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SPECIAL ARTICLE

"It seems like COVID-19 now is the only disease present on Earth": living with a rare or undiagnosed disease during the COVID-19 pandemic

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PURPOSE: Patients with rare and undiagnosed diseases (RUDs) face significant health challenges, which may be exacerbated during the COVID-19 pandemic. The goal of this study was to identify specific impacts of the pandemic on RUD patients, and targets for improving support and health-care access.
METHODS: We conducted an online survey of RUD patients and their family members from 21 April to 8 June 2020, recruited from 76 Facebook groups for RUDs. Questions assessed patient characteristics and impacts of the pandemic on RUD diagnosis and management.
RESULTS: Respondents ($n = 413$), including 274 RUD patients and 139 family members, were predominantly female and white, though income varied. Impacts of the pandemic included (1) barriers to accessing essential health care, (2) specific impacts of restrictive COVID-19 visitation policies on ability to advocate in health-care settings, (3) uncertainty and fear regarding COVID-19 risk, (4) exacerbated physical and mental health challenges, (5) magnified impacts of reduced educational and therapeutic services, and (6) unexpected positive changes due to the pandemic.
CONCLUSION: There are specific, serious challenges affecting RUD patients and families during the COVID-19 pandemic. There is an urgent need to develop approaches to mitigate these challenges both during and beyond the pandemic.

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INTRODUCTION

The COVID-19 pandemic has dramatically impacted communities across the United States, with the most severe impacts on specific subgroups, including racial/ethnic minorities and individuals with disabilities.[1–3] Among those affected are the 30 million patients living with rare and undiagnosed diseases (RUDs).[4–6] For these patients, medical complexity coupled with diagnostic and/or prognostic uncertainty make navigating health care challenging in the best of times,[7] and these challenges may be exacerbated during the pandemic.

Although there are approximately 7,000 rare diseases, patients grappling with RUDs share many challenges.[7–9] RUD patients typically undergo extensive medical testing as part of their diagnostic odysseys, after which an estimated 50% remain undiagnosed.[10–12] Even when diagnosed, most rare diseases lack effective treatments, leaving many RUD patients reliant on clinical research as their primary source of therapy or for achieving a long-sought diagnosis.[13] However, many clinical research studies were halted as a result of the COVID-19 pandemic.[14–17] RUD patients, and particularly pediatric patients, also often rely on diverse educational and therapeutic services, including those delivered through schools, which are essential but not easily translated to remote platforms. Prolonged stay-at-home orders therefore have the potential to dramatically impact the health of this population. At the same time, these patients are, by definition, grappling with complex health conditions that may create additional vulnerabilities to COVID-19 infection. This tension between increased needs and increased risks raises complex ethical and policy questions regarding how best to ensure that essential services are accessible and sufficient to meet the needs of this vulnerable population.

The goal of this study was to explore the challenges facing RUD patients during the COVID-19 pandemic and to suggest targets for action to address these challenges.

MATERIALS AND METHODS

Recruitment

We conducted an online survey from 21 April to 8 June 2020 through Facebook groups for RUDs, identified using broad and targeted keywords. Broad keywords (e.g., "genetic disease") were selected through a series of preliminary searches testing the number and types of groups identified by different keywords. Targeted keywords (e.g., "Aarskog syndrome") were drawn from the National Organization of Rare Diseases (NORD) rare diseases database.[18]

We confirmed that groups were focused on RUDs by cross-checking the group description with rare disease databases published by professional organizations, including NORD,[19] Global Genes,[20] Genetic and Rare Diseases Information Center,[21] and Orphanet.[22] Any disease identified as rare on any of these lists was considered a rare disease for the purpose of this study. We excluded any groups explicitly oriented to participants in countries other than the United States based on the group description. Once identified, a member of the study team contacted the group administrators through private Facebook message. Of 290 group

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administrators contacted, 76 responded and posted the Qualtrics survey link together with the study description. A full list of participating groups is provided in Appendix A.

Eligibility criteria for survey respondents included (1) age 18 or older, (2) self-identified either as an RUD patient or as a family member of an RUD patient, (3) able to read and write in English. Throughout this paper, we refer to individuals with an RUD as a "patient," including both adult RUD patients and the RUD patients described by their family members who completed the survey.

Data collection

We developed survey items through review of existing literature documenting (1) challenges facing RUD patients in general and (2) the broader impacts of COVID-19 pandemic. Whenever possible, survey items were drawn from existing instruments,[23,24] and new items were pretested and revised based on feedback from a small group ($n = 10$) of RUD patients and caregivers. Both structured and open-ended questions were used to assess demographics, COVID-19 risk factors for the RUD patients, and concerns and challenges due to the pandemic. COVID-19 risk factors included those medical conditions identified by the Centers for Disease Control and Prevention as of April 2020.[25] We report here on the demographic and health characteristics of the sample and open-ended responses provided to the question, "What are the most important ways you feel the COVID-19 epidemic is impacting your (*your family member's*) health and your ability to care for your (*your family member with a*) rare or undiagnosed disease?"

Analysis

We analyzed demographic data descriptively using R[26] and open-ended questions through thematic content analysis using Microsoft Excel.[27,28] Three analysts (M.C.H., T.S., and J.M.) reviewed all open-ended responses and generated preliminary codes summarizing the key ideas reflected in the responses. Two coders (T.S. and J.M.) then independently coded 20% of the data set and calculated interrater reliability using a Cohen's kappa statistic in R. Interrater reliability for each code ranged from $\kappa = 0.79$ to $\kappa = 1.0$, with an mean of $\kappa = 0.89$ across all 15 codes used, indicating excellent agreement.[29] A single coder (T.S.) then coded the remaining responses. All authors reviewed the coded data and themes were finalized through consensus.

RESULTS

Respondent characteristics

A total of 497 individuals accessed the survey across all Facebook groups. Of these, 413 (274 RUD patients and 139 caregivers) were eligible and completed at least 50% of all survey questions. Respondents were predominantly female (86.4%), non-Hispanic (91.7 %), white (95.1%), had private insurance (65.1%) and reported at least some college (89.0%), though household incomes were widely distributed (Table 1). The vast majority of family members were caring for an RUD patient who was one of their children (including adult children) (89.7%), and who lived in their home full time (94.0%) (Table 2).

Among all RUD patients (including patients described by family members), the majority were diagnosed with one or more rare conditions (92.8%). Just under half of patients over the age of 5 had some form of disability (45.2%), with RUD patients described by a family member more frequently reported as having a disability (69.7%) than adult RUD patients (35.9%). The majority of RUD patients (67.6%) had at least one known COVID-19 risk factor, with the most common risk factor being immunocompromised for both adult RUD patients (61.5%) and RUD patients described by a family member (39.7%) (Table 3).

Living with an RUD during the COVID-19 pandemic

Seventy percent ($n = 290$) of respondents completed the open-ended question about the impacts of COVID-19 on managing their or their family member's RUD. Responses were summarized in six main themes: (1) sudden and extreme barriers to accessing essential health care, (2) specific impacts of COVID-19 visitation policies on their ability to advocate in health-care settings, (3) uncertainty and fear regarding COVID-19 infection risk, (4) physical and mental health challenges exacerbated by the pandemic, (5) magnified impacts of reduced educational and therapeutic services, and (6) unexpected positive changes due to the pandemic.

1. Sudden and extreme barriers to accessing essential health care

Respondents described significant negative impacts on their access to health care during the pandemic, including to care that they felt was essential to their health and well-being.

> I don't have access to the necessary medical care I usually have. My feeding tube placement was canceled with no alternative ways to get nutrition…. It's nearly impossible to contact my doctors, and even more difficult for them to be able to help me. (Patient with RUD)

Another respondent described a similar challenge to accessing needed care, stating, "Our youngest son [has]…reoccurring vision issues because of his rare disorder [that] haven't been able to be treated (he was supposed to have a procedure scheduled)" (Family member).

This lack of access also exacerbated existing challenges faced by those who were actively seeking a diagnosis, and/or were medically unstable.

> Our genetics [results] should have been back by now but we have yet to hear back from her neurologist…. After fighting for three years trying to get genetic testing done [this] is very frustrating in itself…. COVID-19 has put us at a standstill for something that is destroying my baby. Her health now seems like it is not essential or being treated as seriously as it should, and I am at the end of my rope. (Family member)

Respondents also described significant challenges to accessing medical supplies.

> …[we have an] inability to get medical supplies that we order and pay for out of pocket. Either there's a shortage or the prices have skyrocketed making it difficult to pay…. We are private caregivers but can't get access to basic PPE supplies

Table 1. Respondent demographics.

	Self (*n*)	Self (%)	Family Member (*n*)	Family Member (%)	All	All (%)
Self or Family Member	274	66.3%	139	33.7%	413	100.00%

	Self (*n*)	Self (median, IQR)	Family Member (*n*)	Family Member (median, IQR)	All	All (%)
Year of birth						
Total responses[a]	168	1972 (1944–2001)	122	1981 (1973–1986)	290	1976 (1944–2001)

	Self (*n*)	Self (%)	Family Member (*n*)	Family Member (%)	All (*n*)	All (%)
Education						
Less than high school	2	1.2%	0	0.0%	2	0.7%
High school or GED	22	12.7%	9	7.1%	31	10.4%
Some college	59	34.1%	30	23.8%	89	29.8%
Bachelor's degree	38	22.0%	49	38.9%	87	29.1%
Advanced/graduate level coursework or degree	52	30.1%	38	30.2%	90	30.1%
Total responses[a]	173	100.0%	126	100.0%	299	100.0%
Gender						
Male	24	13.9%	8	6.3%	32	10.6%
Female	145	83.8%	115	89.8%	260	86.4%
Other	4	2.3%	5	3.9%	9	3.0%
Total responses[a]	173	100.0%	128	100.0%	301	100.0%
Income						
Less than \$50,000	54	34.4%	20	17.9%	74	27.5%
50–100	45	28.7%	38	33.9%	83	30.9%
100–150	30	19.1%	30	26.8%	60	22.3%
150+	28	17.8%	24	21.4%	52	19.3%
Total responses[a]	157	100.0%	112	100.0%	269	100.0%
Insurance[b]						
Medicaid, CHIP, or other state-based program	24	14.2%	50	40.7%	74	25.3%
Medicare	41	24.3%	10	8.1%	51	17.5%
Private insurance	102	60.4%	88	71.5%	190	65.1%
Other health insurance	25	14.8%	11	8.9%	36	12.3%
No health insurance	13	7.7%	6	4.9%	19	6.5%
Total responses[a]	169	100.0%	123	100.0%	292	100.0%
Race[b]						
White	159	95.8%	112	94.1%	271	95.1%
Black or African American	0	0.0%	1	0.8%	1	0.4%
Asian or Pacific Islander	3	1.8%	4	3.4%	7	2.5%
American Indian or Alaskan Native	1	0.6%	0	0.0%	1	0.4%
Some other race	5	3.0%	4	3.4%	9	3.2%
Total responses[a]	166	100.0%	119	100.0%	285	100.0%
Hispanic						
No	155	93.9%	109	88.6%	264	91.7%
Yes	10	6.1%	14	11.4%	24	8.3%
Total responses[a]	165	100.0%	123	100.0%	288	100.0%

CHIP Children's Health Insurance Program, *IQR* interquartile range.

[a] Total responses represents the total number of participants who completed a given question. Completion rates per question ranged from 65.1% to 100%. Demographic questions were asked at the end of the survey, which contributed to the lower completion rates for these questions.

[b] Respondents could select multiple responses.

Table 2. Characteristics of RUD patients described by family members.

	n	%
Number of RUD patients cared for		
One	123	88.5%
Two	11	7.9%
More than two	5	3.6%
Total family member responses	139	100.0%
Patient's relationship to family member		
Child	139	89.7%
Spouse/domestic partner	7	4.5%
Parent	4	2.6%
Other family member	5	3.2%
Total patients described[a]	155	100.0%
Patient age		
Less than 1 year	17	11.0%
1–5 years	46	29.9%
6–10 years	29	18.8%
11–17 years	16	10.4%
18 and older	46	29.9%
Total patients described[a,b]	154	100.0%
Lives in household of family member		
Yes, full time	141	94.0%
Yes, part time	8	5.3%
No	1	0.1%
Total patients described[a,c]	150	100.0%

[a] Includes data for first RUD patient and second RUD patient, if reported by family member. Detailed data were collected on a maximum of two RUD patients per caregiver.

[b] Data missing for one patient described by a family member.

[c] Data missing for 5 patients described by a family member.

> to keep our rare sick loved one safe. (Family member)

Respondents also expressed concern that the primary method available to access health care during the pandemic—telemedicine—sometimes felt insufficient for managing an RUD. One family member stated that "[d]octors' appointments are less thorough via telemed[icine] than if he were able to see them in person" and another stated, "All doctors want to do telehealth. Due to this, they missed [diagnosing] [my child] with a life-threatening virus, and he turned blue and had to be taken by ambulance." These challenges in access to care left many feeling that only COVID-19 patients were receiving health care. As one respondent summarized, "It seems like COVID-19 now is the only disease present on Earth" (Patient with RUD).

2. Specific impacts of COVID-19 visitation policies on their ability to advocate in health-care settings

When RUD patients were able to access health care, they and their family members expressed frustration with strict limitations on visitors, companions, and caregivers many health-care organizations instituted to reduce the presence of nonessential personnel. Respondents described the fear of having to access medical care without a companion to act as their advocate.

> …I have to rely on family members to ensure the health-care providers are taking all my diagnoses and medications into consideration for treatment. If they can't be with me, I can't be sure that I will remember to question everyone involved in my health care. (Patient with RUD)

Parents of younger children expressed concern regarding policies that allowed only one parent in the hospital and limited options for taking turns at bedside.

> It has been absolute hell, and from the bottom to the top there has been an appalling lack of compassion. Our previously pretty darn great hospital turned into a prison overnight. Not to mention that we were exposed to [COVID-19] for 5 [solid] days by a provider, yet we as parents were considered not safe enough to be with our own children. (Family member)

On the other hand, parents of adult children with RUDs expressed fears of their child being forced to navigate the health-care system alone. As one described, "I am also concerned that because he is 20, he will be in a situation that I won't be able to advocate for him" (Family member).

While visitation policies were described as emotionally taxing, respondents also described them as adding difficulty to already complex medical decision-making. As one family member stated, "Having only one person at appointments creates stress and difficulty communicating with my husband what is going on with our daughter. My husband lacks a say in what goes on with her care and isn't included in many decision[s] because he can't be there" (Family Member).

3. Uncertainty and fear regarding COVID-19 risk

As illustrated in Table 3, approximately two-thirds of RUD patients had at least one risk factor for COVID-19, while one-third did not. Respondents' perceptions of their risk for severe COVID-19 infection also varied. Some described uncertainly and frustration surrounding the lack of information about their specific risk of COVID-19 conferred by their RUD. As one family member described, "[It is] unclear whether my son is officially considered high risk and whether we should shield him and siblings…longer term." On the other hand, some were extremely fearful that COVID-19 infection would have devastating consequences. As one family member described, "last year my son caught [human metapneumovirus], he spent 38 days in the hospital, the majority of those days in the PICU on a ventilator. I *know* he would not survive COVID." A patient with an RUD simply stated, "If I become infected with [COVID]-19 I will die." Still others expressed their concerns in terms of the potential for COVID-19 to add to existing medical complexity.

Table 3. RUD patient characteristics[a].

	Self (*n*)	Self (%)	Patient of Family Member (*n*)	Patient of Family Member (%)	All (*n*)	All (%)
Diagnosis status						
Diagnosed	187	94.4%	134	90.5%	321	92.8%
Undiagnosed	11	5.6%	14	9.5%	25	7.2%
Total patients	198	100.0%	148	100.0%	346	100.0%
Disability[b,c]						
Deaf or severe hearing loss	17	7.3%	10	11.2%	27	8.4%
Blind or severe vision loss	12	5.1%	13	14.6%	25	7.7%
Serious difficulty doing errands	40	17.1%	35	39.3%	75	23.2%
Serious difficulty remembering, concentrating, or making decisions	24	10.3%	35	39.3%	59	18.3%
Serious difficulty walking or climbing stairs	45	19.2%	27	30.3%	72	22.3%
Serious difficulty dressing or bathing	21	9.0%	20	22.5%	41	12.7%
Serious difficulty communicating	5	3.5%	19	21.3%	24	7.4%
None of the above	150	64.1%	27	30.3%	177	54.8%
Selected at least one category	84	35.9%	62	69.7%	146	45.2%
Total patients	234	100.0%	89	100.0%	323	100.0%
COVID-19 risk factors[b]						
Diabetes	15	6.5%	2	1.4%	17	4.5%
Serious heart condition	16	6.9%	18	12.3%	34	9.0%
Immunocompromised	142	61.5%	58	39.7%	200	53.1%
Chronic kidney disease (undergoing dialysis)	3	1.3%	1	0.7%	4	1.1%
Liver disease	31	13.4%	20	13.7%	51	13.5%
Chronic lung disease or moderate to severe asthma	33	14.3%	24	16.4%	57	15.1%
Severe obesity (body mass index [BMI] of 40 or higher)	29	12.6%	8	5.5%	37	9.8%
Selected at least one category	174	75.3%	81	55.5%	255	67.6%
None of the above	57	24.7%	65	44.5%	122	32.4%
Total patients	231	100.0%	146	100.0%	377	100.0%

[a] Includes data for the first and second RUD patient, as reported by a family member. Detailed data were only collected on a maximum of two RUD patients per family member.

[b] Respondents could select more than one response.

[c] Only asked for respondents who were patients themselves or family members of patients age 6 and above.

> I am worried that my son is more likely to experience severe effects from the virus should he catch it…. I am also concerned that if he were to experience lung damage, or arterial inflammation, or myocarditis the consequences of those side effects would be harder on him than on a heart healthy child. He is already dealing with a lifelong heart defect and any further permanent bodily harm to him would be more catastrophic for him than an otherwise healthy child because it would be compounded. (Family member)

Respondents also expressed fear that, should they contract COVID-19, health-care providers would not know how to care for them due to their RUD.

> I'm very concerned that if I were to come into contact with COVID-19 I will not receive treatment quickly or as aggressively as I feel I would need it. Because I appear healthy, it might be difficult to get a doctor to understand all the problems with my tissues due

> to long-term use of steroids, or the severity of my compromised immune system and multiple medications I take to suppress it for disease purposes. (Patient with RUD)

In response to this fear and uncertainty, some respondents described drastic measures of social isolation, for example, "My loved one is even afraid to go outside because of this virus. We encourage her to just let us take her for a walk or sit in our patio. She's so afraid she's going to catch it and not survive if she did" (Family member).

Respondents also expressed frustration over what they felt was a lack of a clear source of support or information specifically for RUD patients. As one family member stated, "There's no cohesive leadership or organization that offers or reaches out to rare disease patients and their families with offers to help educate us or dampen down our worry and fears" (Family Member).

4. Physical and mental health challenges exacerbated by the pandemic

Respondents described multiple ways in which the complex health challenges caused by their RUD were exacerbated by the pandemic. One patient with an RUD described how, "the stress of it is making my illness flare up [and] affecting my mental health," and another stated that, "the stress of the pandemic brought me out of remission." Similarly, another respondent explained that, "I have two boys who were well controlled in their epilepsy treatment who have had multiple breakthrough seizures due to the stress" (Family member).

The severity of the stress involved in accessing essential health care, when they could, was described as so extreme by some that they were considering forgoing treatment. As one respondent described, "I am still receiving monthly IVIG infusions, but the stress of those appointments…also has me questioning whether my mental health would be better off without it" (Patient with RUD). Respondents similarly considered whether they ought to stop certain treatments because the side effects of the treatments themselves could put them at higher risk of COVID-19. As one described, "I am seriously considering stopping chemotherapy treatment for [my RUD] to lower my risk of a poor outcome should I develop COVID-19, as [being immunocompromised] would no longer be an issue" (Patient with RUD).

Family members also described serious impacts on their own mental health due to the stress of caring for an RUD patient during the pandemic. After discussing how the RUD patient s/he cared for was struggling with the challenges of the pandemic, one family member described how, "we too feel stressed out, anxiety ridden, depressed and unsupported as a family of a sick rare disease loved one. We do our best to manage it so it doesn't affect or add to the same feelings our sick loved one is experiencing" (Family Member).

5. Magnified impacts of reduced educational and therapeutic services

While school closures have presented challenges for families across the country, family members of children with RUDs described the magnifying effect of the school closures due to their children's additional educational needs. Educational services for children with special needs are often provided through an Individualized Education Program (IEP), which may include not only adapted educational programming, but also a range of physical, occupational, speech, and/or behavioral therapies. Family members described how school closures impacted access to these additional therapeutic services, which were critical to their child's continued development. As one described, "He is missing a lot of his important physical, occupational and speech therapy, and he has significant delays and needs to get ready for kindergarten." Another family member stated, "To me so far the biggest impact on my child has been the drastically reduced communication with teachers and therapists (usually multiple sessions per week)" (Family Member).

Family members also described the particular challenges of translating special education to remote platforms. As one respondent described, "…they haven't been able to receive direct services for their academic IEP. All classes were switched to virtual, which isn't conducive to special needs learning" (Family member).

6. Unexpected positive impacts of the pandemic

While respondents primarily focused on the challenges presented by the pandemic, some did describe unexpected positive changes in their ability to manage their RUD. Respondents described how the increased infection prevention measures taken by the general public have made them feel safer.

> Now I think that going to the grocery store is more safe for me, [with] people keeping distance and [disinfecting] their hands, I really think we should do this all of the time. So actually the COVID-19 has been sort of a blessing for me. (Patient with RUD)

Respondents also described how the pandemic removed barriers to alternative work arrangements that actually made it easier to manage their RUD while working.

> I just discovered I'm twice as efficient when working completely remotely [because I] haven't caught a single virus since [the] shutdown almost 3 months ago, when I normally am constantly battling viruses. I'm one of the people who has zero desire to go back to "normal," as it was never working for me anyway. (Patient with RUD)

Further, in contrast to respondents who raised concerns about telemedicine, some respondents described how the pandemic had removed some longstanding barriers in access to health care.

> Insurance would not cover telemedicine in our state so [doctors] did not provide it before. Now instead of having to drive 7 1/2 hours one way to see my specialists for 45 minutes or less I can use a computer to connect and get labs or tests done locally. A huge blessing. (Patient with RUD)

DISCUSSION

This study provides a window into the experiences of RUD patients during the COVID-19 pandemic. Our results suggest that the pandemic is exacerbating longstanding challenges already faced by RUD patients (e.g., further extending an already long diagnostic odyssey) and also introducing new elements to these existing challenges (e.g., new limits on caregiver support impacting advocacy needs). While some aspects of these challenges may be shared by other patient populations grappling with complex health conditions, others may be specific to RUD patients. For example, while there is understandable enthusiasm for expansion of telehealth as a way of increasing health-care access for patients during the pandemic,[30] our results suggest that telehealth may have significant limitations for very complex patients requiring coordination across multiple specialties, such as those with RUDs. In addition, while the impacts of COVID-19 visitation policies and their consequences have been examined in the context of intensive care unit (ICU) care of COVID-19 patients,[31,32] RUD patients' complex health challenges require increased advocacy even when accessing routine care. On the other hand, the limited literature in other patient groups indicates that those grappling with complex health conditions, such as cancer,[33] during the pandemic also are at risk for serious mental health challenges, such as those described by our respondents. Our qualitative data further suggest that the anxiety caused by the pandemic may be leading some RUD patients to forgo treatment altogether, with potentially catastrophic implications for their already complex health. Similarly, while closure of schools has impacted countless families in myriad ways,[34] for children with special needs—including many RUD patients—these closures have resulted in the reduction of critical therapeutic services, many of which do not easily translate to remote platforms. The insights of RUD patients and their families may also suggest challenges faced by other patients and families, beyond the already large RUD community.

Addressing these issues will require urgent action and attention to both new and chronic challenges faced by the RUD community. Addressing these needs quickly is important, given the rapidly changing landscape of COVID-19 mitigation strategies, evolving school reopening plans, and the development of vaccination and treatment approaches. On the other hand, our results suggest that the pandemic has exacerbated longstanding challenges in research and clinical care for RUD patients.[35] As we face the short- and long-term implications of the pandemic, we must take into account the experiences of RUD patients to ensure that we address—rather than exacerbate—existing disparities for this large and complex patient population.

Potential targets include the development of policies and approaches recognizing the specific needs of RUD patients. For example, clinical settings could develop methods for identifying RUD patients within health-care systems and creating policy exceptions for those with increased advocacy needs. They could support coordinated telehealth planning across specialties to ensure that RUD patients can reap the benefits of expanded telehealth while ensuring that their complex health conditions are sufficiently monitored, and that they know when they need in-person care. This includes a need to explicitly reassure RUD patients that in-person care can be delivered safely and, in the case of COVID-19 treatment, with careful consideration of a patient's RUD. Further, any efforts toward a multidisciplinary "one stop" model of highly coordinated care that can individually tailor care and integrate medical and social support needs is likely to improve outcomes for RUD patients both during and well beyond the pandemic.[7,36,37]

Research institutions should consider research focused on diagnosis of undiagnosed patients when crafting their research guidelines in the midst of the ongoing pandemic. For example, the current Stanford School of Medicine guidelines explicitly identify, "research that obtains critical, in-person observations or laboratory measures on vulnerable patients or populations where not obtaining these observations could negatively impact patient outcomes, safety or care," as the highest priority for restarting, together with treatment studies.[38] Johns Hopkins University's research reopening plan similarly emphasizes that studies with the potential for direct clinical benefit to patients should be prioritized.[39] While the language in these policies suggests that studies focused on RUD diagnoses would likely be included, further research is needed to understand how various institutions are approaching this issue.

RUD advocacy groups can use these data to further develop support mechanisms for RUD patients and families to address their pandemic-related concerns. For example, NORD has a number of COVID-19 specific resources for RUD patients,[40] though our findings suggest further outreach may be needed. In addition, as nearly half of all patients in our sample identified as having a disability, the RUD community may benefit from COVID-19 resources designed for the disability community, such as those provided by the American Association on Health and Disability.[41]

Our study has a number of limitations. As is common in online survey research using similar methods,[24] our response rate cannot be empirically determined but is likely low given our broad dissemination strategy. However, our approach did allow us to include patients from a large number of RUD groups, at least partially addressing a longstanding challenge in understanding the shared experiences of the RUD community.[35] It is possible that certain segments of the RUD community are overrepresented in our sample due to a variety of factors, including receptiveness of individual Facebook group administrators to participation. Further research in a representative sample of RUD patients would be needed to confirm generalizability and to examine the frequency and variability of these themes within the RUD community. In addition, women are overrepresented in our study, race/ethnic minority patients are underrepresented, and non-English-speaking patients are not included. Given the known disparities in COVID-19 impacts particularly for racial/ethnic minority groups,[42] their perspectives are key and require attention. Undiagnosed patients also are underrepresented, and our ongoing research suggests that undiagnosed patients are less likely to have a specific rare disease group with which they identify. This survey also was conducted at one time point, and the experiences of RUD patients will likely evolve with the pandemic. In addition, although we focused on groups oriented to patients in the United States, we cannot be certain that all respondents were US residents. Finally, this study was focused on patient perspectives and lacks insights from health-care providers and administrators. Further research should examine the perspectives of other stakeholders to provide a fuller picture of the challenges facing RUD patients and potential mitigation strategies to improve care for this population during and after the pandemic.

Conclusion

COVID-19 is both creating new challenges and exacerbating existing challenges for RUD patients. Some of these challenges are specific to this population, while others may be shared by other patient groups. As the pandemic continues, creativity and flexibility will be critical to ensuring that RUD patients receive the care they need to manage their complex conditions. Health-care providers and institutions can work with advocacy organizations, patients, and families to assess emerging needs, improve access—including through the thoughtful use of telehealth—and consider unique advocacy needs when crafting new visitation policies. Research institutions should also ensure that ongoing research for RUD diagnosis and treatment is safely restarted and continued, as for other health conditions, such as cancer. Though the RUD community is medically heterogeneous, identifying their shared needs and proactively addressing them is essential, perhaps now more than ever, to ensure that these patients' already challenging relationship with the medical community is not further compromised.

DATA AVAILABILITY

Materials, data sets, and protocols utilized in the acquisition of the data presented in this paper may be made available by the corresponding author upon request.

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AUTHOR CONTRIBUTIONS

Conceptualization: M.C.H, H.K.T. Data curation: M.C.H., T.S., J.M. Formal analysis: M.C.H., T.S., J.M., A.G., H.K.T. Writing—original draft: M.H., H.K.T. Writing—review & editing: M.C.H., T.S., J.M., J.A.B., M.W., A.G., H.K.T.

ETHICS DECLARATION

All study procedures were approved by the Stanford University School of Medicine Institutional Review Board. Informed consent was required and obtained from all participants.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

The online version of this article (https://doi.org/10.1038/s41436-020-01069-7) contains supplementary material, which is available to authorized users.

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