IPOPI
United for Immunodeficiency Patients

WHITE PAPER

Improving Respiratory Care for People with PIDs & Associated Conditions

Better respiratory care, every step of life: what needs to change, from the first infection to lifelong care.

A WHITE PAPER BY
IPOPI, the International Patient Organisation for Primary Immunodeficiencies

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Foreword

A message from IPOPI President, Martine Pergent

Respiratory complications remain one of the leading causes of illness and reduced quality of life for people living with primary immunodeficiencies (PIDs). Over the past year, IPOPI has brought together clinicians, researchers, patients, industry and policymakers – through our 2025 Expert Round Table and a dedicated 2026 interview and survey programme – to identify what these challenges actually mean for people living with PIDs, where the greatest gaps remain and what concrete action could close them.

This White Paper is the product of that collective effort. It does not claim to resolve every challenge facing people with PIDs, but it sets out a realistic, evidence-informed set of policy recommendations that European and national decision-makers can act on, bringing patient voices and clinical experience directly to those who shape policy. We are grateful to every clinician, researcher and patient representative who has given their time and expertise to this process, and we look forward to presenting this White Paper at a dedicated event in the European Parliament.

A message from IPOPI Medical Advisory Panel (MAP) Chair, Dr Nizar Mahlaoui

Respiratory infections remain the most common complication faced by people with primary or secondary immunodeficiencies (SIDs), even with appropriate care, and too often the resulting damage to the airways is identified only once it is already established.

As clinicians, we see this gap every day: in the shortage of specialists able to monitor patients properly, in the diagnostic tools needed to detect infection and structural lung damage earlier, in gaps in awareness among primary care providers, and in the collaboration between immunology, ENT and pulmonology that good respiratory care requires. Closing it will take better and more accessible diagnostics, clearer pathways to adequate treatment and monitoring, stronger multidisciplinary working, and sustained investment in the research still needed to understand how this damage develops and how to prevent it.

I am glad to co-chair this initiative and to support IPOPI in turning these priorities into concrete, actionable steps for patients across Europe.

Executive summary

Primary immunodeficiencies (PIDs), also referred to in the clinical literature as inborn errors of immunity (IEI), are a group of more than 550 rare disorders in which the immune system does not work adequately or at all. For individuals living with these conditions, respiratory disease occupies a distinct place: for many, altered immune function combines with structural lung disease, and recurrent infections, chronic inflammation and airway damage can reinforce one another over time.

Chronic complications such as bronchiectasis and interstitial lung disease affect a substantial proportion of people with PIDs and associated conditions, and lung disease remains a leading cause of illness and death in this population – compounded by a changing landscape of respiratory threats, from circulating viruses and antimicrobial resistance to vaccine hesitancy. Crucially, current clinical evidence shows that this cycle of heightened respiratory susceptibility extends to conditions associated with PIDs, within an interconnected and complex patient health landscape.

Primary Immunodeficiencies are frequently diseases of immune *dysregulation*. Autoimmune and inflammatory complications – such as interstitial lung disease or autoimmune pulmonary alveolar proteinosis (aPAP) – significantly aggravate respiratory vulnerability, causing structural tissue damage and impairing local lung defences, which leaves patients highly susceptible to severe, recurrent infections. In addition, an expanding population of patients living with some forms of SIDs, acquired for example via haematological malignancies, chemotherapy, or B-cell-depleting therapies, face a comparable threat to their lungs and could benefit from the same proactive care and preventive models as PID patients.

The policy recommendations laid out as part of this White Paper build on IPOPI's 2025 Expert Round Table and a structured 2026 engagement process with clinicians and experts from around the world.

This process has helped us set out a European policy framework across four themes:

- Prevention and early diagnosis
- Delivering adequate care
- Awareness and patient empowerment
- Research and innovation

Recurring gaps emerge throughout: diagnostic delay caused by limited awareness and uneven access to appropriate diagnostic testing, including in primary and non-specialist care; reimbursement rules that lag clinical practice; the absence of dedicated funding or structures for multidisciplinary care, transition from paediatric to adult care settings and healthy ageing; and a research base constrained by rarity. The recommendations that follow translate these findings into concrete, actionable steps for European and national decision-makers – from extending reimbursement to match clinical practice and embedding routine monitoring and multidisciplinary team (MDT) standards in national guidelines, to dedicated EU support for multinational guidelines, data-sharing and research.

Chapter 1: Prevention and early diagnosis

For many people with immunodeficiencies, respiratory disease carries a heavy and distinctive burden. Altered immune function combines with structural lung disease, and complications such as interstitial lung disease and bronchiectasis are among the most serious drivers of illness and reduced quality of life in this population.

Prevention and early diagnosis can proactively reduce this burden, which is why they are a core pillar of this White Paper.

Early diagnosis and screening

Clinicians and patients describe a long and difficult path to diagnosis. Individuals living with immunodeficiencies and associated conditions often present repeatedly with recurrent or severe infections that are treated individually, without the underlying (primary or secondary) immunodeficiency being recognised as the root cause of their respiratory symptoms, as a normal initial basic immunological screen should not automatically rule this out.

Studies suggest that a substantial share of adults presenting with bronchiectasis have an underlying immunodeficiency, with estimates commonly around 5–10% and up to 30% depending on the immunological tests performed (Aliberti et al. 2022). Some people with interstitial lung disease may also have an underlying immunodeficiency; granulomatous-lymphocytic interstitial lung disease (GLILD), for example, is a complication of common variable immunodeficiency (CVID, the most common PID). It is vital to raise awareness of warning signs among non-immunology clinicians, while addressing delayed referrals, limited testing access, and the lack of standardised screening pathways.

Furthermore, health systems should address the need for comprehensive respiratory health assessment by extending the diagnostic lens beyond the lower airway to include the whole respiratory tract, from the nose and sinuses to the alveoli, given the frequent overlap with ENT disease. Rapid diagnostic differentiation should also be better implemented to distinguish viral from bacterial respiratory infections earlier – for example through rapid diagnostic testing in emergency settings.

Lastly, genetic testing, interpreted alongside clinical findings and the immunological work-up already used in routine diagnosis, can establish a molecular diagnosis and, in selected disorders, inform treatment, respiratory surveillance and family counselling, although its ability to predict the timing and severity of lung disease varies between conditions. Genetic assessment should be considered in particular for unusually severe or opportunistic infections, unexplained early-onset bronchiectasis, or inflammatory lung disease accompanied by autoimmune cytopenias, lymphoproliferation, enteropathy or syndromic features; adult onset or an unremarkable family history should not rule it out. Results require expert interpretation: a finding of a variant of uncertain significance based on next-generation genetic sequencing methods is not a confirmed diagnosis, a negative result should not end evaluation where clinical suspicion remains high, and access to clinically indicated care should not depend on obtaining a molecular diagnosis. However, equitable access to genetic testing in particular – especially outside specialist centres – remains a persistent barrier to timely diagnosis across the European Union.

Policy recommendations

- **Medical education and training**: Embed the respiratory presentation of PIDs and associated conditions into professional education and continuing training for respiratory (including ENT specialists), emergency and primary-care clinicians. **(Medical societies / educators)**

- **Harmonised pathways & multidisciplinary networks**: Develop clear, harmonised referral and screening pathways, supported by national guidelines, patient registries and multidisciplinary care networks. **(Member States)**
- **Newborn screening**: Support equitable access to newborn screening for severe combined immunodeficiency (SCID), linked to rapid confirmatory assessment and treatment, recognising that it identifies severe T-cell lymphopenia rather than all PIDs. **(Member States)**
- **Patient-centred reimbursement policies**: Ensure reimbursement supports diagnostic work-up, including immunological screening, both where a PID or SID is suspected and as part of routine investigation – so that an abnormal result triggers automatic or facilitated referral, rather than depending on individual clinician awareness. **(Member States)**
- **Point-of-care testing**: Implement rapid point-of-care diagnostic testing to distinguish viral and bacterial respiratory infections, including in emergency departments. **(Member States / healthcare systems)**
- **ERN-approved care pathways**: Develop European Reference Network (ERN)-approved care paths for managing viral respiratory tract infections and associated lung disease in people with PIDs, to make consistent care easier to implement. **(ERNs)**
- **Access to advanced diagnostics & genetic testing:**
    - Improve equitable access to genetic and immunological testing across Member States, including appropriate test selection, expert interpretation, genetic counselling and follow-up, building on the expertise of ERNs. **(Member States)**
- **Targeted research funding:** Support EU-funded research linking genetic and immunological profiles to respiratory phenotype in PIDs, including registries that connect molecular findings with standardised respiratory and immunological phenotypes, treatments and long-term outcomes. **(EU institutions)**

Monitoring and surveillance

Regular monitoring and surveillance are central to preventing respiratory complications from progressing. For example, an annual lung-function test for patients with common variable immunodeficiency (CVID) is already recommended in many national guidelines, to catch deterioration early and reduce irreversible lung damage.

Beyond individual monitoring, population-level data on respiratory-infection trends within the PID population is also a priority, to give this need the visibility it currently lacks.

To ensure comprehensive protection, monitoring frameworks should extend beyond lung function alone to include the wider respiratory tract – nose, sinuses and lungs – through regular ENT and pulmonology review, and clearer warning signs or predictive factors are needed to flag deterioration before damage becomes irreversible. Imaging should be individually justified and radiation exposure kept to a minimum, with non-ionising alternatives such as lung MRI considered where diagnostically suitable; this matters particularly for disorders associated with increased radiosensitivity, such as ataxia-telangiectasia. Emerging tools, including AI-assisted analysis of imaging and wearable-based biomarkers, offer innovative non-invasive routes towards simpler monitoring that patients could eventually use at home.

Policy recommendations

- **Standard of care integration**: Embed regular respiratory monitoring (lung-function testing and individually justified imaging) as a standard of care across national clinical guidelines for PIDs and associated conditions. **(Member States)**
- **Epidemiological and viral surveillance**: Invest in dedicated epidemiological and viral surveillance covering vulnerable populations, including people living with PIDs. **(EU institutions)**
- **Multi-specialty assessment**: Ensure individuals diagnosed with PIDs and associated conditions are reviewed by an ENT specialist and a pulmonologist to establish whether they need treatment or regular specialised monitoring tailored to their PID or associated condition. **(Member States / healthcare systems)**
- **Digital health innovation**: Support the development and validation of AI-assisted diagnostic and monitoring tools, including wearable biomarkers, that can flag early functional change before structural lung damage develops, and that give patients data on their own respiratory health to discuss with their treating physician through home-based monitoring. **(EU institutions / research funders)**

Vaccination strategies

Vaccination is a central pillar in preventing long-term and serious respiratory complications in people with PIDs, yet opportunities are still missed. High-dose influenza vaccines, for example, are generally recommended only for older people, even though people with PIDs would be expected to benefit from their higher immunogenicity, which a recent meta-analysis has shown in immunocompromised patients (Rivera-Izquierdo et al., 2025). People with PIDs are also frequently excluded from vaccine trials, and hesitancy plays a role too: in a 2022 US survey of people with cancer, autoimmune disease or other serious comorbidities (a broader immunocompromised population, not PID-specific), 18.6% expressed hesitancy about COVID-19 vaccination and 10.3% said they would not receive it, even though healthcare professionals remain the most trusted source of information (Tsai et al., 2022).

According to a global survey conducted jointly by IPOPI, the European Society for Immunodeficiencies (ESID), and the International Nursing Group for Immunodeficiencies (INGID) across 40 countries, 41.7% of PID patients reported experiencing vaccine hesitancy (Pergent et al., 2023). The primary drivers of this hesitancy stemmed from clinical uncertainty regarding post-vaccination protection related to their underlying PID (82.1%) and concerns regarding potential long-term side effects or disease flares (58.8%), rather than scepticism of immunisation itself.

This underscores an urgent clinical and policy imperative: as healthcare professionals remain the most trusted source of information, clinicians must be supported and equipped with unified guidance to confidently counsel immunodeficient individuals and their close contacts.

Policy recommendations

- **Scale best practices on access**: Support EU-level sharing of national best practices on vaccination age thresholds for people with PIDs, building on existing best-practice examples. **(EU institutions / Member States)**
- **Targeted vaccine efficacy research**: Fund research into vaccine efficacy and uptake in the PID population and invest in patient-organisation-co-designed vaccination communication. **(EU institutions / Patient organisations)**

- **Health literacy & patient support**: Develop targeted health literacy initiatives and co-designed educational resources to empower patients and families in managing respiratory risk and understanding protection measures. **(Patient organisations / Member States)**
- **Clinical immunisation guidance**: Ensure PID-specific vaccination and immunisation guidelines – covering both patients and their household contacts – are consistently integrated and followed in routine clinical practice. **(Healthcare professionals / medical societies)**

Chapter 2: Delivering adequate care

Delivering adequate respiratory care for individuals living with PIDs and associated conditions, including SIDs, largely depends on prevention, access to specialist expertise and effective treatment, strong multidisciplinary collaboration, and life-course structures that support patients through critical transition stages – from paediatric to adult services and into healthy ageing. In many cases, the clinical knowledge and best practice already exist, built up by individual clinicians and specialist centres. What remains missing is the process to turn expert consensus into consistent standards of care, backed by dedicated funding and administrative support needed to implement and sustain them across the EU.

Prevention of long-term respiratory complications

Bronchiectasis and associated lung diseases are characterised by a self-reinforcing cycle in which mucus obstruction, recurrent infection, chronic inflammation and airway damage repeatedly reinforce one another.

National reimbursement rules frequently lag behind clinical practice. Bronchiectasis is traditionally divided into cystic fibrosis (CF) and non-CF bronchiectasis, and many inhaled therapies, such as hypertonic saline and inhaled antibiotics, are approved or reimbursed for CF only. In Germany, for example, 6% hypertonic saline is officially reimbursed only for people with CF, and inhaled antibiotics such as colistin or tobramycin are prescribed off-label in non-CF bronchiectasis, which makes prescribing considerably more time-consuming. The evidence for some of these therapies in non-CF bronchiectasis is still developing, including a recent negative trial of hypertonic saline (Bradley et al., 2025). This underlines the need for reimbursement rules that allow clinicians to individualise treatment where it is clinically indicated, rather than excluding patients on the basis of diagnosis alone.

Policy recommendations

- **Extend and harmonise reimbursement** of established, evidence-based treatments and preventive measures – such as vaccines and, where clinically indicated, inhaled therapies – to clinically similar patient groups, so that off-label prescribing reflecting good clinical practice is not left uncovered by narrow diagnosis-specific reimbursement rules. **(Member States)**
- **Optimised treatment management**: Support responsible antibiotic use and appropriate adjustment of immunoglobulin and prophylactic therapy to prevent infection and preserve treatment effectiveness. **(Healthcare professionals)**
- **Pulmonary rehabilitation access**: Reinforce the value of, and improve access to, adapted physical activity and pulmonary rehabilitation as part of routine preventive care. **(Member States / healthcare systems)**

Access to treatment

Beyond timely diagnosis and monitoring, equitable access to effective treatment is central to adequate respiratory care. While many life-saving interventions are already in clinical use, actual access and reimbursement frameworks remain uneven and fragmented across Member States.

Immunoglobulin replacement therapy (IgRT) remains the backbone of preventive treatment for most antibody deficiencies, including both PIDs and some SIDs. However, its clinical benefit depends on individualised, tailored dosing. Some patients require doses above standard regimens, and subcutaneous administration (SCIg) may improve infection control and quality of life for some. Reimbursement and prescribing systems do not always accommodate these adjustments.

Prophylactic antibiotics, including long-term azithromycin (typically given three times weekly) or trimethoprim/sulfamethoxazole where indicated, pulmonary rehabilitation, and asthma/COPD therapies delivered according to GINA and GOLD guidelines can help reduce exacerbations, but are not consistently offered or reimbursed. For inflammatory complications such as GLILD, treatment may progress from corticosteroids to steroid-sparing agents, rituximab or, in genetically defined disorders such as CTLA4 haploinsufficiency or LRBA deficiency, targeted biologics such as abatacept, where the underlying disease mechanism has been established. A clinical practice guideline for the diagnosis of GLILD in CVID, developed by the ERS e-GLILDnet Clinical Research Collaboration with ESID (the European Society for Immunodeficiencies), was published in 2026 (Bintalib et al., 2026), and a treatment guideline is nearing completion. Similarly, for aPAP, in which neutralising autoantibodies against GM-CSF impair the macrophages that clear surfactant and fight infection, access to targeted, non-invasive therapies or specific protocols is crucial to prevent terminal respiratory failure. Hereditary and secondary forms of PAP have different underlying mechanisms, which changes their diagnostic work-up, treatment and implications for relatives.

Delivering optimal care requires patient-centred access to treatments and preventive services, responsible antimicrobial stewardship, and tailored immunoglobulin and anti-infectious prophylactic regimens. Extending harmonised clinical guidance beyond primary antibody deficiencies is essential to ensure treatment pathways remain closely aligned with each patient's specific immunological profile and respiratory needs. Furthermore, protecting immunodeficient individuals – who frequently exhibit attenuated vaccine responses – demands a shift towards proactive, precision immunisation pathways integrated into routine care.

Policy recommendations

- **Patient-centred reimbursement for IgRT**: Ensure reimbursement and care pathways support individualised immunoglobulin replacement therapy, including adjustments to dose and route of administration. **(Member States)**
- **Harmonised clinical guidance**: Develop harmonised, evidence-based guidance for treating PID-related respiratory disease, including complex inflammatory complications such as GLILD. **(ERNs / medical societies)**
- **Targeted protocols for autoimmune complications**: Ensure access to targeted, non-invasive therapies and specific protocols for patients with autoimmune complications, such as aPAP, to prevent terminal respiratory failure. **(Member States / healthcare systems)**

Access to specialist care, appropriate diagnostics and multidisciplinary teams

Respiratory complications across the immunodeficiency spectrum are common and can be highly complex, but the number of clinicians with relevant expertise is correspondingly small, creating a genuine risk of unequal access across Member States. Ensuring equitable access to specialist respiratory-immunology expertise for countries with limited specialist capacity or for patients living in remote regions is a priority.

Clinicians and patient representatives have identified a shortage of pulmonologists with dedicated experience in PIDs and pointed to microbial diagnostics that often remain limited to a bug-by-bug approach or narrow multiplex panels covering only a handful of pathogens, rather than the comprehensive tests needed to identify pathogens that would not typically cause infection in a healthy population, and are therefore not captured by standard panels. This matters in a population where recurrent respiratory infections are common and can contribute to irreversible lung damage, including bronchiectasis, which once established can drive a progressive cycle of infection, hospitalisation and

reduced quality of life. Timely access to appropriate infectious-disease diagnostics should therefore be considered part of specialist respiratory care, helping clinicians identify the cause of infection and guide management. Better data are also needed on the full range of pathogens that cause respiratory infections in people with PIDs. Stronger, structured collaboration between immunodeficiency specialists and ENT or pulmonology colleagues – rather than ad hoc referral – was identified as a precondition for better care.

Joint respiratory-immunology clinics deliver more coordinated, holistic care; while multidisciplinary working is often already embedded in paediatric services, adult clinics are less likely to have equivalent structures, and demonstrating the clinical and economic value of these models is important for wider adoption.

Multidisciplinary team (MDT) panels currently lack a consistent standard for composition or operation; in many countries, clinicians take on this coordinating role themselves, without a clear framework, because they recognise the benefit it brings to patients. The limited pool of specialists – who already sit on multiple panels each week – makes even ERN-level case discussions hard to schedule. ERN RITA's Clinical Patient Management System (CPMS) was meant to ease this, but uptake remains limited because completing submissions is time-consuming.

Holistic, multidisciplinary care also depends on the wider team, including specialist nurses and allied health professionals who support patients between clinic visits. Physiotherapists, for example, play a central role in teaching the airway clearance techniques that help patients clear sputum from their lungs.

The UK's national MDT model was identified as one that would allow clinicians managing complex cases to draw on specialist input from across the country. While a similar attempt at European level stalled due to unresolved data-privacy challenges, interest in an EU-level model remains – particularly for lower-capacity countries.

Policy recommendations

- **Equitable specialist access mechanisms**: Support and fund robust EU-level mechanisms – including through European Reference Networks – to guarantee that individuals living in remote regions or lower-capacity Member States have equitable, facilitated access to top-tier cross-border respiratory-immunology expertise. **(EU institutions / ERNs)**
- **Institutionalised integrated care pathways**: Mandate and support national care pathways that integrate dedicated specialists with expertise in PIDs and associated conditions – spanning pulmonology, ENT and both paediatric and adult clinical immunology – into the routine, lifetime care of immunodeficient patients presenting with complex respiratory manifestations. **(Member States)**
- **Access to appropriate microbial diagnostics**: Ensure that people with PIDs and associated conditions have timely and equitable access to appropriate microbial diagnostic testing as part of specialist respiratory care, including more comprehensive testing where clinically indicated and where pathogen-by-pathogen approaches or narrow panels may be insufficient. **(Member States)**
- **Minimum standards & administrative support for MDTs**: Develop minimum standards for MDT composition and operation, recognising nursing and allied health professionals, such as physiotherapists, as core members, with access to clinical genetics and genetic counselling where needed, and fund dedicated administrative support for CPMS to reduce the burden on clinicians. **(ERNs)**

- **Resolve European cross-border MDT barriers**: Revisit the case for a European-level MDT model for respiratory complications in rare diseases, resolving the data-privacy barriers that previously stalled this work, prioritising benefit to lower-capacity Member States. **(EU institutions / ERNs)**

Transition of care & healthy ageing with PIDs

Medical progress has ensured that an ever-growing number of individuals living with PIDs and associated conditions in the EU are reaching older age. For example, patients with X-linked agammaglobulinaemia are now routinely living well into their fifties and beyond. However, experts in the field have started to highlight the importance of specific preventive and monitoring needs of this population. As individuals with compromised immunity age, they frequently accumulate additional age-related diagnoses and clinical comorbidities, including severe respiratory complications, making integrated, holistic, and multidisciplinary care more critical than ever.

A well-managed transition from paediatric to adult care is important, but an absence of any real structure or funding to support it results in clinicians often using their own time to coordinate a patient's transfer, with no reimbursement to the clinic.

This also raises the question of continued access to the tests, activities and medical devices that ageing patients need – as they also face a major hurdle in maintaining continuous, lifelong access to specialised diagnostics, physical therapies, and multidisciplinary care – on the same basis as younger patients.

> *"Everyone agrees that transition is important, but there is no real structure to support it. At present, I effectively use my own time to visit the paediatrician, and my clinic receives no reimbursement for doing so."*
> *– Dr Leif Hanitsch*

Policy recommendations

- **Prioritise healthy ageing in immunodeficiencies:** Recognise the ageing PID/SID population as a distinct health policy priority, supporting research into its specific needs and consistent embedding of age-appropriate monitoring – and continued access to the tests, activities and medical devices this requires – in national guidelines. **(Member States)**
- **Support transition care mechanisms:** Introduce dedicated reimbursement codes or funding mechanisms, at national level, recognising the clinical time required to coordinate joint paediatric-to-adult transition consultations and joint specialty clinics, such as immunology-pulmonology clinics. **(Member States)**
- **Ensure lifelong continuity of care and access:** Guarantee that ageing individuals maintain uninterrupted, seamless access to essential diagnostic tests, adapted physical activities and respiratory care across their entire lifespan. **(Member States)**

Chapter 3: Building awareness and empowering patients

Improving respiratory care for people with PIDs depends as much on awareness and empowerment as on clinical services: healthcare professionals outside specialist immunology need the awareness to recognise a possible underlying PID, and patients need to know what good care looks like in order to ask for it.

While patient empowerment is a core function of patient organisations, true empowerment in the context of complex respiratory care requires moving beyond informational support towards active inclusion in clinical and policy decision-making. Patients living with PIDs and associated respiratory conditions must be recognised as active partners in their care pathways, equipped with clear information regarding their rights, care standards, and available treatment options to enable meaningful co-decision-making with healthcare providers.

Patient empowerment

Patients should know what good care looks like and be able to ask for it. Living with a PID requires constant vigilance – hygiene measures, mask use, social precautions – placing a burden on patients and families that extends beyond physical health to social life and mental wellbeing.

This vigilance is especially demanding around respiratory infections, given how frequently and severely they affect this population. Developing guidance that reinforces patient rights and supports access to information and care would be a valuable step towards patient empowerment.

Where a genetic diagnosis is involved, empowerment extends to the wider family. Pre- and post-test counselling, discussion of inheritance and variable penetrance, appropriate testing of relatives and non-directive reproductive counselling all help families make informed decisions, and transition to adult care offers an opportunity to revisit these issues with the young person directly.

> *"People should know what good care looks like and be empowered to ask for it."*
> *– Prof John Hurst, on patient empowerment*

Policy recommendations

- Develop national patient charters for respiratory care in PIDs, setting out what good care looks like, including when to seek care, what monitoring and specialist follow-up to expect, and when diagnostic testing may be needed, and test whether a shared core resource, condition-specific versions, or both, best serve patients. **(Patient organisations)**
- Promote and resource joint clinician-patient advocacy as a model for engaging policymakers. **(Member States)**
- **Public education on hygiene**: Raise awareness and promote education regarding proper hygiene measures among the wider population to complement patient-level preventive behaviours. **(Member States / Patient organisations)**

Healthcare professional education

Clinical experts have independently highlighted the need to raise awareness of PIDs beyond immunology: respiratory physicians and GPs may not recognise recurrent infections as a possible sign of underlying immunodeficiency, unintentionally delaying diagnosis. Stronger education on warning signs, particularly in adult patients, can accelerate diagnosis and equip clinicians with the confidence and time to support immunocompromised patients with respiratory complications.

Clinical and patient experts are calling for increased regional and national educational events to reach healthcare professionals who do not routinely care for people with PIDs, and for awareness-building to start earlier, through dedicated content in medical and nursing school curricula as well as post-graduate training, webinars and interactive formats such as quizzes. Joint scientific meetings bringing together immunodeficiency, ENT and pulmonology specialists alongside patients themselves were also proposed as a way to build shared knowledge and practice.

Policy recommendations

- **Medical curriculum integration:** Integrate PID awareness into professional and continuing medical education for GPs and respiratory physicians and equip them to discuss vaccination confidently. **(Medical societies / educators)**
- **Targeted training and CME**: Organise regional and national educational events for clinicians outside specialist PID care and integrate PID-related respiratory care into medical and nursing school curricula and post-graduate training. **(Medical societies / educators)**
- **Cross-specialty scientific initiatives:** Organise regional and national joint scientific forums that bring together immunology, pulmonology, and ENT specialists to establish unified clinical protocols for managing complex rare lung disease. **(Medical societies / educators)**
- **Immunology input into respiratory guidelines**: Involve immunologists in the development of pulmonology guidelines so that basic immunological work-up, such as serum IgG, IgA, IgM and IgE, is included, as has already happened for bronchiectasis guidelines. **(Medical societies)**

Public awareness & health literacy

Strengthening health literacy can reduce the burden of care and complement clinical care for respiratory complications of PIDs. By co-designing proactive communication strategies and awareness campaigns alongside trusted, empathetic communicators, such as patient organisations and patient voices, public health messaging is likelier to resonate with society.

Public education on everyday preventive behaviours around respiratory illness – such as wearing a mask when unwell, hand hygiene, social distancing and remote working during periods of illness – can reduce transmission risk in shared settings such as public transport, schools and workplaces, while also helping to reduce the stigma sometimes associated with these behaviours.

Policy recommendations

- **Fund health-literacy initiatives:** Support public awareness campaigns and the development of patient-friendly educational resources, targeting younger and older people in school and work settings. **(EU institutions / Member States)**
- **Support public awareness campaigns:** Educate the wider public on preventive behaviours around respiratory illness, such as vaccination against respiratory infections where recommended (including influenza, COVID-19, RSV and pneumococcal disease), mask-wearing when unwell and remote working during periods of respiratory illness when possible, to reduce stigma and the transmission risk of respiratory infections to vulnerable groups, and convey the broader benefits of vaccination for individuals and those around them. **(EU institutions / Member States)**

Chapter 4: Research and innovation for better outcomes

Primary immunodeficiencies and associated conditions encompass a diverse group of conditions that, even collectively, are uncommon. They are, however, accompanied by a rapidly growing group of more common SIDs. Together with their associated rare pulmonary complications, they encompass a vast and diverse spectrum of immune-mediated conditions; yet the clinical evidence base for their respiratory complications remains limited. Strengthening research, encouraging the safe and appropriate inclusion of people with PIDs in clinical trials, resolving data-sharing barriers, and supporting emerging diagnostics and therapies are central to improving outcomes.

Research priorities & data-sharing

Across PID-related respiratory complications more broadly – and particularly for conditions such as GLILD, which affects an estimated one in five people with common variable immunodeficiency (CVID) – building a robust evidence base requires European collaboration. The James Lind Alliance Priority Setting Partnership methodology – a structured process giving equal weight to the views of patients and clinicians in setting research priorities – was used a few years ago by the ERS e-GLILDnet collaboration to identify shared research priorities for GLILD, which are now being worked through. Pan-European collaboration should be encouraged, particularly for older patients, where evidence remains especially limited.

Cross-border collaboration depends on safe, efficient data sharing. Resolving data-privacy challenges at EU level would help overcome a barrier that also affects the pooling of data through international cohorts needed to generate evidence for a small patient population.

Clinicians highlighted a need for better understanding of non-infectious respiratory complications, alongside promising new diagnostic avenues for infections – such as volatolomics (the analysis of volatile organic compounds in breath to detect disease) and integrated host-microbe metagenomics (genetic sequencing of patient and microbial samples together to characterise infection) – that could enable faster, more accurate diagnosis of respiratory tract infections. They also stated that epidemiological research into the impact of climate change and air pollution on respiratory health in this population would be beneficial.

Policy recommendations

- **Support patient-centred research**: Fund patient-involved research priority-setting exercises and pan-European research collaboration to close evidence gaps. **(EU institutions)**
- **Resolve cross-border data-sharing barriers**: Provide EU-level guidance and practical support to resolve cross-border data-sharing barriers affecting European case-discussion platforms and research cohorts. **(EU institutions)**
- **Fund advanced diagnostic research:** Promote better understanding of the mechanisms of respiratory complications in PIDs and support the validation and adoption of emerging diagnostic approaches such as metagenomics and volatolomics in specialist centres. **(EU institutions)**

Clinical trial participation

People with PIDs are frequently excluded from clinical trials, including vaccine trials, on the basis that they are considered a vulnerable population. While this reflects legitimate safeguarding considerations, it also contributes to the evidence gaps that in turn slow or complicate access to treatment and reimbursement.

Policy recommendations

- **Promote inclusive clinical trials:** Encourage regulatory agencies and clinical-trial ethics committees to support the safe, appropriate and structured inclusion of people with immunodeficiencies in relevant clinical trials. **(Regulatory agencies / ethics committees)**
- **Streamline cross-border investigator-led trials:** Simplify EU-level approval processes for investigator-driven, cross-country trials, building on the Commission's ongoing work on patients' rights in cross-border healthcare. **(EU institutions)**

Emerging therapies and diagnostics

Personalised and precision medicine, tailored to each patient's immune profile and pulmonary presentation, represents the future of respiratory care in immunodeficiencies. This includes the clinical roll-out of next-generation targeted therapies such as JAK and PI3K-delta inhibitors, whose use depends on an established disease mechanism rather than the presence of a genetic variant alone, alongside diagnostic advances such as lung MRI. Funding should be allocated to ensure equitable access to advanced treatment options and diagnostics.

Ensuring that these advanced treatment options and diagnostics do not remain confined to a few wealthy regions requires proactive, coordinated European support to guarantee equitable, cross-border access for all immunodeficient patients, particularly those battling complex respiratory manifestations (e.g. GLILD, aPAP).

Policy recommendations

- **Promote advanced respiratory innovation and access**: Support research into, and equitable access (including cross-border) to, emerging respiratory diagnostics and advanced therapies – including magnetic resonance imaging (MRI) – for people with PIDs. **(EU institutions)**
- **Adapt HTA processes for vulnerable populations**: Ensure Health Technology Assessment (HTA) frameworks specifically account for rare immunodeficiencies and vulnerable populations during the evaluation and access decisions for innovative respiratory care technologies. **(EU institutions / Member States)**

Conclusions

Respiratory disease occupies a distinct and often devastating place in the care of individuals living with PIDs and associated conditions, including SIDs. For many, altered immune function combines with progressive structural lung disease, remaining a leading cause of severe illness and reduced quality of life.

The expert contributions and clinical evidence gathered throughout this White Paper point to a consistent, systemic set of gaps across EU healthcare systems:

- Diagnostic delay driven by limited awareness outside specialist immunology and uneven access to appropriate diagnostic testing;
- Rigid reimbursement frameworks that lag behind clinical practice;
- Profound absence of dedicated funding or standards for lifelong multidisciplinary care, transition and healthy ageing;
- Highly fragmented research base constrained by rarity.

None of these gaps require reinventing respiratory or immunology care from first principles – in most cases the clinical practice, evidence or model of care already exists. What is missing is the policy structure and sustainable funding required to turn good practice into common practice and make these standards of care consistent and equitably accessible for all patients living in the EU.

By implementing the expert recommendations outlined in this White Paper, EU institutions and Member States have an opportunity to bridge the gap between primary and secondary immunodeficiencies, eliminate the structural threats of complex respiratory comorbidities for this patient population, thereby guaranteeing that immunodeficient EU citizens can maintain their lifelong right to breathe clearly and live securely.

Political supporters

- **Adam Jarubas** (Poland, European People's Party, EPP)
- **Billy Kelleher** (Ireland, Renew Europe)
- **András Kulja** (Hungary, European People's Party, EPP)
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Authors & Acknowledgements

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- Leire Solis, IPOPI, Spain

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Annex: Policy recommendations at a glance

This matrix summarises the major actions set out in Chapters 1 to 4, by the audience best placed to deliver them. Full recommendations and supporting evidence are set out in each chapter.

Audience	1. Prevention & early diagnosis	2. Delivering adequate care	3. Awareness & empowerment	4. Research & innovation
EU institutions	- Fund research and surveillance covering immunocompromised populations - Coordinate sharing of best practice across PIDs, respiratory conditions and vaccination - Develop care pathways for viral respiratory infections ***(ERNs)***	- Fund ERN-based cross-border access to specialist expertise and MDTs - Harmonise clinical guidance and set minimum MDT standards, with administrative support for CPMS ***(ERNs)***	- Fund health-literacy and public awareness campaigns	- Resolve cross-border data-sharing barriers and simplify cross-border trials - Fund advanced diagnostics and therapies; adapt HTA to vulnerable populations
Member States	- Reimburse diagnostic work-up; - Embed screening, referral, monitoring and vaccination in national guidelines - Ensure equitable access to genetic and point-of-care testing and to newborn screening for SCID	- Align reimbursement with clinical practice and ensure access to appropriate microbial diagnostics - Fund integrated care pathways, transition and healthy ageing	- Resource joint clinician–patient advocacy and public education on prevention	- Adapt HTA to account for vulnerable populations - Enable safe, structured inclusion of people with immunodeficiencies in clinical trials ***(regulators / ethics committees)***

Audience	1. Prevention & early diagnosis	2. Delivering adequate care	3. Awareness & empowerment	4. Research & innovation
Healthcare professionals & medical societies	- Embed PID warning signs in training - Apply PID-specific immunisation guidance	- Ensure responsible antibiotic use and individualised Ig and anti-infectious prophylaxis	- Integrate PID content into curricula, CME and cross-specialty forums, and involve immunologists in pulmonology guidelines	–
Patient organisations	- Co-design vaccination communication and health-literacy resources	–	- Develop national patient charters and co-lead public education	–

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Their insights have shaped every recommendation in these pages.

STAND WITH PEOPLE LIVING WITH PIDs

Read it. Share it. Act on it.

The recommendations in this White Paper offer EU institutions, Member States, European Reference Networks, healthcare professionals and patient organisations a shared agenda for protecting the lung health of people with PIDs, at every step of their lives.

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