Impact of APDS survey on patients and their carers

Activated PI3K delta syndrome (APDS) is a rare primary immunodeficiency. About 40 people in the UK are known to be affected by the condition.

In April 2024 Immunodeficiency UK worked with NICE to develop an online survey to help understand the impact of the rare condition APDS on those affected and their carers. The evidence was used for NICE's technology appraisal of the drug Leniolisib for the treatment of APDS.

The survey was publicised in Immunodeficiency UK's newsletter, on social media and reach out to immunology centres.

Fourteen people with experience of APDS responded to the survey.

Key findings from the survey

- Most respondents reported a time to diagnosis of greater than 3-5 years.
- APDS was shown to have a significant impact on daily and family life affecting education, ability to work, socialise, carrying out daily activities, family activities and hobbies. Significant impacts were also described on carers and siblings of those affected. Only 30% of respondents reported satisfaction with their quality of life.
- Physical pain and discomfort and extreme tiredness were associated with having the condition.
- APDS impacts on mental health with concerns about the health of the person affected, with extreme anxiety about getting infections. Factors impacting on mental health included the burden of treatment and care, dealing with pain, coping with feelings of isolation and loneliness and uncertainty about the future.
- Symptoms of APDS which had the most impact on those affected were bronchiectasis, respiratory infections, chronic cough, autoimmunity problems, hearing problems, enlarged lymph nodes, gastrointestinal problems and having an enlarged spleen.
- Respondents reported an average of 24.6 outpatient visits (range 2 - 200) and 17.6 days in hospital (range 0 – 80 days) over the last year.
- The treatment combinations used to manage APDS varied between individuals. Four respondents indicated they were taking four to six medications. The most used therapies were immunoglobulin therapy, prophylactic antibiotics, followed by immunosuppressants, prophylactic antivirals and Sirolimus.
- There remains an unmet need for treatment of symptoms not addressed by current treatments.
- Six respondents had been treated with Lenioslib. Of these five reported health benefits. These included a reduction in lymph node size, improved blood counts, increased energy and appetite, reduced use of antibiotics and hospital admissions.
- Respondents gave overwhelming support for the drug Leniolisib to be made available to people with APDS.

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- ## About the survey respondents

Fourteen people with experience of APDS responded to the survey.

Four respondents were directly affected by APDS. Ten identified themselves as carers, a family member or friend of the family of a patient with APDS.

Six people confirmed they were being treated with Leniolisib.

Self-reporting of respondent's ethnic group:

10 respondents: English, Welsh, Scottish, Northern Irish, British

1 respondent – Any other white background

1 respondent – Asian

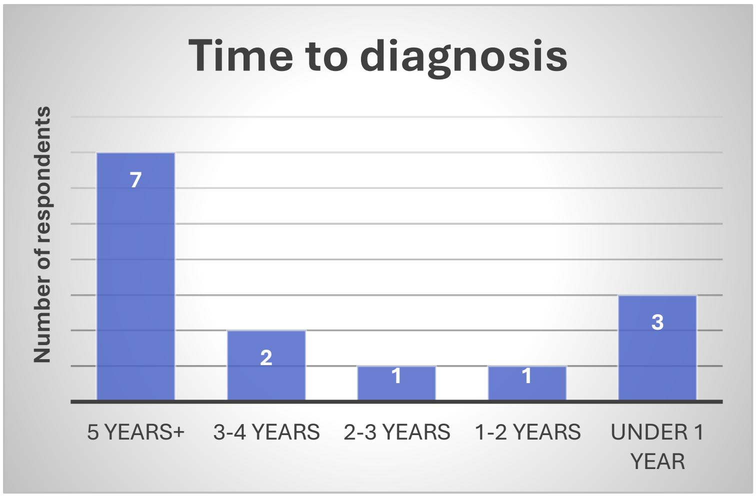
1 respondent – White & Asian

1 respondent – Chinese.

Type of responder	Number of respondents	Sex, age of respondents
Directly affected by APDS	4	*1 male; aged 58. 3 females; ages 21, 37 and *47.
A carer of a patient with APDS	7	2 female; 5 male carers responded. Age range of child affected: 3 -12 years old.
A family member or friend of the family	3	2 female and 1 male responded. Age range of child affected: 3-14 years old.

* Family members also affected by APDS.

- ## Time to diagnosis



The majority of respondents reported a time to diagnosis of greater than 3 years (N=9).

Diagnosis:

“Doctors need to be educated on the condition”.

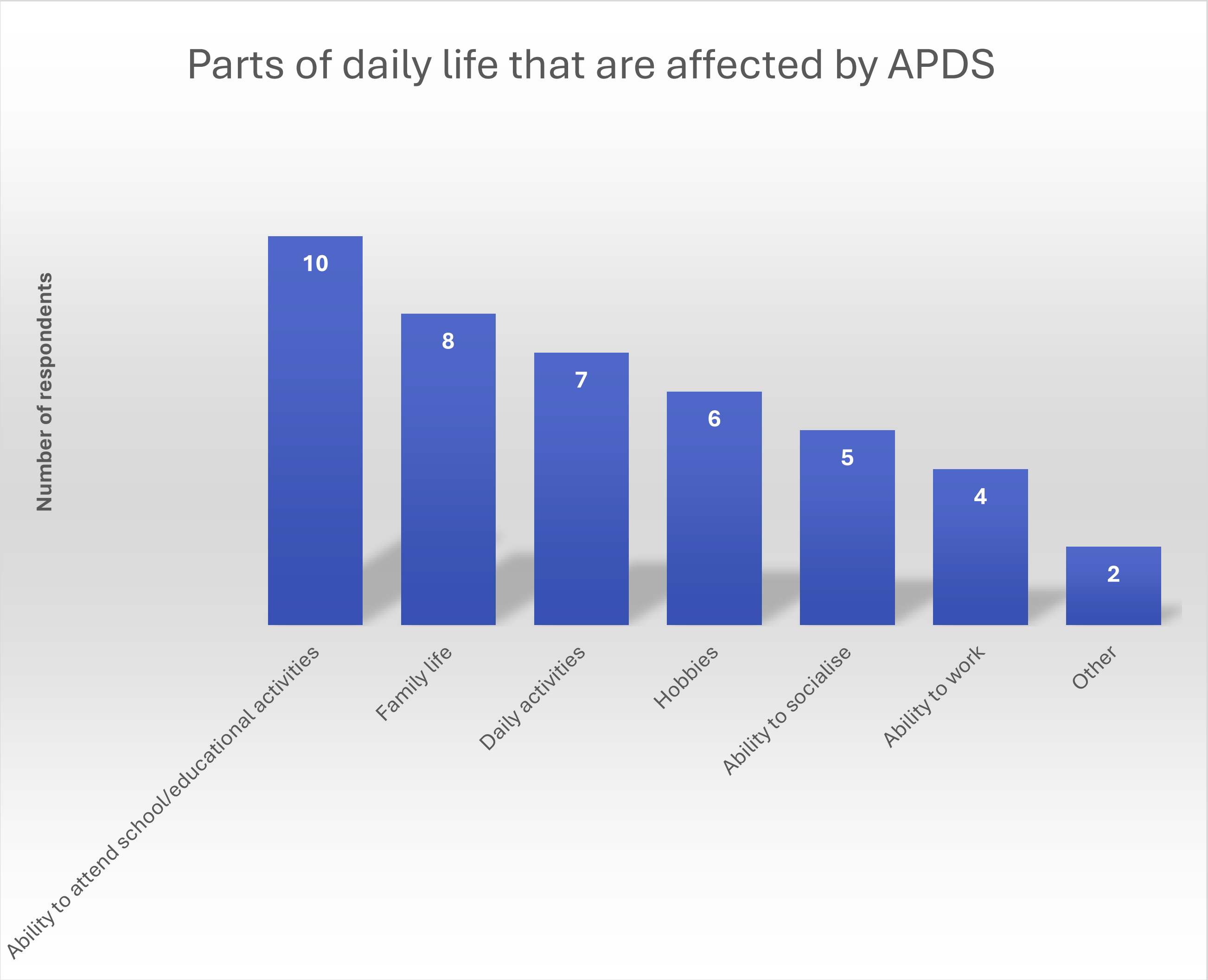
“Undiagnosed for 5 years was so scary, several hospital additions with pneumonia, struggling to breathe, eat and sleep. Parents and medical professions should question if the child has been on several recurring antibiotics and admitted with recurrent chest infections.”

“more awareness needs to be made about this condition. All the doctors who have tried to help [patient] in the past didn’t even know what this condition was when [they] was finally diagnosed. We struggled to get help for 7 years which has led to horrific lung damage. More awareness would help other families who may be suffering from the disease but are unaware they even have it. We as a family are trying our best to do our part in making this condition known.”

“Infant screening at the heal prick test would have saved a lot of problems.”

- **Impact on daily life**

The impact of APDS on daily life is significant.



Impacts on daily life:

“Tough, exhausting, damaging, poorly, sick, irritable from coughing and all the infections, painful”

“tiredness and infections”. “Emotionally distress”

“Torture”.

“[Patient] fell poorly around 1 years old. Despite us not having a diagnosis we knew something was wrong as she was constantly poorly and getting infections. From this point up until the age of 7 [patient] struggled to mix with other children and has only been able to complete a full school year without hospital admission once. This affected her ability to maintain friendships with her peers and to keep up with her education.”

“Lots of vomits and coughing. Took many sick days off school. Had lots of trips to the GP and hospital”

“Bronchiectasis from APDS - 2/3 daily physio and 3 monthly IV hospital antibiotics”.

“Ear and lymph glands problems. Behind in schoolwork and development both socially and academically.”

“Recurrent ear infections resulting in holes in ears so washing and swimming difficult.”

“psychological and emotional effects”

- ## Impact on education

12 respondents reported significant days off school/college. This included several weeks each term (N=1), 1 year (N=1), 2 years (N=1), 4 years (N=1), and unable to attend (N=1).

Missing education

“Missed several days of school. Missed out on dance / gymnastics due to being ill. Walking, plays at the park.”

“Several weeks of school each term.”

“[Patient] missed almost the whole of reception, at least 3 months of year 1, 2 months of year 2 and thankfully only 3 weeks of year 3.”

- **On ability to work and loss of income**

Four respondents also reported the impact APDS had their ability to work. One respondent was not able to work as they looked after their 4-year-old child with APDS.

Impact on work

"I am unable to work due to [patient's] condition as she is constantly getting infections and needs iv medication at least 2/3 monthly."

"Not working as a results to looking after my son."

Loss of income – *"Very much so as one household working and not entitled to any help/benefits"*.

- **Impact on mental health**

Ten respondents reported that APDS impacted their mental health. Reasons included burden of care (N= 3), frustration (N=3), moderate and extreme anxiety (N=2), isolation and loneliness (N=2), confusion (N=1) and depression (N=1).

Mental health impacts:

"Makes me feel so down and depressed, isolated". "Frustration." "Can be lonely."

"Not being able to most things my son should be doing has impact on his mental health."

"Tearful. Frustrated, Unsure if he actually has constant physical or mental pain."

"The amount of hospital appointments and receiving medical care each week at home".

"Recurrent blood tests and hospital appointments."

"Anxiety, uncertainty, having a condition no one understands, frustration at having to have weekly infusions."

"When [patient] cannot go and play with his friends or when [patient] had to miss a family trip away due to being hospitalised [they] asked "why me"."

- **Impact on mobility**

Five respondents reported an impact on mobility.

Impacts were:

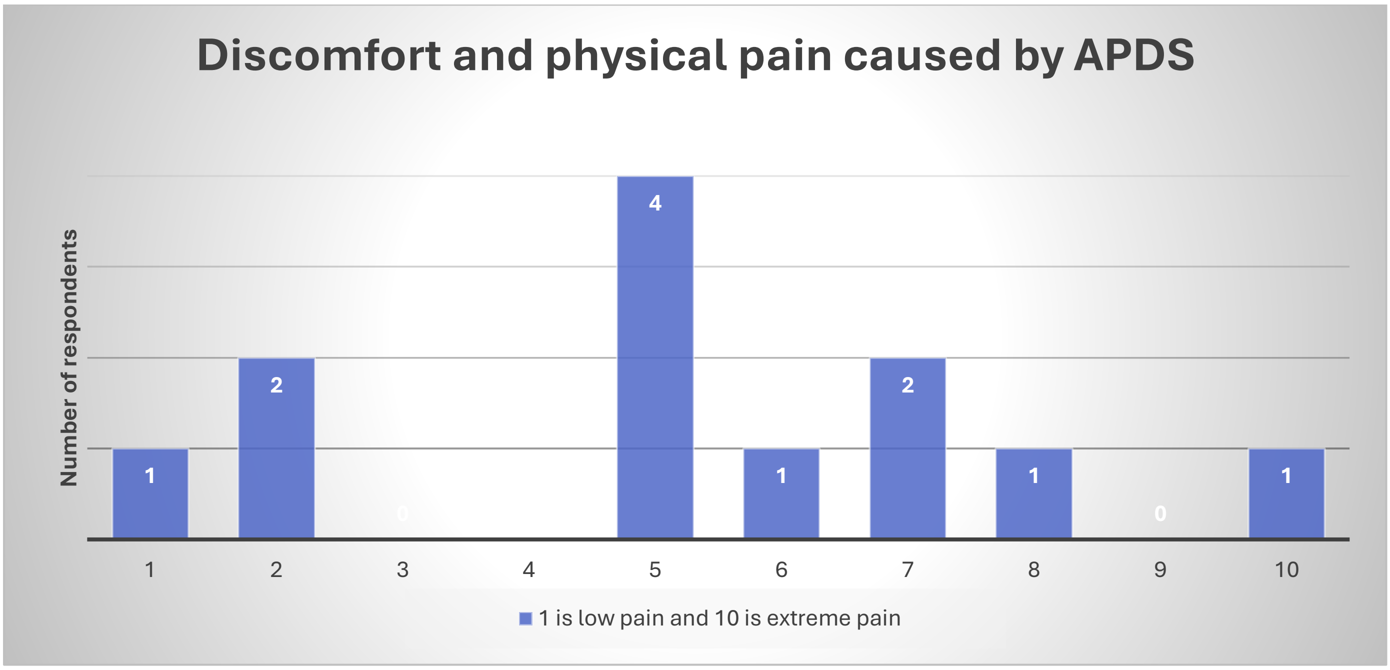
"Painful, breathless, exhausted." "Hypermobility in limbs". "Can get dizzy or lightheaded."

"Slow at learning to crawl and walk. Unable to walk for long distances".

"Legs after the immunoglobulin treatments but so cannot walk as far as his peers."

- **Physical and pain discomfort**

Twelve respondents reported their pain and discomfort in relation to having APDS. One respondent reported that pain had an extreme effect on doing what they needed to do. Six respondents reported a moderate effect and 5 a little. Only 1 respondent said it had no effect.



Examples of physical pain experienced:

"On my worse days I am in pain from weak joints, or headaches from sinus flare ups, chest always hurts with coughing so hard."

"[Patient] struggles with discomfort in [patient's] ears, stomach and chest. [Patient] has had reoccurring lung collapse which would be more on a level of 10 for pain when this occurs."

"pain in knees." *"Hands can lock."* *"Discomfort."* *"Frequent infections."* *"Legs".*

"[Patient] will wake up in the middle of the crying out in pain."

"Only when having blood tests and weekly subcutaneous infusions."

- **Impact on different aspects of quality of life**

Three respondents reported that they experienced an extreme amount of tiredness in relation to having APDS, with a further 7 respondents being moderately affected (Table 1).

Six of 13 respondents indicated they were extremely worried about their health, with a further 5 respondents moderately affected.

A major concern was worry of the risk of infection with 11 of 13 respondents reporting an extreme amount of concern.

Table 1

	Rating				
Quality of life factor	**An extreme amount**	**A moderate amount**	**A little**	**Not at all**	**No of responses**
Amount of tiredness experienced	**3**	**7**	**2**	**1**	**13**
The impact of being tired	**2**	**4**	**6**	**1**	**13**
Extent of worry about health	**6**	**5**	**2**	**0**	**13**
Worry about infections	**11**	**1**	**1**	**0**	**13**
Positivity about the future	**2**	**4**	**5**	**0**	**11**
Extent of enjoying life	**4**	**5**	**1**	**2**	**12**

Fear about infections

“Makes me worried when I get an infection the long term affect it is having on me.”

“I'm terrified to go out or I'm always poorly with either a chest infection or my head feeling like it is about to explode.”

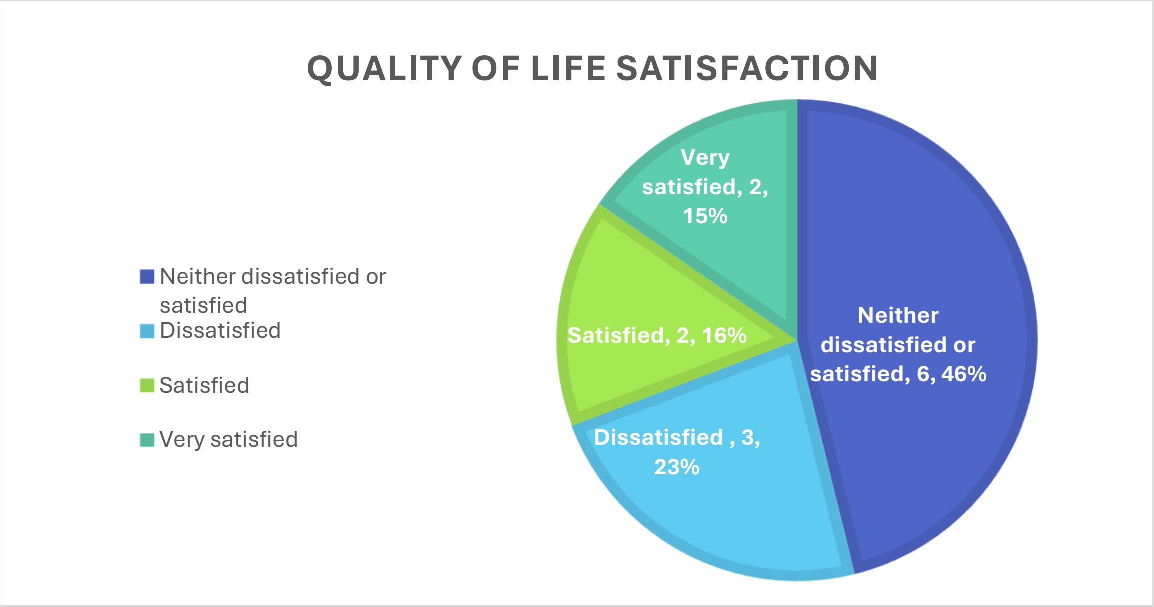
“As a mum I worry a lot about [patient]. Covid being our biggest fear due to how damaged [their] lungs are from the condition. We managed to shield from Covid and [they] didn’t catch the virus untill 2023. [They] had a collapsed lung from Covid so we are very careful about who {they] mixes with who are unwell.”

“Extremely worried as he's unable to fight a cold without being hospitalise and IV antibiotics.”

“Not particularly worried just get on with life as best as possible.”

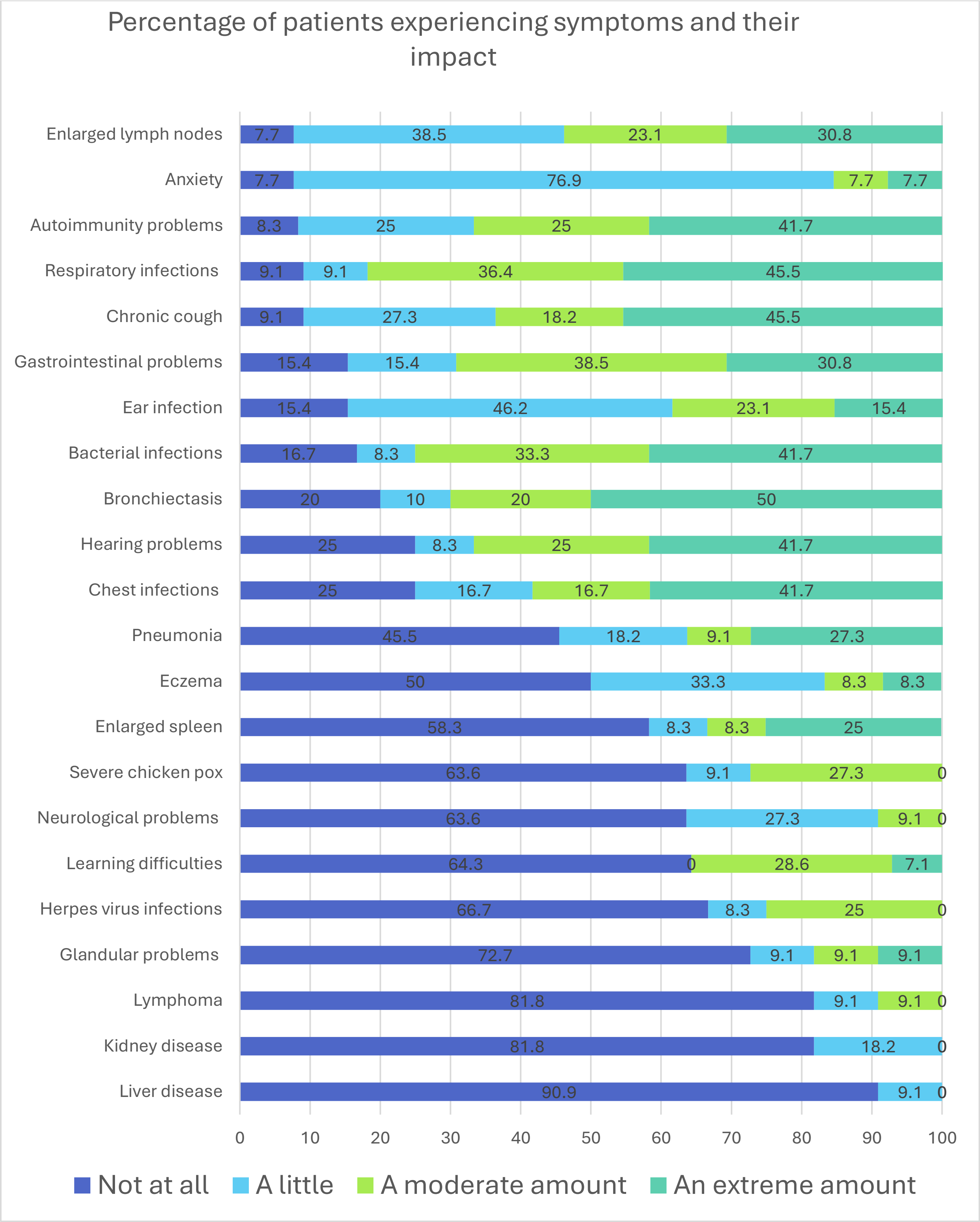
- **Quality of life**

Of 13 respondents only 4 reported satisfaction with quality of life.



- **Symptoms experienced when living with APDS and their impact**

Symptoms which were reported as having an extreme impact were bronchiectasis, respiratory infections, chronic cough, autoimmunity problems, hearing problems, enlarged lymph nodes, gastrointestinal problems and enlarged spleen.



Other symptoms experienced were:

Sinus, kidney pains, bad back, shingles, vertigo spinning head, dizziness, rhinitis, weak bladder(incontinence) due to coughing, vomiting and nausea, holes in ears due to frequent ear infections, enlarged tonsils obstructing airways, causing difficulty to eat and sleep.

- **Impact of living with APDS and on family life**

Of the eight respondents, seven felt APDS highly affected their family and one moderately.

On living with APDS

“Tiredness and chest infections are a major concern as well as the mental anxiety the condition causes.”

“[Patient] has had a long and hard journey to get her diagnosis. It has had a big impact on our family and our relationships with doctors. For 7 years nobody believed anything was wrong with [patient}. On the face of it [the patient] looks like a healthy 8 year old, but [the patient] has struggled with adjusting to life when infections hit. [Patient] loves school and would often get anxiety about returning to school after being off for so long. It also affected me as a mother as I knew something was wrong but was unable to get the help we needed as nobody knew how to help.”

“Not easy, always on the edge always following to the dot the doctors /CNS instructions/ admissions a lot in hospital and missing out on his childhood/not being able to do a lot due to extreme precautions of the condition/not being able to see a lot of the family, etc.”

“Recurrent infections, stunted growth, hearing issues impacting learning in school, ability to do physical sport, coordination issues.”

“getting infections and hospital admissions.” *“Stressful. Requires a lot of patience.”*

“Challenging not having a lot of answers.”

“We as a family with APDS and 4 of us has issues we just got on with life.”

“Short stature incurs teasing and unable to partake in lots of activities. Holes in ears prevent water sports and also hair washing is problematic.”

“It’s a medicalised life with regular blood tests, regular immunoglobulins replacement therapy.”

“Mindful of no soft plays, limit to parks and long walks.”

Impact of APDS on family life:

“Significantly, my mother had to give up work, family holidays had to be cancelled, hobbies for my siblings had to be cancelled, time my parents spent with my siblings was compromised as they were always with me.”

“Unable to work and socialise. Tired and lack of sleep. Difficult to maintain routine.”

“Disproportionately caring for child with APDS over other children, lots of holiday from work spent hospital admissions, days work around physio /. ”

“Restricted activities.” “its stressful.”

“We all have to know about it, the younger sibling has to fit around the treatment, we have to pay extra for travel insurance, we have to be more conscious of infection, we have to fit in hospital appointments and medical supplies ordering.”

“Before diagnosis, we spend 5 years of month after month being an in patient. Every month on antibiotics for 5 years. Couldn’t eat due to in large tonsils causing him to bring his food up after every meal and chocking when sleeping. Couldn’t go for wet weather walks (which we can now) however still can’t walk far distances.”

- **Burden of treatment**

All 14 respondents reported they/the patient were currently taking medication (Table 2). The profile and number of medications taken to manage APDS varied for each respondent. Medication included immunoglobulin therapy (N=12), prophylactic antibiotics (N=9), immunosuppressants (N=6), prophylactic antivirals (N=5), Sirolimus (N=3), Leniolisib (N=6). Two respondents were taking six medications, with two others reporting taking 4-5 medications to manage APDS.

Table 2: Medications taken

Respondent	**Antibiotics**	**IG therapy**	**Immuno-suppressant**	**Antivirals**	**Sirolimus**	Leniolisib
1	🟩	🟦				
2	🟩	🟦	🟨	🟧	🟪	🟥
3	🟩	🟦				🟥 For 1 month only
4	🟩	🟦	🟨	🟧		
5	🟩	🟦	🟨	🟧	🟪	
6	🟩	🟦	🟨			
7	🟩	🟦	🟨	🟧	🟪	🟥
8	🟩			🟧		
9			🟨			Unsure
10	🟩	🟦				
11		🟦				🟥
12		🟦				🟥
13		🟦				
14		🟦				🟥

- ## Impact of disease burden on patients and the NHS

Table 3, below, summarises the number of outpatient, inpatient and days spent in hospital over the last 12 months, as reported by 13 respondents. This varied considerably between respondents.

The overall findings underline the impact on individuals and families in terms of time spent in managing appointments and disruption to their lives by time spent in hospital. The results also indicated a significant healthcare burden to the NHS.

Table 3: Number if outpatient/inpatient and days in hospital

Respondent	Outpatient visits	Inpatient visits	Days in hospital
1	2	0	0
3	16	6	14
4	>20	6	80
5	>200	0	0
6	8	4	30
7	10	0	20
8	0	1	10
9	2	0	0
10	12	42	42
11	12	1	2
12	18	2	4
13	6	0	6
14	14	5	21
Totals	**320+**	**67**	**229**

- ## Help with personal care

Of eleven respondents, three required help with personal care. One of the respondents was a carer for a 14-year-old, and two responders were family members or friends of the patient who was three years old. Personal care included washing (N=3), going to the toilet (N=2), cooking (N=1), mobility (N=1), and administering medication (N=1).

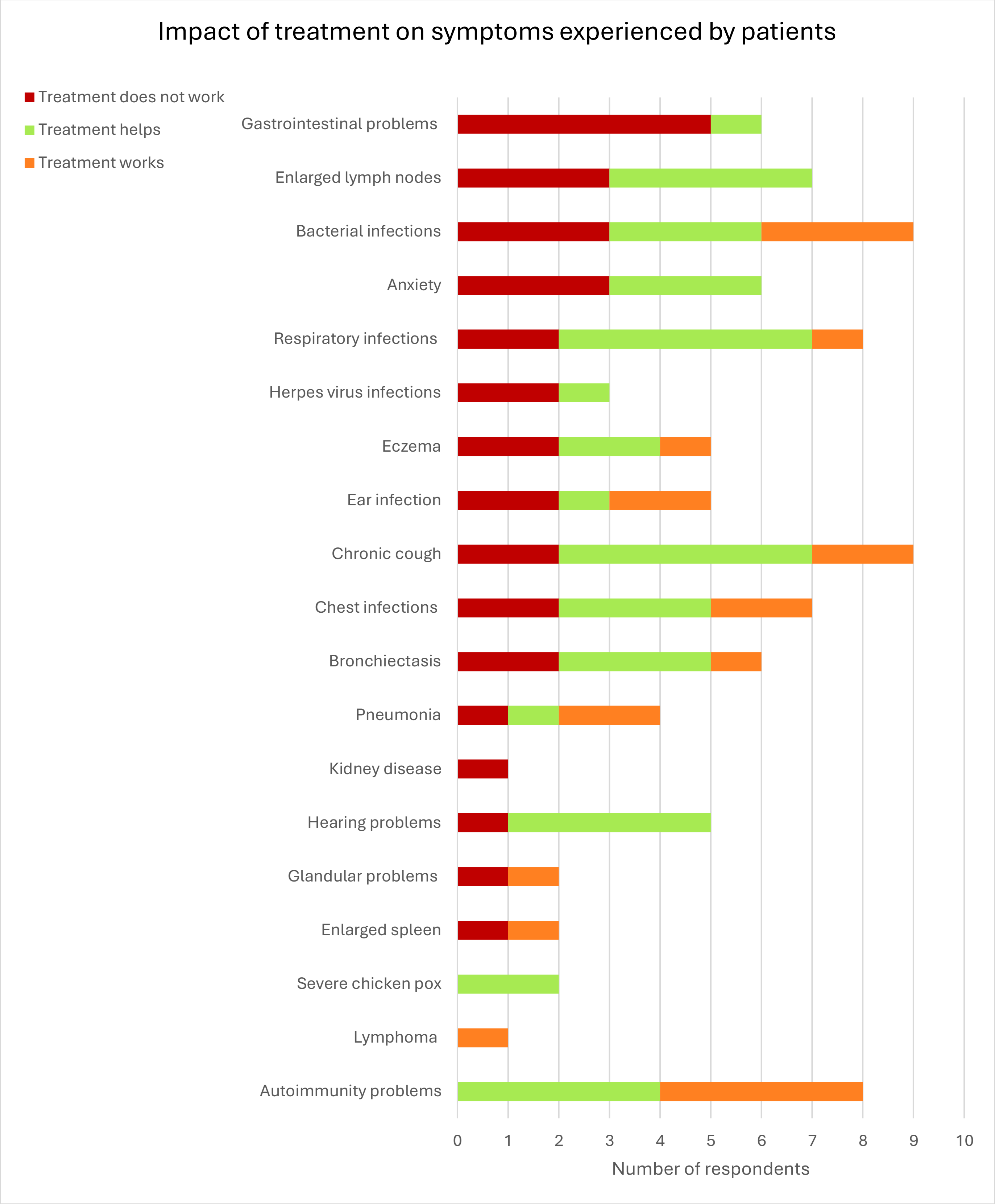
Carers of affected children reported:

“delayed development so not potty trained and can’t wash himself.”

“2-3 physio sessions a day, medicine administered daily, weekly subq infusions, frequent soiling as on antibiotics regularly.”

“Cooking the meals, shower and sometimes mobility assistance.”

- **Symptoms not addressed by current treatments – unmet need**



- **Use of Leniolisib for APDS: side effects, benefits, support for access**

Six of 14 respondents had been treated with Leniolisib, with one respondent saying they were unsure (Table 2).

Three of five respondents had experienced side effects from using Leniolisib. One respondent reported a headache, one respondent reported fatigue and diarrhoea, and one respondent reported mouth ulcers and eye infections.

Benefits of Leniolisib

Of the six respondents who had been treated Leniolisib, five reported benefits of Leniolisib. This included a reduction in antibiotic use (N=2), bring bloods [blood count] up (N=1), increasing energy and appetite (N=2) and reducing coughing (N=1), hospital admissions (N=1) and reduced lymph nodes (N=1).

One respondent did not report any benefits as they had only taken the treatment for one month so were yet to find out.

Benefits noted:

"Reduced coughing, reduced the amount of need of antibiotics."

"it has brought his bloods up."

"Reduced lymph nodes. More appetite and energy."

"Increased energy and appetite."

"[Patient] had been on antibiotics for 5 years with serval Hospital additions where so as starting treatment to date of 8 months [Patient] has only had 3 antibiotics and no Hospital additions."

"I would recommend everyone with Apds try this treatment as I have noticed improvement slightly in my condition which has made me feel a little better."

Support for Leniolisib as a treatment option

Of the eight respondents to this question, all eight would recommend Leniolisib.

"100% would recommend the medication. As a parent you want what is best for your children, just having the chance to try a medication for a condition of this nature gives us just that little bit of hope that [patient] will one day be healthier then what [patient] is today and for that reason I would always recommend it."

Drawbacks

Of the six respondents who had been treated Leniolisib, three reported drawbacks. This included the possible side effects listed (N=1), having mouth and tongue ulcers for the first time (N=1), and Leniolisib not tackling the infection damage that was caused before starting the Leniosilib (N=1).

Patients who might benefit more, or less, from Leniolisib

Of the five respondents to this question, all five reported they thought everyone should have access to the treatment. One respondent identified patients who are unable for other treatments would benefit more from the treatment:

> *"[patient] is unable to have a bone marrow transplant due to [their] ethnicity. I feel like if this medication was used for patients in the UK who are unable to get a transplant they would have more of a chance of living a more fulfilled quality of life."*

Dated 16th August 2024.