ANNUAL REPORT 2024

ALPHA-1 FOUNDATION IRELAND

MISSION STATEMENT

Alpha-1 Foundation Ireland is a charity dedicated to raising awareness, increasing diagnosis, promoting research, and improving the treatment of Alpha-1 Antitrypsin Deficiency (Alpha-1).

VISION

That everyone with Alpha-1 in Ireland is diagnosed and receives specialist care and treatment in a timely fashion.

CORE ACTIVITIES OF ALPHA-1 FOUNDATION IRELAND

ALPHA-1 FOUNDATION IRELAND TEAM

Anne Marie O'Dowd, CEO
Dr Tomás Carroll, Chief Scientist
Ronan Heeney, Medical Scientist
Rosaleen Carroll, Alpha-1 Nurse Specialist

PATRON

Michael D. Higgins, President of Ireland

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Alpha-1 Foundation Ireland Charity Code: CHY22304

ANNUAL REPORT 2024

ALPHA-1 FOUNDATION IRELAND

CONTENTS

1 Executive Summary

Welcome to the Alpha-1 Foundation Ireland 2024 Annual Report. In the pages ahead, you will see an overview of some of the work that took place in 2024.

As part of the National Centre of Expertise for AATD, the weekly Alpha-1 clinic in Beaumont Hospital saw 195 new referrals coming from a diagnosis of AATD via the National Targeted Detection Programme (TDP). It's a busy clinic now and includes a multi-disciplinary team under the leadership of Professors Gerry McElvaney and Cedric Gunaratnam and Dr. Michelle Casey. Working at the clinic is a dedicated medical and research team who continue to carry out important research. This work improves our understanding of Alpha-1 and we are hopeful that some of these research findings will translate to better care and ultimately a cure for this condition.

Patient registries are an important tool for clinical research. We currently have in excess of 700 people with Alpha-1 on the National AATD Registry and the more people that join, the more effective the research is. I really want to encourage our patient community and their families to join the registry and enable the scientists, researchers and doctors to continue the brilliant work they do on behalf of Alpha-1 patients around the world. You can read all about this work in Chapters 2 and 3 – and find an example in Chapter 4 of how the national registry is used to quickly identify people who might benefit from taking part in a clinical trial.

An important part of our work is education and outreach, particularly educating health professionals and students in Ireland about Alpha-1. As part of this education, we visited many groups in 2024 (Chapter 5), including a webinar along with other lung advocacy groups in September hosted by the National Clinical Programme in Respiratory. Representation in the Alpha-1 European Alliance continued in 2024 as did engagement with national groups connected with our work such as Health Research Charities Ireland and IPPOSI. A major event which took place in October was the National Alpha-1 Patient and Family Conference – the first one following the COVID-19 pandemic. We were delighted to welcome people from all over the country and the reports and photos are in Chapter 6.

The National AATD Targeted Detection Programme and the National AATD Registry would not be possible without annual core funding from the HSE for which we are grateful. I want to express a special thanks to the Alpha-1 team based at RCSI Beaumont. Our theme this year is "**Fiche Bliain ag Fás"** – as we celebrate 20 years of working for the Alpha-1 community in Ireland. Our vision is that every Alpha-1 individual in Ireland is diagnosed and receives specialist care and treatment in a timely fashion. Together we are working hard to realise this vision and look forward to continuing to support people with Alpha-1 in 2025.

Anne Marie O'Dowd
CEO, Alpha-1 Foundation Ireland

2 The National Alpha-1 Antitrypsin Deficiency Targeted Detection Programme – An Update

Ronan Heeney, medical scientist on the national Alpha-1 detection programme which tests over 1,200 people each year.

Alpha-1 antitrypsin deficiency (AATD or simply Alpha-1) can be diagnosed by a simple blood test but unfortunately remains hugely under-diagnosed. A diagnosis of Alpha-1 is a unique opportunity for early intervention which can prevent or postpone lung disease in both the affected individual and their relatives. In May 2004, a national targeted detection programme for AATD was launched by Alpha-1 Foundation Ireland thanks to funding from the HSE. By the end of December 2024, the programme had tested more than 24,500 people.

Who Should Be Tested for Alpha-1?

World Health Organisation (WHO), American Thoracic Society (ATS), and European Respiratory Society (ERS) guidelines advocate targeted detection programmes for AATD. These guidelines recommend targeted testing of certain patient groups, with a special focus on chronic obstructive pulmonary disease (COPD)(Table 2.1).

Figure 2.1. *Simple testing process for Alpha-1 involving a visit to a GP, blood sample, laboratory test and a final report.*

Table 2.1. *ATS/ERS recommendations for diagnostic testing for AATD (type A recommendations).*

Who Should Be Tested?
Adults with symptomatic emphysema or COPD (regardless of age or smoking history)
Adults with asthma with airflow obstruction that is incompletely reversible after aggressive treatment with bronchodilators
Asymptomatic individuals with persistent obstruction on pulmonary function tests with identifiable risk factors (e.g. cigarette smoking, occupational exposure)
Adults with panniculitis
Siblings of individuals with Alpha-1
Individuals with unexplained liver disease, including neonates, children, and adults, particularly the elderly

How Do We Test for Alpha-1?

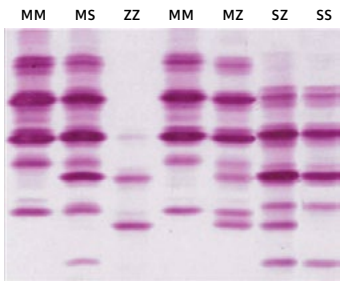


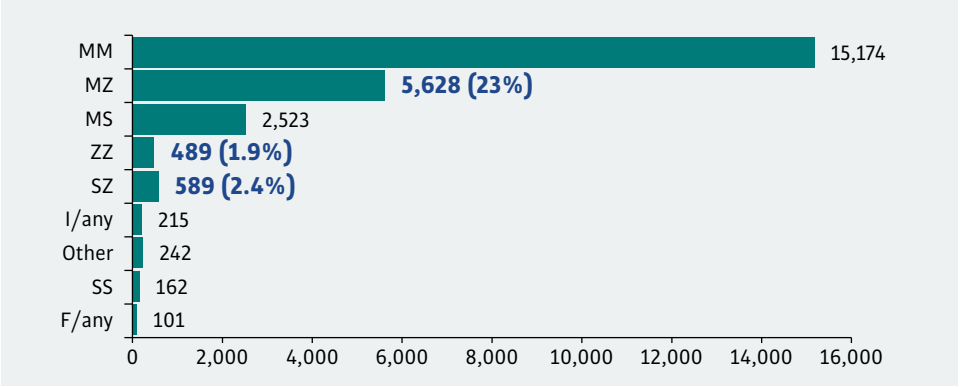
Figure 2.2. *Typical isoelectric focusing gel for AAT phenotype identification with the most common phenotypes included.*

There are two tests needed to correctly diagnose Alpha-1. The first test measures how much alpha-1 antitrypsin (or AAT) is in the blood. The second test looks at what type of AAT protein is present by a method called isoelectric focusing. This method identifies types of AAT protein circulating in human blood and is more commonly known as phenotyping (Figure 2.2). It is the most accurate method of diagnosing Alpha-1 and can recognise common and rare AAT variants.

What Have We Found in Ireland?

Since 2004, more than 24,500 individuals with COPD, asthma, and liver disease, as well as first-degree relatives of people with AATD have been tested in a National Targeted Detection Programme.

Figure 2.3. *Results from the National AATD Targeted Detection Programme showing the major AAT phenotypes identified among more than 24,500 individuals tested.*



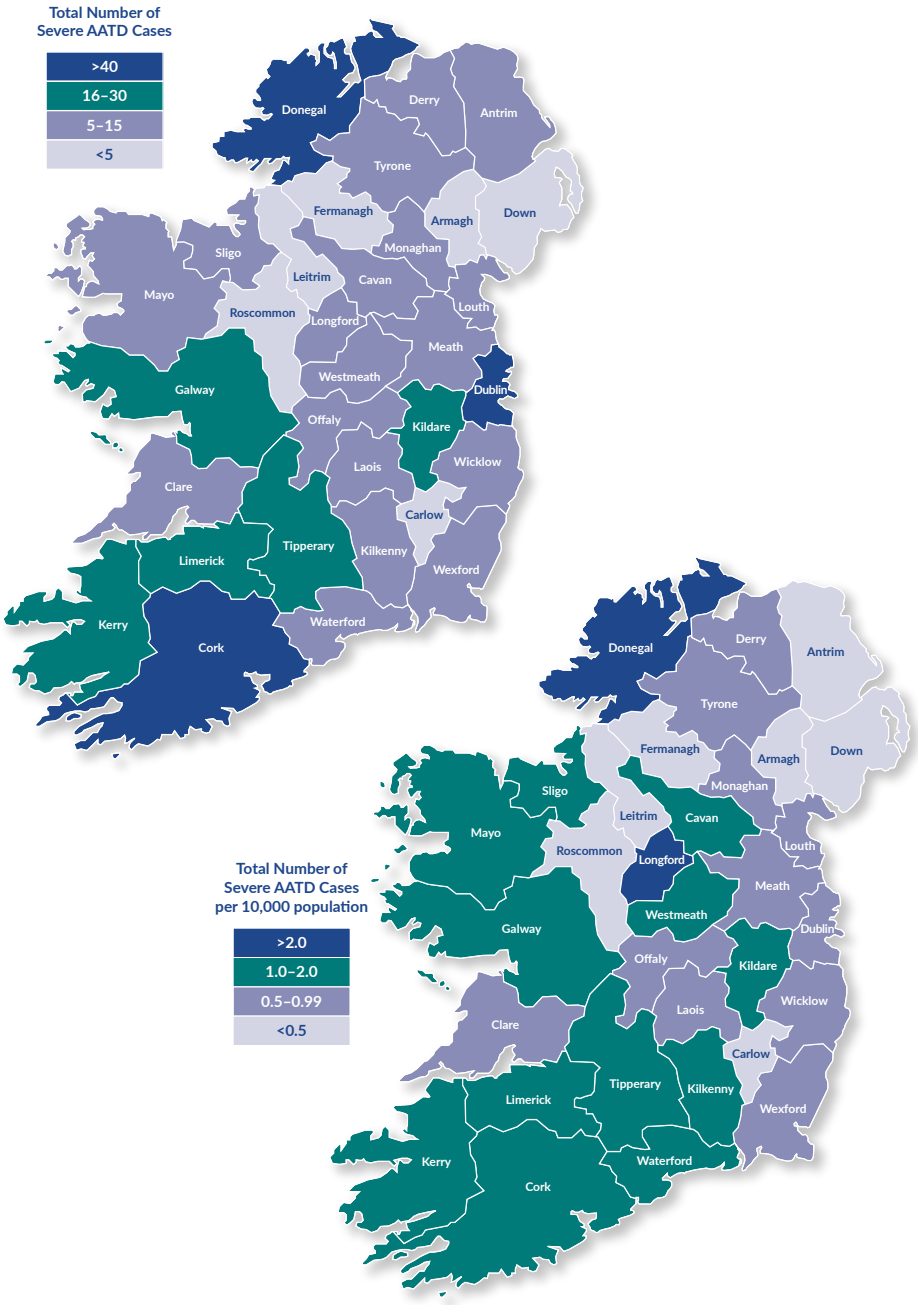
A total of 489 ZZ individuals with severe Alpha-1 have been identified. In addition, a larger number with moderate Alpha-1 who are at risk of developing lung problems if smoking or vaping. Moderate Alpha-1 includes those with MZ (5,628) or SZ (589) forms of Alpha-1 (Figure 2.3). Other clinically significant forms of Alpha-1 have been found including 30 IZ and 17 FZ individuals. A number of very rare deficiency-causing AAT variants have also been identified. These include $M_{heerlen}$, M_{malton}, $M_{wurzburg}$, $N_{whitstable}$, S_{munich}, and $Z_{bristol}$ and six different Null (Q0) mutations ($Q0_{bolton}$, $Q0_{cork}$, $Q0_{dublin}$, $Q0_{lisbon}$, $Q0_{porto}$ and $Q0_{amersfoort}$). $Q0_{cork}$ and $Q0_{dublin}$ were discovered for the first time here in Ireland.

Table 2.2. *Simple explanation of the most common AAT phenotypes.*

AAT Phenotype/ AAT Genotype*	AAT Deficiency?	What does it mean?
MM	No	Does not have the disorder – has two normal copies of the AAT gene.
MS	Mild	No evidence of increased risk of lung or liver disease but does carry one altered AAT gene.
MZ	Moderate	Significantly increased risk of lung disease **in smokers**. Increased risk of liver disease.
SS	Moderate	Presumed increased risk of lung disease **in smokers**. No evidence for increased risk of liver disease.
SZ	Moderate	Significantly increased risk of lung disease **in smokers**. Increased risk of liver disease.
ZZ	Severe	Significantly increased risk of lung disease in **smokers and ever smokers**. Increased risk of liver disease.

The goal of the national detection programme is to ensure people with Alpha-1 are correctly diagnosed and have the opportunity to receive expert medical care, advice, and support. People with Alpha-1 can be referred to the National Centre of Expertise for AATD in Beaumont Hospital under the care of Professor Gerry McElvaney. A strong focus on family screening can discover other family members with Alpha-1, which can help prevent or postpone the development of serious health problems in the wider family. Importantly, a correct diagnosis means people can benefit from lifestyle changes such as stopping smoking and vaping, risk reduction in the workplace, specialist medical care from Alpha-1 experts, and the opportunity to enrol in clinical trials that test new treatments.

Figure 2.4.
LEFT: *Distribution of severe AATD cases detected to date (559 cases across 32 counties – this includes people diagnosed outside of the TDP).*
RIGHT: *Distribution of severe AATD cases adjusted per 10,000 population.*



Alpha-1 Education and Outreach in 2024

Education and raising awareness of AATD is one of our core activities. We held seminars on Alpha-1 to a mixture of respiratory and laboratory teams in Sligo, Newry, Galway, Letterkenny, and Nenagh Hospitals. We also presented to medical students in UCD, nursing students in DCU, M.Sc. Clinical and Diagnostic Biochemistry students in UCD, M.Sc. Precision Medicine students in RCSI, and to Wexford COPD Support Group.
We presented at the Irish Society of Human Genetics, Irish Thoracic Society, and European Respiratory Society conferences. The aim of these presentations is to increase awareness of Alpha-1 among healthcare professionals and to encourage testing. While respiratory (and liver) medical teams care for patients most at risk due to AATD, hospital laboratories measure alpha-1 antitrypsin levels during normal blood investigations and can help reach a diagnosis of AATD.

3 The National Alpha-1 Antitrypsin Deficiency Registry

What is the registry?

The registry is a confidential database that stores relevant medical information of individuals diagnosed with alpha-1 antitrypsin deficiency (AATD). Results of tests that monitor lung and liver function such as blood tests, breathing tests, CT scans of the lungs and ultrasound or transient elastography (also called a Fibroscan) of the liver are recorded in the registry and updated at regular intervals. The registry also collects other information relevant to AATD. For example, smoking status and occupation can help to quickly identify risks to lung health (e.g. a factory worker exposed to fumes or dusts).

Is my data safe?

Yes. The registry is located on a secure server, hosted by Health Atlas Ireland, a key part of the HSE digital landscape. All data is encrypted and only Beaumont Hospital staff have access to the registry.

Figure 3.1. *The Goals of the National Alpha-1 Registry.*

What is the purpose of the registry?

The registry helps to deepen our knowledge and understanding of AATD, improve the clinical care given to people with AATD, and increase recruitment for clinical trials investigating new treatments for AATD. The small number of people affected by a rare condition like AATD means that getting access to the right care, treatment and support can be difficult. Registries play an important role in filling gaps that exist in the care of people with rare disease, particularly in Ireland which has no electronic healthcare record.

What are the key objectives of the Registry?

1. Increase our understanding of AATD (knowledge)
2. Inform and improve clinical care (care)
3. Provide early access to new treatments via clinical trials (treatment)

How can I enrol?

Individuals diagnosed with various forms of AATD are eligible to enrol in the registry. Enrolment is completely voluntary, and an individual must provide their written informed consent prior to enrolment. A member of Alpha-1 Foundation Ireland will provide individuals with an information leaflet and answer any questions at the time of enrolment.

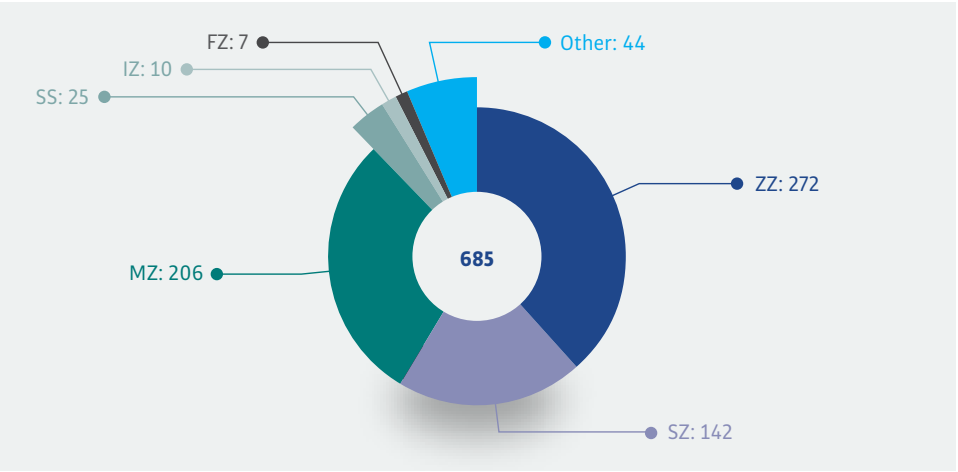
If I have questions?

If you or your family are interested in enrolling or have any questions about the registry, please contact us on 01-8093871. To learn more about our registry visit our website at *https://www.alpha1.ie/irish-alpha-1-registry/*.

Registry Update and Future Plans

At the end of 2024 a total of 706 people with Alpha-1 were taking part in the National AATD Registry (Figure 3.2) and this number is growing all the time. Joining the registry allows us to build knowledge, improve care and help develop new treatments through involvement in clinical trials.

Figure 3.2. Total number of individuals enrolled in the registry according to AATD phenotype (n = 706).

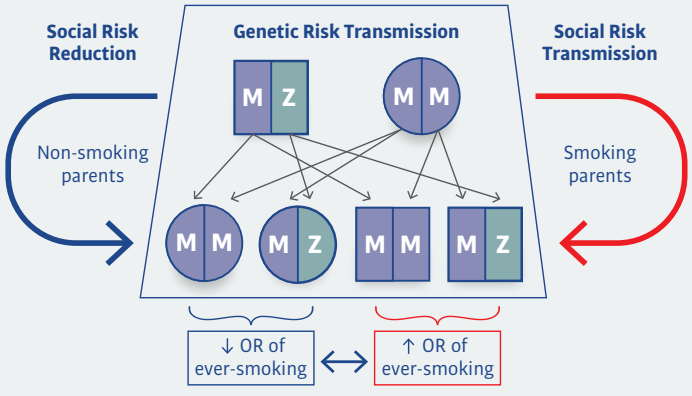


Research using anonymous data from the registry has improved our understanding of the risk factors and symptoms associated with the health problems caused by Alpha-1. For example, a recent study looked at cigarette smoking habits in people with Alpha-1 taking part in the registry. The study [**Alpha-1 Antitrypsin Deficiency and Tobacco Smoking: Exploring Risk Factors and Smoking Cessation in a Registry Population, Franciosi et al, Journal of COPD, 2021**] showed that smokers were highly motivated to stop smoking after finding out they had Alpha-1. In addition, people with one or two parents who smoked were more likely to become smokers themselves (see Figure 3.3).

This important knowledge has led to a greater focus on smoking cessation at the National Centre of Expertise for AATD to prevent lung disease in **current and future generations** within families affected by Alpha-1. The findings once again highlight the importance of an early diagnosis of all types of AATD so positive lifestyle choices (like stopping smoking) can be made.

Another key research study made possible by the National AATD Registry was a three-country study of severe Alpha-1 published in late 2023 [**Augmentation Therapy for Severe Alpha-1 Antitrypsin Deficiency Improves Survival and Is Decoupled from Spirometric Decline-A Multinational Registry Analysis. Fraughen et al, Am J Crit Care Med, 2023**]. This study looked at the health of 615 people with severe AATD in European AATD registries in Ireland, Switzerland, and Austria; three countries where access to standard medical care is equal but access to augmentation therapy is not. This situation allowed us to test the effects of augmentation therapy on survival. We were able to show that people with AATD in Switzerland and Austria benefit from a clear survival advantage due to augmentation therapy that people with AATD in Ireland do not because this treatment is not available. We also showed that a majority of people with AATD are being diagnosed too late by which time severe lung disease has already occurred.

***Figure 3.3.** An example of the new knowledge generated from a survey of smoking habits in people taking part in the National AATD Registry. The diagram shows how two risk factors are inherited in families with a parent who smokes; the genetic risk of Alpha-1 (Z type) and the habit of smoking.*



4 Living with Alpha-1 – Rose's Story

My name is Rose (65) and I live in Cavan. I have four grown children and for years I had been incorrectly diagnosed as having Chronic Asthma suffering with shortness of breath and numerous chest infections. My Alpha-1 Antitrypsin Deficiency journey began when I was 37 and the bouts of infection increased dramatically and my quality of life reduced significantly. My daily life was filled with pain, fatigue where I couldn't get out of bed and I would struggle to do simple tasks without gasping for air. Every night I went to bed I prayed I would wake up in the morning to see my children as I felt I was suffocating. I was a shadow of my former self, a shell that was merely existing not able to experience the joys of life but constantly sucking on inhalers and courses of antibiotics and steroids.

I have seven brothers and one sister, one of my brothers sadly passed away at the age of 23 due to complications from medicine administered for Asthma which we now believe may have been hiding a potential Alpha-1 Antitrypsin Deficiency diagnosis. At the same time as my health was declining so too was my brothers with similar symptoms to me. In 2001, he was referred by his doctor for advanced blood tests to Beaumont Hospital where it was confirmed that he had tested positive as ZZ Alpha-1 and due to this illness being hereditary that his siblings would also need to be tested. When the results came in three brothers were ZZ, three brothers and my sister were MZ and I had my diagnosis as ZZ Alpha-1. It was a relief to finally have answers for why I was so sick, but it also brought a lot of anxiety with it for what the future would hold for me. Just because I had a diagnosis, didn't mean my life suddenly improved as there was little known about Alpha-1 Antitrypsin Deficiency at this time.

I struggled on for five more years, missing out on family events and becoming more reclusive with each year that passed. In 2006 I found out I was going to be a grandmother for the first time and dread filled me that I would not be around to watch my grandchild grow up. I decided that I would travel on a pilgrimage to Medjugorje and ask Our Lady for her help with my health. Our Lady surely smiled on me as on my bus journey I received a call from Professor Gerry McElvaney of Beaumont Hospital inquiring whether my brother Oliver and I would take part in a clinical trial for a new drug called Respreeza being targeted for severe Alpha-1 Antitrypsin Deficiency sufferers. We jumped at the chance of anything that might improve our quality of life. We started to receive weekly intravenous drips. During the trial period, Oliver was making marked improvements whereas I was worsening in my symptoms. This made us think that maybe Oliver was the Test patient receiving the drug and I was in the control group receiving the placebo. On completion of the trial, I went on to receive my weekly Respreeza infusion and have remained on it for the last nineteen years.

My standard of care from the team at Beaumont Hospital has been exceptional and my quality of life has improved substantially. I am now the proud grandmother of 10 grandchildren and I believe if not for this miracle drug I would not have lived to see 50. My young grandchildren keep me on my toes and I get to enjoy experiences with them that were taken away from me with my own children due to my Illness. I try to live life to the fullest now going on family holidays to Spain and being involved in local community events and I feel this is how my life should have been in my 30s and 40s.

I have a special thanks for the following people who have supported me along the way, my family who have always stood by my side through the good and the bad, Dr Eamonn McDwyer (RIP) my GP who pushed to get answers as he believed I had more than Asthma, Dr Gerry McElvaney and his team who gave me the opportunity to take part in a trial that changed my life, and Dr Tomás Carroll who has offered me unwavering support over the years.

NOTE: *During clinical trials for new drugs and treatments, there are usually two groups of people participating – those who receive the active treatment and those who receive a placebo. A placebo is something that appears like the drug and is administered in the same way but it contains no active medicine and is, in actuality, fake. Placebos are used in randomised-controlled clinical trials (RCTs) to test if a drug is effective and working. Patients know in advance that they may not get the real drug when they participate in the study. Whoever gets the real drug or the placebo at the start of the trial is assigned randomly and both patients and staff carrying out the study – the doctor and nurses – do not know which person is getting the real drug. This is known as a double-blinded study. All patients have exactly the same tests throughout the study. In the clinical trial Rose talks about, once that study finished and the drug – Respreeza – was shown to be effective, all patients who participated were offered continuing access. Respreeza and other augmentation therapy medicines are not available yet in Ireland. However, Alpha-1 Foundation Ireland continues to strongly advocate for augmentation therapy for patients who need it and will continue that advocacy until access.*

5 Recent Events

Alpha-1 Education North and South

In early January Alpha-1 Foundation Ireland gave seminars on Alpha-1 to the respiratory teams at Sligo University Hospital and Daisy Hill Hospital in Newry. Next day we discussed the different methods used to correctly diagnose Alpha-1 with students in the Masters in Clinical Chemistry class at Trinity College Dublin. And later in the year we travelled north again to speak at the Ulster Thoracic Society meeting held in Enniskillen, Co. Fermanagh.

Lecture at UCD Medical School

In February Alpha-1 Foundation Ireland visited University College Dublin to discuss Alpha-1 with third year medical students taking the excellent rare disorders module. Running since 2012 this popular module has been showcasing rare conditions like Alpha-1. Thanks to Paula Byrne for the invitation to raise Alpha-1 awareness among the next generation of doctors.

Donegal Visit

In early April Alpha-1 Foundation Ireland visited Donegal to speak about Alpha-1 at the monthly educational meeting in Letterkenny University Hospital. Thanks to Patricia McLaughlin and colleagues for the opportunity to raise #Alpha1Awareness in a region where many people are affected.

Alpha-1 Raises Organ Donor Awareness

Later in April, Alpha-1 Foundation Ireland CEO Anne Marie O'Dowd attended the launch of Organ Donor Awareness Week 2024. The event was hosted by the Irish Kidney Association and Organ Donation Transplant Ireland. Organ donation saves hundreds of lives in Ireland each year. New legislation should lead to an increase in the numbers of lives being saved.

20th Anniversary of Alpha-1 Foundation Ireland - Fiche bliain ag fás

On April 21st 2004 the Alpha-1 Suite was officially opened by Minister for Health Micheál Martin. In the picture are pioneers Professor Gerry McElvaney and the first CEO of Alpha-1 Foundation Ireland Mr. Larry Warren (far right). This office in the RCSI Smurfit building at Beaumont Hospital was the first permanent location for Alpha-1 Foundation Ireland and began 20 years of work for the Alpha-1 community.

The Passing of an Alpha-1 Warrior

In July, the Alpha-1 community lost a dear friend, one of the original Alpha-1 Warriors. Josephine McGuirk was diagnosed with severe Alpha-1 in 1999. A smoker at the time, she stopped soon after her diagnosis, and rolled up her sleeves to begin her next job - raising awareness of Alpha-1 and helping other Alphas to stay healthy and well. Josephine and her family took part in so many awareness campaigns and research studies - with the attitude that it would help those coming after, the next generation of Alphas. Her positive outlook on life, good humour and sharp wit will live long in our memories.

It's a Long Way to Tipperary

In September Alpha-1 Foundation Ireland visited Nenagh General Hospital to talk about Alpha-1. Thanks to Olivia and Anne for the warm welcome. There was lots of interest in Alpha-1 with plenty of excellent questions from the medical teams there.

Alpha-1 visits DCU School of Nursing

Also in September, Alpha-1 Foundation Ireland was invited to DCU to talk about Alpha-1 with the large 2nd year undergraduate nursing class. Thanks to Dr. Ciara White for this valuable opportunity.

Alpha-1 Patient and Family Conference Returns

In October the Alpha-1 Patient and Family Conference finally returned after a five year gap caused by the COVID-19 pandemic. Over 70 people with Alpha-1 attended the meeting to learn all about the latest developments in Alpha-1.

Alpha-1 Attends the National Lung Meeting in Derry

In November Alpha-1 Foundation Ireland attended the Irish Thoracic Society Annual Scientific Meeting in Derry. This conference brings together over 400 doctors, nurses, and physiotherapists to learn about the latest research in lung disease. Our scientist Ronan Heeney was invited to give an update on the national targeted detection programme for Alpha-1 which was a great boost for Alpha-1 awareness.

6 Report on the National Alpha-1 Patient and Family Conference 2024

The Alpha-1 Patient & Family Conference took place on Saturday 5th October 2024 in the Marino Institute of Education after a break of five years caused by the COVID-19 pandemic. Our CEO Anne Marie O'Dowd welcomed the large crowd and the invited speakers who discussed many topics related to Alpha-1.

Professor Gerry McElvaney highlighted the many new and exciting treatments coming down the tracks for Alpha-1. Gene therapies could possibly halt Alpha-1 in its tracks or even cure the condition. All of these are at research stage but the future looks bright and hopeful. Professor Emer Fitzpatrick, Paediatric Hepatologist, from Crumlin Children's Hospital talked about liver disease in Alpha-1 with a focus on infants and children.

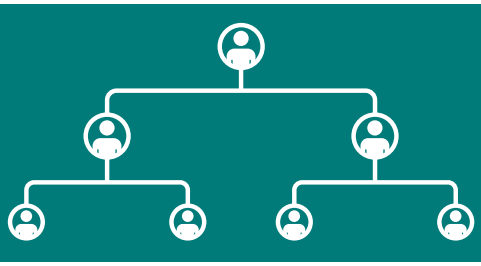
Five up-and-coming young researchers studying Alpha-1 at the Irish Centre for Genetic Lung Disease in RCSI Beaumont Hospital spoke about their work. Dr Tomás Carroll, Chief Scientist, Alpha –1 Foundation Ireland and RCSI gave an update on the National Targeted Detection Programme and the National Alpha-1 Registry. Cathy Ring, Senior Respiratory Physiotherapist, Beaumont Hospital gave a fascinating physiotherapy guide to "Keeping Well with Alpha-1".

To end the day Dorothy Casey, psychotherapist and Alpha-1 patient gave a powerful talk about her own experience of being diagnosed with Alpha-1. She outlined the normal feelings and experiences associated with the stages of grief - denial, anger, bargaining, depression, and acceptance. People can experience these stages in many ways, not necessarily in order and the feelings may be repeated. She described all the ways someone can live well with Alpha-1 and in particular, how emotional wellbeing can be maintained. In closing remarks, Anne Marie O'Dowd thanked everyone for coming and contributing to such an excellent conference.

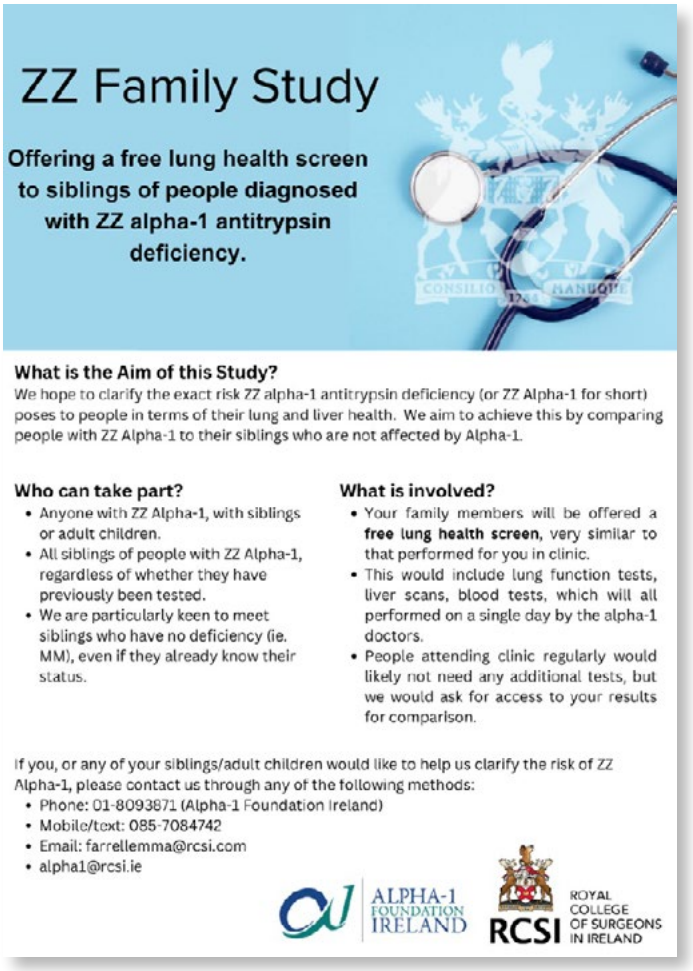
7 Alpha-1 Research Highlights in 2024

Emma Farrell, MD Researcher on ZZ Family Study

New ZZ Family Study



A new **all island** study exploring the risk of lung disease in families containing people with ZZ AATD is ongoing. Funded by the **US Alpha-1 Foundation**, this follows on from two previous successful studies of families containing either MZ or SZ alpha-1 antitrypsin deficiency (AATD) members. We know from how AATD is inherited that if a person in a family is ZZ AATD, the chances of other siblings also having ZZ AATD are quite high. Taking part will involve breathing tests, a liver scan, questionnaires, and some blood tests. In this study we hope to measure to what extent lung disease is present in members of families containing at least one person with ZZ AATD, who have yet to be diagnosed or present themselves to their doctor because of lung problems. This important question remains unanswered and we hope to uncover the hidden burden of ZZ AATD in Ireland among the many families affected.



ZZ Family Study

Offering a free lung health screen to siblings of people diagnosed with ZZ alpha-1 antitrypsin deficiency.

What is the Aim of this Study?

We hope to clarify the exact risk ZZ alpha-1 antitrypsin deficiency (or ZZ Alpha-1 for short) poses to people in terms of their lung and liver health. We aim to achieve this by comparing people with ZZ Alpha-1 to their siblings who are not affected by Alpha-1.

Who can take part?

- Anyone with ZZ Alpha-1, with siblings or adult children.
- All siblings of people with ZZ Alpha-1, regardless of whether they have previously been tested.
- We are particularly keen to meet siblings who have no deficiency (ie. MM), even if they already know their status.

What is involved?

- Your family members will be offered a **free lung health screen**, very similar to that performed for you in clinic.
- This would include lung function tests, liver scans, blood tests, which will all performed on a single day by the alpha-1 doctors.
- People attending clinic regularly would likely not need any additional tests, but we would ask for access to your results for comparison.

If you, or any of your siblings/adult children would like to help us clarify the risk of ZZ Alpha-1, please contact us through any of the following methods:

- Phone: 01-8093871 (Alpha-1 Foundation Ireland)
- Mobile/text: 085-7084742
- Email: farrellemma@rcsi.com
- alpha1@rcsi.ie

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RCSI ROYAL COLLEGE OF SURGEONS IN IRELAND

If you have been diagnosed with ZZ AATD and think your family would be suitable to take part in the study, please email *alpha1@rcsi.ie* to find out more.

Raghad Alfazari, RCSI medical student

Evaluating the benefits of family screening in severe Alpha-1

Raghad Alfazari, an RCSI medical student, carried out a 6-week research project with Alpha-1 Foundation Ireland in early 2024. Raghad looked at the benefits of family screening in severe Alpha-1 by analysing health information stored on the National AATD Registry. When people join the registry, they complete a questionnaire that captures important information such as occupation and smoking or vaping history, as these are risk factors for lung disease.

Of the 261 people with severe AATD included in the study, 36.4% were diagnosed by family screening, meaning they had a sibling who was already diagnosed with severe Alpha-1. Individuals in the family screening cohort had less severe lung disease on spirometry and were less likely to have emphysema on CT scan. A large difference in lung function (FEV1% predicted) was found between ever-smokers and never-smokers, with ever-smokers having worse lung function. The odds ratio (OR) of having CT emphysema (p=0.00001) and of having combined emphysema-bronchiectasis (p=0.00001) were significant in ever-smokers.

Early identification of at-risk individuals with severe AATD through family screening would allow smoking cessation interventions, leading to a reduced risk of lung disease in this highly susceptible population.

Irish Alpha-1 Research Published in 2024

Irish Alpha-1 Research Published in 2024

1. Optimising bronchoalveolar lavage: lessons from alpha-1 antitrypsin deficiency. Malcolm Herron, Suzanne Roche, Daniel D Fraughen, Ronan C Heeney, Lasya Kanchi, Emma J Leacy, Michelle Casey, Cedric Gunaratnam, Tomás P Carroll, Mark P Murphy, Noel G McElvaney. *Thorax*. 2024 Dec 23;80(1):24–31. PMID: 39586664
2. Assessment and monitoring of lung disease in patients with severe alpha-1 antitrypsin deficiency: a European Delphi consensus of the EARCO group. Marc Miravitlles, Alice M Turner, Maria Sucena, Jean-François Mornex, Timm Greulich, Marion Wencker, N Gerard McElvaney. *Respir Res*. 2024 Aug 19;25(1):318. PMID: 39160517.
3. Alpha-1 Antitrypsin Augmentation and the Liver Phenotype of Adults With Alpha-1 Antitrypsin Deficiency (Genotype Pi*ZZ). Malin Fromme, Karim Hamesch, Carolin V Schneider, Noel G McElvaney, Alice M Turner, Christian Trautwein, Pavel Strnad, *Clin Gastroenterol Hepatol*. 2024 Feb;22(2):283–294.e5. PMID: 37716616.
4. Undiagnosed Alpha-1 Antitrypsin Deficiency and the Perpetuation of Lung Health Inequity. Oliver J McElvaney, Jon Hagstrom, Marilyn G Foreman, Noel G McElvaney. *Am J Respir Crit Care Med*. 2024 Jan 1;209(1):3–5. PMID: 37879066
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Financial Report

Alpha-1 Foundation Ireland
(A Company Limited by Guarantee and not having Share Capital)
Financial Statement
Financial year ended 31 December 2024

	2024	2023
TURNOVER	**€**	**€**
Northern Area HSE	119,568	119,568
Donations	8,424	22,426
Fundraising	- 15,000	
Other Funding	2,361	5,189
Charity VAT Compensation	651	108
Gross profit	**129,039**	**145,228**
Gross profit percentage	**100.0%**	**100.0%**
OVERHEADS		
Administrative expenses	(156,043)	(159,881)
Operating (loss)/profit	(25,039)	2,410
Operating (loss)/profit percentage	19.1%	1.5%
(Loss)/profit before taxation	(25,039)	2,410
Overheads		
Administrative expenses		
Wages and salaries	(78,705)	(74,881)
Lab costs	(11,827)	(9,189)
Conference costs	(2,594)	(1,285)
Printing, postage and stationery	(42)	(2,698)
Annual Report	(2,988)	(2,733)
Health professional education programmes	(4,000)	-
Telephone	(180)	(284)
Registry and detection programme	(41,694)	(44,883)
Education and outreach	(1,564)	(3,060)
Consultancy fees	-	(6,458)
Accountancy fees	(6,150)	(6,150)
Bank charges	(99)	(114)
General expenses	(197)	(114)
Charitable Donations – type 2	-	(5)
Subscriptions	(1,940)	(3,964)
Depreciation of tangible assets	(4,063)	(4,063)
	(156,043)	(159,881)

NOTE: Detailed financial statements are available on *www.alpha1.ie*

Acknowledgements

We would like to thank the following:

- Orla Cahalane, Ella Howard, Bríd Holohan, Rabelani Kaela, Dr. Bill Tormey and the Beaumont Hospital Chemical Pathology Department for their continued support and assistance
- Angela McBride and colleagues from the Alpha-1 Foundation (USA) for their continued support
- Dr. Ilaria Ferrarotti and Dr. Stefania Ottaviani, Centre for Diagnosis of Inherited Alpha-1 Antitrypsin Deficiency, University of Pavia, Italy
- RCSI University of Medicine and Health Sciences for their continued support
- Louise Clarke, Lucinda Feeney and colleagues in the Pulmonary Function Laboratory in Beaumont Hospital
- Jean Kirwan and Linda Phoenix, members of the Beaumont Hospital Respiratory Clinic Administration Team
- Raghad Alfazari, RCSI medical student who carried out a research project with Alpha-1 Foundation Ireland in 2024
- Health Research Charities Ireland (HRCI), the Irish Platform for Patients' Organisations, Science & Industry (IPPOSI), the Irish Lung Health Alliance, and the Irish Thoracic Society (ITS)
- President Michael D. Higgins for his continued support as patron of Alpha-1 Foundation Ireland
- A special thank you to everyone who took part in or organised awareness and fundraising events throughout the year

We would also like to thank the Department of Health and Children and the Health Service Executive for their continued financial support

We would also like to acknowledge the participation of the following hospitals;

- Beaumont Hospital
- Blackrock Clinic
- Bon Secours Hospital Tralee
- Bon Secours Hospital Dublin
- Cavan General Hospital
- Children's University Hospital, Temple Street, Dublin
- Coombe Women and Infants University Hospital
- Cork University Hospital
- James Connolly Memorial Hospital Blanchardstown
- Kerry General Hospital
- Letterkenny University Hospital
- Mater Misericordiae University Hospital, Dublin
- Mayo General Hospital
- Midland Regional Hospitals: Tullamore Mullingar, and Portlaoise
- Naas General Hospital
- Our Lady's Children's Hospital, Crumlin
- Our Lady of Lourdes Hospital, Drogheda
- Our Lady's Hospital, Navan
- Peamount Hospital, Dublin
- Roscommon County Hospital
- Rotunda Hospital, Dublin
- Sligo University Hospital
- St. James's Hospital, Dublin
- St. Luke's General Hospital Carlow/ Kilkenny
- St. Vincent's University Hospital, Dublin
- South Tipperary General Hospital, Clonmel
- Tallaght University Hospital
- University Hospital Galway
- University Hospital Kerry
- University Hospital Limerick
- University Hospital Waterford
- Wexford General Hospital


3,000 ZZ
12,000 SZ
250,000 MZ

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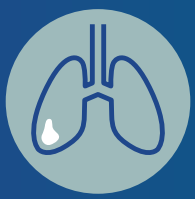
Alpha-1 Foundation Ireland Charity Code: CHY22304

Alpha-1 is the most common genetic cause of COPD

1 in 25 people in Ireland carry the faulty Z Alpha-1 gene



Smokers with the single faulty Z Alpha-1 gene have a **10 fold** increased risk of developing a lung disease called COPD

The Irish Thoracic Society estimates approximately **440,000** people have COPD in Ireland

24,500+ people tested for Alpha-1 to date in a National Targeted Detection Programme

1,000+ people with Alpha-1 attend the National Centre of Expertise for Alpha-1 at Beaumont Hospital

700+ people with Alpha-1 take part in the National Alpha-1 Registry