

PSYCHOLOGICAL INSTRUMENTS TO ASSESS PARENTAL STRESS AND COPING STRATEGIES IN INHERITED METABOLIC DISEASES: A SYSTEMATIC REVIEW

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ABSTRACT – Objective: Parents of patients with inherited metabolic diseases (IMDs) report impaired well-being and a heavy burden in managing their children's disease. Until now, studies focused more on general quality of life, while research on more specific psychological aspects is needed to provide more tailored care. Nevertheless, systematic studies on this topic are not present in the literature. The object of this systematic review is to investigate the instruments used to evaluate stress and coping in parents of patients with different IMDs.

Materials and methods: The literature search was performed on PubMed and Scopus. Inclusion criteria: the presence of instruments exploring stress and/or coping in parents of patients with IMDs, diagnosis of IMD, publication in peer-reviewed journals and English language. Exclusion criteria: sample mostly composed of caregivers different from parents, dissertations, reviews/meta-analysis, full-text not available. Data extracted from the studies: authors, year, country, disease, number and age of patients and parents, design and aim of the study, name and characteristics of instruments for parental stress and/or coping.

Results: Among the included studies (n=39) reported, the use of quantitative and qualitative instruments were different for stress and coping evaluation: almost all studies on parental stress used questionnaires to collect quantitative data, such as standardized questionnaires, instead a larger proportion of studies on coping employed qualitative data (i.e., *ad hoc* questionnaires and interviews).

Conclusions: Qualitative and quantitative instruments can be used to investigate stress and coping in parents of patients with IMDs. Investigating these specific psychological aspects in parents is pivotal in research and clinical practice to provide more tailored family-centered care of IMDS, characterized by the wide variability of symptoms and parental burden.

KEYWORDS: Parents, Stress, Coping, Inherited Metabolic Diseases.

LIST OF ABBREVIATIONS: IMD: Inherited Metabolic Disorder; MI: Malaise Inventory; NBS: Newborn Screening; QoL: Quality of Life; RSA: the Resilience Scale for Adults.

INTRODUCTION

Inherited metabolic disorders (IMDs) are a large group of genetic conditions caused by the impaired functioning of a metabolic pathway that causes the lack of production of an enzyme or its cofactor¹. Nowadays, there are more than 1,400 estimated inborn errors of metabolism²; individually, they are rare diseases but collectively common³. The incidence of IMDs is estimated to be as high as 1 in 800 live births, but it varies depending on the clinical population⁴. IMDs often present with acute events, potentially fatal crises, which require emergency intervention. The clinical course and prognosis of affected patients may depend on early and effective diagnosis and treatment⁵. Patients with IMDs may present different lifelong clinical manifestations, including metabolic decompensations, multiorgan deficit, neurologic alterations, behavioral and intellectual disabilities or delays⁶.

Newborn screening (NBS) is a fundamental tool that allows an early diagnosis and prevents the onset of irreversible organ damage⁷; the goal of NBS is to detect potentially fatal or serious, treatable conditions in newborns as early as possible before symptoms manifest. Unfortunately, the number of IMDs screened via NBS is largely different between countries and clinical centers. NBS for IMDs has gained increasing importance because high throughput assays and new therapies have been developed, improving outcomes and quality of life (QoL) of children and their parents^{8,9}.

Standard of care for a few IMDs may include diet, enzyme and coenzyme replacement, removal of harmful substances, cell and organ transplantation and supportive therapies¹⁰.

Parents of children with IMDs are especially expected to play an important role in their child's disease management; indeed, although caretaking is a natural part of being a parent, having a child with an IMD can bring additional challenges (i.e., clinical management of the child, taking care of healthy siblings, and extra costs and holiday expenditure), leading to additional parenting stress and burden¹¹ and affecting QoL and wellbeing¹². Some studies reported that young patients with an IMD have lower QoL than the general population^{11,13,14}; while research on parents failed in giving consistent results^{15,16}. In addition, a systematic review on health-related QoL in caregivers of children with phenylketonuria reported a poor to moderate health-related QoL and highlighted a need for the use of specific tools in research³.

The majority of literature in IMDs investigates QoL, an indicator that regards the general well-being and adjustment to the disease condition, but there is a need for more research on specific psychological aspects in patients and their parents.

Indeed, the challenges faced by parents of IMD children can be a heavy burden, which can lead to experiencing great stress. Moreover, parents must implement a variety of strategies to cope with their child's illness, which involves increased care, dissatisfaction in non-IMD-specific healthcare settings, financial problems, fear of a child's death, and the restrictions imposed by the diet^{17,18}.

Considering this evidence, tools and guidelines are needed for practitioners and clinicians not only to manage the medical issues of pediatric IMD patients but also to support the psychological needs of their parents.

Nevertheless, the variety and complexity of IMDs make it challenging to decide the appropriate instruments to use, particularly when attempting to evaluate specific psychological features, such as parental stress and coping strategies.

In light of this, we aimed to have a general systematic overview of instruments used to study parental stress and coping in parents of patients affected by IMDs. This can be a starting point for researchers and clinicians to have indications of the quantitative and qualitative instruments that can be used in IMDs. Our specific research question was "Which type of instruments were used to evaluate parental stress and coping in parents of IMD patients?"

MATERIALS AND METHODS

We conducted a systematic review of the literature to investigate the instruments used for studying stress and coping strategies of parents with children affected by IMDs. All the phases were completed according to PRISMA guidelines¹⁹. A study protocol for the study, available on request, was filled in at the initial step of the research. Identifying qualitative and quantitative studies congruent with the inclusion criteria was the objective of the internet search. An electronic search for keywords was undertaken by one researcher on the platforms PubMed and Scopus (a list of full search terms is presented in the [Supplementary Material](#)). The keywords search was constructed, including the name of the most frequent IMDs in order to find a large number of studies, as the literature on this population is scarce. One filter for psychological studies (Subject area: "Psychology") was used in the platform Scopus to include only psychological studies congruent with our research goal.

Study selection

All studies matching the search terms (until 7 February 2024) were screened according to the inclusion and exclusion criteria below.

Inclusion Criteria

The search criteria included articles exploring stress and/or coping in parents of patients with IMDs with different types of instruments, either qualitative or quantitative. Papers were considered only if the authors explicitly said that they used an instrument to study parental stress and/or coping. It was necessary that the patient's disease was diagnosed by a medical team. Moreover, only studies published in peer-reviewed journals and written in English were included.

Exclusion Criteria

Studies on parents of children affected by diseases other than IMDs were excluded. Other exclusion criteria were a sample mainly composed of caregivers different from parents, dissertations, reviews/meta-analysis, full text not available, and absence of parental coping or stress. In particular, studies that investigated non-specific parental stress (e.g., general distress or burden of the parents) or parental coping (e.g., other strategies that were not indicated as coping strategies) were excluded unless differently indicated by the authors (e.g., instruments that did not specifically study parental stress/coping, but authors explicitly declared that they were used for this purpose).

All the researchers took part at the screening phase independently in equal measure; to monitor concordance between the four investigators, a concordance rate on a pool of $n=50$ randomly selected articles was calculated. The researchers agreed on all these 50 studies, anyhow, disagreements or doubts between reviewers were resolved by consensus. If the full text of any eligible study could not be found, the authors were contacted and, as if no response was received, it was excluded.

Data Extraction and Collection

The data extracted from the study included authors and year, type of disease, sociodemographic information of patients with IMDS and their parents (country, type of disease, number and age of parents sample, number and age of patients, presence of control groups, study design, characteristics of the instruments, and main aim of the study).

Data were extracted independently by two reviewers; disagreements were resolved by discussion between all four authors.

Outcome Measures

The main outcome measures were the type and the characteristics of instruments used to assess stress and coping in parents of patients with IMDs.

Risk of Bias of the Studies

Because of the aim of our review, the authors agreed that the risk of bias was not significant.

RESULTS

Study Selection

The search resulted in 1867 studies: 685 in PubMed and 1182 in Scopus. The suitable studies after automatically removing duplicates were $n=1757$ and all these articles were screened on title and abstract. Ultimately, 1716 articles were excluded because they did not fit the inclusion criteria.

The full text of the remaining articles ($n=41$) was read to assess the eligibility, and two were not considered: one was a short report that did not explain the instruments used²⁰, and the other study²¹ was a republication of the same data exposed in a study already included²². Finally, $n=39$ studies²²⁻⁶⁰, all published in English, were included in the review. These works involved 2861 caregivers, mainly mothers and fathers.

The majority of patients were children, although the age range was wide, ranging from a few months to 32 years, encompassing children of widely different ages and adults. The IMD populations came from different countries: the studies were published in USA (n=14), Australia (n=5), UK (n=4), Germany (n=3), Italy (n=2), France (n=2), Turkey (n=2), Tunisia (n=1), Switzerland (n=1), South Korea (n=1), Spain (n=1), Iran (n=1), Canada (n=1) and Ireland (n=1).

The included papers involved a variety of diseases, mainly Phenylketonuria (n=11), Mucopolysaccharidosis (n=7), Pompe disease (n=3), Mitochondrial diseases (n=2), Barth syndrome (n=2); other conditions were phosphomannomutase deficiency (n=1), medium-chain acyl-coenzyme A dehydrogenase deficiency (n=1), X-linked adrenoleukodystrophy (n=1), glycogen storage disease (n=1), Maple syrup urine diseases (n=1), long-chain fatty acid oxidation disorders (n=1), Short-chain acyl-CoA dehydrogenase deficiency and isobutyryl-CoA dehydrogenase deficiency (n=1). The remaining seven studies investigated groups of patients with different diagnoses of IMDs.

Among the 39 included, 17 investigated parental stress, 15 parental coping, and seven studied both stress and coping of parents of IMD patients.

Overall, n=11 validated questionnaires (five for parental stress, six for parental coping), n=5 (three for stress, two for coping) *ad hoc* questionnaires were identified, while in nine studies, qualitative instruments (mainly semi-structured interviews) were used.

A summary of the included studies is presented in [Supplementary Table 1](#). The PRISMA flow diagram, explaining the process of the systematic review, is reported below (Figure 1).

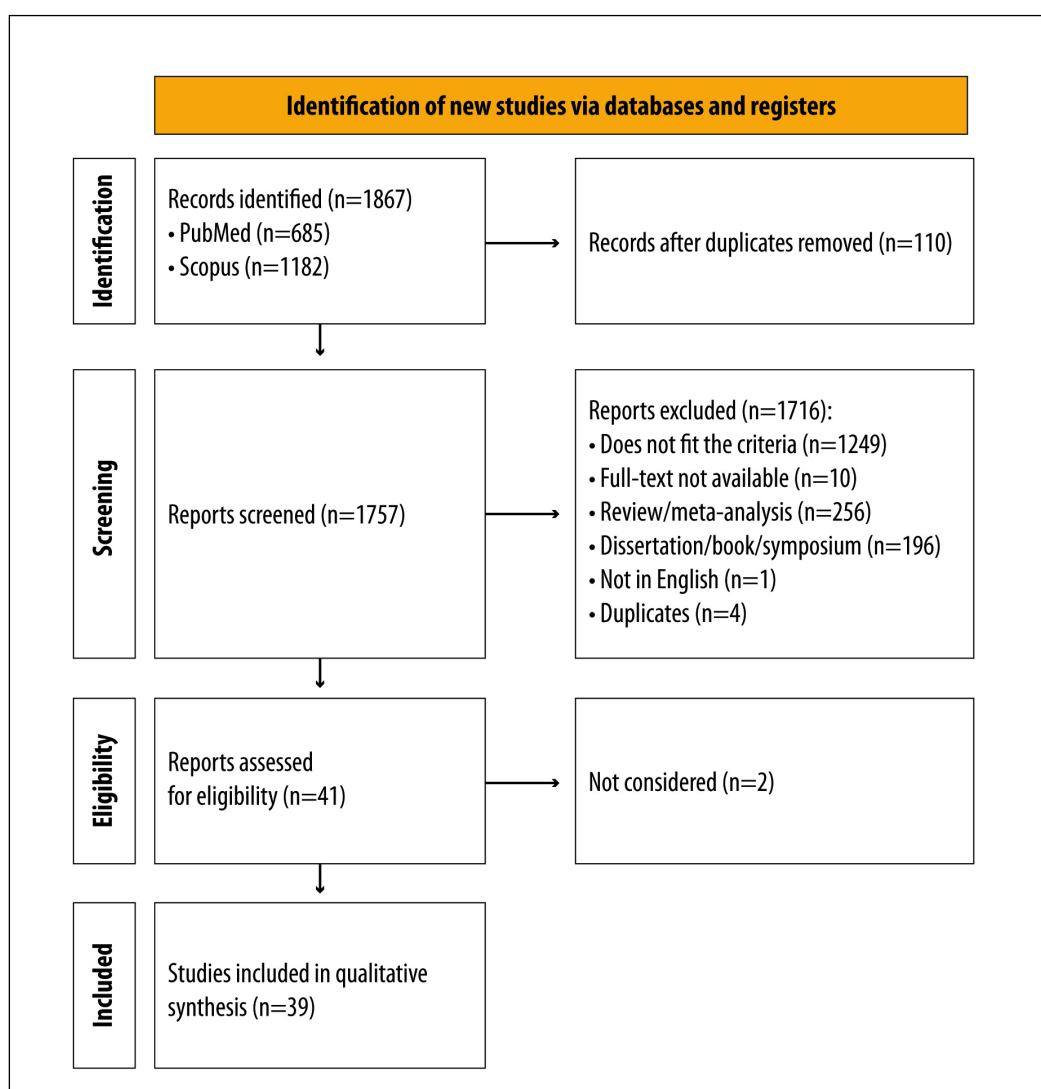


Figure 1. PRISMA flow diagram.

WHICH TYPE OF INSTRUMENTS WERE USED TO EVALUATE PARENTAL STRESS AND/OR COPING STRATEGIES IN PARENTS OF IMD PATIENTS?

Parental stress

Systematic analysis of the 39 included articles identified 24 works discussing parental stress in IMD patients. Of these, 83% (n=20) used standardized instruments, 13% (n=3) *ad hoc* questionnaires, and only 4% (n=1) used qualitative instruments, a semi-structured interview.

Specifically, the most commonly used standardized questionnaires were the Parenting Stress Index - Short Form⁶¹ and the Paediatric Inventory for Parents (PIP)⁶², both of which measure parental stress in relation to the child, but some differences are present.

The Parenting Stress Index–Short Form⁶¹ was chosen to be used in eight articles included^{30,31,36,39,44,45,51,59}. This questionnaire consists of a derivative of the full-length Parenting Stress Index. The full version was created to identify problems between parents and children in normative samples, while the reduced version has been requested for use also on clinical samples as well due to its convenience of use and the shorter time taken for administration (only 10 minutes). Despite the fact that it can also be used in clinical samples, this instrument investigates the general stress that occurs in caring for a child; therefore, it can be used with all parents as it does not investigate stress specific to the physical condition of a possible child's illness. It can be used with parents of children aged 1 month to 12 years old; it is composed of 36 items divided into three subscales: *Parental Distress*, *Difficult Child*, and *Parent-Child Dysfunctional Interaction*, and all contribute to a Total Stress score. Higher scores indicate higher parenting scores.

Also, the Paediatric Inventory for Parents⁶² has been used in eight articles^{22,29,34,43,52,55-57}. It was created specifically for the use of parents of children with chronic diseases to provide information on specific areas of the parental experience that are most relevant to their child's illness. The PIP consists of four subscales: *Communication*, *Medical care*, *Emotional distress*, and *Role function*. Each of these scales is assessed on the basis of two factors: the frequency of the stressful event reported in the item in the last week and the level of difficulty associated with it. These scores are summed separately for each of the four domain scales to form a total frequency score (PIP-F) and a total difficulty score (PIP-D): higher scores indicate greater frequency and difficulty.

In addition, three other questionnaires were used in some of the included articles: the Perceived Stress Scale⁶³, The Malaise Inventory (MI)⁶⁴ and the Depression Anxiety Stress Scale⁶⁵.

The Perceived Stress Scale⁶³ has been used in two studies^{26,37}. Unlike the other instruments, it is used to measure general stress levels in youth and adults aged 12 years and older without being associated with their relationship with their child. The questionnaire consists of 14 questions based on perceived stress over the past month; if the score is close to 56, it means perceived stress was high.

The MI⁶⁴ was used in one article⁴¹ to assess emotional and physical stress symptoms. The MI is derived from the Cornell Medical Index Health Questionnaire and consists of 24 items, of which 15 investigate the psychological aspect, while the rest investigate somatic symptoms; no specific time frame is defined, but in general, reference is made to the recent period. The MI was created for normative samples but has been extensively used with parents of children with chronic conditions.

The Depression Anxiety Stress Scale⁶⁵ was used in one article³⁸, and it consists of 42 items measuring symptoms of anxiety, depression and stress. In this instrument, stress is investigated in one scale focused on symptoms of tension and irritability. The resulting stress score is added to the other two scales of depression and anxiety to compose a total score. It is an instrument that can be used in both clinical and normative samples, and it was developed excluding somatic items to address the need to have a standardized measure that assesses mood only.

In three articles^{35,46,48}, however, an *ad hoc* questionnaire was used to investigate parental stress. Regarding these instruments, it was found that both multiple-choice and open-ended questions were used in their creation, to which parents could freely respond about their difficulties with the disease. All *ad hoc* questionnaires created were composed of a part aimed at collecting demographics and medical information regarding the disease and another part inherent to the parental challenges and difficulties related to their child's condition. Specifically, one study⁴⁶ created an *ad hoc* questionnaire to focus on the impact of a child's illness on the family, particularly on the stress related to the loss of cognitive skills and social/adaptive behavior related to the disorder. The questionnaire was divided into four parts, investigating general information and demographic data, developmental history of the child's disease, behavioral problems, and family issues. The researchers tried to obtain both quantitative data through the use of this questionnaire, and qualitative information, allowing the parents to express their personal point of view via answers in essay form.

Hoffmann et al³⁵ chose to create an *ad hoc* questionnaire in collaboration with the affected families to allow them to express their experiences openly and freely, but also to collect qualitative and comparable data. They used a semi-structured questionnaire with open-ended and direct questions, asking the most frequent and relevant challenges and subjective stresses of parents and children. The main aim of this study was to explore effective day-to-day measures used by parents against challenging behavior in their child's mucopolysaccharidosis. Packman et al⁴⁸ created a questionnaire consisting of 35 closed- and open-ended questions designed to ascertain the stress imposed on families with a child with a urea cycle defect. The five open-ended questions were used to permit parents to discuss more freely specific issues concerning the relationship with hospital and school staff. Additional open questions asked the parents for some suggestions to improve the care of children with that disease.

In only one case⁵⁴, a semi-structured interview was preferred. In this study, this method was chosen to try to understand parents' experiences in managing their child's IMD, specifically focusing on the impact of this condition on the management of the child's and family's daily life and the parental perception of interactions with the healthcare system. The aim of this work was to determine parent's experiences and burdens related to the disease using a qualitative methodology that allowed them to deepen their point of view.

Parental coping strategies

In total, 22 out of 39 included articles investigated coping in parents of children with IMDs. In particular, 59% of the articles (n=13) used *ad hoc* and standardized questionnaires (quantitative instruments), whereas the remaining 36% of the articles (n=8) used qualitative instruments, mainly in-depth interviews and open-ended interviews. Only one article²⁵ (5%) used both self-report questionnaires and interviews to investigate the coping in parents of children with IMDs.

Among the standardized questionnaires, only some instruments were specific to assess coping strategies. The Coping Orientation to the Problems Experienced (Brief COPE)⁶⁶ was the most widely used, present in five studies^{23,34,38,42,47}. It is a self-report questionnaire comprising 28 items split into 14 subscales that measure the strategies used by parents to cope with stressful situations. Specifically, the coping strategies investigated are active coping, use of instrumental support and planning accounting for problem-focused coping, self-distraction, denial, substance use, use of emotional support, behavioral disengagement, venting, positive reframing, humor, acceptance, religion and self-blame accounting for emotion-focused coping. Participants are asked to indicate the degree to which they used different strategies on a 4-point scale from 1 to 4. Higher scores indicate increased utilization of that specific coping strategy.

The Coping Health Inventory for Parents⁶⁷ is another instrument used to study the coping and perceptions of parents, specifically of those having children with serious and/or chronic illnesses. The Coping Health Inventory for Parents was used in four studies^{22,32,33,36}. It consists of 45 items divided into three subsets that identify different coping patterns: maintaining family integration, cooperation and an optimistic definition of the situation (Coping Pattern I); maintaining social support, self-esteem and psychological stability (Coping Pattern II); and understanding the medical situation through communication with other parents and consultation with the Health Care Team (Coping Pattern III). Each item is rated from 0 to 3 according to the usefulness of the parents' coping behavior. A high score represents a higher use of coping strategies.

Finally, the Ways of Coping Questionnaire^{68,69} is an instrument that has been used to investigate the role of coping in dealing with stressful situations⁴¹. It is composed of 66 items, and it indicates how often the subject used eight coping strategies, such as confrontational coping, distancing, self-control, social support seeking, acceptance of responsibility, avoidance of escape, planned problem-solving and positive reappraisal. A high score represents a higher use of coping strategies.

A smaller number of studies^{25,34,41} used other standardized questionnaires, that were not specifically aimed at investigating coping strategies, but in these studies were used to analyze it. These instruments are the Hunter Opinions and Personal Expectations Scale⁷⁰, the Resilience Scale for Adults (RSA)⁷¹ and the Parent Experience of Childhood Illness⁷². The Hunter Opinions and Personal Expectations Scale is an instrument that investigates personal hopefulness; Lord et al⁴¹ added this scale, used to investigate an additional specific coping strategy ("hopefulness"), to the instrument Ways of Coping Questionnaire. The RSA, instead, is a scale that investigates resilience analyzing both personal aspects and cultural aspects; participants evaluate each item using a 7-point semantic differential scale, with higher RSA total

scores indicating greater levels of resilience. Some items regarding personal aspects study factors that can be related to coping skills, but there are no specific scales for coping. In light of this, a discordance was found in our included studies, as one article used this instrument to measure coping²⁵. In contrast, another study³⁴ does not use RSA to investigate coping and places this instrument alongside Brief COPE.

Whereas only one article²⁷ uses the Parent Experience of Childhood Illness⁷², which is an instrument exploring parental adjustment related to caring for the child's illness, with a specific scale investigating coping strategies. It serves as a tool tailored to evaluate emotional adaptation, coping strategies, and the perceived support network accessible to the primary caregiver of children grappling with a chronic illness. It comprises 25 questions distributed over four scales: guilt and worry, unresolved sorrow and anger, long-term uncertainty and emotional resources.

Two studies used an *ad hoc* questionnaire^{35,58}, instead of a standardized questionnaire, to examine coping.

Specifically, Thiel et al⁵⁸ concentrated on utilizing disease-specific questions to evaluate the challenges of parents facing their child's condition and parental coping mechanisms concerning their children's medical condition in everyday life. The survey included various aspects regarding the diagnostic pathway, the clinical trajectory and obstacles in different age groups, dietary rules, sibling dynamics and the perspective of parents towards their child's illness.

Hoffmann et al³⁵ also created an *ad hoc* questionnaire named "Practical coping strategies", in which there was an open-ended assessment of coping strategies supported by exemplary strategies, and also the perceived effectiveness was required. This method encouraged open feedback to indicate individual strategies and allowed for the comparison of potentially effective strategies. The emerged practical coping strategies were classified as: "Distraction/Busying," "Relief/Safety," "Frame Conditions," "Operant Conditioning," "Professional Therapy," "Breathing Support," "Medication" and "Non-medication."

Another widely used tool for investigating coping with metabolic diseases was an interview. Several ways of interviewing emerged in our review: semi-structured interviews were used in seven studies^{24,26,28,40,49,54,60}, open-ended interviews⁵³ and in-depth interviews⁵⁰ in only one study.

Semi-structured interviews investigate well-defined topics using specific questions in no predefined order, allowing participants to explore and elaborate on issues they feel. They are often an effective means of understanding the motivations that drive individuals' choices and behaviors, as well as their attitudes, beliefs and the repercussions of particular events in their lives. Moreover, they often provide valuable insights that the researcher did not initially anticipate.

Despite the need for strong caution in the use of these instruments, qualitative interviews can provide a unique instrument to investigate personal experience⁷³. Open-ended interviews use open and unstructured questions. Open-ended interviews offer a distinct advantage because they provide comprehensive explanations, which can prompt interviewers and researchers to explore new directions, revealing previously overlooked perspectives and opportunities. In addition, participants have the opportunity to clarify their intentions, often revealing underlying motivations.

In-depth interviews, like open-ended interviews, are characterized by large freedom in the interview thanks to unstructured questions. They are a very useful qualitative tool and are usually used with a limited number of participants to delve into their views on a specific concept, initiative or circumstance. The in-depth interview explores a topic in detail to deepen the interviewer's knowledge of the topic.

Among the included articles, a large proportion of them use interviews that don't directly investigate coping, but this theme emerges from the thematic analysis of the answers given by the participants^{24,25,40,49,54,60}; in contrast, a smaller number of articles use interviews that explicitly investigate coping through specific questions on the topic^{28,50,53}.

DISCUSSION

This review allowed us to investigate instruments used for parental stress and coping in different IMDs. Stress and coping of parents of patients with IMD were examined equally: 24 studies were about stress, while 22 were about coping.

Different types of instruments were used to investigate these psychological aspects in parents, probably because of the heterogeneity of IMDs and their clinical manifestations. Many researchers strive to use standardized tools to achieve more normalized and comparable results, but this need often clashes with the desire to have a more specific perspective on the disease and the personal experiences of patients and parents. Indeed, in several studies, authors have decided to create *ad hoc* questionnaires or

use interviews to delve into parents' perspectives on the perceived stress due to their child's disease and strategies used to face this situation; frequently, researchers explicitly declared this intention in using these types of instruments.

A difference emerged in the use of quantitative and qualitative measures between stress and coping: almost all studies concerning stress used quantitative measures by administering questionnaires, while a much larger proportion of studies on coping strategies used qualitative measures. Specifically, a large part of studies on parental stress used standardized questionnaires, while for coping, fewer research studies used these instruments. This is probably due to the characteristics of these psychological factors: stress is a more unified and well-defined concept while coping (often described as coping strategies) is a more varied and multifaceted construct. Indeed, interviews are often used to investigate a complex and miscellaneous theme, such as coping, because these tools can provide a freer method to investigate parents' points of view and approaches to facing and managing the disease and its implications in everyday life.

Lastly, in research on parental coping, some studies have used instruments that are not specific to this construct. This is another point that suggests the difficulty of investigating this construct, especially when research is applied to a population as large and heterogeneous as IMDs.

Many studies often reported increased anxiety and depression and reduced QoL^{12,74} in parents of IMD patients; some authors additionally highlighted that parental distress and coping strategies can be related to QoL. The role of the multidisciplinary team is to investigate the origins of this burden to provide sensible care to patients and their families; for this reason, it is important that clinicians and psychologists can have a wide range of instruments to investigate these aspects due to IMDs' great deal of variability in symptoms and treatments. Indeed, this gives the clinicians the opportunity to choose specific questionnaires to understand the patients and their families in a deep manner.

CONCLUSIONS

This systematic review highlighted different types of instruments, quantitative and qualitative, that can be used to evaluate parental stress and coping in the IMD population for research purposes and/or clinical practice. In research, the use of shared instruments is important in order to combine the need for the obtaining of quantitative data and emphasizing the personal experience of patients and parents. Clinicians and psychologists should investigate the psychological functioning of parents to provide family-centered care tailored to the patient and his disease.

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No Artificial Intelligence-assisted technologies were used in the preparation of the article.

AUTHORS' CONTRIBUTIONS:

Study conception and design: G.G, L.M.; collection and interpretation of data: G.G, S.M, A.G, L.M.; statistical analysis: n/a; manuscript drafting: G.G, S.M, A.G, L.M.; manuscript editing: G.G, S.M, A.G, L.M.; approval to submit: G.G, S.M, A.G, L.M.

AVAILABILITY OF DATA AND MATERIAL:

All data generated or analyzed during this study are included in this published article and its [supplementary material](#).

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The authors declare that they have no conflict of interest to disclose.

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