagement with research</li> </ul>   |
| Baumbusch, J., Mayer, S., & Sloan-Yip, I.<br>2018            | Canada                                   | Semi-structured interviews           | Parents of children with a RD                                    | <ul style="list-style-type: none"> <li>• Acknowledgment from healthcare providers</li> <li>• Support coordinating care</li> <li>• Peer support – information and emotional</li> <li>• Policies and programs to validate their role</li> <li>• Support from genetic counsellor to connect them to others</li> </ul> |

|  |             |                            |   |   |
|--|-------------|----------------------------|---|---|
| Bendixen, R. M., & Houtrow, A.<br>2017                             | USA         | Interviews                 | Parents of children with Duchenne muscular dystrophy          | <ul style="list-style-type: none"> <li>Listened to by healthcare providers</li> <li>Inclusion in the diagnostic process</li> <li>Improved delivery of the diagnosis</li> <li>Improved follow up after diagnosis</li> </ul>  |
| Cañedo-Ayala, M., Rice, D. B., Levis, B., et al.<br>2020           | USA         | Questionnaire              | Informal caregivers   | <ul style="list-style-type: none"> <li>Mental health support</li> </ul>   |
| Currie, G., & Szabo, J.<br>2019                                    | Canada      | Semi-structured interviews | Parents of children with RDs                                  | <ul style="list-style-type: none"> <li>Communication issues need addressed as parents often know more about the disease than healthcare providers.</li> <li>Improved coordination of care between providers and services caring for children with rare diseases.</li> <li>Gap in accessibility to government supports needs addressed.</li> </ul> |
| Currie, G., & Szabo, J.<br>2019                                    | Canada      | Semi-structured interviews | Parents of children with rare neurodevelopmental diseases     | <ul style="list-style-type: none"> <li>Health-care providers need more understanding of rare conditions.</li> <li>More support needed, parents often 'lose themselves' in this demanding caring role.</li> </ul>  |
| Flores D., Ribate M.P., Montolio M., et al.<br>2020                | Spain       | Questionnaires             | Caregivers to patients with Duchenne muscular dystrophy       | <ul style="list-style-type: none"> <li>Financial support.</li> </ul>  |
| Kanters T.A., van der Ploeg Ans. T, Brouwer W.B.F., et al.<br>2013 | Netherlands | Questionnaire              | Caregivers for those with Pompe disease.                      | <ul style="list-style-type: none"> <li>Support needed for informal caregivers.</li> </ul>   |
| Kasparian, N. A., Rutstein, A., Sansom-Daly, et al.                | Australia   | Telephone interviews       | Patients and caregivers affected by Von Hippel-Lindau disease | <ul style="list-style-type: none"> <li>More supportive care services requested.</li> </ul>  |

|   |                         |  |  |   |
|---|-------------------------|--|--|---|
| 2015  |                         |  |  |   |
| Landfelt E., Lindgren P., Bell C.F., <i>et al.</i>                    | Germany, Italy, UK, USA | Visual analogue scale, survey, interview | Caregivers to patients with Duchenne muscular dystrophy        | <ul style="list-style-type: none"> <li>• Screening for depression.</li> <li>• Holistic approach to family mental health needed.</li> </ul>  |
| 2016  |                         |  |  |   |
| Lagae, L., Irwin, J., Gibson, E., <i>et al.</i>                       | Europe                  | Survey                                   | Caregivers for those with Dravet syndrome (DS)                 | <ul style="list-style-type: none"> <li>• Time needed to escape caring duties.</li> <li>• Formal support and respite required.</li> <li>• Stress is common – support needed.</li> </ul>  |
| 2019  |                         |  |  |   |
| Lopez-Bastida J., Pena-Longobardo L.M., Aranda-Reneo I, <i>et al.</i> | Spain                   | Questionnaire                            | Patients and caregivers with Spinal Muscular Atrophy           | <ul style="list-style-type: none"> <li>• Financial support</li> <li>• QoL must be addressed</li> </ul>  |
| 2017  |                         |  |  |   |
| Lyon, M. E., Thompkins, J. D., Fratantoni, K., <i>et al.</i>          | USA                     | Semi-structured interviews               | Caregiving families  | <ul style="list-style-type: none"> <li>• Worries about the future need to be addressed.</li> <li>• More time for themselves needed.</li> <li>• Financial concerns must be addressed.</li> </ul>   |
| 2019  |                         |  |  |   |
| McKnight, A. J. M., Walker, R., Collins, C. (2020).                   | Northern Ireland        | Report                                   | N/A  | <ul style="list-style-type: none"> <li>• Access to accurate information</li> <li>• Access to appropriate services</li> <li>• Improved communication</li> </ul>  |
| 2020  |                         |  |  |   |
| McMullan, J., Crowe, A. L., Bailie, C. <i>et al.</i>                  | Northern Ireland        | Survey and semi-structured interviews    | Rare disease collaborative groups                              | <ul style="list-style-type: none"> <li>• Caregivers often overlooked in RD research – their opinions and experiences must be valued.</li> </ul>   |
| 2021  |                         |  |  |   |
| McMullan J, Crowe A.L., Downes K., <i>et al.</i>                      | Northern Ireland        | Survey and workshop                      | Caregivers of those with a rare disease                        | <ul style="list-style-type: none"> <li>• Improved interactions with healthcare professionals.</li> <li>• Improved emotional, psychological and social support.</li> <li>• Assistance with finances.</li> <li>• Better awareness of support services.</li> </ul> |
| 2015  |                         |  |  |   |
| Mooney J., Graham K. & Watts R.A.                                     | England                 | Semi-structured interviews               | Patients with ANCA-associated vasculitis and their caregivers. | <ul style="list-style-type: none"> <li>• Emotional support is needed.</li> <li>• Reassurance about the future.</li> </ul>   |

|  |           |  |   |   |
|--|-----------|--|---|---|
| 2019   |           |  |   |   |
| Mori, Y., Downs, J., Wong, K., <i>et al.</i>                               | Australia | Survey   | Families with a child with CDKL5 disorder | <ul style="list-style-type: none"> <li>Burden of daily caregiving requires support, particularly in relation to emotional wellbeing, sleep problems, financial difficulties, QoL.</li> </ul>  |
| 2017   |           |  |   |   |
| Mutch, K., Methley, A., Hamid, S., <i>et al.</i>                           | England   | Semi-structured interviews   | Partners of people with NMO               | <ul style="list-style-type: none"> <li>Acknowledgement from HCP regarding the vital role they play in caring.</li> </ul>  |
| 2017   |           |  |   |   |
| Palacios-Cena, D., Famoso-Perez, P., Salom-Moreno, J., <i>et al.</i>       | Spain     | Interviews, focus groups, researcher's field notes, caregiver's personal documents | Caregivers of children with Rett Syndrome | <ul style="list-style-type: none"> <li>Answers needed regarding 'the first symptoms' and 'the need for a diagnosis'.</li> <li>Help with managing day to day life.</li> <li>Financial support.</li> </ul>  |
| 2018   |           |  |   |   |
| Pelentsov, L. J., Fielder, A. L., & Esterman, A. J.                        | Australia | Semi-structured focus group interviews   | Parents of a child with a RD              | <ul style="list-style-type: none"> <li>Social isolation must be addressed.</li> <li>Knowledge of HCP needs to be improved.</li> <li>Support needed as family relationship often impacted due to demands of caring.</li> </ul>                                     |
| 2016   |           |  |   |   |
| Pelentsov, L. J., Laws, T. A., & Esterman, A. J.                           | Australia | Scoping Review   | Parents of child with a RD                | <ul style="list-style-type: none"> <li>Improve parental supportive care – common unmet needs between RDs.</li> </ul>  |
| 2015   |           |  |   |   |
| Rice D.B., Canedo-Ayala M., Carboni-Jimenez A., Carrier M-E, <i>et al.</i> | USA       | Online questionnaire   | Caregivers of people with SSc             | <ul style="list-style-type: none"> <li>Emotional support is required.</li> <li>Help with physical needs.</li> <li>Interventions needed delivered through hardcopy or online resources, including those delivered after the care recipient's diagnosis.</li> </ul> |
| 2020   |           |  |   |   |
| Rice D.B., Carbino-Jimenez A., Canedo-Ayala M. <i>et al.</i>               | USA       | Scoping review   | N/A                                       | <ul style="list-style-type: none"> <li>Psychosocial interventions needed to reduce caregiver's stress, burden and feelings of isolation among caregivers.</li> </ul>  |
| 2020   |           |  |   |   |

|   |             |  |  |   |
|---|-------------|--|--|---|
|   |             |  |  | <ul style="list-style-type: none"> <li>• Future research should design interventions for caregivers.</li> </ul>   |
| Rodriguez A.A., Martinez O., Amayra I, <i>et al.</i><br>2021        | Spain       | Questionnaire  | Carers of children with neuromuscular disease                        | <ul style="list-style-type: none"> <li>• Financial assistance.</li> <li>• Employment support.</li> <li>• Physical and psychological support.</li> </ul>   |
| Selman L.E., Beynon T., Radcliffe S., <i>et al.</i><br>2014         | London      | Semi-structured qualitative interviews                       | Adult informal caregivers of patients with Cutaneous T-cell lymphoma | <ul style="list-style-type: none"> <li>• Easily accessible services are needed that include the family in the unit of care, provide support and information, and understand the process of family adjustment and adaptation.</li> </ul> |
| Sloper, T., & Beresford, B.<br>2006                                 | UK          | Report   | Families of disabled children  | <ul style="list-style-type: none"> <li>• Policies and structures to support social and economic needs.</li> </ul>   |
| Somanadhan, S., & Larkin, P. J.<br>2016                             | Ireland     | In-depth interviews  | Parents of those with Mucopolysaccharidosis                          | <ul style="list-style-type: none"> <li>• Reassurance and certainty needed about the future.</li> </ul>  |
| Wiblin, L., Durcan, R., Lee, M., <i>et al.</i><br>2017              | England     | Qualitative in depth interviews                              | Patients and caregivers living with MSA and PSP                      | <ul style="list-style-type: none"> <li>• Better connections to others to reduce social isolation.</li> <li>• Improved communication.</li> </ul>   |
| Williams, J. K., Skirton, H., Paulsen, J. S., <i>et al.</i><br>2009 | USA, Canada | Focus groups   | Adult caregivers of people with Huntington's disease                 | <ul style="list-style-type: none"> <li>• Emotional distress support should be provided.</li> <li>• Assistance in managing several roles.</li> <li>• Mental health monitoring.</li> </ul>  |
| Wu, Y., Al-Janabi, H., Mallett, A., <i>et al.</i><br>2020           | Australia   | Clinical data was used from Mitochondrial Disease, Epileptic | Parents of those with rare genetic conditions                        | <ul style="list-style-type: none"> <li>• Health effects on family members need to be considered.</li> </ul>   |

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|  |  | Encephalopathy and Brain Malformation projects |  |  |
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# BMJ Open

## The needs of informal caregivers of people with a rare disease: a rapid review of the literature.

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# 1 **The needs of informal caregivers of people with a rare disease: a rapid review** 2 **of the literature.**

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## 13 14 **Abstract**

15 *Objectives:* Many people living with a rare disease are cared for by a family member. Due to a frequent  
16 lack of individual rare disease (RD) knowledge from healthcare professionals, the patient and their  
17 informal caregiver are frequently obliged to become 'experts' in their specific condition. This puts  
18 huge strain on family life and results in caregivers juggling multiple roles in addition to unique caring  
19 roles including as advocate, case manager, and medical navigator. We conducted a rapid review of  
20 literature reporting on the unmet needs of Informal caregivers for people living with a RD. All searches  
21 were conducted on 14 September 2021 followed by a manual searches of reference lists on 21  
22 September 2021.

23  
24 *Setting:* Searches were conducted in Medline, Embase, Web of Science, GreyLit and OpenGrey.

25  
26 *Results:* Thirty-five papers were included in the final review & data extracted. This rapid review  
27 presents several unmet needs identified by informal caregivers of persons with a RD. The related  
28 literature was organised thematically: caregiver burden, support through the diagnosis process, social  
29 needs, financial needs, psychological needs, information and communication needs and  
30 acknowledgement from healthcare professionals.

31  
32 *Conclusions:* This review provides evidence that increased meaningful support is required for  
33 caregivers. Active engagement should be encouraged from this cohort in future research and

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34 awareness raised of the support available to improving the quality of life for families living with an RD.  
35 The unmet needs identified through this review will benefit people living with a RD, caregivers,  
36 healthcare professionals and policy makers.

37

38 **Key words:** burden, informal caregiver, needs, rare disease, review.

39

#### 40 **Strengths and limitations**

- 41 • This study explored a cohort of individuals who frequently go unnoticed and unreported in  
42 the literature – informal caregivers of individuals diagnosed with a rare disease.
- 43 • The rapid review followed the guidelines for conducting a rapid review of the literature.
- 44 • The review was conducted by experienced researchers in the area of RD carer needs who have  
45 a wealth of relevant experience. Additionally, manual searches of reference lists were  
46 conducted to identify any papers not found by the initial search strategy.
- 47 • It is important to acknowledge limitations of this review. Due to resource constraints, only  
48 one author (JM) initially screened the titles and abstracts from the total set of documents  
49 retrieved. This could lead to bias.
- 50 • Conducting a rapid review produced results quickly, including identifying the main self-  
51 identified needs of caregivers of people living with an RD. This is particularly important given  
52 the key role that informal caregivers play, and the fact that earlier research has focused on  
53 the person with an RD and not the caregiver.

54

55 The authors of this paper consider the needs of RD caregivers a priority and recognises the value they  
56 bring to the unique caring needs.

57

#### 58 **Introduction**

59 In Europe, rare diseases (RDs) are those which affect less than 1 in 2000 people in a specified  
60 population<sup>1</sup>. Although each RD occurs infrequently, collectively RDs are a major public health issue  
61 affecting more than 450 million people globally<sup>2 3</sup>. RDs result in a wide variety of healthcare needs  
62 stemming from the involvement of multiple organ systems, such as respiratory complications, the  
63 circulatory system, muscular system, digestive system, and central nervous system. Many RDs are  
64 chronic, complex and associated with physical, intellectual, or neurological disabilities that  
65 significantly affect patients and their families. In addition, many families living with a RD lack peer and  
66 community support services<sup>4-7</sup>

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Although not always the case, family often plays a pivotal role in a person's adjustment to chronic disease and is influenced by behavioural and social factors<sup>8</sup>. Caregivers are defined as individuals who provide care for a person in need/care recipient. On the other hand informal caregivers are defined as family members or close others who provide care for the person in need with no financial benefit in return. In essence, "formal caregivers" or "caregivers" is used to denote a category of professionals or semi-professionals who provide care with financial benefit. In contrast, "informal caregivers" are typically family members or friends who provide care but have no such benefits in return (in most European countries). Caring for someone with an RD affects many areas of life including psychologically, economically, physically and logistically<sup>9</sup>. The importance of good mental and physical health for the informal caregiver is therefore vital for their own wellbeing and to ensure they can sustain the essential role of assisting the person with an RD<sup>10 11</sup>. Individuals with RDs and their families often have limited evidence-based information to guide decisions about disease management and symptom relief<sup>12 13</sup>. Further, the inherent uncertainty that comes with having a RD, including delays in diagnosis (the average time for a diagnosis of a rare disease in Northern Ireland is 5 years) and a lack of knowledge about current and future care needs<sup>14 15</sup>, impact access to services and management of the RD<sup>16</sup>. Research on the experience of having a RD indicates that care and service needs are often not based on the severity of the health condition. Rather, they are associated with poor quality of care and barriers to access leading to less satisfaction with healthcare services and care coordination<sup>15 17</sup>.

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Given the few people with a specific RD, healthcare providers often are not knowledgeable about the condition. Therefore people living with a RD and their carers have to become their own experts<sup>18</sup>. This causes a change to the usual patient-doctor relationship, which can bring challenges such as difficulties in communication and patients struggling to get sufficient accurate information to make informed choices<sup>19 20</sup>.

93

Caring for someone with a RD can be highly demanding often requiring intense and unique care specific to the individuals needs<sup>21</sup>. Delayed diagnosis, lifelong caring, limited capacity for independent living, lack of treatment options and large health service needs have severe impacts on parent's physical and psychosocial wellbeing<sup>22</sup>.

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Rapid reviews are an emerging type of knowledge synthesis used to inform health-related policy decisions and discussions, especially when information needs are immediate<sup>23-26</sup>. Rapid reviews

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2  
3 101 streamline systematic review methods – for example, by focusing the literature search <sup>23</sup> while still  
4 102 aiming to produce valid conclusions. The requirements of the review, which was undertaken with a  
5 103 short deadline, were for a short but in-depth synthesis of the current state of the issues facing  
6 104 caregivers for those with a rare disease.

105

11 106 This review focuses on informal caregivers for people living with a RD. We were particularly interested  
12 107 in their holistic needs when caring for this unique population and how these may differ from other  
13 108 caring populations where there is often more support available e.g. carers of people with dementia or  
14 109 cancer.

110

## 111 **Methodology**

### 112 *Search strategy and inclusion criteria*

113 Three electronic databases were searched -- Medline, Embase and Web of Science -- using the  
114 combined terms 'informal caregiver\*' and 'rare disease\*'. All searches were conducted on 14  
115 September 2021, with no date restrictions. Reference lists of included papers were screened for  
116 further sources. A search was also conducted of grey literature using the databases GreyLit and  
117 OpenGrey. Duplicates and non-English language articles were excluded. The criteria for inclusion  
118 were articles that address caregiving for people living with an RD. Articles on caregiving alone or RD  
119 alone were excluded. A simplified list of databases and the number of papers retrieved is shown in  
120 Table 1.

121

### 122 *Study selection and data extraction*

123 Database searches were last conducted on 14 September 2021 by JM. Titles and abstracts of the  
124 identified articles were downloaded onto Endnote. Duplicate articles were removed and the  
125 remaining papers were screened through analysing their titles and abstracts. Additionally, manual  
126 searches of reference lists were conducted on 21 September 2021 to identify any papers not found by  
127 the initial search strategy. If relevant, the papers were then further screened by reading the full text.  
128 Data were extracted by JM who recorded the follow data for each study:

129

- 130 • Author & year of publication
- 131 • Country in which the study was conducted
- 132 • Data collection method(s)
- 133 • Participants
- 134 • Identified caregiver needs

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5 136 The identified caregiver needs were extracted from the included papers [JM] and presented the data  
6  
7 137 extraction table [AMcK, JM & LL] (Supplementary file 1). From this, common needs were grouped  
8  
9 138 together under headings which became the themes for this review. The themes and content for the  
10  
11 139 themes was agreed between the research team [AMcK, JM & LL].  
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141 **Table 1: Literature search results**

| Database       | No. of articles retrieved | No. of articles included in review |
|----------------|---------------------------|------------------------------------|
| Medline        | 6                         | 5                                  |
| Embase         | 6                         | 5                                  |
| Web of Science | 62                        | 13                                 |
| GreyLit        | 0                         | 0                                  |
| OpenGrey       | 0                         | 0                                  |

142 **This table shows the number of articles identified from each database before reference lists were checked.**

143

144 An illustration of the search strategy including databases searched and screening methods is  
145 displayed in Figure 1, modelled on the PRISMA flow diagram.

146

#### 147 *Patient and Public Involvement*

148 The need for this review was highlighted by a priorities workshop in 2020, which considered  
149 contributions from >2,000 individuals living with rare disease. The review was also shared with  
150 representatives from a local rare disease charity in Northern Ireland (the Northern Ireland Rare  
151 Disease Partnership).

152

## 153 **Results**

### 154 *General description of the literature*

155 Sources initially identified from each database were as follows: MEDLINE  $n=6$ , Embase  $n=6$ , Web of  
156 Science  $n=62$ , OpenGrey  $n=0$  and GreyLit  $n=0$ . The screening process resulted in 30 documents which  
157 were reviewed based on their titles and abstracts. Following the screening 5 duplicate papers were  
158 removed and 25 papers were identified for full text screening. Further studies were identified from  
159 searching the reference lists. Finally, 35 texts were included in the full review, with characteristics of  
160 each source summarised from the completed data extraction table (Supplementary file 1).

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3 161 Of the texts included, publication dates were from 2006 to 2021 and the studies were conducted in  
4  
5 162 Australia, Canada, Germany, Ireland, Italy, Netherlands, Spain, United Kingdom and the United States.  
6  
7 163 The identified studies focus on many rare diseases including Hereditary angioedema, Huntington's  
8  
9 164 Disease, Duchenne muscular dystrophy and Von Hippel-Lindau disease.

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12  
13 166 A narrative review is presented below, highlighting the main needs of caregivers of people living with  
14  
15 167 an RD. The related literature has been organised thematically under the following headings:

- 16  
17 168 • Caregiver burden  
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19 169 • Support through the diagnosis process  
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21 170 • Social needs  
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23 171 • Financial needs  
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25 172 • Psychological needs  
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27 173 • Information and communication needs  
28  
29 174 • Acknowledgement from healthcare professionals

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32 176 Findings from these studies were organised thematically under the following headings as shown  
33  
34 177 visually in Figure 2.

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36 178

37  
38 179 *Caregiver burden*

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40  
41 180 Caring for someone with an RD presents a range of challenges<sup>27 28</sup> that are affected by the severity of  
42  
43 181 the illness and its duration, knowledge about the condition and its changes over time, and one's ability  
44  
45 182 to address the emotional toll involved with long-term care<sup>29</sup>. Despite the stress and difficulties  
46  
47 183 associated with being a family caregiver<sup>30</sup>, often they acknowledge the positive aspects of caring for  
48  
49 184 their loved ones<sup>30</sup>.

50  
51 185

52  
53 186 The quality of life of caregivers is often compromised by their placing others' needs before their own  
54  
55 187 <sup>31</sup>. Previous research has shown that informal caregivers do not have enough time for themselves,<sup>32</sup>  
56  
57 188 and that caring for someone with an RD can negatively impact on all dimensions of family life<sup>33</sup>.  
58  
59 189 Informal caregivers are often forced to miss work or school days due to the demands of their role,  
60  
61 190 frequently address unpleasant events and watch a loved one suffer<sup>28</sup>. Consequently, they would  
62  
63 191 benefit greatly from support to reduce the burden of caring for example from support groups, respite

7

192 care and employment arrangements<sup>34</sup>. This includes both supports for informal carers of people with  
193 a variety of health issues, as well as for RD-related issues<sup>34</sup>.

194

#### 195 *Support through the diagnosis process*

196 In spite of marked medical progress over the past several decades in identifying an RD, there are  
197 substantial delays in diagnosing these conditions<sup>35</sup>. This can have adverse impacts on families, for  
198 example, financial and mental health<sup>12</sup>. Little attention is given to parent concern in the diagnostic  
199 process with previous research reporting concerns regarding how the diagnosis was delivered to  
200 parents, lack of guidance and poor follow-up post diagnosis<sup>35</sup>. Previous research has shown that  
201 families are often dissatisfied by the way in which a diagnosis is given, including an insensitive style of  
202 communication, not offering support or counselling, and inadequate provision of information about  
203 the disease. This can cause emotional stress for caregivers who have not yet learned about the  
204 condition and how it will affect them and their families. Therefore, interventions to support the  
205 following a diagnosis would be useful, delivered either in hardcopy or online<sup>36</sup>.

206

#### 207 *Social needs*

208 Social isolation is common among informal caregivers with the impact on personal relationships being  
209 a reoccurring theme<sup>4 5</sup>. All too often, informal caregivers have little time to themselves and lack  
210 appropriate support and time for respite. This in turn causes further emotional stress and in the case  
211 of parents, uncertainty about their child's future<sup>37</sup>. Parents of children with an RD often feel isolated  
212 from mainstream society and struggle to stay socially connected<sup>4</sup>. It was suggested that the insights  
213 gained through research studies regarding the impact on caregivers' social lives should be considered  
214 in future clinical service planning. Additionally holistic, empathic, and person-centred medical and  
215 psychosocial care is urgently needed for this cohort<sup>6</sup>. Support is needed as relationships among  
216 family members are often impacted due to demands of caring<sup>4</sup>. There is a need for improved parental  
217 supportive care as many common unmet needs exist across RDs<sup>38</sup>.

218

#### 219 *Financial needs*

220 Previous research has indicated that financial issues are a top concern of caregivers of persons with  
221 RD<sup>30 6 39 27</sup>. The high economic costs that families must cover means that financial burden is common  
222 among caregivers of those with an RD, many of whom are forced to exhaust their financial savings<sup>40</sup>.  
223 Purchasing equipment, hiring professionals, and the additional financial burden the illness has on  
224 families poses immense stress on family life<sup>41</sup>. Often financial issues impact on the ability of the  
225 caregiver to meet the individual's healthcare needs, increasing the strain on their lives<sup>42</sup>. Substantial



226 social/economic burden is mostly attributable to high direct non-healthcare costs<sup>43</sup>. Previous  
227 research has shown that caregivers' financial burden might be conditioned by the clinical condition of  
228 the patient<sup>44</sup>. In addition to the direct healthcare costs, caregivers of those with an RD report that  
229 their career choices are influenced due to their caring role. Furthermore, caring duties can result in  
230 missed working days due to emergency caring demands<sup>37</sup> making it difficult for many caregivers to  
231 maintain their job and advance in their careers<sup>41</sup>. Financial hardship adversely effects the mental  
232 health of caregivers<sup>42</sup>.

233

#### 234 *Psychological needs*

235 There is a lack of psychological support for families caring for children with a RD, and many report that  
236 accessing appropriate psychological care is difficult<sup>6,12</sup>. Previous research has suggested that this form  
237 of support should be offered at the time of diagnosis<sup>12,10</sup>. Depressive symptoms are often associated  
238 with caregiving burden and therefore there is a need to develop interventions in addition to  
239 promoting the existing validated tools for caregivers considering their special needs<sup>10</sup>. Caregivers  
240 often express concerns about the future<sup>32</sup>, experiencing emotional distress that can compromise the  
241 well-being of family carers, who attempt to maintain multiple roles<sup>11</sup>. Psychological interventions can  
242 help reduce stress, a sense of being burdened and feelings of isolation that many RD caregivers feel  
243<sup>45</sup>. Research has suggested that screening for depression is needed and emphasises the need for a  
244 holistic approach to family mental health in the context of chronic childhood disease<sup>46</sup>. Peer support  
245 is a key resource in terms of information and emotional support for parents who often begin their  
246 journey feeling isolated and alone<sup>21</sup>.

247

#### 248 *Information and communication needs*

249 Suggestions were made that information about the condition should be given to caregivers at the time  
250 of diagnosis as well as signposting them to groups connecting families who share common experiences  
251<sup>21</sup>. Caregivers require access to accurate information, appropriate services and improved  
252 communication between patients, families, and a range of both health and social care and other public  
253 services<sup>2</sup>. Families require easily accessible services that include the family in the unit of care, provide  
254 support and information, and understand the process of family adjustment and adaptation in the long  
255 term<sup>47</sup>. Policies and structures are needed to support social and economic needs<sup>48</sup>. Engaging  
256 caregivers in future avenues of research is vital to ensure resources and funding are targeted in the  
257 best way<sup>49</sup>.

258

#### 259 *Acknowledgement from healthcare professionals*

260 Out of necessity, informal carers often know more about a particular RD than healthcare providers  
261 do. This often leads to poor communication and collaboration. Furthermore a lack of coordination of  
262 care force carers to fill the gap by juggling multiple roles including that of advocate, case manager,  
263 and medical navigator <sup>50</sup>. Caregivers often experience silencing or being silenced when interacting  
264 with health-care and social care systems and providers <sup>51</sup>. This has been attributed to the lack of  
265 knowledge about RDs by health-care providers who also are unaware of the impact that caring for  
266 someone with RD <sup>50</sup>. This points to the need to improve the knowledge of health care providers on  
267 the medical, social and financial impact these informal carers experience <sup>4</sup>. Health care providers  
268 should also acknowledge the vital role that informal caregivers play in promoting the health and  
269 quality of life of persons with an RD <sup>52</sup>. Caregivers, especially parents caring for someone with an RD,  
270 work hard to be heard and acquire services within health and social systems <sup>50</sup>. Another way that  
271 informal caregivers are silenced is due to how they are overlooked in the world of research despite  
272 growing emphasis on ensuring 'patient and public involvement'. It is vital that this pattern is changed  
273 so that they have an opportunity to be heard <sup>53 27</sup>.

## 275 Discussion

276 The purpose of this rapid review was to synthesise and describe what is currently known about the  
277 needs of informal caregivers for people living with an RD. Based on the findings, several  
278 recommendations for future healthcare practices and policies, as well as for research are evident.  
279 First, it is important to consider the extreme burden often experienced by these caregivers, many of  
280 whom place the need of others ahead of their own while navigating this journey with little or no  
281 support <sup>31</sup>. Support is needed to help caregivers with many aspects of their caring duties from the  
282 initial diagnosis process which has been a difficult time for many families <sup>35</sup>.

284 Social support would be welcomed to enable caregivers to have much needed time away from their  
285 caring duties to recharge and also to relieve them of the emotional strain which impacts on not only  
286 themselves but their wider family <sup>4</sup>. The mental strain of caregiving is evident from previous research,  
287 psychological interventions are required that consider the family as a whole to reduce the emotional  
288 strain and depression too often experienced by caregivers <sup>21 45</sup>. Many caregivers have also reported  
289 struggling financially not only due to the high costs of the practical side of caring but as a result of the  
290 impact caring can have on their ability to maintain a career <sup>41</sup>, financial support therefore a priority.

291

292 Clear information should be provided for caregivers from diagnosis through to their rare disease  
293 journey <sup>2</sup> to replace the current situation of confusion and uncertainty due to unclear and incomplete

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294 or conflicting messages. Lastly, caregivers must be recognised by healthcare professionals for the  
295 integral part they have in caring for someone with a rare disease. This relationship often changes the  
296 dynamic between health professional and patient and so caregivers must be listened to and viewed  
297 as an 'expert'<sup>52</sup>. All of the above-mentioned issues should be taken into consideration when planning  
298 future research, it is vital that informal caregivers views are valued.

299

### 300 **Conclusion**

301 This rapid review presents several unmet needs identified by informal caregivers of persons with a RD.  
302 It is hoped that the findings contribute to increasing the amount of meaningful support for caregivers  
303 as well as encourage their active participation in improving the quality of life for families living with  
304 an RD. It is important that this cohort are engaged in future research to ensure their needs are being  
305 addressed. The insights that are gained through future research in relation to the impact on  
306 caregivers' social lives should be considered in the priorities and strategic directions for clinical  
307 services. Interventions to support them following a diagnosis would be useful, delivered either in  
308 hardcopy or online. Better meeting needs of informal caregivers for people living with a RD is in the  
309 best interests of people with a RD, healthcare professionals and policy makers, as well as caregivers.  
310 It is important that awareness is raised about the range of support options that are available from  
311 health and social care providers, charities and/or support groups for informal caregivers of people  
312 with an RD<sup>27</sup>.

313

### 314 **Abbreviations**

315 RD Rare disease

316

### 317 **Declarations**

- 318 • Ethics approval and consent to participate: Not applicable
- 319 • Consent for publication: Not applicable
- 320 • Availability of data and materials: Not applicable
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- 325 • Authors' contributions: JM contributed to data curation, formal analysis, data interpretation,  
326 drafting and reviewing the original manuscript. LL & AJM contributed to study conception

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3 327 and design, data interpretation, project administration, supervision and reviewing  
 4 328 manuscript drafts. All authors approved the final version of the manuscript for submission.

6 329 • Acknowledgements: Not applicable

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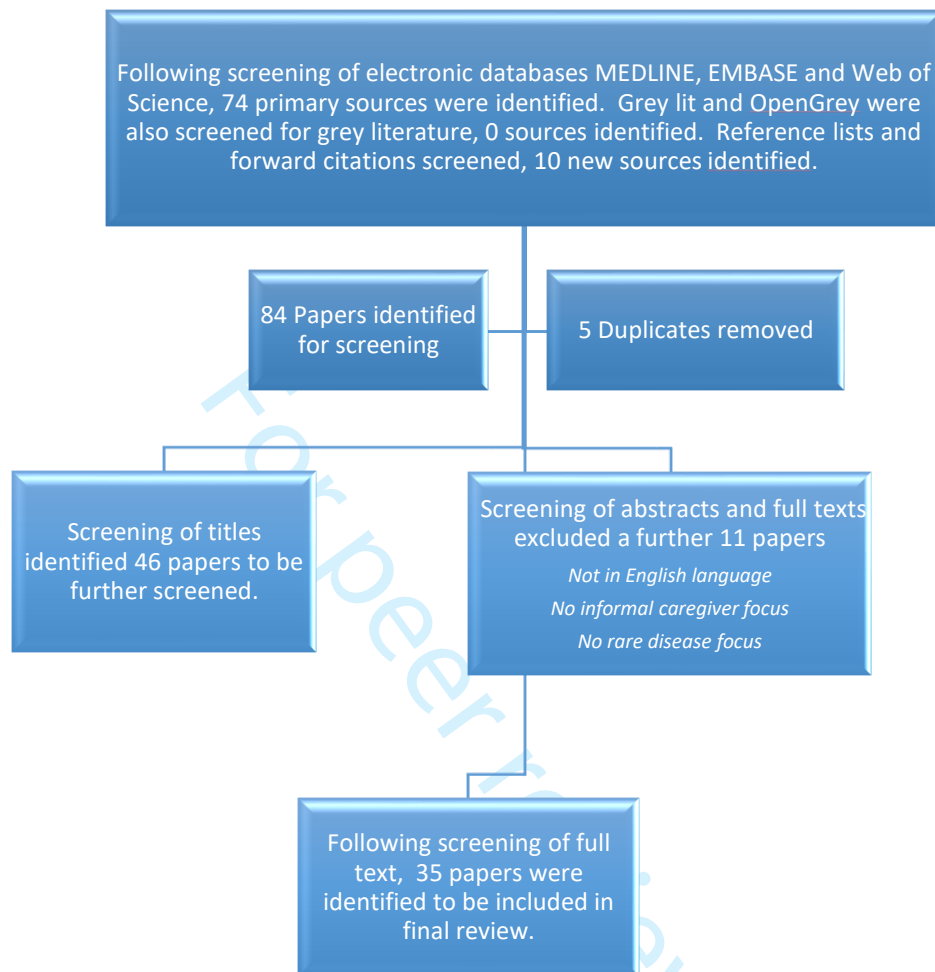


Figure 1 PRISMA flowchart

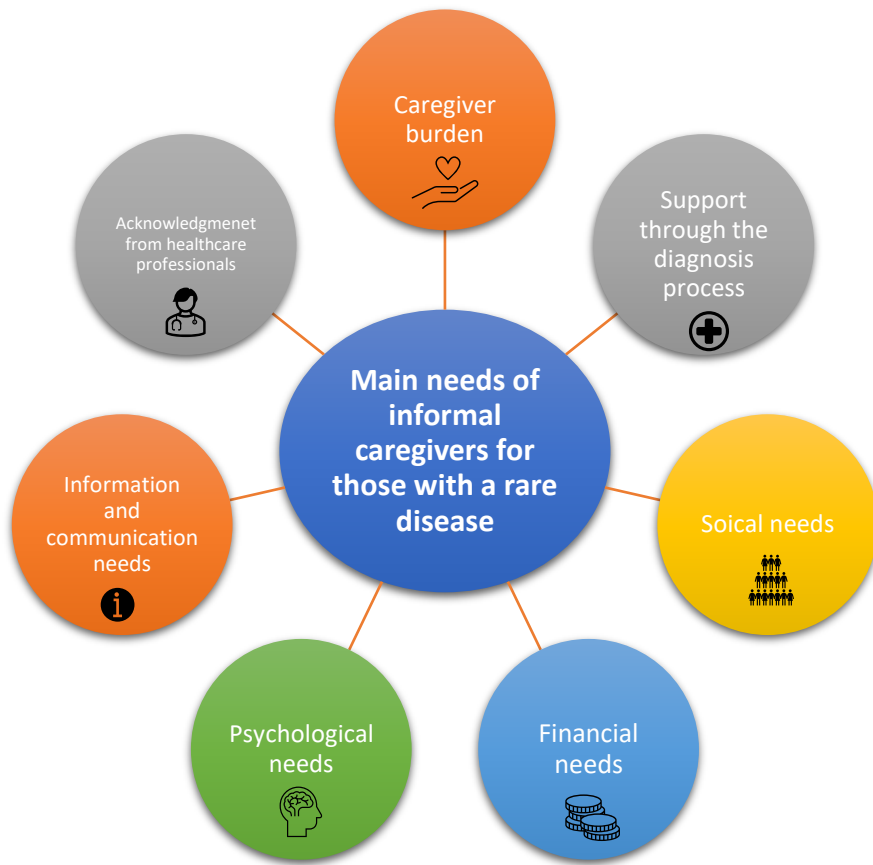


Figure 2 Main needs of caregivers for those with a rare disease

Review only

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| <b>Supplementary file 1: Data extraction table</b>               |   |                                      |  |  |
|--|---|--------------------------------------|--|--|
| <b>Author &amp; year of publication</b>                          | <b>Country in which the study was conducted</b> | <b>Data collection method(s)</b>     | <b>Participants</b>  | <b>Identified caregiver needs</b>  |
| Anderson, M., Elliott EJ, Zuryski YA.<br><br>2009                | Australia                                       | Survey                               | Parents/carers   | <ul style="list-style-type: none"> <li>• Support around diagnosis.</li> <li>• Access to peer support groups.</li> <li>• Psychological support.</li> </ul>  |
| Applebaum A.J., Polacek L.C., Walsh L. <i>et al.</i><br><br>2020 | USA   | Survey and semi-structured interview | Caregivers of patients with Erdheim-Chester disease              | <ul style="list-style-type: none"> <li>• Social connections to prevent extreme isolation</li> </ul>  |
| Aubeeluck A.V. Buchanan H.E., Stupple E.J.N.<br><br>2011         | England   | Focus groups                         | Caregivers of those with Huntington's Disease                    | <ul style="list-style-type: none"> <li>• More time to focus on themselves.</li> </ul>  |
| Craig T.J., Banjerji A., Riedl M.A., <i>et al.</i><br><br>2021   | USA   | Online survey                        | Adults caring for an individual with Hereditary angioedema (HAE) | <ul style="list-style-type: none"> <li>• Recognition for the important role they have.</li> <li>• Inclusion in treatment discussions.</li> </ul>   |
| Hanbury A, Smith AB & Buesch K<br><br>2021                       | England   | Vignettes were developed             | Caregivers   | <ul style="list-style-type: none"> <li>• Engagement with research</li> </ul>   |
| Baumbusch, J., Mayer, S., & Sloan-Yip, I.<br><br>2018            | Canada  | Semi-structured interviews           | Parents of children with a RD                                    | <ul style="list-style-type: none"> <li>• Acknowledgment from healthcare providers</li> <li>• Support coordinating care</li> <li>• Peer support – information and emotional</li> <li>• Policies and programs to validate their role</li> <li>• Support from genetic counsellor to connect them to others</li> </ul> |

|  |             |                            |   |   |
|--|-------------|----------------------------|---|---|
| Bendixen, R. M., & Houtrow, A.<br>2017                             | USA         | Interviews                 | Parents of children with Duchenne muscular dystrophy          | <ul style="list-style-type: none"> <li>Listened to by healthcare providers</li> <li>Inclusion in the diagnostic process</li> <li>Improved delivery of the diagnosis</li> <li>Improved follow up after diagnosis</li> </ul>  |
| Cañedo-Ayala, M., Rice, D. B., Levis, B., et al.<br>2020           | USA         | Questionnaire              | Informal caregivers   | <ul style="list-style-type: none"> <li>Mental health support</li> </ul>   |
| Currie, G., & Szabo, J.<br>2019                                    | Canada      | Semi-structured interviews | Parents of children with RDs                                  | <ul style="list-style-type: none"> <li>Communication issues need addressed as parents often know more about the disease than healthcare providers.</li> <li>Improved coordination of care between providers and services caring for children with rare diseases.</li> <li>Gap in accessibility to government supports needs addressed.</li> </ul> |
| Currie, G., & Szabo, J.<br>2019                                    | Canada      | Semi-structured interviews | Parents of children with rare neurodevelopmental diseases     | <ul style="list-style-type: none"> <li>Health-care providers need more understanding of rare conditions.</li> <li>More support needed, parents often 'lose themselves' in this demanding caring role.</li> </ul>  |
| Flores D., Ribate M.P., Montolio M., et al.<br>2020                | Spain       | Questionnaires             | Caregivers to patients with Duchenne muscular dystrophy       | <ul style="list-style-type: none"> <li>Financial support.</li> </ul>  |
| Kanters T.A., van der Ploeg Ans. T, Brouwer W.B.F., et al.<br>2013 | Netherlands | Questionnaire              | Caregivers for those with Pompe disease.                      | <ul style="list-style-type: none"> <li>Support needed for informal caregivers.</li> </ul>   |
| Kasparian, N. A., Rutstein, A., Sansom-Daly, et al.                | Australia   | Telephone interviews       | Patients and caregivers affected by Von Hippel-Lindau disease | <ul style="list-style-type: none"> <li>More supportive care services requested.</li> </ul>  |

|   |                         |  |  |   |
|---|-------------------------|--|--|---|
| 2015  |                         |  |  |   |
| Landfelt E., Lindgren P., Bell C.F., <i>et al.</i>                    | Germany, Italy, UK, USA | Visual analogue scale, survey, interview | Caregivers to patients with Duchenne muscular dystrophy        | <ul style="list-style-type: none"> <li>• Screening for depression.</li> <li>• Holistic approach to family mental health needed.</li> </ul>  |
| 2016  |                         |  |  |   |
| Lagae, L., Irwin, J., Gibson, E., <i>et al.</i>                       | Europe                  | Survey                                   | Caregivers for those with Dravet syndrome (DS)                 | <ul style="list-style-type: none"> <li>• Time needed to escape caring duties.</li> <li>• Formal support and respite required.</li> <li>• Stress is common – support needed.</li> </ul>  |
| 2019  |                         |  |  |   |
| Lopez-Bastida J., Pena-Longobardo L.M., Aranda-Reneo I, <i>et al.</i> | Spain                   | Questionnaire                            | Patients and caregivers with Spinal Muscular Atrophy           | <ul style="list-style-type: none"> <li>• Financial support</li> <li>• QoL must be addressed</li> </ul>  |
| 2017  |                         |  |  |   |
| Lyon, M. E., Thompkins, J. D., Fratantoni, K., <i>et al.</i>          | USA                     | Semi-structured interviews               | Caregiving families  | <ul style="list-style-type: none"> <li>• Worries about the future need to be addressed.</li> <li>• More time for themselves needed.</li> <li>• Financial concerns must be addressed.</li> </ul>   |
| 2019  |                         |  |  |   |
| McKnight, A. J. M., Walker, R., Collins, C. (2020).                   | Northern Ireland        | Report                                   | N/A  | <ul style="list-style-type: none"> <li>• Access to accurate information</li> <li>• Access to appropriate services</li> <li>• Improved communication</li> </ul>  |
| McMullan, J., Crowe, A. L., Bailie, C. <i>et al.</i>                  | Northern Ireland        | Survey and semi-structured interviews    | Rare disease collaborative groups                              | <ul style="list-style-type: none"> <li>• Caregivers often overlooked in RD research – their opinions and experiences must be valued.</li> </ul>   |
| 2020  |                         |  |  |   |
| McMullan J, Crowe A.L., Downes K., <i>et al.</i>                      | Northern Ireland        | Survey and workshop                      | Caregivers of those with a rare disease                        | <ul style="list-style-type: none"> <li>• Improved interactions with healthcare professionals.</li> <li>• Improved emotional, psychological and social support.</li> <li>• Assistance with finances.</li> <li>• Better awareness of support services.</li> </ul> |
| 2021  |                         |  |  |   |
| Mooney J., Graham K. & Watts R.A.                                     | England                 | Semi-structured interviews               | Patients with ANCA-associated vasculitis and their caregivers. | <ul style="list-style-type: none"> <li>• Emotional support is needed.</li> <li>• Reassurance about the future.</li> </ul>   |

|  |           |  |   |   |
|--|-----------|--|---|---|
| 2019   |           |  |   |   |
| Mori, Y., Downs, J., Wong, K., <i>et al.</i>                               | Australia | Survey   | Families with a child with CDKL5 disorder | <ul style="list-style-type: none"> <li>Burden of daily caregiving requires support, particularly in relation to emotional wellbeing, sleep problems, financial difficulties, QoL.</li> </ul>  |
| 2017   |           |  |   |   |
| Mutch, K., Methley, A., Hamid, S., <i>et al.</i>                           | England   | Semi-structured interviews   | Partners of people with NMO               | <ul style="list-style-type: none"> <li>Acknowledgement from HCP regarding the vital role they play in caring.</li> </ul>  |
| 2017   |           |  |   |   |
| Palacios-Cena, D., Famoso-Perez, P., Salom-Moreno, J., <i>et al.</i>       | Spain     | Interviews, focus groups, researcher's field notes, caregiver's personal documents | Caregivers of children with Rett Syndrome | <ul style="list-style-type: none"> <li>Answers needed regarding 'the first symptoms' and 'the need for a diagnosis'.</li> <li>Help with managing day to day life.</li> <li>Financial support.</li> </ul>  |
| 2018   |           |  |   |   |
| Pelentsov, L. J., Fielder, A. L., & Esterman, A. J.                        | Australia | Semi-structured focus group interviews   | Parents of a child with a RD              | <ul style="list-style-type: none"> <li>Social isolation must be addressed.</li> <li>Knowledge of HCP needs to be improved.</li> <li>Support needed as family relationship often impacted due to demands of caring.</li> </ul>                                     |
| 2016   |           |  |   |   |
| Pelentsov, L. J., Laws, T. A., & Esterman, A. J.                           | Australia | Scoping Review   | Parents of child with a RD                | <ul style="list-style-type: none"> <li>Improve parental supportive care – common unmet needs between RDs.</li> </ul>  |
| 2015   |           |  |   |   |
| Rice D.B., Canedo-Ayala M., Carboni-Jimenez A., Carrier M-E, <i>et al.</i> | USA       | Online questionnaire   | Caregivers of people with SSc             | <ul style="list-style-type: none"> <li>Emotional support is required.</li> <li>Help with physical needs.</li> <li>Interventions needed delivered through hardcopy or online resources, including those delivered after the care recipient's diagnosis.</li> </ul> |
| 2020   |           |  |   |   |
| Rice D.B., Carbino-Jimenez A., Canedo-Ayala M. <i>et al.</i>               | USA       | Scoping review   | N/A                                       | <ul style="list-style-type: none"> <li>Psychosocial interventions needed to reduce caregiver's stress, burden and feelings of isolation among caregivers.</li> </ul>  |
| 2020   |           |  |   |   |

|   |             |  |  |   |
|---|-------------|--|--|---|
|   |             |  |  | <ul style="list-style-type: none"> <li>• Future research should design interventions for caregivers.</li> </ul>   |
| Rodriguez A.A., Martinez O., Amayra I, <i>et al.</i><br>2021        | Spain       | Questionnaire  | Carers of children with neuromuscular disease                        | <ul style="list-style-type: none"> <li>• Financial assistance.</li> <li>• Employment support.</li> <li>• Physical and psychological support.</li> </ul>   |
| Selman L.E., Beynon T., Radcliffe S., <i>et al.</i><br>2014         | London      | Semi-structured qualitative interviews                       | Adult informal caregivers of patients with Cutaneous T-cell lymphoma | <ul style="list-style-type: none"> <li>• Easily accessible services are needed that include the family in the unit of care, provide support and information, and understand the process of family adjustment and adaptation.</li> </ul> |
| Sloper, T., & Beresford, B.<br>2006                                 | UK          | Report   | Families of disabled children  | <ul style="list-style-type: none"> <li>• Policies and structures to support social and economic needs.</li> </ul>   |
| Somanadhan, S., & Larkin, P. J.<br>2016                             | Ireland     | In-depth interviews  | Parents of those with Mucopolysaccharidosis                          | <ul style="list-style-type: none"> <li>• Reassurance and certainty needed about the future.</li> </ul>  |
| Wiblin, L., Durcan, R., Lee, M., <i>et al.</i><br>2017              | England     | Qualitative in depth interviews                              | Patients and caregivers living with MSA and PSP                      | <ul style="list-style-type: none"> <li>• Better connections to others to reduce social isolation.</li> <li>• Improved communication.</li> </ul>   |
| Williams, J. K., Skirton, H., Paulsen, J. S., <i>et al.</i><br>2009 | USA, Canada | Focus groups   | Adult caregivers of people with Huntington's disease                 | <ul style="list-style-type: none"> <li>• Emotional distress support should be provided.</li> <li>• Assistance in managing several roles.</li> <li>• Mental health monitoring.</li> </ul>  |
| Wu, Y., Al-Janabi, H., Mallett, A., <i>et al.</i><br>2020           | Australia   | Clinical data was used from Mitochondrial Disease, Epileptic | Parents of those with rare genetic conditions                        | <ul style="list-style-type: none"> <li>• Health effects on family members need to be considered.</li> </ul>   |

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|  |  | Encephalopathy and Brain Malformation projects |  |  |
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## PRISMA 2020 Checklist

| Section and Topic             | Item # | Checklist item   | Location where item is reported |
|-------------------------------|--------|--|---------------------------------|
| <b>TITLE</b>                  |        |  |                                 |
| Title                         | 1      | Identify the report as a systematic review.  | N/A                             |
| <b>ABSTRACT</b>               |        |  |                                 |
| Abstract                      | 2      | See the PRISMA 2020 for Abstracts checklist.   | N/A                             |
| <b>INTRODUCTION</b>           |        |  |                                 |
| Rationale                     | 3      | Describe the rationale for the review in the context of existing knowledge.  | 97-107                          |
| Objectives                    | 4      | Provide an explicit statement of the objective(s) or question(s) the review addresses.   | 104-107                         |
| <b>METHODS</b>                |        |  |                                 |
| Eligibility criteria          | 5      | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.  | 111-118                         |
| Information sources           | 6      | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.  | 111-126                         |
| Search strategy               | 7      | Present the full search strategies for all databases, registers and websites, including any filters and limits used.   | 111-126                         |
| Selection process             | 8      | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.                     | 121-137                         |
| Data collection process       | 9      | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | 122-139                         |
| Data items                    | 10a    | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.                        | N/A                             |
|                               | 10b    | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.   | N/A                             |
| Study risk of bias assessment | 11     | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.                                    | N/A                             |
| Effect measures               | 12     | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.  | N/A                             |
| Synthesis methods             | 13a    | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).   | N/A                             |
|                               | 13b    | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.  | N/A                             |
|                               | 13c    | Describe any methods used to tabulate or visually display results of individual studies and syntheses.   | N/A                             |
|                               | 13d    | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.  | N/A                             |
|                               | 13e    | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).   | N/A                             |
|                               | 13f    | Describe any sensitivity analyses conducted to assess robustness of the synthesized results.   | N/A                             |
| Reporting bias assessment     | 14     | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).  | N/A                             |
| Certainty                     | 15     | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.  | N/A                             |



# PRISMA 2020 Checklist

| Section and Topic                     | Item # | Checklist item   | Location where item is reported   |
|---------------------------------------|--------|--|---|
| assessment                            |        |  |   |
| <b>RESULTS</b>                        |        |  |   |
| Study selection                       | 16a    | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.   | Figure 1  |
|                                       | 16b    | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.  | 114-117   |
| Study characteristics                 | 17     | Cite each included study and present its characteristics.  | Supp file 1   |
| Risk of bias in studies               | 18     | Present assessments of risk of bias for each included study.   | N/A   |
| Results of individual studies         | 19     | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.   | N/A   |
| Results of syntheses                  | 20a    | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.   | N/A   |
|                                       | 20b    | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | N/A   |
|                                       | 20c    | Present results of all investigations of possible causes of heterogeneity among study results.   | N/A   |
|                                       | 20d    | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.   | N/A   |
| Reporting biases                      | 21     | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.  | N/A   |
| Certainty of evidence                 | 22     | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.  | N/A   |
| <b>DISCUSSION</b>                     |        |  |   |
| Discussion                            | 23a    | Provide a general interpretation of the results in the context of other evidence.  | 273-296   |
|                                       | 23b    | Discuss any limitations of the evidence included in the review.  | 38-51   |
|                                       | 23c    | Discuss any limitations of the review processes used.  | 38-51   |
|                                       | 23d    | Discuss implications of the results for practice, policy, and future research.   | 299-310   |
| <b>OTHER INFORMATION</b>              |        |  |   |
| Registration and protocol             | 24a    | Provide registration information for the review, including register name and registration number, or state that the review was not registered.   | N/A   |
|                                       | 24b    | Indicate where the review protocol can be accessed, or state that a protocol was not prepared.   | a review protocol was prepared and followed as described in the methods |
|                                       | 24c    | Describe and explain any amendments to information provided at registration or in the protocol.  | N/A   |
| Support                               | 25     | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.  | 320-322   |
| Competing interests of review authors | 26     | Declare any competing interests of review authors. <a href="http://bmjopen.bmj.com/site/about/guidelines.xhtml">http://bmjopen.bmj.com/site/about/guidelines.xhtml</a>   | 319   |





# PRISMA 2020 Checklist

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| Section and Topic                              | Item # | Checklist item   | Location where item is reported |
|--|--------|--|---------------------------------|
| interests                                      |        |  |                                 |
| Availability of data, code and other materials | 27     | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | 318                             |

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# BMJ Open

## The needs of informal caregivers of people with a rare disease: a rapid review of the literature.

|                                 |  |
|---------------------------------|--|
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| Date Submitted by the Author:   | 08-Nov-2022  |
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| <b>Primary Subject Heading</b>: | Public health  |
| Secondary Subject Heading:      | Public health  |
| Keywords:                       | Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PUBLIC HEALTH   |
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# 1 **The needs of informal caregivers of people with a rare disease: a rapid review** 2 **of the literature.**

## 3 4 **Authors**

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## 13 14 **Abstract**

15 *Objectives:* Many people living with a rare disease are cared for by a family member. Due to a frequent  
16 lack of individual rare disease (RD) knowledge from healthcare professionals, the patient and their  
17 informal caregiver are frequently obliged to become 'experts' in their specific condition. This puts  
18 huge strain on family life and results in caregivers juggling multiple roles in addition to unique caring  
19 roles including as advocate, case manager, and medical navigator. We conducted a rapid review of  
20 literature reporting on the unmet needs of Informal caregivers for people living with a RD. All searches  
21 were conducted on 14 September 2021 followed by a manual searches of reference lists on 21  
22 September 2021.

23  
24 *Setting:* Searches were conducted in Medline, Embase, Web of Science, GreyLit and OpenGrey.

25  
26 *Results:* Thirty-five papers were included in the final review & data extracted. This rapid review  
27 presents several unmet needs identified by informal caregivers of persons with a RD. The related  
28 literature was organised thematically: caregiver burden, support through the diagnosis process, social  
29 needs, financial needs, psychological needs, information and communication needs and  
30 acknowledgement from healthcare professionals.

31  
32 *Conclusions:* This review provides evidence that increased meaningful support is required for  
33 caregivers. Active engagement should be encouraged from this cohort in future research and

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34 awareness raised of the support available to improving the quality of life for families living with an RD.  
35 The unmet needs identified through this review will benefit people living with a RD, caregivers,  
36 healthcare professionals and policy makers.

37

38 **Key words:** burden, informal caregiver, needs, rare disease, review.

39

#### 40 **Strengths and limitations**

- 41 • This study explored a cohort of individuals who frequently go unnoticed and unreported in  
42 the literature – informal caregivers of individuals diagnosed with a rare disease.
- 43 • The rapid review followed the guidelines for conducting a rapid review of the literature.
- 44 • The review was conducted by experienced researchers in the area of RD carer needs who have  
45 a wealth of relevant experience. Additionally, manual searches of reference lists were  
46 conducted to identify any papers not found by the initial search strategy.
- 47 • It is important to acknowledge limitations of this review. Due to resource constraints, only  
48 one author (JM) initially screened the titles and abstracts from the total set of documents  
49 retrieved. This could lead to bias.
- 50 • Conducting a rapid review produced results quickly, including identifying the main self-  
51 identified needs of caregivers of people living with an RD. This is particularly important given  
52 the key role that informal caregivers play, and the fact that earlier research has focused on  
53 the person with an RD and not the caregiver.

54

55 The authors of this paper consider the needs of RD caregivers a priority and recognises the value they  
56 bring to the unique caring needs.

57

#### 58 **Introduction**

59 In Europe, rare diseases (RDs) are those which affect less than 1 in 2000 people in a specified  
60 population<sup>1</sup>. Although each RD occurs infrequently, collectively RDs are a major public health issue  
61 affecting more than 450 million people globally<sup>2 3</sup>. RDs result in a wide variety of healthcare needs  
62 stemming from the involvement of multiple organ systems, such as respiratory complications, the  
63 circulatory system, muscular system, digestive system, and central nervous system. Many RDs are  
64 chronic, complex and associated with physical, intellectual, or neurological disabilities that  
65 significantly affect patients and their families. In addition, many families living with a RD lack peer and  
66 community support services<sup>4-7</sup>

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Although not always the case, family often plays a pivotal role in a person's adjustment to chronic disease and is influenced by behavioural and social factors<sup>8</sup>. Caregivers are defined as individuals who provide care for a person in need/care recipient. On the other hand informal caregivers are defined as family members or close others who provide care for the person in need with no financial benefit in return. In essence, "formal caregivers" or "caregivers" is used to denote a category of professionals or semi-professionals who provide care with financial benefit. In contrast, "informal caregivers" are typically family members or friends who provide care but have no such benefits in return (in most European countries). Caring for someone with an RD affects many areas of life including psychologically, economically, physically and logistically<sup>9</sup>. The importance of good mental and physical health for the informal caregiver is therefore vital for their own wellbeing and to ensure they can sustain the essential role of assisting the person with an RD<sup>10 11</sup>. Individuals with RDs and their families often have limited evidence-based information to guide decisions about disease management and symptom relief<sup>12 13</sup>. Further, the inherent uncertainty that comes with having a RD, including delays in diagnosis (the average time for a diagnosis of a rare disease in Northern Ireland is 5 years) and a lack of knowledge about current and future care needs<sup>14 15</sup>, impact access to services and management of the RD<sup>16</sup>. Research on the experience of having a RD indicates that care and service needs are often not based on the severity of the health condition. Rather, they are associated with poor quality of care and barriers to access leading to less satisfaction with healthcare services and care coordination<sup>15 17</sup>.

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Given the few people with a specific RD, healthcare providers often are not knowledgeable about the condition. Therefore people living with a RD and their carers have to become their own experts<sup>18</sup>. This causes a change to the usual patient-doctor relationship, which can bring challenges such as difficulties in communication and patients struggling to get sufficient accurate information to make informed choices<sup>19 20</sup>.

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Caring for someone with a RD can be highly demanding often requiring intense and unique care specific to the individuals needs<sup>21</sup>. Delayed diagnosis, lifelong caring, limited capacity for independent living, lack of treatment options and large health service needs have severe impacts on parent's physical and psychosocial wellbeing<sup>22</sup>.

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Rapid reviews are an emerging type of knowledge synthesis used to inform health-related policy decisions and discussions, especially when information needs are immediate<sup>23-26</sup>. Rapid reviews

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3 101 streamline systematic review methods – for example, by focusing the literature search <sup>23</sup> while still  
4 102 aiming to produce valid conclusions. The requirements of the review, which was undertaken with a  
5 103 short deadline, were for a short but in-depth synthesis of the current state of the issues facing  
6 104 caregivers for those with a rare disease.

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9  
10 106 This review focuses on informal caregivers for people living with a RD. We were particularly interested  
11 107 in their holistic needs when caring for this unique population and how these may differ from other  
12 108 caring populations where there is often more support available e.g. carers of people with dementia or  
13 109 cancer.

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## 19 111 **Methodology**

### 20 112 *Search strategy and inclusion criteria*

21 113 Three electronic databases were searched -- Medline, Embase and Web of Science -- using the  
22 114 combined terms 'informal caregiver\*' and 'rare disease\*' (Supplementary file 1). All searches were  
23 115 conducted on 14 September 2021, with no date restrictions. Reference lists of included papers were  
24 116 screened for further sources. A search was also conducted of grey literature using the databases  
25 117 GreyLit and OpenGrey. Duplicates and non-English language articles were excluded. The criteria for  
26 118 inclusion were articles that address caregiving for people living with an RD. Articles on caregiving  
27 119 alone or RD alone were excluded. A simplified list of databases and the number of papers retrieved is  
28 120 shown in Table 1.

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### 38 122 *Study selection and data extraction*

39 123 Database searches were last conducted on 14 September 2021 by JM. Titles and abstracts of the  
40 124 identified articles were downloaded onto Endnote. Duplicate articles were removed and the  
41 125 remaining papers were screened through analysing their titles and abstracts. Additionally, manual  
42 126 searches of reference lists were conducted on 21 September 2021 to identify any papers not found by  
43 127 the initial search strategy. If relevant, the papers were then further screened by reading the full text.  
44 128 Data were extracted by JM who recorded the follow data for each study:

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- 51 130 • Author & year of publication
- 52 131 • Country in which the study was conducted
- 53 132 • Data collection method(s)
- 54 133 • Participants
- 55 134 • Identified caregiver needs

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136 The identified caregiver needs were extracted from the included papers [JM] and presented the data  
 137 extraction table [AMcK, JM & LL] (Supplementary file 2). From this, common needs were grouped  
 138 together under headings which became the themes for this review. The themes and content for the  
 139 themes was agreed between the research team [AMcK, JM & LL].

140

141 **Table 1: Literature search results**

| Database       | No. of articles retrieved | No. of articles included in review |
|----------------|---------------------------|------------------------------------|
| Medline        | 6                         | 5                                  |
| Embase         | 6                         | 5                                  |
| Web of Science | 62                        | 13                                 |
| GreyLit        | 0                         | 0                                  |
| OpenGrey       | 0                         | 0                                  |

142 This table shows the number of articles identified from each database before reference lists were checked.

143

144 An illustration of the search strategy including databases searched and screening methods is  
 145 displayed in Figure 1, modelled on the PRISMA flow diagram.

146

#### 147 *Patient and Public Involvement*

148 The need for this review was highlighted by a priorities workshop in 2020, which considered  
 149 contributions from >2,000 individuals living with rare disease. The review was also shared with  
 150 representatives from a local rare disease charity in Northern Ireland (the Northern Ireland Rare  
 151 Disease Partnership).

152

## 153 **Results**

### 154 *General description of the literature*

155 Sources initially identified from each database were as follows: MEDLINE  $n=6$ , Embase  $n=6$ , Web of  
 156 Science  $n=62$ , OpenGrey  $n=0$  and GreyLit  $n=0$ . The screening process resulted in 30 documents which  
 157 were reviewed based on their titles and abstracts. Following the screening 5 duplicate papers were  
 158 removed and 25 papers were identified for full text screening. Further studies were identified from  
 159 searching the reference lists. Finally, 35 texts were included in the full review, with characteristics of  
 160 each source summarised from the completed data extraction table (Supplementary file 2).



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3 161 Of the texts included, publication dates were from 2006 to 2021 and the studies were conducted in  
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5 162 Australia, Canada, Germany, Ireland, Italy, Netherlands, Spain, United Kingdom and the United States.  
6  
7 163 The identified studies focus on many rare diseases including Hereditary angioedema, Huntington's  
8  
9 164 Disease, Duchenne muscular dystrophy and Von Hippel-Lindau disease.

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13 166 A narrative review is presented below, highlighting the main needs of caregivers of people living with  
14  
15 167 an RD. The related literature has been organised thematically under the following headings:

- 16  
17 168 • Caregiver burden  
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19 169 • Support through the diagnosis process  
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21 170 • Social needs  
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23 171 • Financial needs  
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25 172 • Psychological needs  
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27 173 • Information and communication needs  
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29 174 • Acknowledgement from healthcare professionals

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32 176 Findings from these studies were organised thematically under the following headings as shown  
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34 177 visually in Figure 2.

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38 179 *Caregiver burden*

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41 180 Caring for someone with an RD presents a range of challenges<sup>27 28</sup> that are affected by the severity of  
42  
43 181 the illness and its duration, knowledge about the condition and its changes over time, and one's ability  
44  
45 182 to address the emotional toll involved with long-term care<sup>29</sup>. Despite the stress and difficulties  
46  
47 183 associated with being a family caregiver<sup>30</sup>, often they acknowledge the positive aspects of caring for  
48  
49 184 their loved ones<sup>30</sup>.

50  
51 185

52  
53 186 The quality of life of caregivers is often compromised by their placing others' needs before their own  
54  
55 187 <sup>31</sup>. Previous research has shown that informal caregivers do not have enough time for themselves,<sup>32</sup>  
56  
57 188 and that caring for someone with an RD can negatively impact on all dimensions of family life<sup>33</sup>.  
58  
59 189 Informal caregivers are often forced to miss work or school days due to the demands of their role,  
60  
61 190 frequently address unpleasant events and watch a loved one suffer<sup>28</sup>. Consequently, they would  
62  
63 191 benefit greatly from support to reduce the burden of caring for example from support groups, respite

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3 192 care and employment arrangements<sup>34</sup>. This includes both supports for informal carers of people with  
4  
5 193 a variety of health issues, as well as for RD-related issues<sup>34</sup>.

194

#### 195 *Support through the diagnosis process*

196 In spite of marked medical progress over the past several decades in identifying an RD, there are  
197 substantial delays in diagnosing these conditions<sup>35</sup>. This can have adverse impacts on families, for  
198 example, financial and mental health<sup>12</sup>. Little attention is given to parent concern in the diagnostic  
199 process with previous research reporting concerns regarding how the diagnosis was delivered to  
200 parents, lack of guidance and poor follow-up post diagnosis<sup>35</sup>. Previous research has shown that  
201 families are often dissatisfied by the way in which a diagnosis is given, including an insensitive style of  
202 communication, not offering support or counselling, and inadequate provision of information about  
203 the disease. This can cause emotional stress for caregivers who have not yet learned about the  
204 condition and how it will affect them and their families. Therefore, interventions to support the  
205 following a diagnosis would be useful, delivered either in hardcopy or online<sup>36</sup>.

206

#### 207 *Social needs*

208 Social isolation is common among informal caregivers with the impact on personal relationships being  
209 a reoccurring theme<sup>4 5</sup>. All too often, informal caregivers have little time to themselves and lack  
210 appropriate support and time for respite. This in turn causes further emotional stress and in the case  
211 of parents, uncertainty about their child's future<sup>37</sup>. Parents of children with an RD often feel isolated  
212 from mainstream society and struggle to stay socially connected<sup>4</sup>. It was suggested that the insights  
213 gained through research studies regarding the impact on caregivers' social lives should be considered  
214 in future clinical service planning. Additionally holistic, empathic, and person-centred medical and  
215 psychosocial care is urgently needed for this cohort<sup>6</sup>. Support is needed as relationships among  
216 family members are often impacted due to demands of caring<sup>4</sup>. There is a need for improved parental  
217 supportive care as many common unmet needs exist across RDs<sup>38</sup>.

218

#### 219 *Financial needs*

220 Previous research has indicated that financial issues are a top concern of caregivers of persons with  
221 RD<sup>30 6 39 27</sup>. The high economic costs that families must cover means that financial burden is common  
222 among caregivers of those with an RD, many of whom are forced to exhaust their financial savings<sup>40</sup>.  
223 Purchasing equipment, hiring professionals, and the additional financial burden the illness has on  
224 families poses immense stress on family life<sup>41</sup>. Often financial issues impact on the ability of the  
225 caregiver to meet the individual's healthcare needs, increasing the strain on their lives<sup>42</sup>. Substantial

226 social/economic burden is mostly attributable to high direct non-healthcare costs<sup>43</sup>. Previous  
227 research has shown that caregivers' financial burden might be conditioned by the clinical condition of  
228 the patient<sup>44</sup>. In addition to the direct healthcare costs, caregivers of those with an RD report that  
229 their career choices are influenced due to their caring role. Furthermore, caring duties can result in  
230 missed working days due to emergency caring demands<sup>37</sup> making it difficult for many caregivers to  
231 maintain their job and advance in their careers<sup>41</sup>. Financial hardship adversely effects the mental  
232 health of caregivers<sup>42</sup>.

233

#### 234 *Psychological needs*

235 There is a lack of psychological support for families caring for children with a RD, and many report that  
236 accessing appropriate psychological care is difficult<sup>6,12</sup>. Previous research has suggested that this form  
237 of support should be offered at the time of diagnosis<sup>12,10</sup>. Depressive symptoms are often associated  
238 with caregiving burden and therefore there is a need to develop interventions in addition to  
239 promoting the existing validated tools for caregivers considering their special needs<sup>10</sup>. Caregivers  
240 often express concerns about the future<sup>32</sup>, experiencing emotional distress that can compromise the  
241 well-being of family carers, who attempt to maintain multiple roles<sup>11</sup>. Psychological interventions can  
242 help reduce stress, a sense of being burdened and feelings of isolation that many RD caregivers feel  
243<sup>45</sup>. Research has suggested that screening for depression is needed and emphasises the need for a  
244 holistic approach to family mental health in the context of chronic childhood disease<sup>46</sup>. Peer support  
245 is a key resource in terms of information and emotional support for parents who often begin their  
246 journey feeling isolated and alone<sup>21</sup>.

247

#### 248 *Information and communication needs*

249 Suggestions were made that information about the condition should be given to caregivers at the time  
250 of diagnosis as well as signposting them to groups connecting families who share common experiences  
251<sup>21</sup>. Caregivers require access to accurate information, appropriate services and improved  
252 communication between patients, families, and a range of both health and social care and other public  
253 services<sup>2</sup>. Families require easily accessible services that include the family in the unit of care, provide  
254 support and information, and understand the process of family adjustment and adaptation in the long  
255 term<sup>47</sup>. Policies and structures are needed to support social and economic needs<sup>48</sup>. Engaging  
256 caregivers in future avenues of research is vital to ensure resources and funding are targeted in the  
257 best way<sup>49</sup>.

258

#### 259 *Acknowledgement from healthcare professionals*

260 Out of necessity, informal carers often know more about a particular RD than healthcare providers  
261 do. This often leads to poor communication and collaboration. Furthermore a lack of coordination of  
262 care force carers to fill the gap by juggling multiple roles including that of advocate, case manager,  
263 and medical navigator <sup>50</sup>. Caregivers often experience silencing or being silenced when interacting  
264 with health-care and social care systems and providers <sup>51</sup>. This has been attributed to the lack of  
265 knowledge about RDs by health-care providers who also are unaware of the impact that caring for  
266 someone with RD <sup>50</sup>. This points to the need to improve the knowledge of health care providers on  
267 the medical, social and financial impact these informal carers experience <sup>4</sup>. Health care providers  
268 should also acknowledge the vital role that informal caregivers play in promoting the health and  
269 quality of life of persons with an RD <sup>52</sup>. Caregivers, especially parents caring for someone with an RD,  
270 work hard to be heard and acquire services within health and social systems <sup>50</sup>. Another way that  
271 informal caregivers are silenced is due to how they are overlooked in the world of research despite  
272 growing emphasis on ensuring 'patient and public involvement'. It is vital that this pattern is changed  
273 so that they have an opportunity to be heard <sup>53 27</sup>.

## 275 Discussion

276 The purpose of this rapid review was to synthesise and describe what is currently known about the  
277 needs of informal caregivers for people living with an RD. Based on the findings, several  
278 recommendations for future healthcare practices and policies, as well as for research are evident.  
279 First, it is important to consider the extreme burden often experienced by these caregivers, many of  
280 whom place the need of others ahead of their own while navigating this journey with little or no  
281 support <sup>31</sup>. Support is needed to help caregivers with many aspects of their caring duties from the  
282 initial diagnosis process which has been a difficult time for many families <sup>35</sup>.

284 Social support would be welcomed to enable caregivers to have much needed time away from their  
285 caring duties to recharge and also to relieve them of the emotional strain which impacts on not only  
286 themselves but their wider family <sup>4</sup>. The mental strain of caregiving is evident from previous research,  
287 psychological interventions are required that consider the family as a whole to reduce the emotional  
288 strain and depression too often experienced by caregivers <sup>21 45</sup>. Many caregivers have also reported  
289 struggling financially not only due to the high costs of the practical side of caring but as a result of the  
290 impact caring can have on their ability to maintain a career <sup>41</sup>, financial support therefore a priority.

292 Clear information should be provided for caregivers from diagnosis through to their rare disease  
293 journey <sup>2</sup> to replace the current situation of confusion and uncertainty due to unclear and incomplete

10

294 or conflicting messages. Lastly, caregivers must be recognised by healthcare professionals for the  
295 integral part they have in caring for someone with a rare disease. This relationship often changes the  
296 dynamic between health professional and patient and so caregivers must be listened to and viewed  
297 as an 'expert'<sup>52</sup>. All of the above-mentioned issues should be taken into consideration when planning  
298 future research, it is vital that informal caregivers views are valued.

299

### 300 **Conclusion**

301 This rapid review presents several unmet needs identified by informal caregivers of persons with a RD.  
302 It is hoped that the findings contribute to increasing the amount of meaningful support for caregivers  
303 as well as encourage their active participation in improving the quality of life for families living with  
304 an RD. It is important that this cohort are engaged in future research to ensure their needs are being  
305 addressed. The insights that are gained through future research in relation to the impact on  
306 caregivers' social lives should be considered in the priorities and strategic directions for clinical  
307 services. Interventions to support them following a diagnosis would be useful, delivered either in  
308 hardcopy or online. Better meeting needs of informal caregivers for people living with a RD is in the  
309 best interests of people with a RD, healthcare professionals and policy makers, as well as caregivers.  
310 It is important that awareness is raised about the range of support options that are available from  
311 health and social care providers, charities and/or support groups for informal caregivers of people  
312 with an RD<sup>27</sup>.

313

### 314 **Figure legends**

315 Figure 1 PRISMA flowchart

316 Figure 2 Main needs of caregivers for those with a rare disease

317

### 318 **Abbreviations**

319 RD Rare disease

320

### 321 **Declarations**

- 322 • Ethics approval and consent to participate: This study does not involve human participants  
323 and ethical approval was not required
- 324 • Consent for publication: Not applicable
- 325 • Availability of data and materials: Not applicable
- 326 • Competing interests: The authors declare that they have no competing interests.

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- 6  
7  
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9 331 drafting and reviewing the original manuscript. LL & AJM contributed to study conception  
10 332 and design, data interpretation, project administration, supervision and reviewing  
11 333 manuscript drafts. All authors approved the final version of the manuscript for submission.
- 12  
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14 334 • Acknowledgements: Not applicable
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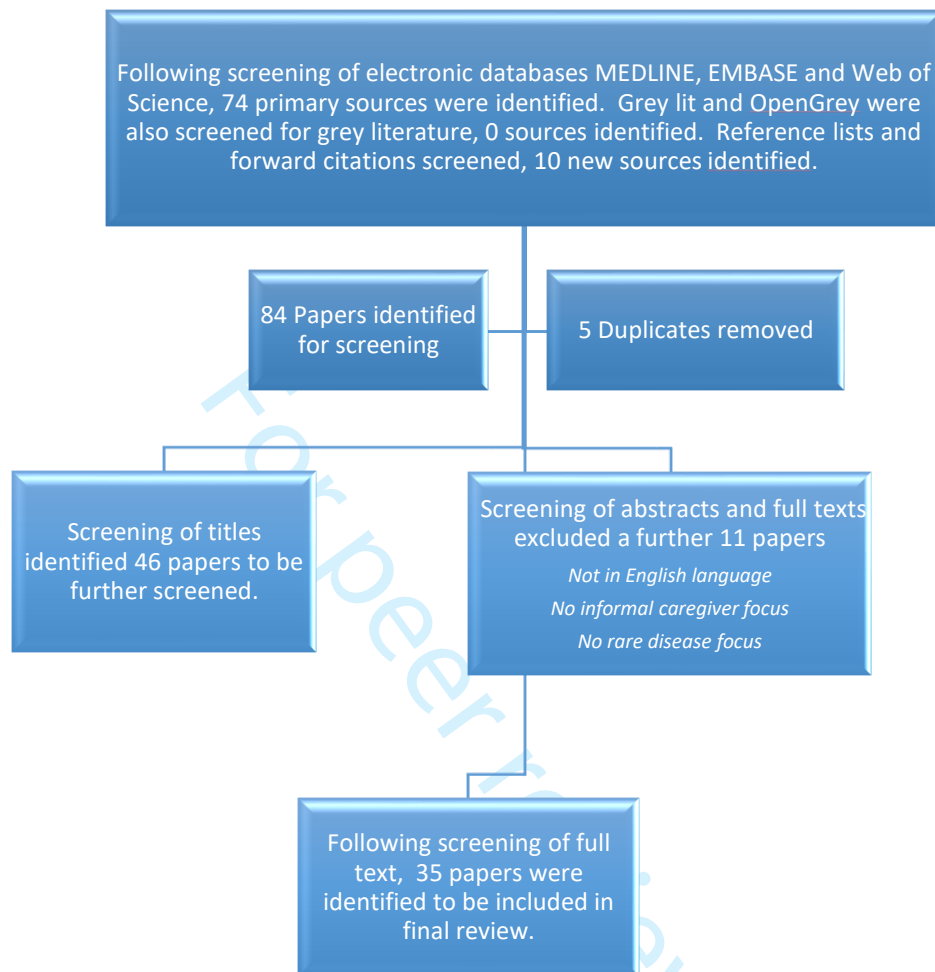


Figure 1 PRISMA flowchart

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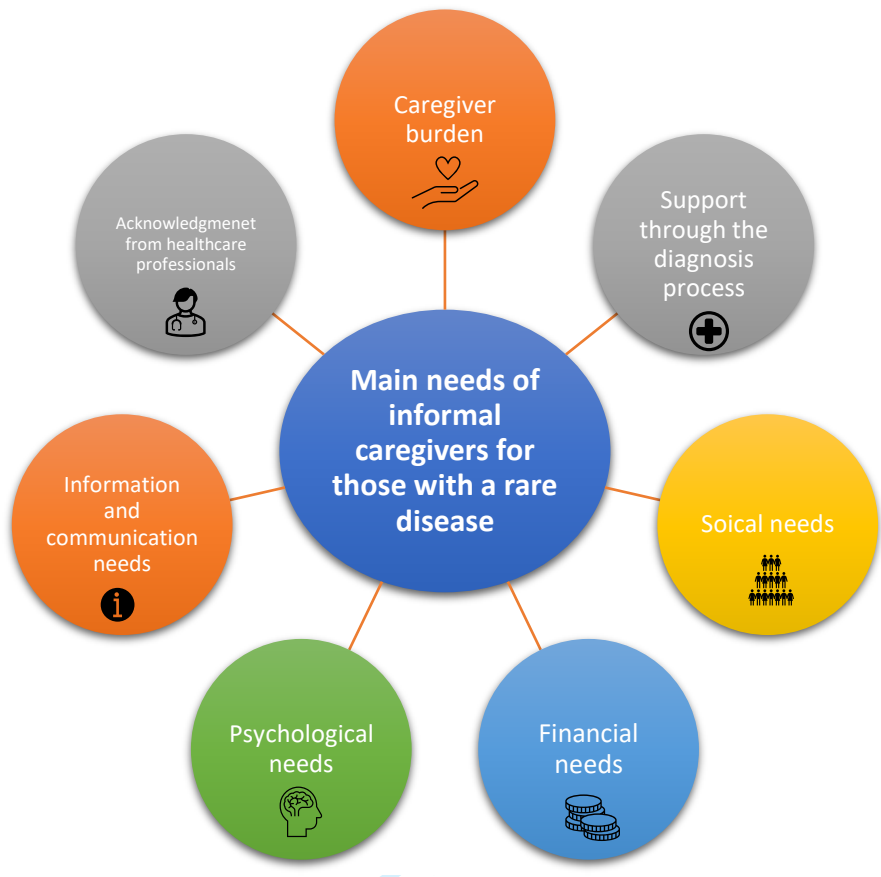


Figure 2 Main needs of caregivers for those with a rare disease

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3 **, Supplementary file 1: Detailed search strategy**  
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6 'informal caregiver\*' AND 'rare disease\*'  
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| Supplementary file 2: Data extraction table                  |  |                                      |  |  |
|--|--|--------------------------------------|--|--|
| Author & year of publication                                 | Country in which the study was conducted | Data collection method(s)            | Participants   | Identified caregiver needs   |
| Anderson, M., Elliott EJ, Zuryski YA.<br>2009                | Australia                                | Survey                               | Parents/carers   | <ul style="list-style-type: none"> <li>• Support around diagnosis.</li> <li>• Access to peer support groups.</li> <li>• Psychological support.</li> </ul>  |
| Applebaum A.J., Polacek L.C., Walsh L. <i>et al.</i><br>2020 | USA                                      | Survey and semi-structured interview | Caregivers of patients with Erdheim-Chester disease              | <ul style="list-style-type: none"> <li>• Social connections to prevent extreme isolation</li> </ul>  |
| Aubeeluck A.V. Buchanan H.E., Stupple E.J.N.<br>2011         | England                                  | Focus groups                         | Caregivers of those with Huntington's Disease                    | <ul style="list-style-type: none"> <li>• More time to focus on themselves.</li> </ul>  |
| Craig T.J., Banjerji A., Riedl M.A., <i>et al.</i><br>2021   | USA                                      | Online survey                        | Adults caring for an individual with Hereditary angioedema (HAE) | <ul style="list-style-type: none"> <li>• Recognition for the important role they have.</li> <li>• Inclusion in treatment discussions.</li> </ul>   |
| Hanbury A, Smith AB & Buesch K<br>2021                       | England                                  | Vignettes were developed             | Caregivers   | <ul style="list-style-type: none"> <li>• Engagement with research</li> </ul>   |
| Baumbusch, J., Mayer, S., & Sloan-Yip, I.<br>2018            | Canada                                   | Semi-structured interviews           | Parents of children with a RD                                    | <ul style="list-style-type: none"> <li>• Acknowledgment from healthcare providers</li> <li>• Support coordinating care</li> <li>• Peer support – information and emotional</li> <li>• Policies and programs to validate their role</li> <li>• Support from genetic counsellor to connect them to others</li> </ul> |

|  |             |                            |   |   |
|--|-------------|----------------------------|---|---|
| Bendixen, R. M., & Houtrow, A.<br>2017                             | USA         | Interviews                 | Parents of children with Duchenne muscular dystrophy          | <ul style="list-style-type: none"> <li>Listened to by healthcare providers</li> <li>Inclusion in the diagnostic process</li> <li>Improved delivery of the diagnosis</li> <li>Improved follow up after diagnosis</li> </ul>  |
| Cañedo-Ayala, M., Rice, D. B., Levis, B., et al.<br>2020           | USA         | Questionnaire              | Informal caregivers   | <ul style="list-style-type: none"> <li>Mental health support</li> </ul>   |
| Currie, G., & Szabo, J.<br>2019                                    | Canada      | Semi-structured interviews | Parents of children with RDs                                  | <ul style="list-style-type: none"> <li>Communication issues need addressed as parents often know more about the disease than healthcare providers.</li> <li>Improved coordination of care between providers and services caring for children with rare diseases.</li> <li>Gap in accessibility to government supports needs addressed.</li> </ul> |
| Currie, G., & Szabo, J.<br>2019                                    | Canada      | Semi-structured interviews | Parents of children with rare neurodevelopmental diseases     | <ul style="list-style-type: none"> <li>Health-care providers need more understanding of rare conditions.</li> <li>More support needed, parents often 'lose themselves' in this demanding caring role.</li> </ul>  |
| Flores D., Ribate M.P., Montolio M., et al.<br>2020                | Spain       | Questionnaires             | Caregivers to patients with Duchenne muscular dystrophy       | <ul style="list-style-type: none"> <li>Financial support.</li> </ul>  |
| Kanters T.A., van der Ploeg Ans. T, Brouwer W.B.F., et al.<br>2013 | Netherlands | Questionnaire              | Caregivers for those with Pompe disease.                      | <ul style="list-style-type: none"> <li>Support needed for informal caregivers.</li> </ul>   |
| Kasparian, N. A., Rutstein, A., Sansom-Daly, et al.                | Australia   | Telephone interviews       | Patients and caregivers affected by Von Hippel-Lindau disease | <ul style="list-style-type: none"> <li>More supportive care services requested.</li> </ul>  |

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|---|-------------------------|--|--|---|
| 2015  |                         |  |  |   |
| Landfelt E., Lindgren P., Bell C.F., <i>et al.</i>                    | Germany, Italy, UK, USA | Visual analogue scale, survey, interview | Caregivers to patients with Duchenne muscular dystrophy        | <ul style="list-style-type: none"> <li>• Screening for depression.</li> <li>• Holistic approach to family mental health needed.</li> </ul>  |
| 2016  |                         |  |  |   |
| Lagae, L., Irwin, J., Gibson, E., <i>et al.</i>                       | Europe                  | Survey                                   | Caregivers for those with Dravet syndrome (DS)                 | <ul style="list-style-type: none"> <li>• Time needed to escape caring duties.</li> <li>• Formal support and respite required.</li> <li>• Stress is common – support needed.</li> </ul>  |
| 2019  |                         |  |  |   |
| Lopez-Bastida J., Pena-Longobardo L.M., Aranda-Reneo I, <i>et al.</i> | Spain                   | Questionnaire                            | Patients and caregivers with Spinal Muscular Atrophy           | <ul style="list-style-type: none"> <li>• Financial support</li> <li>• QoL must be addressed</li> </ul>  |
| 2017  |                         |  |  |   |
| Lyon, M. E., Thompkins, J. D., Fratantoni, K., <i>et al.</i>          | USA                     | Semi-structured interviews               | Caregiving families  | <ul style="list-style-type: none"> <li>• Worries about the future need to be addressed.</li> <li>• More time for themselves needed.</li> <li>• Financial concerns must be addressed.</li> </ul>   |
| 2019  |                         |  |  |   |
| McKnight, A. J. M., Walker, R., Collins, C. (2020).                   | Northern Ireland        | Report                                   | N/A  | <ul style="list-style-type: none"> <li>• Access to accurate information</li> <li>• Access to appropriate services</li> <li>• Improved communication</li> </ul>  |
| McMullan, J., Crowe, A. L., Bailie, C. <i>et al.</i>                  | Northern Ireland        | Survey and semi-structured interviews    | Rare disease collaborative groups                              | <ul style="list-style-type: none"> <li>• Caregivers often overlooked in RD research – their opinions and experiences must be valued.</li> </ul>   |
| 2020  |                         |  |  |   |
| McMullan J, Crowe A.L., Downes K., <i>et al.</i>                      | Northern Ireland        | Survey and workshop                      | Caregivers of those with a rare disease                        | <ul style="list-style-type: none"> <li>• Improved interactions with healthcare professionals.</li> <li>• Improved emotional, psychological and social support.</li> <li>• Assistance with finances.</li> <li>• Better awareness of support services.</li> </ul> |
| 2021  |                         |  |  |   |
| Mooney J., Graham K. & Watts R.A.                                     | England                 | Semi-structured interviews               | Patients with ANCA-associated vasculitis and their caregivers. | <ul style="list-style-type: none"> <li>• Emotional support is needed.</li> <li>• Reassurance about the future.</li> </ul>   |

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|--|-----------|--|---|---|
| 2019   |           |  |   |   |
| Mori, Y., Downs, J., Wong, K., <i>et al.</i>                               | Australia | Survey   | Families with a child with CDKL5 disorder | <ul style="list-style-type: none"> <li>Burden of daily caregiving requires support, particularly in relation to emotional wellbeing, sleep problems, financial difficulties, QoL.</li> </ul>  |
| 2017   |           |  |   |   |
| Mutch, K., Methley, A., Hamid, S., <i>et al.</i>                           | England   | Semi-structured interviews   | Partners of people with NMO               | <ul style="list-style-type: none"> <li>Acknowledgement from HCP regarding the vital role they play in caring.</li> </ul>  |
| 2017   |           |  |   |   |
| Palacios-Cena, D., Famoso-Perez, P., Salom-Moreno, J., <i>et al.</i>       | Spain     | Interviews, focus groups, researcher's field notes, caregiver's personal documents | Caregivers of children with Rett Syndrome | <ul style="list-style-type: none"> <li>Answers needed regarding 'the first symptoms' and 'the need for a diagnosis'.</li> <li>Help with managing day to day life.</li> <li>Financial support.</li> </ul>  |
| 2018   |           |  |   |   |
| Pelentsov, L. J., Fielder, A. L., & Esterman, A. J.                        | Australia | Semi-structured focus group interviews   | Parents of a child with a RD              | <ul style="list-style-type: none"> <li>Social isolation must be addressed.</li> <li>Knowledge of HCP needs to be improved.</li> <li>Support needed as family relationship often impacted due to demands of caring.</li> </ul>                                     |
| 2016   |           |  |   |   |
| Pelentsov, L. J., Laws, T. A., & Esterman, A. J.                           | Australia | Scoping Review   | Parents of child with a RD                | <ul style="list-style-type: none"> <li>Improve parental supportive care – common unmet needs between RDs.</li> </ul>  |
| 2015   |           |  |   |   |
| Rice D.B., Canedo-Ayala M., Carboni-Jimenez A., Carrier M-E, <i>et al.</i> | USA       | Online questionnaire   | Caregivers of people with SSc             | <ul style="list-style-type: none"> <li>Emotional support is required.</li> <li>Help with physical needs.</li> <li>Interventions needed delivered through hardcopy or online resources, including those delivered after the care recipient's diagnosis.</li> </ul> |
| 2020   |           |  |   |   |
| Rice D.B., Carbino-Jimenez A., Canedo-Ayala M. <i>et al.</i>               | USA       | Scoping review   | N/A                                       | <ul style="list-style-type: none"> <li>Psychosocial interventions needed to reduce caregiver's stress, burden and feelings of isolation among caregivers.</li> </ul>  |
| 2020   |           |  |   |   |



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|---|-------------|--|--|---|
|   |             |  |  | <ul style="list-style-type: none"> <li>• Future research should design interventions for caregivers.</li> </ul>   |
| Rodriguez A.A., Martinez O., Amayra I, <i>et al.</i><br>2021        | Spain       | Questionnaire  | Carers of children with neuromuscular disease                        | <ul style="list-style-type: none"> <li>• Financial assistance.</li> <li>• Employment support.</li> <li>• Physical and psychological support.</li> </ul>   |
| Selman L.E., Beynon T., Radcliffe S., <i>et al.</i><br>2014         | London      | Semi-structured qualitative interviews                       | Adult informal caregivers of patients with Cutaneous T-cell lymphoma | <ul style="list-style-type: none"> <li>• Easily accessible services are needed that include the family in the unit of care, provide support and information, and understand the process of family adjustment and adaptation.</li> </ul> |
| Sloper, T., & Beresford, B.<br>2006                                 | UK          | Report   | Families of disabled children  | <ul style="list-style-type: none"> <li>• Policies and structures to support social and economic needs.</li> </ul>   |
| Somanadhan, S., & Larkin, P. J.<br>2016                             | Ireland     | In-depth interviews  | Parents of those with Mucopolysaccharidosis                          | <ul style="list-style-type: none"> <li>• Reassurance and certainty needed about the future.</li> </ul>  |
| Wiblin, L., Durcan, R., Lee, M., <i>et al.</i><br>2017              | England     | Qualitative in depth interviews                              | Patients and caregivers living with MSA and PSP                      | <ul style="list-style-type: none"> <li>• Better connections to others to reduce social isolation.</li> <li>• Improved communication.</li> </ul>   |
| Williams, J. K., Skirton, H., Paulsen, J. S., <i>et al.</i><br>2009 | USA, Canada | Focus groups   | Adult caregivers of people with Huntington's disease                 | <ul style="list-style-type: none"> <li>• Emotional distress support should be provided.</li> <li>• Assistance in managing several roles.</li> <li>• Mental health monitoring.</li> </ul>  |
| Wu, Y., Al-Janabi, H., Mallett, A., <i>et al.</i><br>2020           | Australia   | Clinical data was used from Mitochondrial Disease, Epileptic | Parents of those with rare genetic conditions                        | <ul style="list-style-type: none"> <li>• Health effects on family members need to be considered.</li> </ul>   |

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|  |  | Encephalopathy and Brain Malformation projects |  |  |
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