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Morality as experienced: A scoping review of moral matters encountered by adults living with rare diseases

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Abstract

Most rare diseases are poorly understood, affected individuals struggle tobe timely diagnosed and to access tailored, appropriate, and affordablecare. Following pragmatist theory, individuals living with rare diseasesmay experience these obstacles as morally problematic situations, wherethey struggle with actualizing their cherished values amid their lifecircumstances. These embedded and contextualized lived episodes aredistinct from moral challenges and moral issues, which are more abstract,decontextualized, and speculative moral matters. We sought to uncoverthe moral matters of adults living with rare diseases in the qualitativeliterature while elucidating the moral dimensions of morally problematicsituations. Moral matters were extracted from 25 qualitative studies andsubjected to thematic and interpretive analyses. The uncovered moralissues addressed abstract considerations relating to accessibility, limitedknowledge, and unpredictability of illness manifestations. Moralchallenges and morally problematic situations spanned across the fourphases of the medical trajectory: the diagnostic odyssey, the diagnosis,clinical care and treatment, and medical follow-up. Moral challengesnamely pertained to poor communication of diagnoses, lack of shareddecision-making, and lack of holistic support. Morally problematicsituations featured moral dimensions, namely (1) internal tensions (e.g.,being misunderstood), (2) constraints to agency (e.g., powerlessness anddisempowerment), in addition to (3) empowerment and selfadvocacystrategies (e.g., being assertive and demanding), notably in episodeswhere support from clinicians lacked. This study highlights the usefulnessof distinguishing these three types of moral matters in ethical analysis. Italso shows how moral dimensions of morally problematic situations carryexistential importance for affected individuals.

Keywords

rare diseases, pragmatism, morally problematic situations, moral challenges, moral issues, ethics

Introduction

Rare diseases are conventionally defined as diseases with a prevalence less than 1 in 2000.[1] Many rare diseases are highly incapacitating or life-threatening conditions. While 80% of rare diseases arise from genetic mutations, others may also result from immune dysfunction or exposure to infectious or toxic agents.[2] Despite the current era of precision medicine, several rare diseases' mechanisms of action, symptomatology, and therapeutic avenues are poorly understood.[2] Due to this lack of scientific evidence or their presentation with indeterminate symptoms, clinicians frequently have limited knowledge on the diagnosis, treatment, and prognosis of rare diseases.[3] This is partly understandable as there are several thousand rare diseases.

Scientific and clinical limitations prevent individuals living with rare diseases from accessing timely, appropriate, and affordable care, in addition to adequately personalized

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treatment.[4] For example, these individuals often go through what is called a diagnostic odyssey, the tireless pursuit of several clinical routes to obtain a diagnosis or a certain medical understanding of their situation.[5,6] In other words, before obtaining a diagnosis, the reality of patients with rare disease is that of suffering from medically unexplained symptoms and conditions. Accordingly, they are also often accused of malingering and receive a high proportion of unrelated psychiatric diagnoses to explain their symptoms.[7] Upon being diagnosed, a minority of individuals living with rare diseases may be candidates for pharmaceutical drugs. Even then, these drugs more often only alleviate symptoms and provide support, rather than present any curative functions. However, these expensive treatment avenues raise complex issues regarding insurability, healthcare coverage, and equity due to their high costs, as pharmaceutical companies recoup costs on a very small pool of patients.[8]

Such significant obstacles relating to diagnosis and care profoundly impact the lives of individuals living with rare diseases and their families, often experiencing these obstacles as *morally problematic situations*.[9,10] In these situations, they struggle with actualizing their cherished values and meaningful life experiences.[11] Important human values, such as respectful interpersonal communication and the ability to listen to often marginalized patients, are at stake.[12,13] We approach those situations following pragmatist social and ethics theory,[14–16] according to which these life events should be understood as embodied and socially constituted life experiences, thus moving away from more universalizing ethics theory relying on notions of dilemmas and tough choices. Failing to do so risks simplifying situations to more rationalistic and academic understandings, which do not correspond to or express what is at stake in the situations for those who experience them.[17,18] For instance, situations where patients encounter issues with access to expensive treatments could be rationalized as mere theoretical or conceptual "justice issues," which fall under the premise of a major ethical principle. Such attenuated descriptions of lived situations risk reducing lived experiences to simplified abstract terms such that ethical principles are, following Fiester, used against patients' interests in ways that do not do justice to their experiences and relies on a vocabulary which is largely inaccessible to them.[18]

Pragmatism, ethics, and morally problematic situations

Ethics is often considered to be a field of the humanities whose purpose is to remediate difficult dilemmas or choices. Most often, ethics is scaffolded in the architecture of general, even universal principles that would then be applied to such cases. Fesmire writes apropos that (p.55):

> There is a central dogma of ethical theory, namely that it rests on revealing or constructing a moral bedrock that tells us the right way to think about moral problems. Moral skeptics accept this dogma, plausibly reject that such a foundation can be discovered or erected, and hear the bell toll for ethics. Many self-described normative ethicists hear no such bell. They argue, or uncritically assume, that the fundamental fact of morality is the capacity to set aside our patchwork of customary beliefs and then to discern and apply moral laws or rules derived from one or more foundational principles. This is indeed an ineliminable assumption of ethics, moral skeptics rejoin, but we sadly we all lack such a capacity.[15]

An alternative to deductive ethics and its implementationist orientations is offered by philosophical pragmatism. This epistemological approach invites espousing a view of ethics that is reliant on an embodied and situated account of moral agency and human rationality, and thus of ethics.[19] Following this approach, moments of existence traditionally described as dilemmas or choices are foremost social situations involving moral agents. Situations are transactional in nature; they represent the experiential unit through which an organism interacts with an environment.[19,20] Some of these situations can be experienced as being morally problematic.

For pragmatist social and ethical theory, the morally problematic situation constitutes the basic and most concrete unit of moral experience and ethical analysis upon which other more rationalized interpretations such as dilemmas and choices are derived.[21] A morally problematic situation challenges an agent's self-worth, integrity, and overall sense of flourishing.[19,22] Faced with the situation, the agent may experience internal tensions attesting to the "disturbed, troubled, ambiguous, confused, full of conflicting tendencies, obscure, etc." nature of the situation, compatible with the "conflicting desires and alternate apparent goods" it elicits.[23] A morally problematic situation arising in clinical settings may be perceived as "very difficult" and "very complex," as eliciting "conflicts," as a "crisis," and as "emotionally charged," amplifying internal tensions.[24] These felt difficulties may be accompanied by constraints to agency, making the agent feel "stuck in a difficult situation" and "cornered and [not knowing] how to solve the problem."[24] A morally problematic situation may elicit a negative moral experience for the agent that may "sense that values that he or she deems important are being […] thwarted in everyday life."[11]

A morally problematic situation may be tackled through ethical inquiry, which enables the agent to more thoroughly understand the internal tension experienced, imagine action scenarios that could alleviate this tension, select and adopt the most promising scenario, and evaluate its outcomes. Ethical inquiry is iterative and empirical, meaning that if the agent observes that the implemented scenario does not

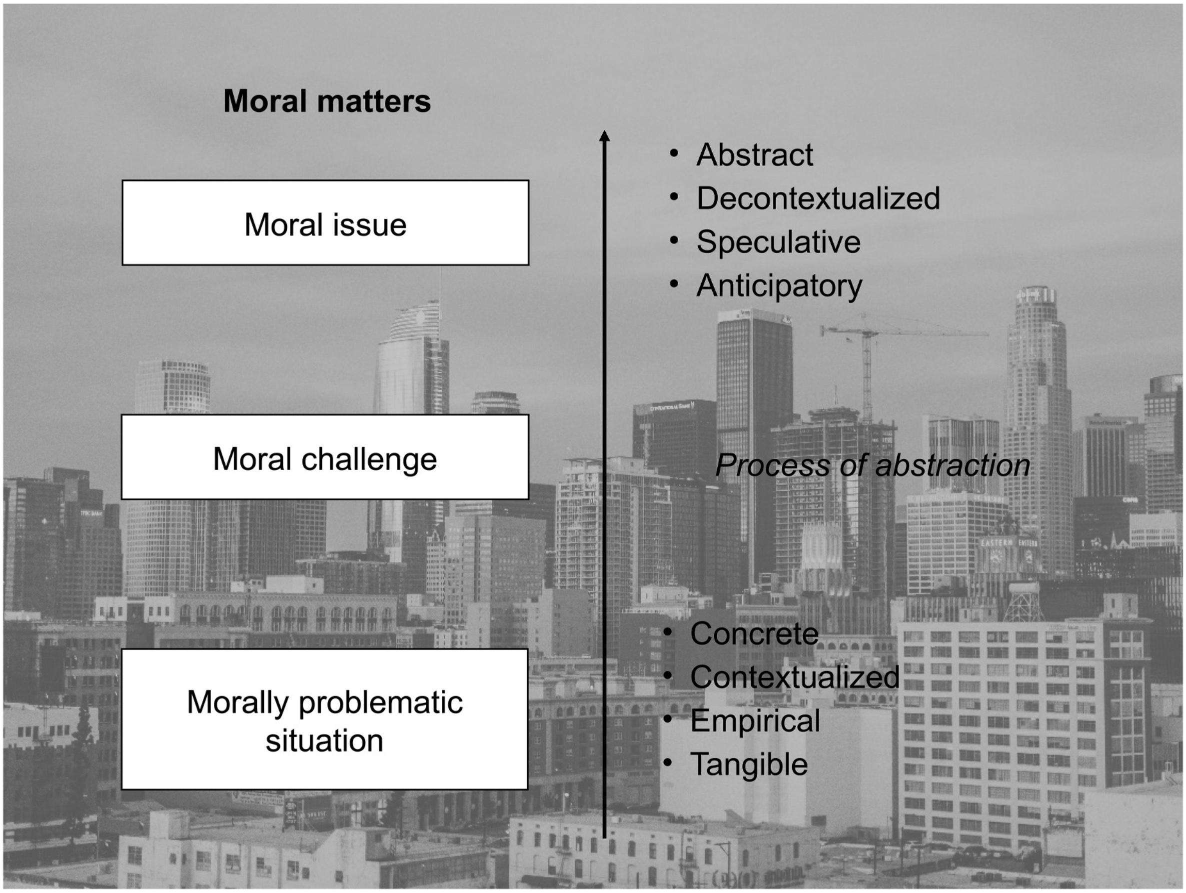


Figure 1. Types of moral matters and their levels of abstraction.

deescalate the felt tension, a refined scenario will need to be imagined and adopted.[25] Ultimately, the resolution of the situation through a fruitful scenario will restore the lost equilibrium in the agent's life.[9,26–28] Through this experience, the agent's well-being, growth, and flourishing will have been nurtured through the empowerment and self-advocacy strategies he or she mobilized to overcome the situation.[29]

Moral matters and their levels of abstraction

The notion of morally problematic situations invites comparison with other terms used to describe different types of moral matters, as well as greater refinement in the terminology used to describe them. Bogossian and colleagues[10] have defined various types of moral matters and have suggested that they can be represented along a continuum. These moral matters can be distinguished based on their level of abstraction and physical existence (i.e. from concrete and existing experiences to more abstracted and generalized forms) and their temporal level of immediacy (i.e. from arising in the present moment to being anticipated in a distant future).[10] An adaptation of the typology put forward by these authors is presented in Figure 1. The typology was adapted to account for recent advances in pragmatist theory and terminology,[30] and is comprised of three types of moral matters, namely morally problematic situations, moral challenges, and moral issues, for methodological reasons such as simplifying data extraction.

Morally problematic situations, as described above, are a type of moral matters representing concrete and contextualized episodes of lived life occurring in a here and now form. Since they are actively experienced by agents, they warrant timely resolution, notably through processes of moral inquiry inspired by pragmatist ethics.[10,22] On the contrary, moral issues are abstract, decontextualized, and anticipatory in essence. Given their more speculative nature, they do not necessarily require immediate action and are generally addressed through anticipatory analyses relying on more abstract ethical language.[10,31,32] Moral challenges are situated halfway between morally problematic situations and moral issues.[10] We suggest that morally problematic situations, as experienced uniquely by individuals, are instantiations of moral challenges that are more abstract. In other words, moral challenges can be derived from similar morally problematic situations through a process of abstraction. Moral challenges have an empirical basis but aremore abstract and decontextualized than morally problematic situations since they do not retain each of their unique spatial and temporal characteristics. Despite seemingly staunch barriers, the differences between morally problematic situations, moral challenges, and moral issues are understandably not clear-cut (see Figure 1).

Such theoretical distinctions between types of moral matters have significant methodological implications for bioethics research through their unique value and function.[35] Experiential and situated language, such as values and constraints at play, could be fruitfully used to describe morally problematic situations, which are experientially entrenched. In contrast, more abstract and decontextualized language, such as jeopardized principles originating from Beauchamp and Childress' principlism for example,[33] could be used to describe moral challenges and moral issues, which are increasingly abstract.

Morality, ethics, and rare diseases

To our knowledge, the experiences of adults living with rare diseases have not been previously studied through the lens of morally problematic situations, moral challenges, and moral issues. While previous reviews and studies reveal the practical difficulties these individuals face,[34] they fall short of discussing at length their moral implications at different levels of abstraction, a gap common in qualitative literature with ethical relevance.[35] Moreover, several studies feature individuals living solely with specific rare diseases,[36,37] thereby failing to highlight common struggles arising in relation to the rarity of various illnesses. More clarity on the moral experiences of individuals living with rare diseases could be gained by understanding the morally problematic situations they face, using a pragmatist ethics lens. This explains our stated goals to uncover experienced moral matters through a scoping review methodology, and then to analyze the moral dimensions of morally problematic situations using this pragmatist concept. In this context, our first objective was to uncover the moral matters (i.e. moral issues, moral challenges, and morally problematic situations) of relevance to adults living with rare diseases discussed in the qualitative literature. Our second objective was to investigate the moral dimensions of morally problematic situations, specifically to see whether this concept helps to better understand moral experiences of adults living with rare diseases.

Materials and methods

This study was designed based on a scoping review methodology developed by Arksey and O'Malley.[38] We followed Arksey's and O'Malley's seven stages: (a) formulating research questions; (b) identifying relevant studies; (c) study selection; (d) data extraction; (e) consultation exercise; (f) thematic and interpretive coding; and (g) reporting results.[38] Figure 2 summarizes the number of studies identified and selected through these stages in a PRISMA-like flowchart.[39]

Research questions

The scoping review was designed to answer the two following research questions:

What are the moral matters (i.e. moral issues, moral challenges, and morally problematic situations) discussed in qualitative studies conducted among adults living with rare diseases?

What are the dimensions of moral matters classified as morally problematic situations, and does the concept of morally problematic situation enhance the understanding of the moral experiences of adults living with rare diseases?

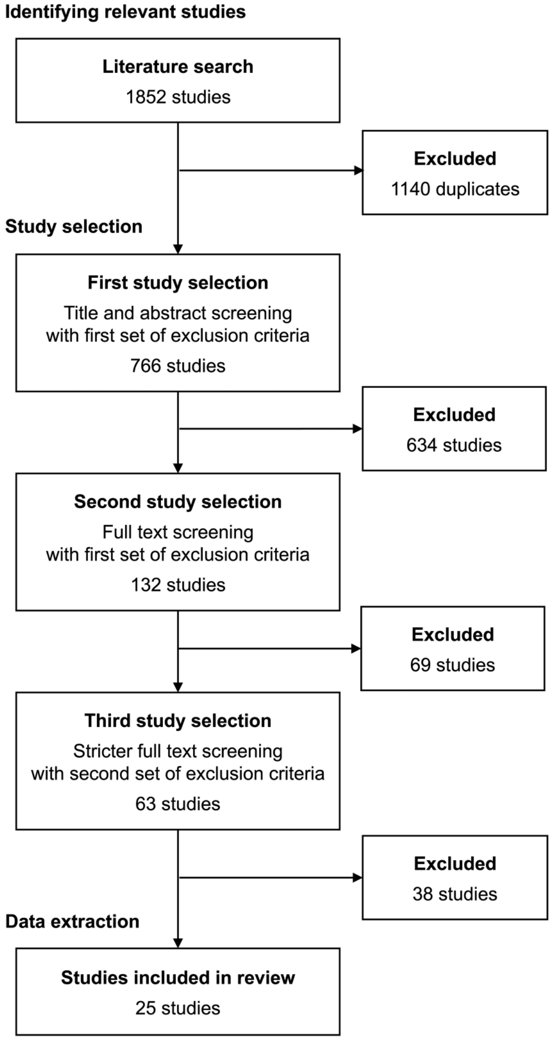


Figure 2. Studies identified and selected through the scoping review.

Identifying relevant studies

The search strategy was designed around two concepts, notably rare diseases and qualitative research methods, in addition to five subconcepts relating to qualitative research: narrative approaches, interviews, focus groups, ethnographic methods, and qualitative analysis methods. An initial search strategy was prepared for the PubMed bibliographic database (see Additional File 1). The search strategy combined medical subject headings (MeSH), non-MeSH search terms applied to the Title and Abstract fields, and filters. The literature search was conducted on 23 July 2020, and targeted journal articles published since 1 January 2000. Older articles were excluded from the search because some of the difficulties reported in these studies could be less relevant today due to the general advancement of specialized healthcare.[40] The strategy was subsequently adapted for the following additional bibliographic databases, notably Web of Science, CAIRN, CINAHL, Ebsco Host (ERIC, Academic Search Complete, Anthropology Plus, APA PsycBooks, Applied Science & Technology Index [H.W. Wilson], CINAHL Plus with Full Text, Gender Studies Database, Humanities International Index, Social Sciences Index Retrospective: 1907–1983 [H.W. Wilson], SocINDEX with Full Text), and Embase.

Study selection

The study selection proceeded in three stages, according to broad inclusion criteria and narrow exclusion criteria, using the Covidence online platform (https://www.covidence.org). During the first selection stage, titles and abstracts of studies obtained through the literature search were assessed for the inclusion criteria. The inclusion criteria of the studies were: being written or translated in English or French (understood by the authors); being primary qualitative studies conducted with adults living with rare diseases; and targeting the experiences of the health conditions in these adults' everyday lives or in clinical settings. Rare diseases were defined as having a prevalence inferior to 1/2000 in accordance with the European Organization for Rare Diseases.[1] Studies whose titles or abstracts were incompatible with these criteria were excluded. Moreover, studies targeting rare psychiatric disorders or exclusively targeting rare cancers or undiagnosed rare diseases were excluded. Rare psychiatric disorders were excluded because they involve markedly different medical trajectories than organic illnesses, which include rare diseases. Rare cancers were excluded since they represent an entirely different clinical context, as patients have access to cancer care centers with ample resources. Undiagnosed rare diseases were excluded given that, by definition, the rarity of an undiagnosed medical condition cannot be confirmed without a diagnosis. During the second selection stage, the remaining studies' full texts were assessed for the inclusion criteria. Studies for which full texts were unavailable online or later found incompatible with these criteria were excluded.

During the third selection stage, new exclusion criteria were introduced to limit the number of included articles, given the depth (as opposed to the breadth) of the data extraction strategy. These new exclusion criteria were: studies not conducted exclusively with adults living with rare diseases;[41] studies designed to understand lived experiences with rare diseases only with the aim to improve care or services (e.g. therapeutic education, coverage, telephonic support, quality of clinical care, or peer connect services;[42] studies providing a qualitative description of symptoms to guide clinical practice;[43] and studies investigating individuals living with rare diseases' information seeking strategies.[44]

Data extraction

The characteristics of included studies were extracted. These characteristics were: rare disease(s) featured in the study accompanied by a short description, country where the study was conducted (or the corresponding author's country if the study's location was not specified), study objective, number of participants and targeted demographic group when specified (e.g. women, men, young adults), qualitative data collection method, and qualitative data analysis method.

Data extraction forms were respectively prepared for morally problematic situations, moral challenges, and moral issues based on the definitions provided in the *Theoretical and conceptual framework* section. Every time a moral matter was encountered in a selected study, a corresponding data extraction form was filled with key aspects of the moral matter, its moral salience, and a text excerpt. The data extraction was conducted by the first author and reviewed by the third author. The fields of the three data extraction forms (see Additional File 2) slightly differ for each type of moral matter. More detailed key aspects were extracted for morally problematic situations notably because, unlike moral issues and moral challenges, they involve precise agents (rather than broad groups of stakeholders) that interact in a specific context.[9,45]

Moral salience was reported differently across types of moral matters. Due to their experiential nature, morally problematic situations were determined to be morally salient if an agent experienced a tension such as uncertainty, discomfort, distress, hesitancy, frustration, uneasiness, or an inner dilemma that impacted their well-being or flourishing. These tensions, to qualify as moral in nature, also needed to engage the agent's values or feature a constraint or constraints preventing the agent from actualizing their values. Hence, for each morally problematic situation, the tension in addition to the value(s) or constraint(s) at play were extracted. Values encompassed priorities, needs, preoccupations, desires, or preferences, while constraints included roles, obligations, or practices.[45]

In contrast, because of their less experiential nature, issues and challenges were determined to be morally problematic using more abstract ethical language that reflected the nature of these moral matters. Accordingly, we relied on Beauchamp and Childress' principlist framework,[33] which is based on four principles, namely respect for autonomy, beneficence, nonmaleficence, and justice.[33] Issues and challenges were morally significant if they jeopardized at least one principle or if they featured a tension between some of the principles. Therefore, for each moral issue or moral challenges, the principle(s) that was or were in tension or jeopardized was noted in extraction forms. Overall, throughout this interpretive exercise, principles were conceptualized as being abstract and decontextualized, unlike values and constraints which are experientially and contextually relevant for agents in accordance to the definitions provided above.[22]

Main consultation exercise

This scoping review is part of a greater multistep research project aiming to understand the morally problematic situations experienced by adults living with rare diseases. Throughout this participatory-action project,[46] a working group composed of patient partners, representatives from the Canadian province of Québec's rare disease association (i.e. the Regroupement québécois des maladies orphelines), and two clinician researchers specialized in rare diseases has been involved in each step of the project. Participatory-action research, operationalized through a working group, is consistent with the intersubjective tenets of pragmatist ethics that recognize the usefulness of deliberation and experiential knowledge in understanding morally problematic situations and supporting their resolution.[9,22,46] At this stage, working group members were asked to identify the most important morally problematic situations to them among those extracted. These situations, along with related moral matters, are emphasized in the Results and Discussion sections.

Thematic and interpretive coding

Two successive coding phases were applied to the extracted data to further guide the reporting of results.[47,48] Figure 3 summarizes these two coding phases, which are thematic analysis and interpretive analysis, and their relationship to the study objectives.

Thematic analysis. The thematic analysis[49] aimed to classify moral challenges and morally problematic situations according to their contexts of emergence in order to facilitate their reporting, following the first objective of the review. Contexts of emergence corresponded to the environments in which moral matters took place, consistently with a transactional account of human experience.[20] This initial coding phase was conducted using the software MAXQDA (Berlin, Germany).[50] The coding logic presented in Figure 3 is compatible with the definitions of moral challenges and morally problematic situations provided above. The generated thematic coding guide classified these moral matters under their corresponding contexts of emergence, which were healthcare, personal life, relationship with the illness, social environment, and career and studies. Due to space limitations, only the matters coded under healthcare are reported in this manuscript, apart from a few excerpts related to medical expenses that have been coded under personal life. Moreover, moral matters pertaining to healthcare were subsequently classified according to the phases of the medical trajectory: diagnostic odyssey, diagnosis, clinical care and treatment, and medical follow-up.

Interpretive analysis. The interpretive analysis[51] aimed to identify how the moral dimensions of morally problematic situations materialize across situations, following the second objective of the review. The interpretive coding guide was initiated with three primary codes designating moral dimensions introduced above, which were *internal tensions*, *constraints to agency*, and *empowerment and self-advocacy strategies*. These codes are in line with the account of lived experience of an agent within a situation, in addition to the pragmatist understanding of agency.[19] Secondary codes emerged inductively and were refined iteratively,[50] designating types of internal tensions, types of constraints to agency, and types of empowerment and self-advocacy strategies. Under each secondary code, situations were coded based on the medical environments in which they arose, as explained in Figure 3.

Reporting results. We used a narrative review to synthesize findings and illustrate examples. Examples of morally problematic situations, which have been selected by the working group, are provided. These examples are accompanied by explanations of their moral dimensions as identified through the interpretive analysis in addition to the profiles of those who experienced them when specified by the authors (e.g. age, gender, and rare disease). The working group reviewed this manuscript, and the resulting feedback was taken into account.

Results

Included studies

A total of 25 studies were included in the review. The studies included participants living with 23 different rare diseases, not including the rare diseases of the participants of the Bryson et al.'s (2021) study, which were not

Coding strategy	**Thematic analysis**	**Interpretive analysis**
Aims of the analyses	Classify **moral challenges** and **morally problematic situations** according to their contexts of emergence to facilitate their reporting. *(~objective 1 of the study)*	Identify how the **moral dimensions** of **morally problematic situations** materialize across situations. *(~ objective 2 of the study)*
Coded excerpts	• Extracted **moral challenges** • Extracted **morally problematic situations** • Given that few moral issues have been extracted, they were not integrated to the coding guide.	• Extracted **morally problematic situations**

Coding guide structure	• Primary codes: **Contexts of emergence**
	  • i.e., **healthcare**, personal life, relationship with the illness, social environment, career and studies
	• Secondary codes: **More precise contexts of emergence**
	  • For healthcare: **Medical environments**
	    • i.e., Diagnostic odyssey; diagnosis; clinical care and treatment; and medical follow-up *(e.g., Figure 4)*
	• Tertiary codes: **Even more precise contexts of emergence**
	  • e.g., For Diagnosis: Diagnoses poorly communicated, usefulness of a diagnosis, uselessness of a diagnosis, examples of difficult decisions *(e.g., Figure 4)*
	• Quaternary codes: **Moral challenges** *(e.g., Figure 4)*
	• Quinquennary codes: **Morally problematic situations**
		• Primary codes: **Moral dimensions of morally problematic situations**
		  • Internal tensions
		  • Constraints to agency
		  • Empowerment and self-advocacy strategies
		• Secondary codes: **Types of…**
		  • Internal tensions
		  • Constraints to agency
		  • Empowerment and self-advocacy strategies
		  • *(e.g., Figure 5)*
		• Tertiary codes: **Medical environments**
		• Quaternary codes: **Morally problematic situations**

Figure 3. Coding strategies and coding guide structure.

specified. Table 1 below briefly defines the rare diseases represented in the included studies and provides study characteristics.

Moral issues

Moral matters were extracted as moral issues if they were abstract, decontextualized, and speculative in nature. Eight moral issues pertaining to healthcare were identified. Moral issues relating to accessibility addressed the obstacles in accessing appropriate treatment with respect to epoch, geographical location, and financial situations, and highlighted the difficulties in obtaining specialized and timely care.[37,54,67] Other moral issues alluded to clinicians' limited knowledge on rare diseases, which sometimes involved poor recognition of patients' expertise, and stigmatization of patients.[57,69] Moral issues linked to illness management addressed the unpredictability of illness manifestations and the resulting loss of control, in addition to difficulties with finding credible information on the Internet and in online support groups.[55,70]

Moral challenges

Moral matters were identified as moral challenges if they had empirical basis while featuring indefinite individuals. Seventy-five distinct moral challenges relating to healthcare were identified. These moral challenges arose across various medical environments, notably the diagnostic odyssey, diagnosis, clinical care and treatment, and

Table 1. Rare diseases and characteristics of the studies included in this scoping review.

Rare disease(s) featured in the study, based on information provided in the study	References	Country	Study objective	Participants	Qualitative data collection method	Qualitative data analysis method, using the authors' terminology
Studies featuring single rare diseases						
Autoimmune Addison's disease: Adrenal glands fail to produce essential hormones. The illness is managed through replacement therapies.	53	Sweden	"Exploring challenges and possibilities situated in everyday life"	5 adults	Photovoice method	Thematic analysis
Congenital hypogonadotropic hypogonadism: Insufficient production of gonadotropin releasing hormone, which limits or prevents puberty and leads to infertility.	54	Switzerland	"Explore specific patient-identified targets for care and to examine the acceptability of possible online interventions"	26 men	Focus group discussion	Thematic analysis
Dystonia: A family of diverse movement disorders featuring muscle spasms of variable frequency which may impact posture.	7	United Kingdom	"Exploring the experience of living with dystonia"	8 adults	Semi-structured interviews	Phenomenological interpretive analysis
Hereditary hemorrhagic telangiectasia: Arteriovenous malformations leading to the dilatation of small blood vessels near the surface of the skin, causing frequent nosebleeds.	55	France	"Accurate description of health-related quality of life of hereditary hemorrhagic telangiectasia patients."	13 adults	Semi-structured interviews	Grounded theory analysis with a phenomenological perspective
Hermansky-Pudlak syndrome: Multisystemic syndrome characterized by visual impairment, albinism, and a bleeding disorder.	36	United States	"Explore the experience of individuals with this rare genetic disease"	23 adults	Semi-structured interviews	Colaizzi's phenomenological data analysis method
Holt-Oram syndrome: Diverse upper limb and cardiac malformations.	56	France	"Shed light on individuals' subjective perceptions of their diseases, how these perceptions provide meaning, and the consequences the syndrome can have in daily life and across all life stages"	10 adults	Semi-structured interviews	Interpretative phenomenological analysis
(Recessive) limb-girdle muscular dystrophy: A family of degenerative neuromuscular disorders	57	Sweden	"Young adults' experiences of living with recessive limb-girdle muscular dystrophy"	14 young adults	Semi-structured interviews	Content analysis guided by a salutogenic orientation

(continued)

Table 1. Continued.

Rare disease(s) featured in the study, based on information provided in the study	References	Country	Study objective	Participants	Qualitative data collection method	Qualitative data analysis method, using the authors' terminology
impacting shoulder girdle, pelvic girdle, and other proximal limb muscles.						
See previous.	58	United States	"Issues that have the greatest impact on their quality of life"	20 adults	Semi-structured interviews	Framework technique application
Lipodystrophy: Diminished or absent body fat with metabolic abnormalities (e.g. severe insulin resistance).	59	United Kingdom	"Impact of lipodystrophy on body image and how this affects patients' daily lives"	11 adults	Semi-structured interviews	Inductive thematic analysis
Indolent systemic mastocytosis: Abnormal and chronic mobilization of mast cells in organs, typically in the digestive system, skin, and bone marrow.	60	Denmark	"Patients' perspectives on everyday life with (indolent systemic mastocytosis) and how they experience, understand and manage the symptoms and challenges in everyday life"	7 adults	Semi-structured interviews	Giorgi's phenomenological data analysis method
Moebius syndrome: Facial paralysis.	61	United States	"Social interaction experiences and strategies"	12 adults	Focus groups	Content analysis
Pemphigus: Autoimmune disease leading to severe and painful blistering.	62	France	"(Individuals living with pemphigus) critiques of the medical work conducted during the trying diagnostic period"	54 adults	Interviews with discourse co-construction (Kaufmann 1996) with one initial question	Constant comparative method
See previous.	63	France	"Experience of illness—in this case, pemphigus—reconfigures engagement in leisure activities, and how these activities are integrated into the biographies of persons with a rare chronic illness"	25 adults	Interviews with one initial question	Constant comparative method
Phenylketonuria: Congenital enzyme deficiency managed through a protein-restricted diet.	64	Norway	"Everyday life for young adults with PKU"	11 young adults	Semi-structured interviews	Grounded theory analysis
See previous.	37	Norway	"Young and early treated Norwegian adults' experiences"	11 young adults	Semi-structured interviews	Grounded theory analysis
Progressive ataxia: Family of movement disorders impacting movement, balance, and speech.	65	United Kingdom	"Patients' experiences of ataxia and its symptoms."	38 adults	Semi-structured interviews	Thematic analysis

(continued)

Table 1. Continued.

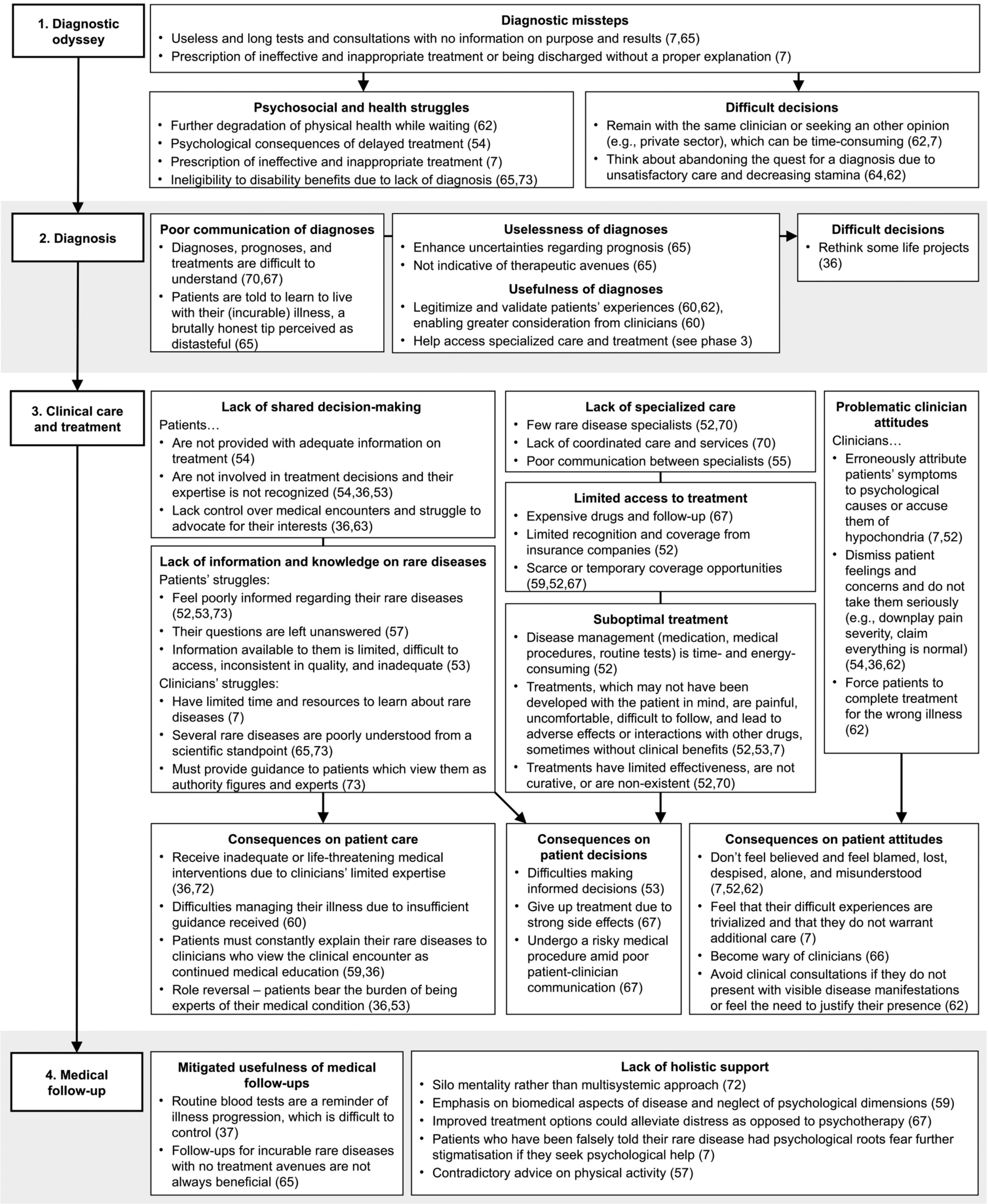
Rare disease(s) featured in the study, based on information provided in the study	References	Country	Study objective	Participants	Qualitative data collection method	Qualitative data analysis method, using the authors' terminology
Pulmonary hypertension: High blood pressure within the pulmonary arteries resulting in breathlessness and limited energy.	66	Italy	"Investigating the illness experience of PH"	11 women	Written illness narratives	Giorgi's phenomenological data analysis method
See previous.	67	Taiwan	"Explore and understand the treatment experiences of patients with PH"	17 adults	Semi-structured interviews	Thematic analysis
Scleroderma: Multisystemic disease characterized by progressive fibrosis and immune dysfunction.	68	Turkey	"Daily life experiences of patients"	16 adults	Demographic survey and semi-structured interviews	Colaizzi's phenomenological data analysis method
See previous.	69	Canada	"Understand, from the individual's perspective, the experience of living with scleroderma"	13 women	Focus group discussion	Data analyzed for themes
See previous.	70	Canada	"Coping strategies employed by individuals living with scleroderma"	22 adults	Focus group discussion	Content analysis inspired by Lazarus' and Folkman's theoretical model on coping strategies and anchored in a social constructionist epistemology
See previous.	71	Canada and United States	"Understand how patients with scleroderma perceive the social support they need and receive from close relationships to better manage their disease"	19 adults	Semi-structured focus group discussions	Thematic analysis anchored in a social constructionist epistemology
Studies featuring multiple rare diseases						
Arthrogryposis multiplex congenita: Congenital joint contractures severely limiting mobility and muscle strength. *Dysmelia*: Various limb reductions. *22q11 deletion syndrome*: Congenital tissue and organ alterations accompanied by immune deficits. *Klinefelter syndrome*: Presence of more than one X chromosome in	72	Sweden	"Investigate the experiences of adults living with different rare diagnoses, how they perceived their difficulties, needs and participation in everyday life, and to identify some common issues and problems"	38 adults	Focus group discussion	Content analysis

(continued)

Table 1. Continued.

Rare disease(s) featured in the study, based on information provided in the study	References	Country	Study objective	Participants	Qualitative data collection method	Qualitative data analysis method, using the authors' terminology
men leading to low testosterone and limited sperm production.						
Neurofibromatosis type 1: Development of tumors in the skin, brain, nerves, and other body parts accompanied by changes in skin pigmentation. *Primary sclerosing cholangitis*: Alteration of the bile ducts preventing bile from adequately exiting the liver. *Pulmonary hypertension*: See definition above. *Marfan syndrome*: Congenital connective tissue alterations in the bones, nervous system, lungs, skin, heart, and eyes.	73	Germany	"Perceived burden of patients with rare chronic diseases and identify commonalities and differences in the experiences of patients with four heterogeneous conditions."	18 adults	Diversified focus groups	Qualitative content analysis
Various unspecified rare diseases, mostly limited to rare neurological diseases and rare cancers	52	United States	"Which challenges, in participants' own words, are most prevalent across a sample of individuals"	1157 adults	One open-ended question	Content analysis

Note. PH: pulmonary hypertension.



1. Diagnostic odyssey

Diagnostic missteps
- Useless and long tests and consultations with no information on purpose and results (7,65)
- Prescription of ineffective and inappropriate treatment or being discharged without a proper explanation (7)

Psychosocial and health struggles
- Further degradation of physical health while waiting (62)
- Psychological consequences of delayed treatment (54)
- Prescription of ineffective and inappropriate treatment (7)
- Ineligibility to disability benefits due to lack of diagnosis (65,73)

Difficult decisions
- Remain with the same clinician or seeking an other opinion (e.g., private sector), which can be time-consuming (62,7)
- Think about abandoning the quest for a diagnosis due to unsatisfactory care and decreasing stamina (64,62)

2. Diagnosis

Poor communication of diagnoses
- Diagnoses, prognoses, and treatments are difficult to understand (70,67)
- Patients are told to learn to live with their (incurable) illness, a brutally honest tip perceived as distasteful (65)

Uselessness of diagnoses
- Enhance uncertainties regarding prognosis (65)
- Not indicative of therapeutic avenues (65)

Usefulness of diagnoses
- Legitimize and validate patients' experiences (60,62), enabling greater consideration from clinicians (60)
- Help access specialized care and treatment (see phase 3)

Difficult decisions
- Rethink some life projects (36)

3. Clinical care and treatment

Lack of shared decision-making

Patients…
- Are not provided with adequate information on treatment (54)
- Are not involved in treatment decisions and their expertise is not recognized (54,36,53)
- Lack control over medical encounters and struggle to advocate for their interests (36,63)

Lack of information and knowledge on rare diseases

Patients' struggles:
- Feel poorly informed regarding their rare diseases (52,53,73)
- Their questions are left unanswered (57)
- Information available to them is limited, difficult to access, inconsistent in quality, and inadequate (53)

Clinicians' struggles:
- Have limited time and resources to learn about rare diseases (7)
- Several rare diseases are poorly understood from a scientific standpoint (65,73)
- Must provide guidance to patients which view them as authority figures and experts (73)

Lack of specialized care
- Few rare disease specialists (52,70)
- Lack of coordinated care and services (70)
- Poor communication between specialists (55)

Limited access to treatment
- Expensive drugs and follow-up (67)
- Limited recognition and coverage from insurance companies (52)
- Scarce or temporary coverage opportunities (59,52,67)

Suboptimal treatment
- Disease management (medication, medical procedures, routine tests) is time- and energy-consuming (52)
- Treatments, which may not have been developed with the patient in mind, are painful, uncomfortable, difficult to follow, and lead to adverse effects or interactions with other drugs, sometimes without clinical benefits (52,53,7)
- Treatments have limited effectiveness, are not curative, or are non-existent (52,70)

Problematic clinician attitudes

Clinicians…
- Erroneously attribute patients' symptoms to psychological causes or accuse them of hypochondria (7,52)
- Dismiss patient feelings and concerns and do not take them seriously (e.g., downplay pain severity, claim everything is normal) (54,36,62)
- Force patients to complete treatment for the wrong illness (62)

Consequences on patient care
- Receive inadequate or life-threatening medical interventions due to clinicians' limited expertise (36,72)
- Difficulties managing their illness due to insufficient guidance received (60)
- Patients must constantly explain their rare diseases to clinicians who view the clinical encounter as continued medical education (59,36)
- Role reversal – patients bear the burden of being experts of their medical condition (36,53)

Consequences on patient decisions
- Difficulties making informed decisions (53)
- Give up treatment due to strong side effects (67)
- Undergo a risky medical procedure amid poor patient-clinician communication (67)

Consequences on patient attitudes
- Don't feel believed and feel blamed, lost, despised, alone, and misunderstood (7,52,62)
- Feel that their difficult experiences are trivialized and that they do not warrant additional care (7)
- Become wary of clinicians (66)
- Avoid clinical consultations if they do not present with visible disease manifestations or feel the need to justify their presence (62)

4. Medical follow-up

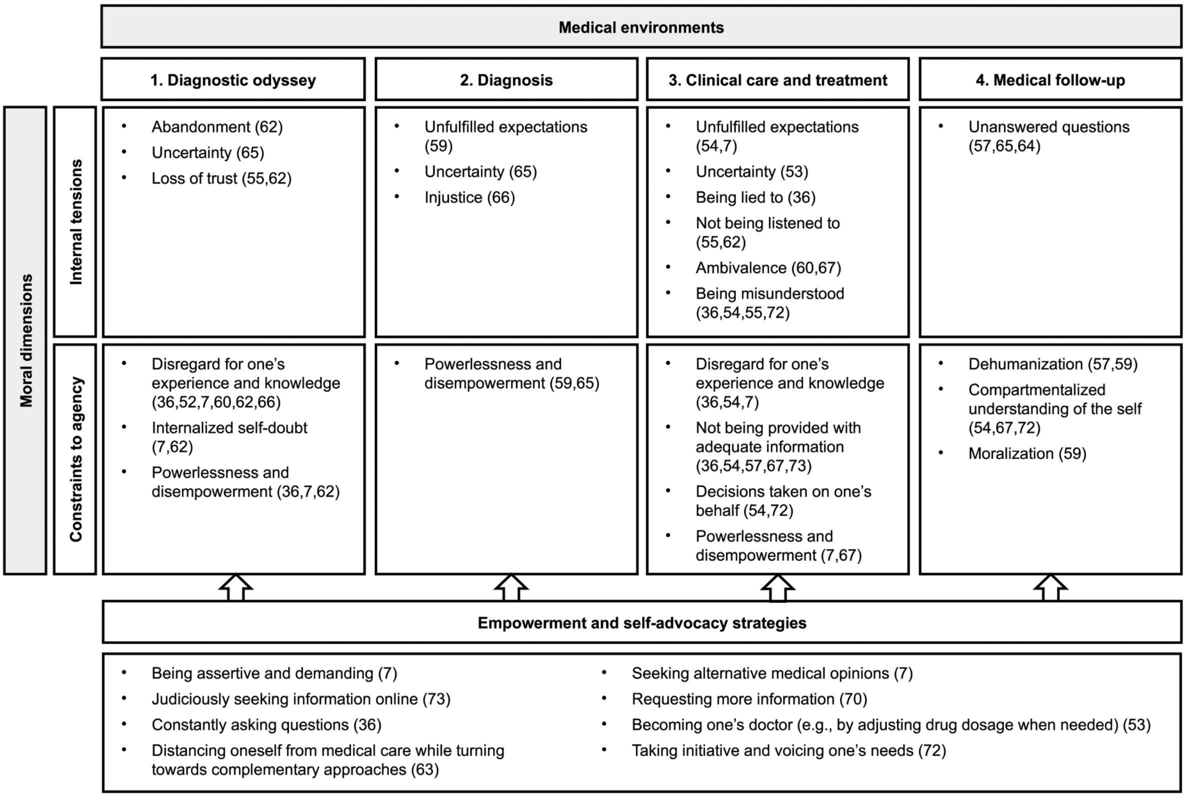
Mitigated usefulness of medical follow-ups
- Routine blood tests are a reminder of illness progression, which is difficult to control (37)
- Follow-ups for incurable rare diseases with no treatment avenues are not always beneficial (65)

Lack of holistic support
- Silo mentality rather than multisystemic approach (72)
- Emphasis on biomedical aspects of disease and neglect of psychological dimensions (59)
- Improved treatment options could alleviate distress as opposed to psychotherapy (67)
- Patients who have been falsely told their rare disease had psychological roots fear further stigmatisation if they seek psychological help (7)
- Contradictory advice on physical activity (57)

Figure 4. Moral challenges arising across various medical environments.

medical follow-up. These moral challenges are summarized in Figure 4.

Briefly, undergoing a diagnostic odyssey involved diagnostic missteps, such as useless medical consultations and diagnostic tests or inappropriate treatment. Waiting for a diagnosis had striking psychological and health-related consequences and prompted difficult decisions. Diagnoses were often poorly communicated, through information difficult to understand and with a lack of sensitivity towards patients' distressing life situations. Some diagnoses sometimes relieved patients by validating their experiences and granting them with longed access to specialized care,



Medical environments

Moral dimensions		1. Diagnostic odyssey	2. Diagnosis	3. Clinical care and treatment	4. Medical follow-up
	Internal tensions	• Abandonment (62) • Uncertainty (65) • Loss of trust (55,62)	• Unfulfilled expectations (59) • Uncertainty (65) • Injustice (66)	• Unfulfilled expectations (54,7) • Uncertainty (53) • Being lied to (36) • Not being listened to (55,62) • Ambivalence (60,67) • Being misunderstood (36,54,55,72)	• Unanswered questions (57,65,64)
	Constraints to agency	• Disregard for one's experience and knowledge (36,52,7,60,62,66) • Internalized self-doubt (7,62) • Powerlessness and disempowerment (36,7,62)	• Powerlessness and disempowerment (59,65)	• Disregard for one's experience and knowledge (36,54,7) • Not being provided with adequate information (36,54,57,67,73) • Decisions taken on one's behalf (54,72) • Powerlessness and disempowerment (7,67)	• Dehumanization (57,59) • Compartmentalized understanding of the self (54,67,72) • Moralization (59)

Empowerment and self-advocacy strategies

- Being assertive and demanding (7)
- Judiciously seeking information online (73)
- Constantly asking questions (36)
- Distancing oneself from medical care while turning towards complementary approaches (63)
- Seeking alternative medical opinions (7)
- Requesting more information (70)
- Becoming one's doctor (e.g., by adjusting drug dosage when needed) (53)
- Taking initiative and voicing one's needs (72)

Figure 5. Experiences of internal tensions and constraints to agency across morally problematic situations.

although other diagnoses failed to clarify uncertain prognoses or therapeutic avenues. Diagnoses also elicited emotional struggles, especially if the illness was incurable, and led to heartbreaking life decisions.

Once clinical care and treatment were made available, patients had to face insufficient specialized care for their rare diseases, the lack of conditions conducive to shared decision-making, poor information and knowledge on rare disease provided by clinicians, in addition to suboptimal or inaccessible treatment, which prompted additional disheartening decisions. Patients were also met with problematic attitudes from clinicians. Together, these challenges had immediate and long-lasting consequences on patients. The process of seeking medical follow-ups over time turned out to be not always desirable or useful and was marked by a lack of holistic support from clinicians.

Morally problematic situations

Moral matters were classified as morally problematic situations if they featured concrete life episodes experienced by specific individuals. These situations were unsettling and distressing, and often left these individuals feeling like they could not make an authentic and fulfilling choice. Seventy distinct morally problematic situations relating to healthcare were identified. These situations arose across medical environments: diagnostic odyssey, diagnosis, clinical care and treatment, and medical follow-up. These situations were morally problematic because they elicited a diversity of internal tensions within agents and hindered their capacity to intervene upon the situation, although some agents reclaimed control over the situation through empowerment and self-advocacy.

Internal tensions were defined as subjective discomfort experienced by agents who were confronted with important questions regarding their values and existence within a morally problematic situation. Constraints to agency hindered the agents' ability to intervene upon morally important aspects of the situation they were confronted with. Empowerment and self-advocacy were achieved through various strategies mobilized by agents to take leadership and control of the situation they faced, strategies that were unfortunately perceived negatively by clinicians. The moral dimensions elicited through the interpretive coding of the situations are summarized in Figure 5. Examples of these situations are provided below, with their moral dimensions evidenced in bold and using the same terminology presented in Figure 5.

Diagnostic odyssey. Adults living with rare diseases experienced a myriad of morally problematic situations during their diagnostic odysseys. Examples of these situations included skepticism expressed by clinicians regarding the suffering of the patients, the existence of their rare diseases, and the severity of their associated symptoms.[36,52] Clinicians also failed to take patients seriously, accusing them of lying, claiming they were hypochondriac or hysteric, and falsely believing that their illness had psychosomatic roots.[36,60,62,66] As the diagnostic odyssey was prolonged, some patients' physical health deteriorated, while others became more worried, and some began to doubt their own symptoms.[62,65] In one of these tragic situations, a woman living with pemphigus felt abandoned and lost trust in the medical establishment. After a diagnostic odyssey of 3 years, she realized that she hid a lot of information from the clinicians to avoid eliciting their skepticism or facing their inability to offer treatment avenues. Upon that revelation, she stopped seeking medical care.[62]

Other situations arising during the diagnostic odyssey limited the agents' ability to act in their unique situations. For instance, another woman from the same study living with pemphigus experienced powerlessness and disempowerment in the face of the severe health crisis she endured. Her experiences and knowledge were disregarded by the clinicians she saw. Over the course of her diagnostic odyssey of 2 months, she became dangerously unable to eat, sleep, or speak, and was close to dying. It was only after several medical appointments with a general practitioner and an otolaryngologist, some erroneous psychiatric diagnoses (e.g. she was suspected of having an eating disorder), and inconclusive treatment for other medical conditions, that she was diagnosed with pemphigus by a stomatologist.[62]

Another woman endured a similar course of events for 9 months. After meeting seven doctors of different medical specialties, she was told by the last one that her illness had psychosomatic origins, which made her feel "completely anxious and disoriented" and lead to internalized self-doubt. As she briefly doubted her illness experience, she was attentive to her physical sensations and later reiterated her initial understanding of having a physical illness. As she contemplated seeking medical care again, she feared not being listened to: "Because if I tell the same story over again and then he [the new doctor] tells me the same thing, I am going to start asking myself, 'But, I am sick, or am I imagining it?' [I am afraid] of not being listened to, afraid of hearing, 'I believe what your doctor told you' [from the new doctor]."[62]

Some individuals living with rare diseases were able to overcome situations of skepticism from clinicians during their diagnostic odyssey, notably by becoming assertive self-advocates. This was the case for Jennifer, a 50-year-old retired British woman living with dystonia. She surmounted clinicians' prejudices by becoming a strong self-advocate and having a "more demanding and aggressive" attitude: "To be told by [clinicians], 'pull yourself together, don't be so stupid' […] I don't have to put up with that, that's just not right. So, ermm, I, I've had to learn to stand my ground […] it's made me a stronger person."[7]

Diagnosis.

Being diagnosed with a rare disease elicited various morally problematic situations for affected individuals. Diagnoses of rare incurable diseases elicited vivid feelings and emotions of isolation, fear, and anger. Similarly, a woman diagnosed with pulmonary hypertension felt poignant injustice. She explained: "you feel detached from reality, like you're at the center of the world but you're alone, you cannot accept to suffer from a rare disease especially when you do not find the cause, you continuously ask yourself 'Why me? What did I do wrong?' But you are not allowed to have an answer."[66]

In another situation, a woman felt desolate due to her diagnostic not fulfilling her expectations of leading to a cure: "I kind of had it in my mind then they're going to find what's wrong and then I'm going to be fixed and I'm going to go back to normal… and [that not happening] was just devastating."[59]

In some situations, a diagnosis was synonymous with unclear benefits and even more questions, leading to uncertainty in addition to powerlessness and disempowerment regarding one's health management. This was the case of a man in his mid-fifties, who had not been prescribed a treatment once diagnosed with idiopathic ataxia. He explained: "nobody's prescribed treatment as of yet… basically waiting and see what happens."[65]

Due to such ambiguity and lack of adequate information regarding one's illness and prognosis, some individuals may feel profoundly unsettled and experience existential anguish. Empowerment strategies, such as judiciously seeking information online, could help mitigate some of these disabling feelings. Plagued with unknowns, a person living with primary sclerosing cholangitis claimed to have "approached Doctor Google, even though I know I have to be very careful."[73]

Clinical care and treatment.

When seeking clinical care and treatment after being diagnosed, individuals living with rare diseases encountered diverse morally problematic situations. When poorly informed about their treatment, some individuals nurtured unrealistic expectations about its effectiveness, which later translated in disappointment and unfulfilled expectations.[7,54] Others were confronted with clinicians' inability to understand their situations, which offered compartmentalized care, rather than holistic care.[36,72] This was the case of a man living with congenital hypogonadotropic hypogonadism, who felt profoundly misunderstood after seeing clinicians: "There's no sense from anyone… about them trying to understand or even that it crosses their mind that you are going through anything. You know, that, it's painful. They are just 'Mr fix-it' give you a prescription and you are gone."[54]

Similarly, an individual living with Hermansky-Pudlak syndrome felt lied to and misunderstood by clinicians. The clinicians had erroneously claimed that this individual was in perfect health uniquely based on good blood markers, which contradicted the individual's subjective experience of the illness. The individual would have preferred a humbler posture from the clinicians, marked by an acknowledgement of their limited understanding of the rare disease and by an openness to learning more.[36] Such negative care experiences alarmingly discouraged some individuals to stop seeking care in emergency departments.[55]

When individuals living with rare diseases interacted with clinicians to receive clinical care and treatment, they were not always supported to act upon their health. Some of these individuals were given insufficient explanations on their rare diseases and their treatment.[54,57,67] In one situation, a man living with congenital hypogonadotropic hypogonadism felt that his experience and knowledge had been promptly dismissed by a clinician. The latter withheld information from him, as if he "wasn't considered intelligent enough to understand what [he] was being treated for."[54] Some individuals were not offered to participate in shared decision-making.[36,54,72] Another man living with congenital hypogonadotropic hypogonadism recalled facing a similar situation. The doctor took a decision on his behalf, thereby disempowering him from his care. He explained, to his dismay, that "He (doctor) didn't give me any treatment options. He just said 'take this gel.' We didn't discuss what was the best treatment."[54]

Conversely, some individuals employed self-advocacy strategies to overcome such situations of misunderstanding and exclusion from medical decisions. For example, an individual living with Hermansky-Pudlak syndrome **constantly asked questions** to the care team about treatment procedures: "I'm very vigilant when I'm in the hospital because if I have an IV (intravenous), I'm like, they have straight access to my blood stream, so I'm like 'Who are you? What's in the syringe? Who ordered it and why?"[36]].

Medical follow-up. As individuals living with rare diseases seek medical follow-ups, they encounter additional unnerving morally problematic situations, such as receiving vague information regarding potential treatment, prognosis, or rare disease management.[37,57,65] For example, a young adult living with recessive limb-girdle muscular dystrophy struggled with clinicians' lack of knowledge regarding prognosis or best practices to prevent physical decline associated with the illness. The upset young adult explained that his questions remained unanswered: "The most frustrating thing about healthcare is that I always get the answer 'Everybody is different so it's not possible to say what it will be like,' whereas I have a clearer picture of what it will be like and I want to be ahead of things… ."[57]

Similarly, a woman living with phenylketonuria also had unanswered questions when she was pregnant: "I had a lot of thoughts about giving birth, if there was anything special I had to consider, other than the diet. You have a lot of questions, you sit and wonder, and nobody at the local hospital knows the answers, because they don't know anything."[37]

Over the course of medical follow-ups, some individuals deplored, feeling merely reduced to their medical conditions as they interacted with clinicians, which could compromise their ability to take charge of their health. A young adult living with recessive limb girdle lamented this dehumanization: "because they don't see the whole … they don't see me as a person and individual but as the disease, so they can't try to suggest creative solutions for me … I think they ought to think a bit for themselves about how they behave and what they say, because we are well aware that we are sick … it gets very palpable."[57]

Such medical follow-ups marked by unanswered questions and dehumanization may not result in clear clinical benefits for some patients. This was the case for a patient, who lived with pemphigus for nearly 17 years and who progressively strived to become a true self-advocate. Faced with clinicians' limited understanding of her condition, she decided to stop taking immunosuppressants. She chose to distance herself from the medical realm while turning to complementary approaches such as stress management, psychotherapy, relaxing hobbies, and physical activity to tackle the triggers of her illness, which she identified as partly psychological.[63]

Critical analysis and proposed taxonomy

In this review, we highlight the state of the literature on moral matters encountered in rare diseases and discussed in qualitative studies. Following proposals to advance ethics theory and terminology to more accurately describe moral matters,[10] the latter were delineated as moral issues, moral challenges, and morally problematic situations. Challenges and situations were further categorized with respect to the various medical environments in which they occurred, which were the diagnostic odyssey, diagnosis, clinical care and treatment, and medical follow-up.

This pragmatist conceptual taxonomy of moral matters showed great promise in understanding moral problems relating to rare diseases at various levels of abstraction. While morally problematic situations are concretely experienced, moral issues are more speculative and anticipated.[10] More importantly, the moral dimensions ascribed to morally problematic situations (i.e. internal tensions, constraints to agency, and empowerment and self-advocacy), provide an enriched outlook on the existential implications of morality for individuals as agents in a specific clinical context. Below, we highlight the distinctiveness of each moral matter with key examples from the study, their usefulness to address morality in practice, their limits, and how they could be expanded upon in future research when applicable.

Moral issues

Moral issues are abstract, decontextualized, and speculative in nature. They are amenable to anticipatory analyses relying on abstract language to be addressed.[10,31,32] A key moral issue extracted in the literature review was accessibility to specialized and timely care and treatment, which depended on geographical location, financial situation, and epoch.[37,67,54] Other moral issues addressed clinicians' limited knowledge of rare diseases and difficulties for patients to access credible information on the Internet and on online support groups about their rare diseases.[70] Addressing moral issues such as accessibility considerations, for example, is often necessary for establishing health policies and funding priorities. Some have advocated for fairer allocation policies for orphan drugs in order to limit accessibility issues, such as high costs for patients and poor financial incentives for developers.[74] Such reflections are often supplemented with the use of abstract moral principles, utilitarian approaches, and rights-based theories.[75]

From a pragmatist ethics perspective, moral claims are fallible and have an instrumental value, meaning that they constitute tools to be refined with improved knowledge of the problem at hand.[30,76] Through empirical data collection, moral issues would be specified and take the shape of moral challenges and morally problematic situations. These contextualized moral matters would be more efficient in informing localized decision-making, like in organizational ethics or clinical ethics. For example, to improve accessibility to emergency care among individuals living with rare diseases in a given metropolis, a survey study would likely need to explore the moral challenges, as opposed to the moral issues, faced by these individuals. In sum, moral issues could either guide the development of health policies or be viewed as "moral intuitions" warranting further investigation for more targeted decision-making. They are helpful to anticipate and eventually prevent the conversion of moral issues into more substantive challenges or situations. However, as seen in discussions about the actual worth of anticipatory analyses of more speculative moral issues, the ability to foresee the materialization of moral issues is limited.[31,77,78]

Moral challenges

Moral challenges are derived from the more poignant moral matter of morally problematic situations through a process of generalization. They retain the empirical basis of the morally problematic situations they refer to, but may lack references to temporal, spatial, or individual elements.[10] Important moral challenges reported in this review included being poorly informed about one's rare disease, associated treatment options, and not being able to readily access comprehensive and adequate information on these topics. Being an expert of one's medical condition was another salient moral challenge identified. Similarly, siloed care, as opposed to multisystemic approaches, was insufficient to tackle patients' needs. Through their concise formulations, moral challenges abstract moral problems from intersubjective and agential outlooks,[28] setting aside their existential salience to seize their general impact on a more considerable number of individuals.

Given their synthesized format, moral challenges are useful for compilations and overviews. For example, a list of moral challenges (e.g. Figure 4) may optimally communicate the diversity and scope of empirically documented moral problems relevant to a given context. Since moral challenges emerge from or point to similar morally problematic situations, they often describe phenomena with significant prevalence. Alternatively, they constitute more concretized iterations of abstract moral issues. As a result, moral challenges may simultaneously inform improvements to clinical practices regarding rare diseases while offering a rationale for undertaking these changes, given that they refer to prevalent or generalized problems with established empirical foundations. In contrast, a morally problematic situation discussed in isolation may not have sufficient weight to warrant changes in broader clinical practices.

Acknowledging the important moral challenges highlighted above could inspire improvements in clinical practices relating to rare diseases. First, an increased use of rare disease reference websites (e.g. https://www.orpha.net/) by clinicians could foster their knowledge of rare diseases, enabling them to provide higher quality information to their patients. This would alleviate some of the burden experienced by patients forced to be solely responsible for their health. Second, hospitals could aim to offer more holistic support to individuals living with rare diseases, as opposed to siloed care. Such support, which would extend to nonmedical specialties (e.g. nutritionists, psychologists, physiotherapists, occupational therapists), would help patients better cope and live with their rare diseases. Such models could be inspired by existing multidisciplinary care models that exist for selected rare diseases such as cystic fibrosis.[79] A list of recommendations for improving clinical practices in the context of rare diseases could be derived more extensively from such moral challenges through eventual deliberative exercises with stakeholders.

Morally problematic situations

Morally problematic situations provide in-depth accounts of morality as experienced through episodic and concrete life experiences.[22] In pragmatist accounts of human experience, situational occurrences of morality are *tripartite*, featuring agents, contexts, and experiences occuring through transactions.[76,80]

What makes these situations *morally problematic* are their moral dimensions, such as internal tensions, constraints to agency, or strategies of empowerment and self-advocacy deployed in response to the situation, as revealed by this review. Of particular importance in this review, three morally problematic situations featured women living with pemphigus being met with various forms of skepticism, denial, and disbelief from clinicians regarding their illness.[62] Each of these situations is morally salient because they elicited internal tensions among these women such as abandonment, loss of trust, and not feeling listened to. The women were also constrained in their ability to act in these situations because they were rendered powerless and disempowered, their knowledge and experience were disregarded, they internalized self-doubt, and they were not listened to. Thus, the concept of the morally problematic situation valuably exhibits how agents interact with their environments, in ways which create important and detrimental internal tensions and constraints to agency.

Moreover, these disturbing examples, along with their moral dimensions, convey the emotional salience of morally problematic situations, that is, as profoundly unsettling, destabilizing, and distressing life episodes. By being deprived of proper recognition and care, individuals living with rare diseases risk profound biographical disruptions well beyond their medical trajectory.[81] Lacking an official diagnosis, which can often be conducive to prognosis and treatment, may markedly jeopardize these individuals' life paths and the accomplishment of their dreams and aspirations. In addition, diagnoses hold epistemic value notably by validating and legitimizing one's arduous illness experience, including in the eyes of other agents,[82,83] which can include friends, family, employers, and medical evaluators for insurance companies. Without benefiting from this epistemic credibility,[76,84] individuals living with rare diseases must face, often alone, the emotional hardships of experiencing incapacitating and unexplained health struggles that threaten their flourishing in all spheres of their lives, including work, leisure, and significant relationships. Morally problematic situations thus elegantly bring forth the embodiment of moral problems within agents, the existential importance of such problems, their emotional salience, and their devastating consequences if left unexamined.[28] As a result, these situations warrant further examination through moral inquiry to pave the way for their eventual mitigation or resolution.[10,28]

While the concept of the morally problematic situation constitutes a valuable tool for understanding and analyzing moral experiences, its inattentive use may inadvertently lead to essentialist or reductionist accounts of moral experiences. In such cases, moral experiences put forward through bioethics research could risk trivializing agonizing experiences. Unfortunately, this pitfall may be in part inevitable. The richness of moral experiences may not be perfectly accounted for through second-hand accounts, and even less through an interpretation of the literature as opposed to primary data collection. The peculiarities of moral experience are poorly captured with traditional bioethical analysis methods because of their tendency to reduce moral problems to the more rationalistic formulations of dilemmas, decisions, and choices.[28] To mitigate this issue, bioethics research should seek to comprehend moral experiences through an in-depth investigation of agents' characteristics and context, and without eclipsing the emotions and tensions they feel in relation to the situations at hand. To that end, empirical research may be more promising than a literature review due to the value of first-hand accounts.

In response to the existential struggles embedded within morally problematic situations, pragmatist ethics points to empowerment and encourages agents to take ownership of situations through a process of inquiry.[29] This orientation resonates with the empowerment and self-advocacy strategies identified in the literature on rare diseases.[85] For example, in one situation identified in the review, a woman living with dystonia had strived to be more assertive to overcome the skepticism of clinicians.[7] Insights stemming from such situations could inform interventions to improve the integration of ethics in patient–clinician interactions. First, adults living with rare diseases could be exposed to the empowerment and self-advocacy strategies identified in the current study, such as adamantly asking questions, requesting more information, taking initiative, and voicing one's needs, through an ethical intervention (e.g. brochure). Knowledge of such strategies could empower these individuals to assume greater leadership and control over the situations they face, thereby limiting the aforementioned constraints to their agency. Indeed, the first step in a process of empowerment is to understand one's situation and one's ability to act upon it in ways that lead to a greater sense of control and greater efficacy in dealing with the situation.[86]

Second, tools for shared decision-making designed for clinicians could be enriched with the results of this study to become effective ethical interventions. Decision aides, which foster respectful and reciprocal exchanges between clinicians and patients, do not always address ethics explicitly.[87,88] Including examples of internal tensions felt by patients (e.g. not being listened to, unfulfilled expectations, unanswered questions), in addition to examples of constraints to patients' ability to act (e.g. disregard for the patient's experience and knowledge, decisions taken on the patient's behalf) in these tools could help clinicians better understand the moral importance of fostering shared decision-making with each patient. Such ethical interventions could be developed with the help of stakeholders through participatory action research approaches reminiscent of pragmatist inquiry.[25]

Strengths and limitations of the study

A first limitation of this study is that it only addresses the experiences of adults living with rare diseases in healthcare settings and, as a result, the identified moral dimensions could manifest quite differently in other contexts. Future studies could investigate whether agents experience these dimensions differently in their daily lives, in relation to their friends and family, in their participation in society, and in their career and studies, for example. Similarly, due to their contextual nature, the situations identified may not be generalizable to all rare diseases or all healthcare settings. A second limitation of this study is that the qualitative data addressing morally problematic situations in the literature was very succinct. As evidenced by the examples provided in the Results section, little information was provided on the study participants' life experiences and context. A truly holistic understanding of morally problematic situations, as recommended by pragmatist ethics, was therefore impossible to achieve. Empirical bioethics research featuring data collection guided by the concept of the morally problematic situation may be promising in enabling in-depth investigations of embedded and situated moral experience. A third limitation of this literature review is that, by design, narrowing data collection to qualitative studies did not enable the identification of several moral issues. Targeting other types of publications featuring higher-level reflections on the ethics of rare diseases might have provided more insights on the moral issues reported in relation to this topic. A fourth limitation of this study is that it did not feature a gender-based analysis of morally problematic situations reported in the literature, notably since gender was not reported in some of the reviewed studies.[73] It is plausible that morally problematic situations, along with their moral dimensions, could be experienced differently based on gender. Future research could seek to illuminate whether gender shapes such moral experiences.

Conclusion

This literature review identified moral issues, moral challenges, and morally problematic situations of importance for adults living with rare diseases. It showcased the possible contributions of a proposed new ethical taxonomy for ethical analysis, while highlighting the added value of the concept of the morally problematic situation to understand moral experiences. The existential importance of these situations is reflected in the internal tensions and constraints to agency they elicit among agents, while empowerment and self-advocacy strategies show promise in overcoming such tensions, to the benefit of the agents' growth and flourishing.

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Data availability statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Supplemental material

Supplemental material for this article is available online.

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