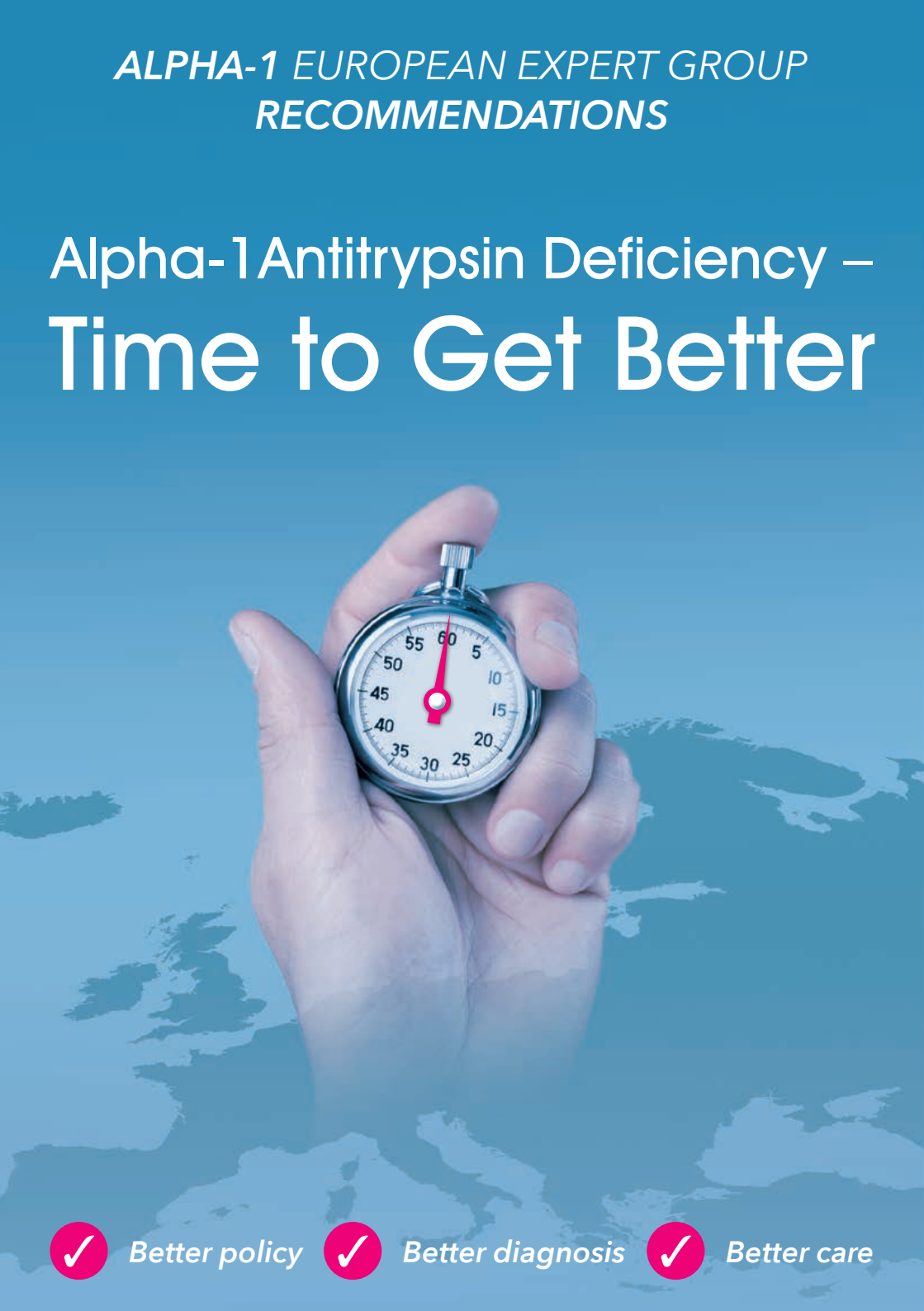
ALPHA-1 *EUROPEAN EXPERT GROUP*
RECOMMENDATIONS

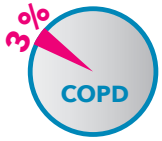
Alpha-1 Antitrypsin Deficiency – Time to Get Better



✓ *Better policy* ✓ *Better diagnosis* ✓ *Better care*

Alpha-1 European Expert Group Recommendations

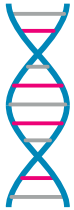
ALPHA-1 – A RARE DISEASE, A REAL NEED TO ACT



3% of COPD patients are *Alpha-1* patients

COPD will be a **leading cause of death** worldwide by 2020

2020



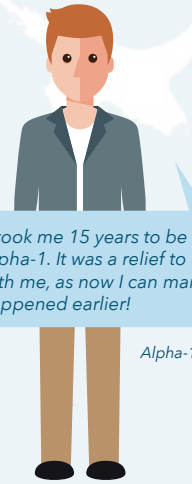
Alpha-1 is the most widely recognised **rare genetic cause** of COPD

Alpha-1 is the only form of COPD with **specific treatment** and with the **highest level of data** for that treatment

Alpha-1 causes cirrhosis **not attributable** to alcohol consumption and accelerates progression of other liver diseases

Alpha-1 antitrypsin deficiency was discovered more than 50 years ago, but most of its roles and properties are not known yet. We need more support for research.

Dr. Ilaria Ferrarotti, University of Pavia, Italy



It took me 15 years to be diagnosed with Alpha-1. It was a relief to know what is wrong with me, as now I can manage it. I wish it happened earlier!

Alpha-1 patient from Denmark

Despite rare diseases is being a public health priority, we need to ensure that all Alpha-1 patients have access to early diagnosis and care, and can benefit from opportunities stemming from research and innovation.

Marlene Mizzi,
Member of the European Parliament, Malta

More than 66m people have COPD in the European Region, of which at least 2m cases are caused by AAT deficiency. All COPD patients must be tested for Alpha-1, just this simple step would significantly improve diagnosis.

Prof. Joanna Chorostowska-Wynimko, National Institute of Tuberculosis and Lung Disease, Poland

A test for Alpha-1 antitrypsin deficiency is essential in all cases of liver disease of unknown origin in newborn, children and adults.

Prof. Christian Trautwein, University Hospital Aachen, Germany

Particularly if there is a family history of Alpha-1!

PD Pavel Strnad, University Hospital Aachen, Germany

Lung-related uncontrolled *Alpha-1* complications

Liver-related uncontrolled *Alpha-1* complications

INTRODUCTION

Alpha-1* antitrypsin deficiency** (henceforth referred to as ***Alpha-1) is an **inherited condition** that **increases the risk of lung, liver and other diseases**. *Alpha-1* is present **worldwide**, but the prevalence of its severe form varies across Europe, affecting about **1 in 1,500 to 3,500 individuals**,[1] whereas mild forms are much more common.[2]

The principal difficulty in managing *Alpha-1* is **achieving early diagnosis**, something which most patients will not receive until severe symptoms have begun, despite the cheap and effective means of diagnosis that exist. Many times, the symptoms of **chronic obstructive pulmonary disease (COPD)** and **liver disease** do not lead to appropriate referrals to *Alpha-1* centres of excellence. This challenge requires a **consolidated approach of educated healthcare professionals and patients**. In addition, *Alpha-1* patients require policy that facilitates sharing of expertise, encourages preventive measures such as screening and allows a tailored approach to evaluating medicines for *Alpha-1* patients. Policy at the European level also must recognise that diseases like *Alpha-1* benefit from a **great deal of information sharing** and at EU and national level, and consequently *Alpha-1* should be considered in **many policy areas** such as in **environmental, economic and educational policy**.

The burden of *Alpha-1* is not about the number of affected patients but about each individual's life which can be **significantly impacted** by the **delayed diagnosis** and **limited access to treatment**. What is more, *Alpha-1* is a **life-threatening disease**, and without proper treatment and care patients have a **decreased life expectancy**. The social aspect of *Alpha-1* disease should not be forgotten: many *Alpha-1* patients need to deal with **stigma associated** with **lung disease** as a **"smokers' disease"** and **liver disease** as **"alcoholics' disease"**.

!

This document highlights how the European community can improve care for patients, and calls on all citizens to be more aware of the need to diagnose, treat and care for *Alpha-1* patients.

Alpha-1 Policy Recommendations

The use for policy makers

To improve policy for patients, to make healthcare systems more sustainable and to consider *Alpha-1* patients in wider policy topics

The use for healthcare professionals

To increase the awareness around when to test for *Alpha-1*, how to recognise it and how to connect with centres of excellence

To consolidate best practices amongst centres of excellence and recommend good networking practices

The use for individuals and carers

To increase knowledge about *Alpha-1* condition, to encourage all COPD patients to be tested for *Alpha-1*, know what to say to your doctor and what more you can do

OVERARCHING RECOMMENDATIONS

This paper calls on **policy makers, healthcare professionals**, **individuals** and **carers** to pursue these recommendations:

Recommendations for Policy Makers

- All Member States should develop an ***Alpha-1* diagnosis programme** in their **rare disease plan**. The European Commission should develop a project to **generate minimum credentials** for ***Alpha-1* centres of exellence.**
- National paying agencies should develop **reimbursement decisions** by distinguishing rapid or non-rapid declining *Alpha-1* patients.
- National governments should **ensure that legislation does not deter individuals from genetic testing for rare diseases** by ensuring that non-symptomatic patients do not have **higher insurance premiums.**

Recommendations for Healthcare Professionals (HCP)

- HCPs should **consider a diagnosis of *Alpha-1* in patients with COPD, emphysema, bronchial asthma, bronchiectasis, unexplained liver disease, panniculitis, unexpected vasculitis and any patients with family histories of *Alpha-1*.**
- **Test all the above listed patients** with a simple **blood test** and refer all positive tests to centres of excellence (specified on page 22).
- Centres of excellence should work through **networks** such as the **European Reference Networks to share expertise, refer patients** and **educate healthcare professionals across Europe.**

Recommendations for Individuals and Carers

- If you have unexplained symptoms of lung, liver or skin disease, **ask your doctor to be tested for *Alpha-1*.**
- *Alpha-1* patients should **adjust their lifestyles** to reduce the chance of the onset, or aggravation of lung, liver or skin disease.
- *Alpha-1* patients and carers should **seek support from the patient and/or support groups.**

Alpha-1 European Expert Group Recommendations

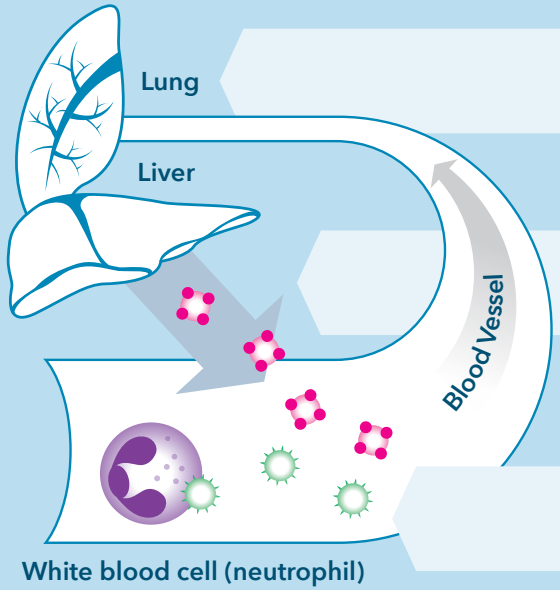
WHAT IS ALPHA-1?

Alpha-1 is a **genetic inherited condition**, which is passed from parents to children through genes.

Alpha-1 occurs when there is a **lack of a protein** in the **blood called *Alpha-1* antitrypsin, or AAT.** AAT, the *Alpha-1* protein, is **mainly produced by the liver.** The main function of AAT is to **protect the lungs from inflammation** caused by **infection and inhaled irritants** such as tobacco smoke.

The low level of AAT in the blood occurs because the AAT is abnormal and **cannot be released from the liver at the normal rate.** This leads to a build-up of abnormal AAT in the liver that can cause **liver disease** and a **decrease of AAT** in the blood that can lead to **lung disease in adults.**[3]

Normal

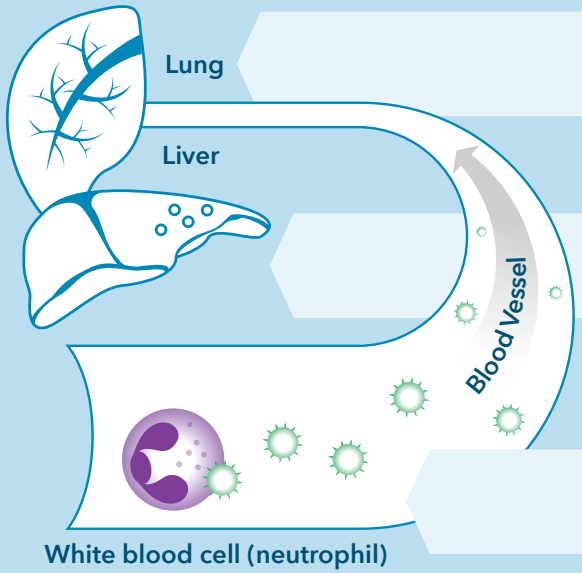


Alpha-1 antitrypsin coats lungs, protecting them from neutrophil elastase

Alpha-1 antitrypsin
produced in the liver protects lungs from neutrophil elastase

Neutrophil elastase
Produced by white blood cells to break down harmful bacteria. Potentially damaging to lungs

Alpha-1 Antitrypsin Defiency



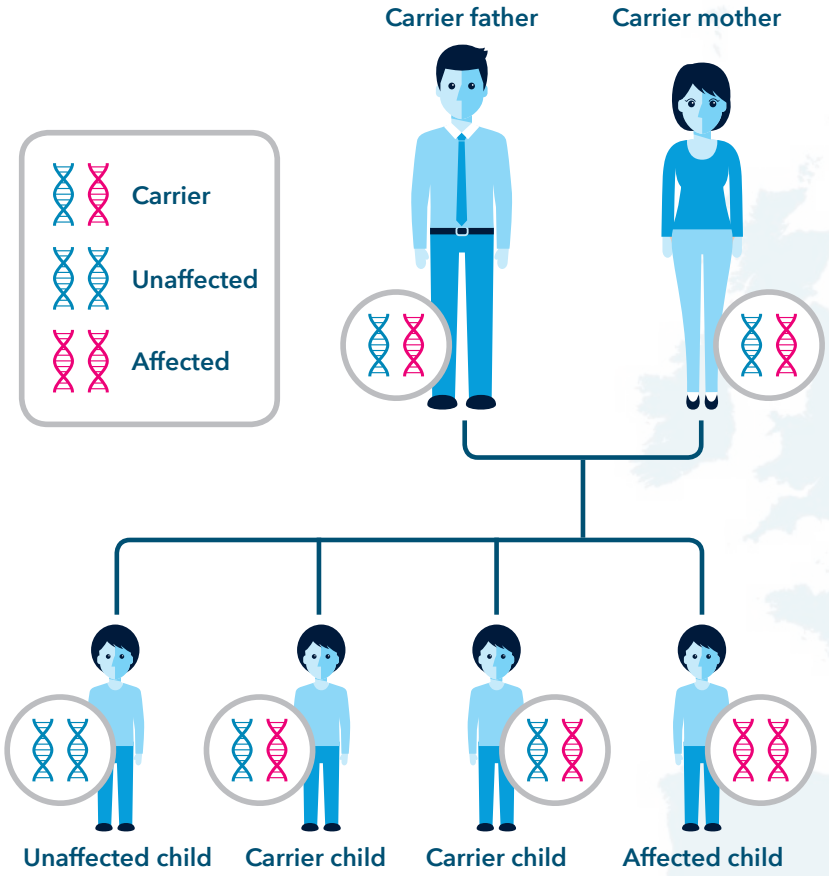
Lungs lack Alpha-1 antitrypsin coating, leaving them open to damage by neutrophil elastase

Alpha-1 antitrypsin
Trapped in liver, causing liver damage

Neutrophil elastase
Unhibitited, causing lung damage

HOW IS ALPHA-1 INHERITED?

As a **genetic disorder**, to inherit severe *Alpha-1*, a so-called **Z-AT gene** (or another severely impaired AT variant) must be passed on by both parents. If an individual carries two Z-AT, his/her level of AAT would be 10 to 20 % of what it should be. The AAT protein affected by the Z-AT gene **builds up in the liver**, which means that the individual does not have enough AAT released to control the enzyme in his/her body.[4] The defective production of AAT protein in the liver mainly results in **compromised pulmonary protection**.[5]



STANDARD OF CARE FOR ALPHA-1 PATIENTS

Symptoms can be treated by **appropriate therapeutic measures.** Besides specific treatments for the lungs and liver, all *Alpha-1* patients should take **precautions to avoid infections**, which includes **vaccinations, sensible consumption of alcohol** (unless liver disease is established in which case it should be avoided) and **no tobacco.**[6]

Alpha-1 patients with **lung disease such as asthma, COPD or bronchiectasis** can be treated by the **same drugs that are used by non-*Alpha-1* patients** for these conditions.

Specific therapy available to ***Alpha-1* patients with lung disease** called **augmentation therapy.** This therapy consists of intravenous infusions, usually weekly, of AAT protein in order to increase the level of the protein in the blood and lungs. The therapy has shown to reduce the rate of lung decline, and improve survival. The augmentation therapy cannot restore lost lung function, thus it is crucial for patients to receive it as early as possible if they have evidence of deteriorating lung function.[7]

For **liver diseases, liver transplantation** is the **only viable therapy** today.[8] Other treatment options may include adjustment of alcohol intake, hepatitis A&B vaccinations and nutrition adjustment.[9]

RECOMMENDATIONS FOR POLICY MAKERS

Act, coordinate and evaluate

Challenge 1: Late or incorrect diagnosis

Although ***Alpha-1* is one of the most common hereditary disorders in Europe**, lack of correct and timely diagnosis is a major challenge due to lack of awareness on the disease and thus its exclusion from systematic screenings programmes. *Alpha-1* is diagnosed through the simple and low-cost way – a **blood test**. However, *Alpha-1* diagnosis should also trigger **family screening**. While genetic testing is crucial for patients with a higher likelihood of *Alpha-1* these patients might be hesitant to seek screening because of the fear of correspondingly increased insurance premiums.

The Call to Action

- The European Commission should **update their CORDIS study from 2002** to find the current status of genetic testing for rare diseases and to issue subsequent recommendations for countries to promote an approach based on maintaining a high level of human health and not discriminating against patients taking effective steps to avoiding both human and health system costs.
- All Member States should **develop an *Alpha-1* diagnosis programme** as part of the rare disease plan and ensure that guidelines for related diseases such as COPD and liver cirrhosis include mandatory tests for *Alpha-1*.
- Consider **newborn screening** for *Alpha-1* recognising the importance in avoiding expensive organ transplantation, dangerous and expensive non-controlled disease progression.

Challenge 2: Reimbursement

***Alpha-1* currently has no cure**, however, there are number of treatments developed for better disease management. One of the most progressive treatments for *Alpha-1* lung and skin affected patients is called **augmentation therapy**, aimed to slow down or prevent progression of lung disease and is often recommended for *Alpha-1* patients. Despite promising results and proven cost-effectiveness[10] of the augmentation therapy, there are only few countries which reimburse it.

The Call to Action

- Payers must consider the number of **"rapid decliners"**[11] that would receive augmentation therapy rather than the whole patient population when assessing cost-benefit.
- Consider assessment by a **Computed Tomography (CT) Scan.**
- **Augmentation therapy** has been proven to be **cost-efficient**[12] and *Alpha-1* is the only form of COPD with specific treatment and has one of the **highest levels of data and hence** it should be made available for all patients who need it.

Alpha-1 European Expert Group Recommendations

Challenge 3: Coordination

Centres of excellence are the cornerstone of rare disease care in the EU. Across all countries, centres of excellence must have a **more coordinated approval process** so that patients know where expert care exists and where appropriate referrals can take place. This is crucial for the development of European Reference Networks (ERNs) in all disease areas and so that detected *Alpha-1* patients can be appropriately managed. In 2017, the were two ERNs launched, in which Alpha-1 is included: the European Reference Network on Rare Respiratory Diseases (ERN LUNG) and the European Reference Network on Rare Hepatological Diseases (ERN RARE-LIVER). In addition, there are 63 designated centres of excellence listed on the Orphanet website but these are self-assigned by national health services and 24 of these centres are in a single country.[13]

The Call to Action

- **Implement EU Cross-Border Healthcare Directive** to support the right of patient to get the best possible care, also abroad, if deemed appropriate.
- The European Commission should incorporate a project under the 3rd Health Programme generating an ***Alpha-1* centre of excellence accreditation.**
- The development of an "EU Stamp", recorded on the **Orphanet database** denoting a centre of excellence by disease area. This stamp would be the same processing form for ERN applications and comparatively applicable for patients to know where they will receive expert care.

Challenge 4: Holistic policy on *Alpha-1*

Alpha-1 does not just require **strong health policy** but also a considered approach that environmental issues such as **pollution** (indoor and outdoor) and the **toxicity of chemicals in employment settings** have a **major impact on human health**. *Alpha-1* patients experience organ degeneration noticeably faster than other patients with COPD in environments with more pollutants in the air.[14]

What can be done?

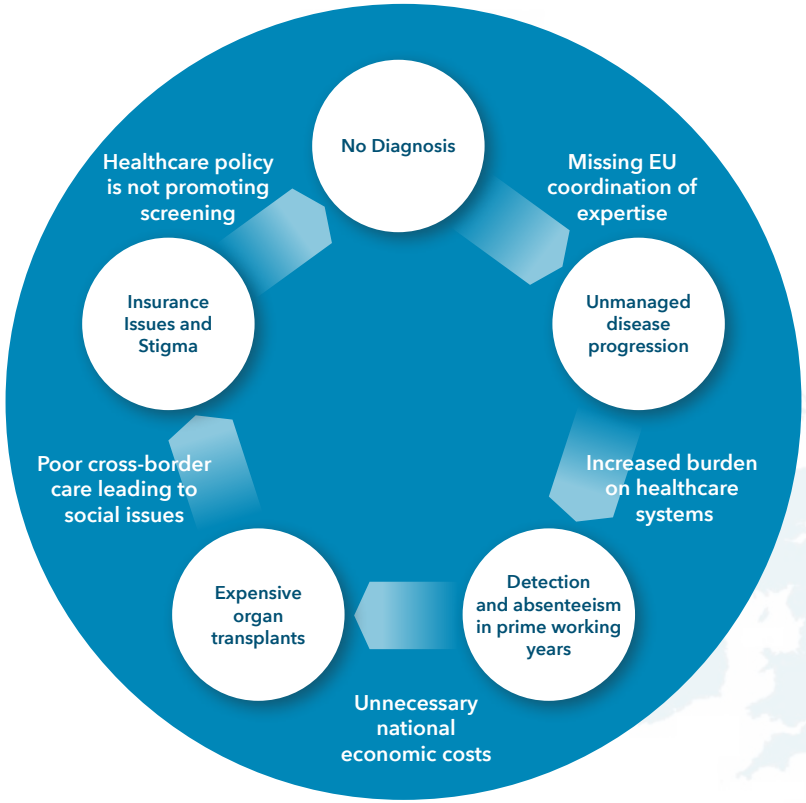
- The EU Member States should improve **ambient air quality** through effective implementation of the EU and WHO developed **air quality standards.**
- The EU should **develop comprehensive strategy on indoor air quality.**

Poor air quality is an invisible killer which currently affects 90% of city dwellers in the EU, particularly lung disease patients. Achieving the highest outdoor and indoor air quality standards is just one measure that legislators can take to improve health for Alpha-1 patients.

Seb Dance, Member of the European Parliament, UK

Alpha-1 European Expert Group Recommendations

WHY IS IT IMPORTANT TO ACT NOW?



Rare diseases, such as *Alpha-1*, require a **combination of coordinated EU policy work** to harmonise standards and benefit from **differential expertise**, and **strong national plans** to ensure patients are cared for in a **holistic way within resource-constrained health systems.**

Effective policy solutions for *Alpha-1* are not necessarily complicated, but the lack of awareness around this disease has simply meant policy has omitted key elements for these patients. This is an area where European and national policy makers can make **rapid changes to patients' lives**, which will improve not only the **prosperity of patients**, but the **socio-economic functioning of European societies.**

Lack of political action creates a **vicious circle**, where an unaddressed issue leads to another unaddressed issue and deepens, contributing to an **increased burden for *Alpha-1* patients and healthcare systems.**

A message from the European Parliament

Rare diseases, including *Alpha-1*, affect only a **small group of the population**, and for a long time the needs of such patients were neglected: limited knowledge on rare diseases, high cost of specialised services and effective therapies resulted in lack of consideration and investment in research and healthcare services in this area.

However, for the last decade, the **EU has been actively contributing to the changing perspective on rare diseases:** the legislative developments at EU level have led to the development of national rare disease plans and centres of expertise in most Member States, as well as the facilitation of research and clinical trials and the possibility to receive diagnosis, treatment and care abroad. Many useful tools for rare diseases are already in place, including but not limited to the EU Regulation on Orphan Medicinal Products, the EU Directive on Patients' Rights to Cross-Border Healthcare, the EU Public Health Programme and the Clinical Trials Regulation although it is paramount to continuously evaluate and ameliorate existing legislative instruments, develop new solutions to enhance diagnosis, care and research.

In the upcoming years, **special attention should be paid to development of *Alpha-1* diagnosis programmes**, as a part of rare disease plans in the Member States. Better diagnosis is needed to efficiently tackle the disease and to avoid higher costs in the future. To ensure access to a quality care for all Europeans, the tools provided by the cross-border health provisions should be fully exercised by all Member States. As elected European citizens representatives we would like to express our continuous commitment to work on the health and well-being of all Europeans, with a great focus on rare disease patients.

Seb Dance, Member of the European Parliament, S&D, UK
Marlene Mizzi, Member of the European Parliament, S&D, Malta
Sirpa Pietikäinen, Member of the European Parliament, EPP, Finland

RECOMMENDATIONS FOR HEALTHCARE PROFESSIONALS

Key Recommendations for Healthcare Professionals

- Healthcare professionals should keep the tear-out as a **reminder of all patients who could have *Alpha-1*.** You are the key to identifying the undetected population of *Alpha-1* patients and to ensure that all can receive good care.
- In addition to striving to consider *Alpha-1* in more patients, healthcare professionals should aim at **attending and participating in respiratory and other *Alpha-1* related medical events** to increase knowledge and enhance networking.
- There are many centres of excellence around Europe with the **expertise to diagnose and care for *Alpha-1* patients** appropriately. Look to establish links with these centres of excellence and contact them in all cases.
- Centres of excellence should work through networks such as the **European Reference Networks to share expertise, refer patients and educate healthcare professionals** across Europe. The full list of centres of excellence in your country can be found at the end of this document.

Recommendations for Recognising *Alpha-1* Patients

Conditions indicating risk of *Alpha-1*:	Test all patients with:
• Bronchiectasis • Panniculitis • Vasculitis (in particicular ANCA) • Hepatocellular carcinoma • Unexplained liver disease	• COPD • Asthma • Family history of *Alpha-1* • Chronic liver disease • Patients with frequent infections • On lung and liver transplant lists

1. Positive for low levels of Alpha-1 Antitrypsin? › 2. Refer to centre of excellence (see page 22) › 3. Treatment and care at centre of excellence

RECOMMENDATIONS ON TREATING AND CARING FOR ALPHA-1 PATIENTS

Initial Visit(s)

Undertake baseline assessment after obtaining a full clinical history

- Full physical examination
- A high-resolution CT of the lungs or a posteroanterior (PA) and Lateral Chest X-Ray
- Pulmonary function test (spirometry, lung volumes, diffusion capacity, oximetry, or arterial blood gases)
- Liver function test (AST, ALT, total and direct bilirubin, Albumin, INR, liver ultrasound or fibroscan examination, non-invasive assessment of liver fibrosis)
- Other appropriate tests for specific associations including vasculitis screen

Discuss need for liver evaluation with appropriate referral to a liver specialist (paediatric or adult)

Discuss need for lung evaluation or referral to a pulmonologist

Discuss use of drug therapy for lung problems

- Use of bronchodilators
- Use of corticosteroids
- Early identification and treatment of lung infections

Discuss active management and treatment of liver complication symptoms

Discuss need for vaccinations

- Influenza (annual)
- Pneumococcal vaccine
- Hepatitis A
- Hepatitis B

Assess smoking status and provide strong message on the harm, reason to and appropriate advice on how to quit if patient smokes any form of tobacco, including cigars, pipes and cigarettes

Discuss risk of occupational and environmental exposures including second hand tobacco smoke, dusts, chemicals

Discuss alcoholic beverage consumption

RECOMMENDATIONS ON TREATING AND CARING FOR ALPHA-1 PATIENTS

- Discuss developing an exercise programme if relevant
- Discuss developing a nutrition plan if relevant
- Discuss reducing stress if relevant
- Discuss referring patient to a psychologist (if necessary)
- Refer patients to the joint resources listed at the end of the recommendations after discussing the reasons with the patient
- Discuss patient at a relevant MDT if appropriate, and provide advice to patient

Subsequent Visit(s)

- Discuss the results and implications of the initial baseline assessment
- Discuss requirements and frequency of follow-up visits
- Discuss the potential prognosis and treatment options
- Discuss potential benefits of augmentation therapy specific for the individual patient
- Discuss the use and benefits of supplemental oxygen (if necessary)
- Discuss the benefit of surgical options (if appropriate)
- Discuss referring patient to a psychologist (if necessary)
- Discuss referring patient to a genetic counsellor (if necessary)

RECOMMENDATIONS FOR HEALTHCARE PROFESSIONALS

Healthcare professionals hold the ultimate key to **improving care for *Alpha-1* patients** but the lack of adequate education about identifying the disease and awareness on how to react to appropriate symptoms obstructs good care. This section aims to provide healthcare professionals with the key tools for identifying and appropriately dealing with *Alpha-1* patients.

The Key Steps

RECOGNISING – It is more common than you think![15]

Who to test? The World Health Organisation and the European Respiratory Society recommend the testing of all patients with COPD, emphysema, a diagnosis of adult onset asthma especially with incompletely reversible airflow obstruction, individuals with unexplained liver disease, and adults with necrotizing panniculitis or multisystem vasculitis.[16]

Any patients on lung and liver transplant lists should be tested, and keep in mind that bronchiectasis, panniculitis, vasculitis, hepatocellular carcinoma and unexplained liver disease are all potential indicators of *Alpha-1*.

REACTING – Testing is cheap and can be life saving

What to do? All patients who have been recognised within the above groups should be tested for *Alpha-1*. Testing can be conducted on a single blood sample (blood draw or finger prick test).[17]

Once this has been done, more specific tests and evaluations may be necessary please consult the tear out for more information.

REFERING – Centres of Excellence exist across Europe

Now what? All tests for *Alpha-1* on the above groups should be referred immediately to a centre of excellence in your country for a full examination, diagnosis and expert information. The list of centres of excellence can be found at the end of this document.

Our greatest opportunity to care better for Alpha-1 patients is to increase the recognition of the disease amongst healthcare professionals so that patients can be referred to specialists linked to multidisciplinary teams. Doctors are the essential bridge between a huge community of undiagnosed patients and the centres of excellence.

Prof. Robert Stockley, University Hospital Birmingham, UK

RECOMMENDATIONS FOR INDIVIDUALS AND CARERS

Do I have *Alpha-1*?

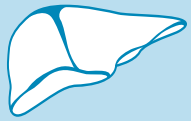
Alpha-1 can be **confused with other lung and liver diseases**. If you have any of the symptoms described below, it is suggested to **ask your doctor to conduct some tests**, especially if you are under the age of 40.[18]

Lungs[19]

- Frequent infections
- Frequent coughs, phlegm production
- Shortness of breath
- Wheezing

Liver[20]

- Elevated liver enzymes
- Discomfort in right upper abdomen
- Easier bruising
- Fatigue
- Eyes and skin turning yellow
- Dark urine
- Distressing itching
- Weight faltering
- Swelling of the abdomen (ascites)
- Vomiting blood or passing blood in the stool



When should I seek screening?

It is suggested to go through screening if you have **family history of *Alpha-1***, if you have **symptoms listed previously**, as well as any of the **following diseases:**

Lungs[21]

- COPD
- Emphysema
- Chronic bronchitis
- Chronic bronchiectasis
- Suspected allergies and or asthma

Liver[22]

- Chronic liver disease
- Cirrhosis
- Unexplained liver disease
- Unexplained paediatric liver disease
- Hepatocellular carcinoma

Skin[23]

- Panniculitis
- Unexplained Vasculitis

Depending on experienced symptoms, lung screening should be done irrespective of age

Some people experiencing *Alpha-1* symptoms are hesitant to seek diagnosis, preferring **"better not to know"** about the **potential disease.** However, it is **highly recommended to get screened**, as timely and correct diagnosis will **significantly improve your quality of life and can stop disease progression.**

QUESTIONS TO ASK YOUR DOCTOR

- What is my **diagnosis?** What is ***Alpha-1*?**
- **Will I need a test? What is the test for?** What will the **results** tell me?
- Should my **family members** take the **test for *Alpha-1*?**
- What are my **treatment options?** What are the **benefits of each option?** What are the **side effects?**
- What will the **medicine** you are prescribing do? **How do I take it?** Are there any **side effects?** Can they adversely **interact with other medications** you are prescribing for me?

- Why do I need **surgery?** Are there **other ways to treat my condition? How often do you perform this surgery?**
- Do I need to change my **daily routine?** What I can do to maintain and improve my health?
- If my **symptoms worsen**, what should I do **on my own? When should I contact you?**

- ✓ Do annual flu vaccination
- ✓ Do vaccination against pneumonia
- ✓ Do vaccination against hepatitis A&B
- ✓ Keep your ideal body weight
- ✓ Eat a balanced vitamin-rich high fiber diet, including lots of vegetables and fruits but not too much meat and fat
- ✓ Develop an exercise programme suitable for your condition
- ✓ Consult use of any food supplements and/or medicines with your physician
- ✗ Do not smoke: *Alpha-1* and smoking is a deadly combination
- ✗ Avoid exposure to the second hand smoke
- ✗ Avoid sources of infections
- ✗ Be careful with alcohol
- ✗ Avoid medications and supplements that may harm your liver such as certain painkillers
- ✗ Avoid outdoor pollution, including pollen, smoke, dust and other irritants
- ✗ Avoid indoor pollution and exposure to household chemicals and dust
- ✗ Reduce your stress

FOR YOUR NOTES

How are diagnosis made?

Alpha-1 can be diagnosed through a **simple blood test.** One type of blood test measures the **body's level of AAT.** If the AAT level is lower than normal, your health care provider may order a **genotype or a phenotype blood test.** The genetic analysis looks at the changes in the genetic code and shows if the person is an *Alpha-1* carrier. To have a better understanding of how genetic testing is done and what the outcomes may be, please seek genetic counselling beforehand.

Can I be treated?

Alpha-1 is not yet curable, however, **treatments for symptoms are available.** The same medicines which are used by non-*Alpha-1* patients for lung conditions such as COPD, asthma or bronchiectasis can help *Alpha-1* patients with lung diseases. In addition, in some European countries, lung-affected *Alpha-1* patients may receive infusions of AAT, which is known as **augmentation therapy.** The therapy is a **preventive measure**, it can protect against further lung damage but it cannot restore it. Augmentation therapy might also be suggested for the **treatment of panniculitis.**[24] In case of the presence of one or more additional diseases co-occurring with *Alpha-1* (comorbidities), please seek advice from your doctor on the treatment.

For the *Alpha-1* liver condition there is no specific treatment, the only currently available treatment, when liver disease is most severe, is **surgery** or **liver transplantation.** Augmentation therapy is not used for the liver disease patients.

Where can I find support?

Check if there are **support groups** and/or **patient organisations** in the area where you live. Join this network to get the support and information you may need. Patient groups are also essential for providing information to patients, and working on their behalf on policy and medical levels. In addition, they connect *Alpha-1* patients to deal together with ongoing issues and to support each other. All patients are encouraged to find their local *Alpha-1* patient group, please check page 22, if you have a patient group near you, otherwise please contact *Alpha-1* Global for further information.

Being diagnosed with Alpha-1 is one of the most stressful experiences in a person's life. Patient organisations are the best place to share experiences and to learn from others who are in similar situation. You will find support in your country by visiting ***http://www.alpha-1global.org/en***

Dr. Frank Willersinn, Alpha-1 Global (Belgium)

Alpha-1 European Expert Group Recommendations

USEFUL LINKS/QR CODES

European Reference Network on Rare Respiratory Diseases (ERN LUNG)
http://ern-lung.org/

List of Centres of Excellence

Please visit Orphanet – the portal for rare diseases and orphan drugs – to find *Alpha-1* centre of excellence in your country: www.orpha.net

List of Patient Organisations

***Alpha-1* Austria**
www.alpha1-oesterreich.at

***Alpha-1*-France**
www.alpha1-france.org

***Alpha-1* Plus Belgium**
www.alpha1plus.be

***Alpha-1* Germany**
www.alpha1-deutschland.org

***Alpha-1* Denmark**
www.alfa-1.dk

***Alpha-1* Ireland**
www.alpha1.ie

***Alpha-1* Italy**
www.alfa1at.it

***Alpha-1* Norway**
www.alfa1foreningen.word-press.com

***Alpha-1* Netherlands**
www.alpha-1nederland.nl

***Alpha-1* Poland**
www.a1at.wordpress.com

***Alpha-1* Portugal**
www.aa1p.pt

***Alpha-1* Switzerland**
www.alpha-1.ch

***Alpha-1* Romania**
www.unutest.webcentral.eu

***Alpha-1* UK Support Group**
www.alpha1.org.uk

***Alpha-1* Spain**
www.alfa1.org.es

***Alpha-1* Awareness UK**
www.alpha1awareness.org.uk

***Alpha-1* Sweden**
www.alfa-1.se/news.php

***Alpha-1* Global**
www.alpha-1global.org

Alpha-1 European Expert Group Recommendations

PAST SUCCESS TABLE

This table of success should serve as an overview of what has **successfully been achieved from the list of policy recommendations** developed in 2011 and what remains to be done.

Recommendation 2011	Status of achievement 2017
Recognition of *Alpha-1* as rare condition	**Partially achieved**
Increased *Alpha-1* awareness	**Partially achieved** Through establishment of patient organisations, awareness campaigns, meetings with MEPs, distribution of the previous set of the expert recommendations
Diminishing health inequalities affecting *Alpha-1* and other rare disease patients	**Partially achieved** Through Cross-Border Health Directive, which sets framework to ensure better access to cross-border treatment, however it requires positive reimbursement decisions in more Member States to truly reduce inequalities
EU definition of rare diseases is respected by all Member States	**Partially achieved** Member States with adopted plans or strategies on rare diseases comply with the EU definition. Those without plans in place usually do not have any official definition of rare disease[2]
Development of the EU and national policies with a relevance to rare diseases	**Achieved** • European policy in the field of rare diseases has improved European cooperation • European policy encouraged national policies in the field • 22 national plans for rare diseases were adopted (as of 2016) • National policies are guided by recommendations issued at the European level • Over 80 orphan drugs authorised as a result of the European incentives (as of 2016)
Increased access to treatment through implementation of the Cross-Border Healthcare Directive	**Partially achieved** Although possibilities for treatment abroad have expanded, there are still not many patients using them and the barriers to achieving treatment remain prohibitive to good cross-border care
Better standardisation of treatments and devices supporting breathing	**Partially achieved** Revised Medical Devices Regulations will come into force as from 2019, resulting in safer medical devices supporting breathing
EU Strategy on information to patients	**Not achieved**
Need of lung transplants is reduced through the optimal *Alpha-1* treatment	**Partially achieved** No available data - for some EU countries (e.g. Belgium) number of persons waiting for a lung transplant is reducing, however, there is no data of which disease patients are waiting for a transplant. On the other hand, number of transplantations within the EU countries is increasing, although it is linked to increased availability of organs, rather than better treatment
Patients should be given a possibility to decide whether and when they should undergo organ transplantation	**Partially achieved** Patient empowerment is gaining greater international importance in the healthcare. Reflecting the shift in Western culture towards increasing individualism, institutional culture in healthcare is slowly moving towards an ethic of empowering patients to make informed decisions. This is demonstrated by interest in developing and implementing more equitable and collaborative approaches to the healthcare relationship, including shared decision-making
***Alpha-1* Expert Groups, including academic and patients are supported by the EU and Member States**	**Partially achieved** The EU has allocated €449.4 million (2014-2020) through the Third Health Programme to support cooperation projects at EU level, actions jointly undertaken by Member State health authorities, functioning of nongovernmental bodies, cooperation with international organisations. Particular attention of the programme is given to rare diseases
Establishment of *Alpha-1* patient registries	**Partially achieved** 63 *Alpha-1* centres of excellence in Ireland, Italy, Netherlands, France, UK, Belgium, Denmark, France, Spain, Switzerland (24 of 63 reference centres are in Italy) (as of 2017)

EXPERT GROUP OVERVIEW

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Time to Stop Reading, Time to Act!

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