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ORIGINAL ARTICLE

Provider Perceptions of Quality of Life, Neurocognition, Physical Well-being, and Psychosocial Health in Patients with Primary Immunodeficiency/Immune Dysregulation Conditions

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Abstract

Purpose Both pediatric and adult patients with a primary immunodeficiency/immune dysregulation (PID/PIDR) diagnosis report inferior quality of life (QOL) and patient-reported outcomes (PROs) as compared with their healthy peers. Recognition of the negative impact on QOL and PROs provides an opportunity for clinicians to intervene with supportive measures. However, provider perceptions of PID/PIDR patients' quality of life, physical well-being, psychosocial health and neurocognition, and access to supportive resources have yet to be systematically evaluated.

Methods We report specialty providers' perception of the QOL and psychosocial and physical well-being of their pediatric and adult patients with PID/PIDR through the utilization of an online survey assessing QOL and the impact of disease or its associated treatment on their physical well-being, mental health, social relationships, neurocognition, and work/school performance.

Results Clinicians trended towards believing adult PID/PIDR patients had worse overall QOL than children with PID/PIDR. Providers additionally identified their adult patients' QOL to be more deleteriously affected by co-morbidities than their pediatric patients. Clinicians distinguished anxiety and social relationships as the psychosocial aspects most often affected by a complex immunological diagnosis in all patients. Of physical health considerations, energy, rather than mobility or pain, was perceived to be more negatively influenced by PID/PIDR in both adult and pediatric patients.

Conclusions Knowledge of these clinician perceptions can affect communication of findings with patients, as well as ongoing management, and thus, it is important to understand these fully to improve healthcare delivery to, and clinical management of, these patients.

Keywords Primary immunodeficiency/immune dysregulation · quality of life · patient-reported outcomes · provider perceptions

Abbreviations

CIS	Clinical Immunology Society
HRQoL	Health-related quality of life
IAPIDS	International Alliance of Primary Immunodeficiency Societies
PID/PIDR	Primary immunodeficiency/immune dysregulation
PROs	Patient-reported outcomes
QOL	Quality of life

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Introduction

The psychosocial aspects of chronic disease, in general, and their impact on morbidity and mortality are being increasingly recognized and identified as an area of opportunity for improving care and optimizing overall patient health [1]. Evaluations of QOL and psychosocial and physical well-being, however, remain inadequate in those diagnosed with a PID/PIDR disorder [2–5]. Moreover, it is unknown if provider

perceptions of patient QOL and psychosocial and physical well-being parameters are an accurate reflection of patient-reported outcomes or are discordant.

Prior studies of patients with a PID/PIDR observed that the health-related QOL (HRQoL) of both adult and pediatric PID/PIDR patients is decreased compared with normal controls [1, 2, 4]. Co-morbidities and additional health conditions also appear to negatively impact the QOL of adult PID/PIDR patients [4]. Kuburovic et al. showed that school functioning was significantly lower in children with a PID/PIDR. In the same study, 26.3% and 10.5% of children with PID/PIDR reported significant anxiety or depressive symptoms, respectively [3]. Additionally, numerous studies note a negative impact of a PID/PIDR diagnosis on the social and physical functioning of adult and pediatric patients [2].

No prior studies have assessed medical provider perceptions of their PID/PIDR patients' QOL, physical well-being, neurocognition, social relationships, work/school performance, or mental health. Studies have evaluated the ability of medical clinicians to accurately assess patient-reported symptoms and quality of life in patients receiving palliative care treatment and those with oncologic, urologic, renal, cardiac, and hematologic disorders. These studies demonstrate that healthcare workers are often inaccurate in judging patient mental/physical health symptoms and QOL [6–16]. Interestingly, the degree and type of discordance between patient and provider can be affected by the healthcare provider's specific profession [6, 11, 13]. Understanding whether such dichotomies between provider and patient perceptions exist in PID/PIDRs will be critical to improving the clinical management of PID/PIDRs. Herein, we provide data from an international survey of specialty clinicians and their assessment of their PID/PIDR patients' QOL, physical condition, neurocognition, and psychosocial health.

Methods

Specialty clinicians in multiple disciplines (allergy/immunology, bone marrow transplantation, hematology/oncology, general pediatrics, genetics, & infectious disease) who routinely care for PID/PIDR patients were contacted through the Clinical Immunology Society (CIS) and International Alliance of Primary Immunodeficiency Societies (IAPIDS). Those who expressed an interest in participating in the survey were directed to an online questionnaire administered via a secure online website, QuestionPro®. Participants answered an eleven-question demographic survey evaluating such aspects as gender, birth year, medical practice statistics/location, area of focus and support staff availability (Table 1). In addition to demographic information, fifteen novel Likert scale-based survey questions assessed provider perceptions of their adult and/or pediatric patients' overall QOL and the impact of disease or its associated treatment on their physical well-being, mental health, social relationships, neurocognition, and work/school performance as a whole (Tables 2 and 3). Likert scale responses were scored (one through five) to facilitate analyses. Statistical comparisons were generated via ANOVA and *t* test analyses. Analyses were completed via SAS 9.4 software. Participant questionnaire responses were collected and managed securely and electronically using QuestionPro®. Study approval was granted via the institutional review board at the University of Michigan (HUM00148246). Informed consent was obtained from all individual participants included in the study.

Results

Study participants (n = 67) were primarily from the United States (42/66; 64%), but respondents were noted to practice globally, including within Africa, Asia, Europe, South America, and Australia. Of those practicing within the USA, survey takers most commonly provided care in Michigan (6/41; 15%), Ohio (6/41; 15%), and California (5/41; 12%). Most were born between 1965 and 1979 (29/66; 44%) and were trained in allergy/immunology (47/62; 77%), although the specialties of hematology/oncology and bone marrow transplantation were also well represented (10/62; 16% of participants). Eighty-five percent (55/65) of survey takers practiced within an academic center and 52% (33/64) were female. Forty percent (27/67) cared for both adults and children, 52% (35/67) cared exclusively for pediatric patients and 8% (5/67) only treated adults (Table 1). The vast majority of study participants, 98.5% (64/65), obtained a doctoral degree or equivalent. Thirty-two percent (21/65) of respondents spent their academic time split equally between clinical and research endeavors, and 77% (50/65) of providers saw an average of 250 or less of PID/PIDR patients annually. In assessing support staff accessibility to healthcare providers, only spiritual care had less than 50% (27/58; 47%) availability to survey takers (Table 1).

There was nearly a statistically significant difference (p = 0.07) in the perceived overall QOL of pediatric versus adult PID/PIDR patients with 41% of clinicians feeling as though their pediatric patients had a good QOL while only 25% believed their adult patients had a good QOL (Fig. 1a). No survey respondents felt their PID/PIDR patients had very poor or excellent QOL, while 18% of providers felt their adult patients had a poor QOL. Compared with children with PID/PIDR, providers believed adult PID/PIDR individuals had more difficulties related to associated co-morbidities rather than their actual PID/PIDR (p = 0.046). There was no significant difference when comparing providers' perceptions of adult and pediatric patients' difficulties related directly to PID/PIDR manifestations or treatment (p = 0.83 and p = 0.93, respectively) (Tables 2 and 3). Of note, medical providers practicing within

Table 1 Medical provider demographics

Sex ($N = 64$)	Percentage
Female	52.0%
Male	48.0%
Year of Birth ($N = 66$)	**Percentage**
Prior to 1925	0.0%
1925–1944	0.0%
1945–1964	24.2%
1965–1979	43.9%
1980–1995	31.8%
Location of medical practice by nation($N = 66$)	**Percentage**
United States of America	63.6%
Mexico	4.5%
Belgium	3.0%
Brazil	3.0%
Canada	3.0%
Peru	3.0%
Australia	1.5%
Chile	1.5%
China	1.5%
Egypt	1.5%
Finland	1.5%
India	1.5%
Japan	1.5%
Malaysia	1.5%
Netherlands	1.5%
Pakistan	1.5%
Qatar	1.5%
Spain	1.5%
Sweden	1.5%
Location of medical practice by state ($N = 41$)	**Percentage**
Michigan	14.6%
Ohio	14.6%
California	12.2%
Florida	7.3%
New York	7.3%
Pennsylvania	7.3%
Texas	7.3%
Georgia	4.9%
Maryland	4.9%
Tennessee	4.9%
Arkansas	2.4%
Connecticut	2.4%
Illinois	2.4%
Minnesota	2.4%
Missouri	2.4%
North Carolina	2.4%
Highest degree obtained ($N = 65$)	**Percentage**
Doctor of Medicine (M.D.)	78.5%

Table 1 (continued)

Sex ($N = 64$)	Percentage
Doctor of Philosophy (Ph.D.)	10.8%
Doctor of Osteopathic Medicine (D.O.)	3.1%
Doctor of Medicine/Doctor of Philosophy (M.D./Ph.D.)	3.1%
Bachelor of Medicine, Bachelor of Surgery (M.B.B.S.)	1.5%
Fellow of College of Physicians and Surgeons Pakistan (F.C.P.S.)	1.5%
Master of Science (M.Sc.)	1.5%
Advanced nursing degree	0.0%
Specialty/primary area of focus ($N = 62$)	Percentage
Allergy/immunology	77.4%
Bone marrow transplantation	9.7%
Hematology/oncology	6.5%
General pediatrics	3.2%
Genetics	1.6%
Infectious disease	1.6%
Primary duties ($N = 65$)	Percentage
Clinical duties (greater than 50% of the time)	56.9%
Both research and clinical duties equally	32.3%
Research duties (greater than 50% of the time)	10.8%
Primarily practices within ($N = 65$)	Percentage
Academic medical center	84.6%
Private practice	10.8%
Community hospital/clinic	4.6%
Average number of unique primary immunodeficiency patients seen annually ($N = 65$)	Percentage
Less than 100	53.8%
101–250	23.1%
251–500	16.9%
Greater than 500	6.2%
Primarily treat ($N = 67$)	Percentage
Pediatric primary immunodeficiency patients (< 18 years old)	52.2%
Both adult and pediatric primary immunodeficiency patients	40.3%
Adult primary immunodeficiency patients (> 18 years old)	7.5%
Support staff that is easily accessible within your practice ($N = 58$)	Percentage
Social Work	81.0%
Dietician	79.3%
Geneticist/genetic counselor	79.3%
Psychologist/psychiatrist/mental health counselor	70.7%
Physical therapy	69.0%
Speech therapy	60.3%
Child life specialist	51.7%
Nurse educator	51.7%
Occupational therapy	51.7%
Spiritual care	46.6%

the United States trended towards believing their adult ($p = 0.06$) and pediatric ($p = 0.1$) PID/PIDR patients have a higher overall QOL when compared with clinician perceptions internationally but this finding did not reach statistical significance.

Table 2 Responses from medical providers who care for pediatric patients

	Very poor	Poor	Fair	Good	Excellent	Mean Likert Scale Score
Pediatric quality of life						
In general, how would you rate your pediatric primary immunodeficiency patients' overall quality of life? (*N* = 58)	0.0%	13.8%	44.8%	41.4%	0.0%	3.28
In general, how significantly do you think your primary immunodeficiency pediatric patients are affected by the following:	Not at all	A little bit	Moderately	Quite a bit	Extremely	Mean Likert Scale Score
Difficulties related directly to their primary immunodeficiency (*N* = 58)	1.7%	6.9%	48.3%	36.2%	6.9%	3.40
Difficulties related to co-morbidities other than their primary immunodeficiency (*N* = 58)	3.4%	17.2%	44.8%	27.6%	6.9%	3.17
Difficulties related to treatment of their primary immunodeficiency (*N* = 58)	0.0%	22.4%	48.3%	17.2%	12.1%	3.19
Average Score						3.25
Pediatric psychosocial health						
How often do you feel your primary immunodeficiency pediatric patients:	Never	Almost never	Sometimes	Often	Almost always	Mean Likert scale score
Have anxiety symptoms related to their disease or treatment? (*N* = 58)	0.0%	5.2%	56.9%	34.5%	3.4%	3.36
Have depressive symptoms related to their disease or treatment? (*N* = 58)	3.4%	10.3%	67.2%	19.0%	0.0%	3.02
Have anger symptoms related to their disease or treatment? (*N* = 58)	1.7%	24.1%	62.1%	10.3%	1.7%	2.86
Peer/social relationships are negatively impacted by their disease or treatment? (*N* = 58)	1.7%	3.4%	55.2%	32.8%	6.9%	3.40
Average Score						3.16
Pediatric physical health						
How often do you feel your primary immunodeficiency pediatric patients':	Never	Almost never	Sometimes	Often	Almost always	Mean Likert scale score
Mobility or level of physical activity is negatively impacted by their disease or treatment? (*N* = 58)	0.0%	22.4%	60.3%	17.2%	0.0%	2.95
Energy is negatively impacted by their disease or treatment? (*N* = 58)	0.0%	3.4%	41.4%	48.3%	6.9%	3.59
Have pain/physical discomfort related to their disease or treatment? (*N* = 58)	0.0%	17.2%	63.8%	17.2%	1.7%	3.03
Average Score						3.19
Pediatric neurocognition and school performance						
How often do you feel your primary immunodeficiency pediatric patients':	Never	Almost Never	Sometimes	Often	Almost Always	Mean Likert scale score
Memory is negatively impacted by their disease or disease treatment? (*N* = 58)	6.9%	50.0%	41.4%	1.7%	0.0%	2.38
Attention or concentration is negatively impacted by their disease or disease treatment? (*N* = 58)	5.2%	25.9%	63.8%	3.4%	1.7%	2.71
Miss school due to their disease or treatment? (*N* = 58)	0.0%	5.2%	34.5%	48.3%	12.1%	3.67
School performance is negatively impacted by their disease or treatment? (*N* = 58)	1.7%	6.9%	46.6%	41.4%	3.4%	3.38
Average Score						3.04

Table 3 Responses from medical providers who care for adult patients

	Very poor	Poor	Fair	Good	Excellent	Mean Likert scale score
Adult quality of life						
In general, how would you rate your adult primary immunodeficiency patients' overall quality of life? (***N*** >= 28)	0.0%	17.9%	57.1%	25.0%	0.0%	3.07
In general, how significantly do you think your adult primary immunodeficiency patients are affected by the following:	Not at all	A little bit	Moderately	Quite a bit	Extremely	Mean Likert scale score
Difficulties related directly to their primary immunodeficiency (*N* = 28)	0.0%	0.0%	57.1%	42.9%	0.0%	3.43
Difficulties related to co-morbidities other than their primary immunodeficiency (*N* = 28)	0.0%	7.1%	39.3%	46.4%	7.1%	3.54
Difficulties related to treatment of their primary immunodeficiency (*N* = 28)	0.0%	25.0%	35.7%	32.1%	7.1%	3.21
Average score						3.39
Adult psychosocial health						
How often do you feel your adult primary immunodeficiency patients:	Never	Almost Never	Sometimes	Often	Almost Always	Mean Likert Scale Score
Have anxiety symptoms related to their disease or treatment? (N = 28)	0.0%	3.6%	42.9%	42.9%	10.7%	3.61
Have depressive symptoms related to their disease or treatment? (N = 28)	0.0%	7.4%	48.1%	44.4%	0.0%	3.37
Have anger symptoms related to their disease or treatment? (N = 28)	3.6%	28.6%	42.9%	25.0%	0.0%	2.89
Social or family relationships are negatively impacted by their disease or treatment? (N = 28)	0.0%	10.7%	35.7%	46.4%	7.1%	3.50
Average score						3.34
Adult physical health						
How often do you feel your primary immunodeficiency adult patients':	Never	Almost never	Sometimes	Often	Almost always	Mean Likert scale score
Mobility or level of physical activity is negatively impacted by their disease or treatment? (*N* = 28)	0.0%	14.3%	64.3%	21.4%	0.0%	3.07
Energy is negatively impacted by their disease or treatment? (*N* = 28)	0.0%	3.6%	35.7%	50.0%	10.7%	3.68
Have pain/physical discomfort related to their disease or treatment? (*N* = 28)	3.6%	14.3%	53.6%	25.0%	3.6%	3.11
Average score						3.29
Adult neurocognition and work performance						
How often do you feel your adult primary immunodeficiency patients:	Never	Almost never	Sometimes	Often	Almost always	Mean Likert scale score
Memory is negatively impacted by their disease or disease treatment? (*N* = 28)	7.1%	35.7%	46.4%	10.7%	0.0%	2.61
Attention or concentration is negatively impacted by their disease or disease treatment? (*N* = 28)	3.6%	10.7%	67.9%	17.9%	0.0%	3.00
Have trouble shifting back and forth between different activities that require thinking? (*N* = 28)	3.6%	21.4%	64.3%	10.7%	0.0%	2.82
Work performance or daily mental functioning is negatively impacted by their disease or treatment? (*N* = 28)	3.6%	17.9%	53.6%	21.4%	3.6%	3.04
Average Score						2.87

There was a trend towards providers feeling that the neurocognition and school performance of children was more negatively impacted by a PID/PIDR diagnosis than the neurocognition and work performance of adults ($p = 0.1$), although this finding did not reach significance (Fig. 1b). Only 4% of those who care for adults believe their patients' work performance or daily mental functioning is never negatively impacted while clinicians believe children with PID/PIDR had more severe difficulties related to their concentration than memory ($p = 0.01$). Sixty percent of survey respondents believe pediatric PID/PIDR patients miss school often or almost always due to their disease or its associated treatment (Tables 2 and 3).

Anxiety symptoms and social relationships were viewed as being more negatively affected by PID/PIDR or treatment than anger or depressive symptoms in both children and adults ($p < 0.01$ and $p < 0.01$). Thirty-eight percent of pediatric providers feel their PID/PIDR patients experience anxiety symptoms often or almost always, while 67% felt their pediatric patients sometimes had depressive symptoms related to their immunodeficiency diagnosis or its associated treatment. Fifty-four percent of those who responded believed their adult PID/PIDR patient had social or family relationships negatively impacted by their disease or treatment often or almost always (Tables 2 and 3).

There was no statistically significant difference between provider-perceived impact of a primary immunodeficiency diagnosis on the physical or psychosocial health of adult versus pediatric PID/PIDR patients ($p = 0.27$ and $p = 0.11$, respectively) (Fig. 1b).

Of physical health considerations, energy was deemed to be more deleteriously influenced by a PID/PIDR diagnosis in both adult and pediatric patients than mobility or pain ($p < 0.01$ and $p < 0.01$). Although adult and pediatric PID/PIDR patients are perceived by 82% and 83% of providers as at least sometimes being affected by pain related to their diagnosis or associated treatment (Tables 2 and 3).

Discussion

The recognition of and appreciation for the negative impact decreased QOL and psychosocial and physical well-being can have on the overall health of patients with PID/PIDR is central to identifying opportunities for screening and supportive care. Our work showed that providers believe that their adult and pediatric patients' overall QOL, psychosocial health, physical well-being, school/work performance, and neurocognition are negatively impacted by their PID/PIDR diagnosis or

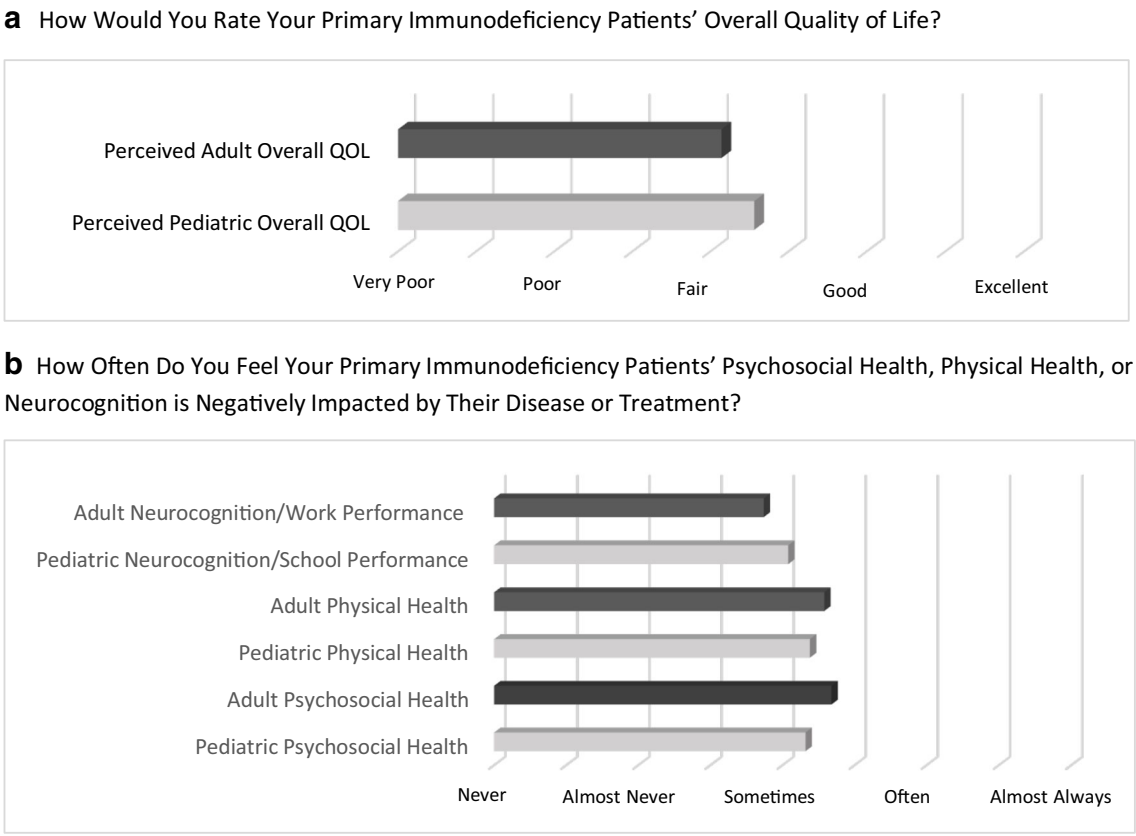

Fig. 1 **a** How would you rate your primary immunodeficiency patients' overall quality of life? **b** How often do you feel your primary immunodeficiency patients' psychosocial health, physical health, or neurocognition is negatively impacted by their disease or treatment?

treatment; although there are differences in the perceived influence of such a disorder between adults and children for each of the assessed parameters. Clinicians trended towards believing the QOL of adults is more negatively impacted than the QOL of children by a PID/PIDR diagnosis or its treatment. While neurocognition and school/work performance are felt to be impacted; energy, anxiety, and social relationships are believed to be more severely negatively influenced in PID/PIDR patients by their providers. Past studies analyzing the QOL of PID/PIDR patients showed that one's QOL was strongly associated with the burden of other health conditions [4], clinicians seem to agree with 54% of those who care for adults surveyed noting that their patient's QOL was "quite a bit" or "extremely" affected by co-morbidities. Clinicians do appear though to overestimate the frequency of anxiety and depressive symptoms in their pediatric PID/PIDR patients with 38% and 19% noting that their patients often or almost always experience anxiety or depressive symptoms, respectively, while actual patient assessments previously performed showed that 26.3% and 10.5% of children with PID/PIDR reported significant anxiety or depressive symptoms, respectively [3].

Interestingly, our study also demonstrated the accessibility of support staff to most PID/PIDR clinicians. This may be a manifestation of the fact that a majority of survey respondents were pediatric clinicians and practiced within an academic medical center with expanded resources. This finding is important as having well-trained ancillary support staff not only improves the satisfaction of health care received, but additionally provides patients and their families with resources to address issues, once identified, that may be negatively affecting their QOL, physical well-being or psychosocial health [17].

This study has several limitations, most notably the requirement that study participants answer survey questions based on their PID/PIDR population as a whole. We recognize that this may have been difficult for some providers as the patients they care for likely have varied disease manifestations and severity with diverse impact on their quality of life and mental/physical/psychosocial health. A study evaluating direct comparisons of patient and provider responses to survey questions would have been optimal but given the rarity of specific PID/PIDRs the feasibility of such an approach was not practical.

Despite these limitations, our current data provides meaningful information and insight into provider perceptions of how a PID/PIDR diagnosis impacts the quality of life, neurocognition, physical well-being and psychosocial health of adult and pediatric patients. In relation to their perception of their PID/PIDR patients' QOL/patient-reported outcomes, medical providers are largely harmonized with patients except when it comes to individual mental health concerns, in which clinicians appear to overestimate the impact of a PID/PIDR condition on patient anxiety and depression. Previous studies have also shown discordance in patient and provider perceptions of QOL thus highlighting the importance of regularly inquiring about a patient's quality of life and physical/mental/psychosocial health at medical appointments rather than relying on a clinician's perceived assessment of these parameters. In the current healthcare model in most countries, this rarely occurs despite a patient's desire for such interactions, and evidence that care is improved with these non-traditional assessme nts [18, 19]. Therefore, we suggest that patient-reported outcome and HRQoL assessments become a regular part of the clinical care of PID/PIDR patients. General tools for such assessments are readily available for provider use, such as the PedsQL™ and the National Institutes of Health developed patient-reported outcomes measurement information system (PROMIS®). Unfortunately, there are limited PID/PIDR-specific validated questionnaires at this time [2, 20–24]; the creation of an easily administered and freely available QOL/patient-reported outcomes assessment tool targeting this patient population would likely be beneficial to patients and providers alike. This study represents the "tip of the iceberg" and much work is required to validate these findings and do correlative studies in patient populations. The cumulative data has the potential to dramatically alter clinical practice and the approach to pediatric and adult patients with PID/PIDR.

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Author Contributions Drs. Michniacki and Walkovich conceptualized and designed the study. Dr. Michniacki drafted the manuscript as well as analyzed/interpreted the study data. Dr. Abraham, Dr. Walkovich, Dr. Merz and Ms. Sturza assisted in editing the manuscript. Dr. Merz also assisted in constructing the online surveys. Ms. Sturza additionally provided statistical support.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (University of Michigan; HUM00148246) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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