

ARTICLE

Inborn errors of immunity at school: How can we do better?

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Adolescents with inborn errors of immunity (IEI) face physical limitations, social difficulties, psychological issues, and school absenteeism. Improving their school integration is essential. 13 adolescents with confirmed IEI attending high school, along with their parents, classmates, and teachers, participated in the study to evaluate social and academic adaptation indicators. A questionnaire was developed to gather perceptions on diagnosis, adaptation, understanding, socialization, coordination, and challenges. 13 adolescents (median age 13.8, IQR 13–15), 21 parents, 13 teachers, and 74 classmates participated. The illness impacted education, making it difficult for 50% of the students to keep up. 11 tutor teachers lacked specific knowledge and demanded more training. Most schools, 7/13, lacked absenteeism protocols, and 8/13 teachers were unaware of patient associations. Most classmates did not observe discriminatory behavior. IEI affect adolescents' education. There is a need for better information, protocols to prevent absenteeism, improved coordination with healthcare teams, and contact with patient associations to enhance school adaptation.

Introduction

Primary immunodeficiencies (PIDs), also known as inborn errors of immunity (IEI), comprise more than 550 diseases of genetic origin that lead to an increased risk of severe and/or recurrent infections, autoimmunity, inflammation, allergic reactions, and neoplasms (1, 2).

IEI-related complications usually lead to recurrent hospital admissions and visits that increase the likelihood of restricted social contact, making these patients more susceptible to negative self-image, as well as a reduced perception of their own health-related quality of life and increased general fatigue (3, 4). Thus, a multidisciplinary approach to IEI patients and their families that includes psychological support is essential to improve patients' quality of life, reducing the occurrence of general adaptation problems and the risk of suffering signs of anguish and depression (3, 5). In this sense, the International Patient Organization for Primary Immunodeficiencies (IPOPI) drafted a booklet that discusses the psychological effects that IEI can have on patients, parents, carers, and families and suggests ways to address them (6). In a broader view, rare disease impacts >300 million people globally, with 70% of these conditions starting in childhood (7). Some individuals living with a rare disease have physical or mental disabilities, which may have a greater impact

on their health, and face various barriers that may hinder their full and effective participation in society on an equal basis with others. To that matter, the World Health Organization urges that those chronic conditions can increase school absenteeism and require individualized adaptations in educational (8, 9).

The educational community is a space for socializing and learning that contributes to normalizing the lives of children with chronic disease and enables them to define their personal and group identity. Intermittent absenteeism resulting from hospitalizations and long-term treatments is common in IEI students. This prompts the need to offer personalized counseling (10). All stakeholders in the field should aim to enable access to an equal educational opportunity and nondiscriminatory education for these children and adolescents by applying the necessary measures to face different educational stages (11). This need stands out especially as students with IEI become adolescents, considering its negative impact on social spheres (4). It is well known that the lack of knowledge on rare diseases and their consequences often limits social interaction with peers, as rejection or isolation leads to socio-affective problems and decreased academic performance (12, 13). However, implementing an inclusive approach in the schooling of teenagers with chronic

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diseases is challenging and, to date, in most countries, the welfare-state model does not resolve the majority of issues of children with IEI and their families (14).

Appropriate communication and coordination between healthcare professionals and schools is extremely important, with patients' families being a key link between them (15, 16). However, due to the fear of discrimination, some family members may be reticent in providing information about the disease to their school (12, 15). Moreover, students themselves report difficulties associated with open communication, based on exclusion from school life, teachers' reactions, and relationships with peers and friends (17, 18). Thus, communication and coordination strategies need reinforcing, as does the knowledge of health conditions through interprofessional education programs (11, 12).

The Barcelona PID Foundation is a nonprofit organization that was founded in 2014 at the initiative of a group of professionals dedicated to the care of IEI patients and their families. Its "I have a PID. I'm not alone." program started in 2015 to provide psychological support and comprehensive care to children and adolescents with IEI. It is carried out in collaboration with a pediatric reference unit for IEI care in Catalonia, Northern Spain, that currently performs follow-up for more than 500 children and adolescents with a confirmed IEI diagnosis. As part of the program, the "PID at schools" project was created in 2016 with the aim to optimize the integration of children and adolescents with IEI at school and to conduct research activities to detect areas for improvement. Pediatric immunologists, researchers, nurses, and psychologists carry out specific coordination activities at patients' schools with the active participation of patients, their teachers, and classmates.

In this setting, we conducted an observational study to evaluate the indicators of social and academic adaptation as reported by adolescents with IEI, their main caregivers, their classmates, and teachers.

Results

20 adolescents with IEI aged between 12 and 18, who attended high school and were involved in the "I have a PID. I'm not alone." program, were invited to participate. 13 of them—from 13 different schools—accepted (8 males; median age 13.8 [interquartile range [IQR]: 13–15]). Additionally, 21 parents (mothers 12/21), 13 tutor teachers, and 74 classmates (5.7 per patient) agreed to participate (see Table 1 for detailed demographic and clinical data). Reasons for not participating varied, with mistrust regarding confidentiality being the most common. Nine out of 13 participating schools were previously involved in the PID at schools project, with at least one coordination activity carried out between the school and the medical team.

Regarding diagnostic results, 8/13 patients and 10/21 parents felt that their tutor teachers knew about the patient's disease, 7/13 patients liked to be asked by their teachers about their illness, and 14/21 parents thought that it would be beneficial for their child if their tutor teachers and classmates knew they had an IEI. However, 12/21 answered that their child's classmates did not know about their child's illness. Regarding tutor teachers,

Table 1. Main characteristics of PID patients and schools

PID patients (N = 13)		
Age	Median/IQR	13.8/ 13–15
Sex	M/F	8/5
Level of functioning	Level 0/1/2/3	4/3/4/ 2
Treatment	IgRT/SCT	6/1
PID Dx	X-linked agammaglobulinemia	3
	Ataxia telangiectasia	2
	Chronic granulomatous disease	2
	STAT3-LOF hyper IgE syndrome	1
	Autoimmune lymphoproliferative syndrome	1
	SAVI	1
	Combined immunodeficiencies with associated or syndromic features	1
	Autoinflammatory disorders (non-inflammasome-related conditions)	1
Frequency of psychology visits	Weekly/monthly/quarterly	2/7/4
	Parents (N = 21)	Father/mother
Schools (N = 13)		
Type of school	Public/private	11/2
Prior school coordination	Yes/no	9/4
Schools with classmate participation	Yes/no	9/4
Classmates (N = 74)	Male/female/non-binary	34/39/ 1

To calculate the patient's level of functioning, we used the Eastern Cooperative Oncology Group performance status scale (19). CVID, Common variable immunodeficiency; Dx, diagnosis; IgRT, immunoglobulin replacement therapy; SAVI, STING-associated vasculopathy with onset in infancy; SCT, stem cell transplantation.

11/13 would be interested to learn more about IEI, and 8/13 stated that they lacked detailed information about the medical conditions of the student in question. Finally, 40/74 of classmates stated that they knew that their classmate had an IEI and were aware of the consequences, but 41 of them felt they lacked information about the specific repercussions on the daily school life of the student in question. As occurred with tutor teachers, 50 of them would have been interested in receiving more information about IEI, and 53 believed that this would help them to provide optimal support to their affected classmates (see Fig. 1 for detailed answers).

 Patients	D	N	A	 Parents	D	N	A
Do you think your teacher knows about your disease?	1/13	4/13	8/13	Do you think that most of your child's classmates know about their illness?	12/21	4/21	5/21
Does it make you feel good if your teachers ask about your illness?	1/13	5/13	7/13	Do you think your child's teacher knows about their illness?	4/21	7/21	10/21
If you need to explain the details of your illness to a teacher, is it difficult to find the right moment?	4/13	4/13	5/13	Have any of the teachers asked you for a specific description of your child's illness?	8/21	7/21	6/21
Does it make you feel good if your classmates ask you about your illness?	1/13	7/13	5/13	Do you think it would be beneficial for your child if their teachers and classmates know they have a PID?	3/21	4/21	14/21
Do you think your teacher knows how your disease affects you?	3/13	6/13	4/13				
Do you think most of your classmates know about your disease?	6/13	3/13	4/13				
Do you think your classmates are aware of the consequences of your IEI?	6/13	4/13	3/13				
 Teachers	D	N	A	 Classmates	D	N	A
Would you like to know more about primary immunodeficiencies?	0/13	2/13	11/13	Do you think if you knew more about their disease you could support them better?	4/74	17/74	53/74
Do you know what primary immunodeficiencies are?	1/13	2/13	10/13	Would you like to know more about primary immunodeficiencies?	10/74	14/74	50/74
Do you feel that you lack good, detailed information about your student's medical condition?	5/13	0/13	8/13	Do you feel you lack information about how their disease affects their daily school life?	14/74	19/74	41/74
Do you know your student's medical condition and its consequences?	3/13	3/13	7/13	Do you know that your classmate has a PID and what the consequences are?	10/74	24/74	40/74
Do you feel that you have enough information to properly manage health problems that may arise?	6/13	3/13	4/13	Would you feel insecure if your classmate had medical problems at school?	15/74	23/74	36/74
Do you feel able to manage sudden medical problems that may arise at school?	7/13	3/13	3/13	Do you know what primary immunodeficiencies are?	18/74	23/74	33/74

*A=(Agree + Totally agree), D=(Disagree + Totally Disagree), N=Neutral

Figure 1. **Diagnostic results.** Top left: patient responses; top right: parent responses; bottom left: tutor teachers; bottom right: peer responses. Answers with agreement exceeding half of the participants are highlighted in bold.

In this area, we would like to highlight a comment that appeared in the free-text field of the questionnaires: “At times, being able to detect anxiety processes in our child has been complicated. These states of nervousness have been caused by returning to school after a long period of hospitalization and wanting to be at the same level as the rest of classmates” (parent).

Regarding adaptation, 7/13 students with IEI said that they were allowed to hand in assignments or exams on a different day or via a different route. A total of 9/13 students felt that the amount of work that they are expected to do is in line with their capacity, but 11/21 parents gave a neutral score regarding whether the school had an established action procedure on dealing with school absenteeism due to medical reasons, and 11/21 reported that there are academic or social needs not covered by school actions. Moreover, teachers reported that 7/13 schools lacked a specific policy of action for students’ absenteeism, but

11/13 reported they had changed the curriculum or methodology to meet the students’ specific needs. Regarding classmates, 38/74 said they helped students with IEI with missed homework and classwork, but 46 felt they could do more. Only 15/74 responded that IEI students asked for more details about homework and class notes than other students (see Fig. 2 for detailed answers).

In this area, we would like to highlight these two comments from the free-text field of the questionnaires: “I think that knowing the diagnosis would allow me to better help my friend” (classmate); “I think that information about the disease at school is very important to help our child feel more supported and confident” (parent).

Regarding comprehension, 10/13 patients answered that there are tutor teachers they trust enough to tell them how their disease and treatments affect their academic performance, and 8/13 felt like their tutor teachers have been able to help them

 Patients	D	N	A	 Parents	D	N	A
Do you think the amount of work that you are expected to do is consistent with your capacity?	1/13	3/13	9/13	Do you feel that the way the school handles the impact of the disease helps your child feel satisfied?	5/21	8/21	8/21
Does the school allow you to hand in assignments or exams in alternative ways or on alternative deadlines?	2/13	4/13	7/13	Do you think that some of your child's academic or social needs are not covered by the school's actions?	11/21	3/21	7/21
Do you think that missing school for medical reasons makes it difficult for you to keep up with the course content?	6/13	2/13	5/13	Do you think that the school has an established action procedure on dealing with school absenteeism due to medical reasons?	3/21	11/21	7/21
When you can't attend school, is it hard to find out what the homework is and what was explained in class?	7/13	2/13	4/13	Does your child verbalize that it is difficult for them to catch up after a period of school absenteeism due to medical reasons?	8/21	7/21	6/21
				Do you feel that your child is distressed or worried about their school?	9/21	5/21	7/21
 Teachers	D	N	A	 Classmates	D	N	A
Has the curriculum or methodology been changed to meet this student's specific needs?	1/13	1/13	11/13	Do you think you could help them with schoolwork more?	5/74	23/74	46/74
Is there a common approach among the teaching staff regarding the application of specific measures to help the student?	2/13	2/13	9/13	Do you help this student with homework and classwork they have missed?	11/74	24/74	38/74
Is there any individual, social or academic support available in place for the student?	1/13	5/13	7/13	Do you think your classmate with IEI asks for details about homework and class notes more than other students?	30/74	28/74	15/74
Is there a policy to deal with absenteeism for students with an IEI?	7/13	3/13	3/13				

*A=(Agree + Totally agree), D=(Disagree + Totally Disagree), N=Neutral

Figure 2. **Adaptation results.** Top left: patient responses; top right: parent responses; bottom left: tutor teachers; bottom right: peer responses. Answers with agreement exceeding half of the participants are highlighted in bold.

with social or academic problems. A total of 12/21 parents said that their children feel adequately supported by the school in dealing with the challenges their illness may cause. Moreover, 9/13 tutor teachers said that there are preventive/inclusive activities to increase awareness of the students' disease among their classmates, and 11/13 believed that IEI students are able to freely express their feelings and concerns. Furthermore, 52/74 classmates expressed a willingness to receive more information on IEI from the medical team, and 63 reported not having any discriminatory behavior towards their classmate with IEI due to their illness (Fig. 3).

In this area, we would like to highlight these two comments: "Having a protocol would be very helpful to train teachers how to act properly, since, despite their willingness, what to do is not clear" (parent); "I think that I already have enough information to be able to help the student, but any additional educational activity would be highly welcomed" (tutor teacher).

When examining coordination, results revealed that 7/13 patients with IEI expressed a desire for improved coordination between their tutor teachers and healthcare team, including regular updates on their health status, and 7/13 wanted their family to give more information about their illness to their teachers. A total of 17/21 parents also felt that increasing communication between the school and the medical team could improve their child's social and academic performance. In that

regard, 7/13 teachers felt that parents were actively and sufficiently involved when reporting on the course of their child's disease or the emergence of new needs, and 8/13 answered that they coordinated with the family on a regular basis to closely monitor the student's status to discuss their progress, taking into account their special needs. A total of 13/21 parents felt that they were frequently informed about their child's academic performance (Fig. 4).

The comment "It would be beneficial to regularly coordinate with the clinical unit in order to adjust universal, additional and intensive measures at school" (tutor teacher) is of relevance in this section.

Finally, when analyzing socialization, all 13 patients reported that they felt treated properly by their classmates, and 10/13 felt fully integrated. This was also expressed by 67/74 and 57/74 of their classmates, respectively. A total of 12/13 tutor teachers and 17/21 parents mentioned that students with IEI were well accepted by their classmates. Moreover, 46/74 classmates thought that they showed a proactive attitude when it came to helping their classmates socialize, and 48/74 did not observe any discriminatory behavior from other students towards their peers with an IEI. Regarding patient associations, 8/13 tutor teachers did not know that IEI foundations or associations existed, but 16/21 parents and 8/13 patients thought that it would be useful for teaching staff to meet with IEI patient associations (Fig. 5).

 Patients	D	N	A	 Parents	D	N	A
Are there any teachers you trust enough to tell them how your disease and treatments affect your academic performance?	2/13	1/13	10/13	Do you think that the teaching staff has a proactive attitude when it comes to addressing the poorer school performance due to medical visits or hospital admissions?	4/21	6/21	10/21
Do you feel like your teachers have been able to help you with any social or academic problems?	3/13	1/13	8/13	Do you think that all the teachers treat your child the same?	4/21	6/21	11/21
Do you think that all your teachers treat you the same?	4/13	5/13	4/13	Do you think that the teachers are sympathetic to your child when their illness might make them feel worried, frustrated or stressed?	3/21	8/21	9/21
Did your school explain what you have to do when you miss school for medical reasons?	6/13	4/13	3/13	Has your child expressed to you that they don't feel adequately supported by the school in dealing with the challenges their illness may cause?	12/21	4/21	5/21
Have you ever felt rejected or discriminated against by a teacher because of your illness?	11/13	1/13	1/13				
 Teachers	D	N	A	 Classmates	D	N	A
Is the student able to freely express their feelings and concerns?	0/13	2/13	11/13	Would you like to receive more information about IEI from the medical team?	6/74	16/74	52/74
Are there any preventive/inclusive activities to increase awareness of the student's disease among their classmates?	3/13	1/13	9/13	Do the teachers tell you how you can help the student with PID with their schoolwork?	20/74	16/74	37/74
Is there a policy in place to deal with academic problems caused by long hospital stays?	3/13	5/13	5/13	Are you interested in this student's medical visits or hospital treatments?	23/74	30/74	21/74
Is there an action policy for the social area to deal with prolonged hospital admissions?	5/13	4/13	4/13	Have you ever discriminated against this student due to their illness?	63/74	8/74	3/74

*A=(Agree + Totally agree), D=(Disagree + Totally Disagree), N=Neutral

Figure 3. **Comprehension results.** Top left: patient responses; top right: parent responses; bottom left: tutor teachers; bottom right: peer responses. Answers with agreement exceeding half of the participants are highlighted in bold.

Upon examining the most challenging areas to manage, 8/13 patients emphasized having active clinical manifestations of the disease as the most challenging situation, while 11/21 parents reported that the main challenge was the consequences of school absenteeism due to the disease. These two areas were also chosen by 6/13 tutor teachers. Finally, 50/74 classmates reported that the most difficult area to manage when helping a patient with IEI is their lack of knowledge about the disease (see Fig. 6 for detailed answers).

Discussion

This study shows IEI's impact on adolescents' schooling at different levels and that there is a need to provide recommendations for home, school, community, and healthcare settings to improve the quality of life of individuals with rare diseases during childhood and adolescence. Disease complications, frequent hospitalization, and medical visits contribute to school absenteeism and social isolation, as shown by Kuburovic et al. (3). This is particularly true in emotional, social, and school psychosocial domains, as these children are at an increased risk of experiencing severe anxiety and depressive symptoms. The current study adds to the evidence in the literature that, while students and

families report positive social acceptance in schools, the educational and healthcare system lacks preparedness to meet their needs effectively.

School absenteeism due to disease complications significantly impacts quality of life and emotional well-being due to restricting social contact. Patients are thus more susceptible to experiencing negative self-perception, decreased perception of their own health, and an increase in general fatigue, as previously demonstrated by our group (4). The study by Xiao et al. represents a literature review focusing on health-related quality of life (HRQoL) in IEI patients. It stresses the need for more extensive and systematic research in this area, emphasizing the importance of a multidisciplinary approach. Despite advances in medical treatments for IEI, there is a crucial need to focus on HRQoL to improve patient satisfaction and overall well-being (20). Our findings reveal a lack of structured and systematic protocols within schools to address school absenteeism and its consequences and emphasize the need for early biopsychosocial assessment and support to prevent long-term mental health consequences. Digital or hybrid education might help minimize absenteeism in chronic diseases (21). However, when implementing them, it is crucial to manage the possible increase of inequities and digital breaches to avoid creating new barriers (21).

 Patients	D	N	A	 Parents	D	N	A
Would it make you feel good if your teacher received more information about your illness from your healthcare team?	2/13	4/13	7/13	Do you think that increasing communication between your child's school and medical team would improve your child's social and academic performance?	0/21	4/21	17/21
Do you want your family to give more information about your illness to your teachers?	1/13	5/13	7/13	Do you feel that you spend enough time giving information and justification of your child's needs in order to obtain a proactive attitude from their school?	1/21	7/21	12/21
Does your teacher liaise with any member of your healthcare team?	4/13	3/13	6/13	Are you frequently informed about your child's academic performance?	4/21	4/21	13/21
Do you think your teacher is aware of the course of your illness?	2/13	6/13	4/13	Do you feel that the school is prepared to address the specific needs of your child?	5/21	5/21	11/21
				Does the school inform you frequently about your child's social development?	5/21	6/21	10/21
 Teachers	D	N	A				
Is there regular coordination with the student's family to discuss the student's progress, taking into account their special needs?	1/13	4/13	8/13				
Do you think the student's family is sufficiently involved when reporting the course of the disease or the emergence of new needs?	5/13	1/13	7/13				
Does the educational center coordinate with the student's healthcare team?	5/13	4/13	4/13				

*A=(Agree + Totally agree), D=(Disagree + Totally Disagree), N=Neutral

Figure 4. **Coordination results.** Top left: patient responses; Top right: parent responses; bottom left: tutor teachers. Answers with agreement exceeding half of the participants are highlighted in bold.

In addition to specific protocols dealing with school absenteeism, our study emphasizes gaps in disease-related knowledge among educators and peers. Our data show that, despite more than half of classmates being aware of the existence of the disease, the vast majority reported lacking specific knowledge about the disease and its repercussions on daily school life. Lack of knowledge is described by almost every stakeholder as a limiting factor. As observed by Hinton et al., teachers often lack formal training in chronic condition management, and this may limit their ability to address the needs of students with IEI (22). Even when aware of the disease, truly understanding the academic consequences and implications is inadequate. As expressed by García-Perales et al., there is an urgent need for widespread educator training to foster true inclusive education, using knowledge and understanding of the characteristics and potential of students with rare diseases (23). Across contexts, teachers commonly face limited condition-specific training, workload, resource constraints, and the absence of a designated school-health liaison, which hinder implementation of inclusive practices (9, 22, 24). We also acknowledge that policies and accommodations vary internationally; settings with nationwide school-health frameworks may face different barriers, whereas our findings reflect the Spanish/Catalan context, where condition-specific guidance for rare diseases remains fragmented. A brochure from the IPOPI tries to fill this gap by offering guidance on how schools can best support these students from a health point of view but also addressing education, absenteeism, and bullying, among other

issues. In Spain, several associations and foundations dedicated to various rare diseases are actively advocating for better support within schools and providing guidance tailored to specific conditions. We believe in the importance of merging forces from the different stakeholders to carry out common protocols in the future, using expertise networks for dissemination, such as European Reference Networks (ERNs), the corresponding scientific societies, as well as patient associations or foundations (19).

Coordination between healthcare teams, schools, and families is also a recurrent unmet need highlighted by our study. Although essential, it is usually insufficiently implemented, as shown by Verger et al. and Rosselló et al., who stress the importance of interdisciplinary approaches to meet the needs of children with rare diseases (15, 24). Our findings support these observations, highlighting the need for regularly updated structured communication pathways. Moreover, coordination should explicitly extend to healthcare transition from pediatric to adult services and its interface with postsecondary education/employment supports; although consensus recommendations exist in IEI (e.g., ERN for Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases), empirical data linking transition processes to education or work outcomes are currently lacking (19). At our center, a hospital-wide transition program is in place; future work will formalize links with schools/universities and vocational services to close this gap.

Patient associations play a pivotal role in raising awareness, providing resources, and advocating inclusive education. As

 Patients	D	N	A	 Parents	D	N	A
Do you feel that you are treated well by your classmates?	0/13	0/13	13/13	Do you think that your child is well integrated into their class?	2/21	3/21	16/21
Do you feel like a fully integrated member of your class?	1/13	1/13	10/13	Do you think it would be useful for teaching staff to meet with IEI associations?	3/21	2/21	16/21
Do you think it would be appropriate for your teachers to meet with IEI associations?	2/13	3/13	8/13	Do you feel that your child is well accepted by their classmates?	1/21	3/21	17/21
Do you think that your teacher has made it easier for your classmates to understand your illness?	5/13	4/13	2/13	Has your child ever said that they don't feel sufficiently supported by their classmates regarding their disease?	14/21	4/21	3/21
 Teachers	D	N	A	 Classmates	D	N	A
Is the student well accepted by their classmates?	0/13	1/13	12/13	Do you think the class group treats your classmate well?	1/74	6/74	67/74
Do you think the school enables the students to understand this disease?	2/13	4/13	7/13	Do you think your classmate with IEI is well integrated into the class?	5/74	12/74	57/74
Are you aware of the existence of associations that support the student's illness?	8/13	0/13	5/13	Do you think that you have a proactive attitude when it comes to helping your classmate socialize?	4/74	22/74	46/74
Have you ever observed students discriminate against the IEI students because of their disease?	11/13	0/13	2/13	Are you aware of any associations that support children with IEI?	36/74	14/74	24/74
				Have you observed discriminatory behavior by your classmates towards the student with IEI?	48/74	16/74	9/74

*A=(Agree + Totally agree), D=(Disagree + Totally Disagree), N=Neutral

Figure 5. **Socialization results.** Top left: patient responses; top right: parent responses; bottom left: tutor teachers; bottom right: peer responses. Answers with agreement exceeding half of the participants are highlighted in bold.

Gaintza et al. demonstrate, these organizations enhance community understanding of rare diseases and promote positive attitudes within school communities (25). Paz-Lourido et al. also

show a high acceptance of educational agents for the school environment in rare disease both in primary and secondary schools (26). Our study aligns with these findings, showing

 Patients	No	Yes	 Parents	No	Yes
Clinical manifestations	5/13	8/13	Academic consequences of school absenteeism	10/21	11/21
Academic consequences of school absenteeism	8/13	5/13	People at school are not aware of the disease	11/21	10/21
Teachers and classmates do not have enough information about the disease	10/13	3/13	Clinical manifestations	11/21	10/21
Socializing with classmates	10/13	3/13	Socializing with classmates	13/21	8/21
Other	11/13	2/13	Other	20/21	1/21
 Teachers	No	Yes	 Classmates	No	Yes
Academic consequences of school absenteeism	7/13	6/13	People at school are not aware of the disease	24/74	50/74
Clinical manifestations	7/13	6/13	Academic consequences of school absenteeism	37/74	37/74
Other	9/13	4/13	Clinical manifestations	42/74	32/74
Socializing	10/13	3/13	Socializing	61/74	13/74
People at school are not aware of the disease	11/13	2/13	Other	68/74	6/74

Figure 6. **Challenging areas results.** Top left: patient responses; top right: parent responses; bottom left: tutor teachers; bottom right: peer responses. Answers with agreement exceeding half of the participants are highlighted in bold.

strong support from educators, classmates, and families for the involvement of patient associations to foster adaptive measures and prevent discrimination. Empowering children and adolescents with IEI by following a specific and well-structured program improves their QoL, as shown by Fasshauer et al. (27). Despite the lack of specific protocols and knowledge, one distinguishing trait of our findings is that our data suggest that social acceptance among peers is generally positive, in contrast to other studies like that by Adama et al., where stigma and bullying were highly prevalent among patients with rare diseases (28). This difference might be explained by one of the main limitations of our study: the relatively small sample size of schools and individuals with an IEI, though comparable to that of similar studies, and also by the differences regarding the rare diseases studied for the 41 families in Adama's studies. Additionally, the inclusion of participants already enrolled in psychological support programs like PID at schools may have created a selection bias, potentially underestimating the challenges faced by others without such resources. Given the heterogeneity of rare diseases and even within IEI, differences across studies are expected. Likely determinants include: IEI groups, Eastern Cooperative Oncology Group performance status, sex/gender, socioeconomic context, school settings (public vs. private; urban vs. rural), prior exposure to support programs, and parental engagement. Many of these variables are inconsistently reported in the literature, which limits comparability and interpretation. In our cohort, the sample size precluded adjusted or stratified analyses by these dimensions. Exploratory stratifications by school sector and parent sex were performed but not presented in our study because group sizes were extremely imbalanced and underpowered, yielding no consistent trends. By May 2021, restrictive measures related to the COVID-19 pandemic had already been considerably relaxed in our school settings, and students attended classes wearing ear-loop face masks, generally with a greater sense of normalcy compared to the most acute moments of the pandemic. However, the health situation could have influenced perceptions of special attention toward children with immunodeficiencies, which constitutes another possible bias. Lastly, the cross-sectional design limits the evaluation of long-term outcomes and the impact of interventions over time, highlighting the need for larger, multicenter, longitudinal studies. With those limitations in mind, in the following years, our group is aiming to apply a broader, multicenter, validated evaluation, including the use of the RE-AIM framework, to enable greater coverage to overcome most of these limitations (29). Also, a stepwise validation program including psychometric modeling has been planned with the goal of producing a robust, adoptable instrument for IEI school settings more scalable and comparable to other settings.

Conclusion

Adolescents with IIEs face significant challenges impacting their education, emotional well-being, and overall QoL. This study highlights critical gaps and unmet needs in educational and healthcare systems to support disease impact in the school environment. Specifically, the absence of structured protocols to address absenteeism, limited disease-related knowledge among

educators, and insufficient coordination between families, schools, and healthcare teams continue to be significant barriers. Patient associations and foundations already advocate for stronger school support and condition-specific guidance. Building on these efforts, we propose co-developing standardized protocols and resources with education authorities and disseminated them through expert networks—such as ERNs, relevant scientific societies, and patient associations. Co-development should include all stakeholders. Our next steps are to develop, pilot, and evaluate these materials with stakeholders to enable scalable, system-level adoption.

Despite these challenges, the findings highlight positive social acceptance from peers and the important role of patient associations in promoting awareness and fostering inclusivity. Addressing the identified gaps through interdisciplinary collaboration, educator training, and the development of structured action plans is essential. Future multicenter studies with larger samples are needed to confirm these findings and guide the implementation of effective, inclusive educational strategies to improve the quality of life for adolescents with an IEI.

Materials and methods

Study design

A 2-mo, prospective, cross-sectional, observational study was initiated in May 2021. At that time, children in Catalonia attended school with the sole restriction of wearing an ear-loop face mask to class.

Questionnaire design and measures

Four different questionnaires (one for each category: patients, parents, tutor teachers [teachers who are primarily responsible for the students in a specific class], and classmates) were co-created by a multidisciplinary team, including pediatric immunologists, pediatric psychologists, a specialist nurse practitioner together with the advisory patient council of the Barcelona PID Foundation, composed of 12 adolescents and adults with IEI. This co-design provided the basis for initial face and content validity and ensured that items were context-specific and age/role appropriate. Because the aim of this study was an exploratory mapping across informants, items were tailored to each respondent group rather than forced to be parallel. The questionnaire comprised five evaluative specific areas (knowledge of the IEI diagnosis, perception of patient's adaptation at school, the school's understanding of the disease's impact, perception of patient-family-school coordination, and perception of patients' socialization) and one final area that asked for a selection of the two most challenging disease-related areas to sustain individually. A Likert rating scale was used to evaluate answers. Furthermore, a free-text comments section was available to add reflections if needed for all questions and areas.

Results with consensus of more than half of the participants were considered relevant, included in the Results section of this manuscript, and bolded in Fig. 1, 2, 3, 4, 5, and 6.

Data collection

Data were collected at one time point during the study period. Patients, parents, and tutor teachers were invited to participate

by telephone or email, whereas classmates were invited by their own tutor teachers.

The questionnaires were sent to all participants via email through a link to the REDCap platform (Vanderbilt University). Each patient, at least one parent, the head teacher, and all classmates willing to participate answered the questionnaires.

Statistical analysis

Qualitative variables were described as numbers and percentages. Quantitative variables were described as mean and standard deviation or median and IQR. Confidence intervals for all analyses were considered at 95%. All statistical analyses were performed with R software, Version 4.2.0 (2022-04-22 ucrt), The R Foundation for Statistical Computing. This study was not powered for psychometric modeling; no factor or test-retest analyses were performed in the present pilot, which focuses on descriptive results across informants.

Ethics

All the information collected during the study was strictly confidential. Participants signed the study informed consent (IC); participants ≥ 12 and < 18 years signed the informed assent along with their legal guardian. The study followed the World Medical Association's Declaration of Helsinki and obtained ethical approval from Vall d'Hebron Barcelona Hospital Campus Research Ethics Committee (PR(AMI)192/2021). IC was obtained from all participants.

Data availability

All data generated or analyzed during this study are included in this published article. If needed, detailed data are available from the corresponding author upon reasonable request.

Acknowledgments

We are deeply grateful to the affected individuals and their families who participated in this study. The authors thank Clare Butler for English language assistance and acknowledge Santiago Pérez-Hoyos and Anna Martínez for carrying out the statistical analysis. The authors would also like to thank patients and their caregivers, their teachers, and the schools that participated in the study: Escola Pia Terrassa (Terrassa), Institut Celestí Bellera (Granollers), Escola Ginebró (Granollers), Institut Valldemosa (Barcelona), Institut Sant Feliu de Guíxols (Sant Feliu de Guíxols), Institut Ridaura (Palamós), Institut Joaquina Pla i Ferreras (Sant Cugat del Vallès), Institut Quatre Cantons (Barcelona), Institut Sa Palomera (Blanes), Institut Banús (Cerdanyola del Vallès), Institut Mediterrània (Castelldefels), and Institut Maremar (Masnou).

This research is supported by the European Reference Network for Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases and the Jeffrey Modell Foundation. This research is included in the "I have a PID. I'm not alone." program carried out with the support of the Barcelona PID Foundation, the Catalan Association of Primary Immunodeficiencies, private

grants from La Caixa Foundation social work (AD21-01447), and public grants from the Generalitat de Catalunya social area (DDS004/22/000724).

Author contributions: Laura Lopez-Seguer: conceptualization, data curation, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, and writing—original draft, review, and editing. Sonia Rodriguez-Tello: conceptualization, data curation, formal analysis, investigation, methodology, project administration, supervision, validation, visualization, writing—original draft, and writing—review and editing. Miriam Gonzalez-Amores: conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing—original draft, and writing—review and editing. Andrea Martin-Nalda: conceptualization and writing—review and editing. Stephany Zelada: conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, visualization, and writing—review and editing. Saida Ridao Manonellas: conceptualization, investigation, methodology, resources, and writing—review and editing. Sonia Galindo-Maycas: conceptualization and writing—review and editing. Carlota Villar: supervision and writing—review and editing. Jacques G. Riviere: conceptualization, data curation, investigation, methodology, project administration, supervision, validation, visualization, writing—original draft, and writing—review and editing. Pere Soler-Palacin: conceptualization, methodology, supervision, validation, writing—original draft, and review, and editing.

Disclosures: J.G. Riviere reported grants from Grifols, personal fees from Grifols, personal fees from Takeda, grants from Pharming, personal fees from Pharming, and personal fees from CSL Behring outside the submitted work. P. Soler-Palacin reported grants from CSL Behring, grants from Grifols, and non-financial support from Takeda outside the submitted work. No other disclosures were reported.

Submitted: 1 July 2025

Revised: 9 September 2025

Accepted: 2 February 2026

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