ANNUAL REPORT 2023

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

STAFF OF ALPHA-1 FOUNDATION IRELAND

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 2023

ALPHA-1 FOUNDATION IRELAND

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1 Executive Summary

2023 was again a busy year for Alpha-1 Foundation Ireland and the team. The biggest event was the Global Alpha-1 Research and Patient Congress hosted in Dublin in April. The last time the Congress was in Ireland was over 20 years ago. This year there were 350 delegates from 25 countries with presentations on cutting-edge research and wide-ranging information. You can read a conference report in Chapter 6. Big congratulations to all involved in its organisation.

Outreach and education continued throughout the year with talks given all over the country. These talks always increase the number of requests for tests for Alpha-1 from health care staff and new diagnoses are often made on foot of these presentations. From 2004 to end 2023, the Alpha-1 lab based in RCSI Beaumont has tested 23,500+ people with 458 diagnosed with ZZ, 5,109 with MZ and 544 with SZ. A number of rare variants have also been found.

The Alpha-1 research team, led by Professor Gerry McElvaney, continued to publish throughout 2023 and an outline is given in Chapter 7. We are learning more about Alpha-1 with new research and clinical trials ongoing. The research team in Beaumont are world experts, presenting their work at conferences both nationally and internationally and bringing hope to the Alpha-1 community.

The Alpha-1 European Alliance continued its work in 2023 with the official launch of the Alliance taking place in November. The Alliance advocates for patients on a European level lobbying for better care, access to treatment and raising awareness. Partnering with other advocacy organisations both nationally and internationally leverages our work. As well as the Alliance, we continued to engage with national groups such as Health Research Charities Ireland, Irish Platform for Patients Science and Industry, and Rare Disease Ireland to name a few.

In 2023, we welcomed Rosie Carroll to the team. Rosie is a Clinical Nurse Specialist and joined the Alpha-1 team at the end of November to carry out research and to attend the Wednesday clinic. We are delighted to have Rosie on board, a fantastic addition to Alpha-1 Foundation Ireland and the clinical team.

The end of 2023 also saw Geraldine Kelly retire as CEO from the organisation. Geraldine's tenure saw some very challenging times, particularly during the COVID-19 pandemic, and her ongoing support for patients throughout that time was absolutely crucial. More recently, Geraldine was a key organiser for the International Congress and I know she went far beyond the call of duty. I had the privilege of working with Geraldine for a short time during the handover period for the CEO job and I quickly realised I had big shoes to fill. I know the whole Alpha-1 community, the clinical and research team, and the team in Alpha-1 Foundation Ireland wish Geraldine the very best in her retirement.

Personally, I look forward to taking up the mantle and hope to represent the organisation and the community well. I'm looking forward to meeting people and forging relationships and networks in order to support the patient community. I want to thank the whole team at Alpha-1 Foundation Ireland for all their hard work and support as well as the Board of the Foundation and look forward to the coming year.

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 1,000 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 and 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 with core funding from the HSE. By the end of December 2023, the programme had tested more than 23,500 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?

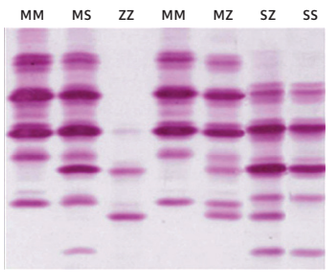


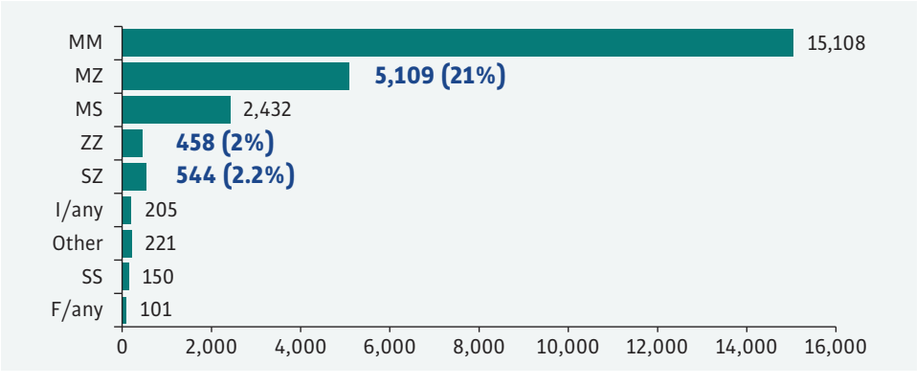
***Figure 2.2.** Typical isoelectric focusing gel for AAT phenotype identification with the most common phenotypes included.*

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 23,500 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 23,500 individuals tested.*



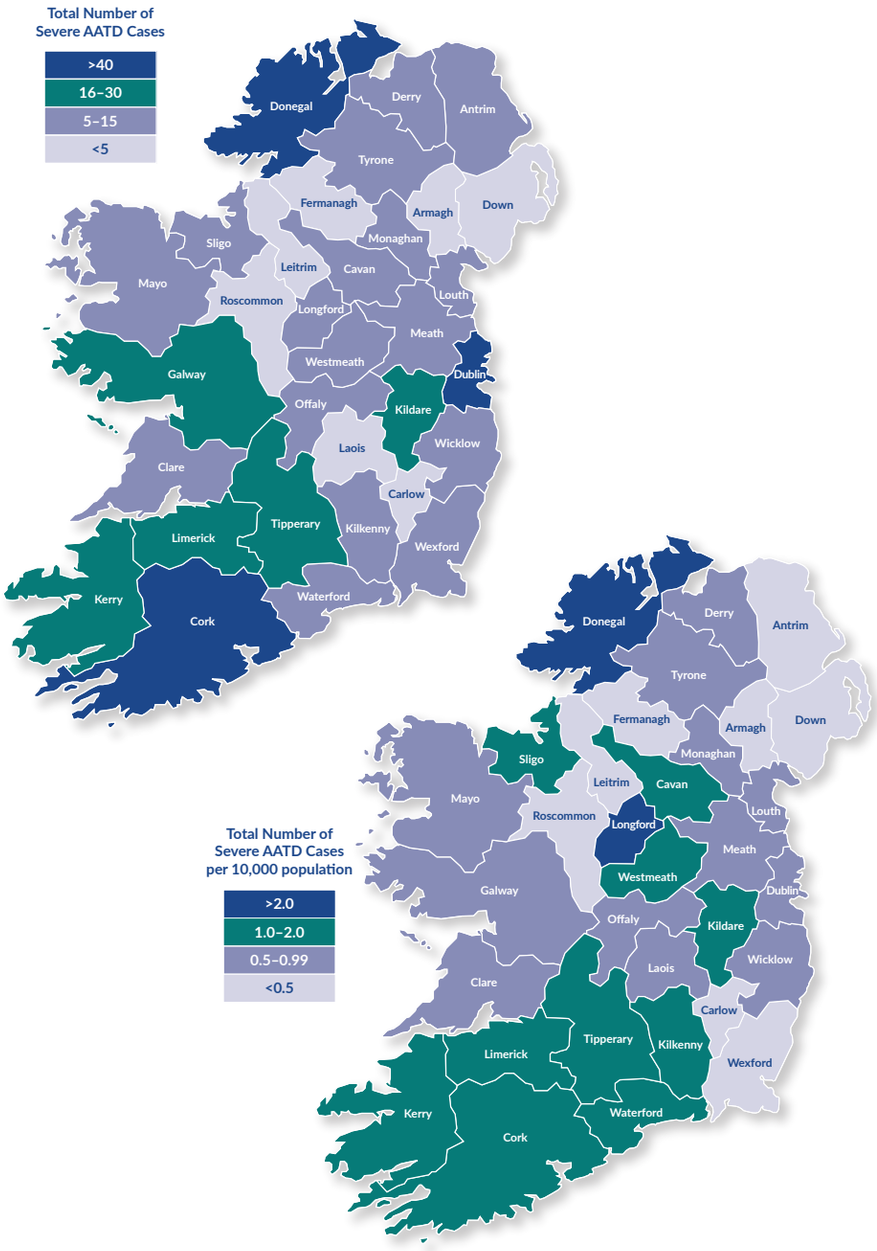
A total of 458 ZZ (severe Alpha-1) individuals have been identified, as well as 544 SZ individuals, who are also at risk of developing lung if smoking or vaping (Figure 2.3). In addition, a large number of other clinically significant phenotypes have been detected including 5109 MZ, 26 IZ, and 14 FZ. A number of rare and very rare deficiency-causing AAT mutations have also been identified. These include $M_{heerlen}$, M_{malton}, $M_{wurzburg}$, S_{munich}, and $Z_{bristol}$ and six different Null (Q0) mutations ($Q0_{bolton}$, $Q0_{cork}$, $Q0_{dublin}$, $Q0_{lisbon}$, $Q0_{porto}$ and $Q0_{amersfoort}$). The rare Q0 mutations cause no AAT protein to be produced. Two were discovered for the first time here in Ireland ($Q0_{cork}$ and $Q0_{dublin}$).

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 are given the opportunity to receive expert medical care, advice, and support. Newly diagnosed individuals 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 smoking cessation, 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 (515 cases across all 32 counties – total includes people diagnosed outside of the TDP).*
RIGHT: *Distribution of severe AATD cases adjusted per 10,000 population.*



Alpha-1 Education and Outreach in 2023

Education and raising awareness of AATD is one of our core activities. In 2023, we held seminars on Alpha-1 to a mixture of respiratory and laboratory teams in Naas Hospital, Kerry and Mayo University Hospitals, Beaumont Hospital, and St. James's Hospital. 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 the Wexford COPD Support Group. We also presented about Alpha-1 at the Irish Society of Human Genetics, the Irish Thoracic Society, and the European Respiratory Society conferences as well as attending the ANÁIL respiratory nurse meeting. We also spoke to over 100 respiratory healthcare professionals in a webinar organised by the HSE National Clinical Programme for Respiratory. 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 tests 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).

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.

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

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.

WANT TO TAKE PART?

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

Registry Update and Future Plans

At the end of 2023 a total of 685 people were taking part in the National AATD Registry (Figure 3.2) and this number is growing all the time. An improved version of the registry was launched in 2023, thanks to the hard work of Dr. Daniel Fraughen from the Alpha-1 team at Beaumont Hospital and Irish healthcare IT company OpenApp. Enhancements to the registry include new sections to capture e-cigarettes and vaping use, and a new section to capture results from **oscillometry** and **transient elastography (Fibroscan)**, two new tests that look in closer detail at the lung and liver, respectively.

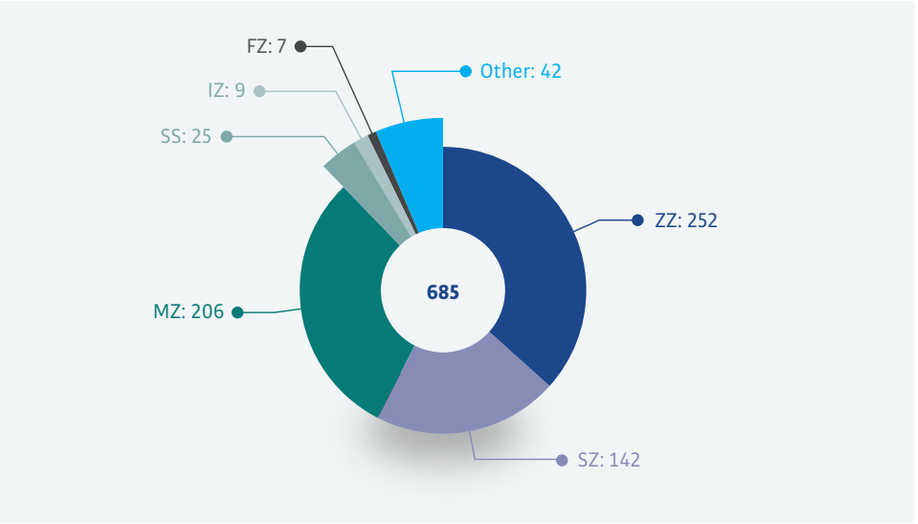


Figure 3.2. Total number of individuals enrolled in the registry according to AATD phenotype (n = 685).

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 inherited 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.

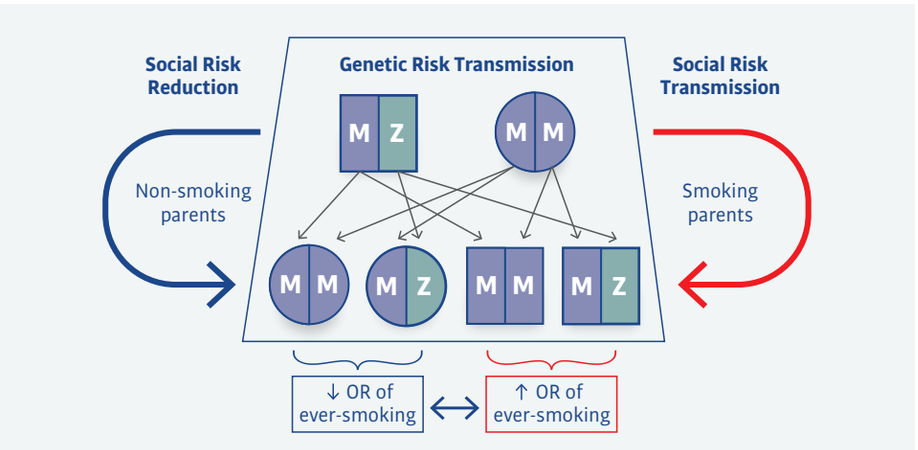


***Figure 3.3.** An example of the new knowledge generated from a survey of smoking habits in people taking part in the National AATD Registry. The diagram shows how two risk factors are inherited in families with a parent who smokes; the genetic risk of Alpha-1 (Z type) and the habit of smoking.*

Living with Alpha-1 – Declan's Story

My name is Declan. I am 71 years old and married with four adult children and five grandchildren. I am a retired psychiatric nurse. I was diagnosed with alpha-1 antitrypsin deficiency (AATD) and cirrhosis of the liver in August 2000, age 47.

My journey in life since then until I received a liver transplant in May 2016 has been interesting and at times challenging. However, the extraordinary thing was that during that period I remained in good health, free of sickness of any serious nature. The diagnosis came about purely by chance. Following an annual blood donation in 2000, I received notice from the Blood Transfusion Board to cease future blood donations as some irregularity was evident in my recent blood donation.

My GP followed this up by referring me to Professor Dermot Kelleher, consultant gastroenterologist at St James Hospital in Dublin. He investigated my bloods for suspected haemochromatosis. The results were negative for haemochromatosis but showed my alpha-1 antitrypsin (AAT) level was very low at 0.3 g/L. A subsequent liver biopsy revealed active cirrhosis of the liver with evidence of AATD. No evidence of respiratory problems was diagnosed at that juncture, and the type (genotype) was ZZ. The professor explained what the consequences of this would be eventually leading to end stage liver disease. My lifestyle would require important changes. I was a non-smoker since my late 20's but enjoyed a regular few pints of Guinness every week. I was advised to give up alcohol completely. For the following eight years, I attended St James Hospital at Prof. Kelleher's clinic for blood tests and consultation on the continued deterioration of my liver.

In 2009 I was then referred to Professor Aiden McCormick at the liver clinic in St Vincent's Hospital in Dublin. He took over the continued monitoring of my liver disease every three months at the clinic. He also referred me to Professor Gerry McElvaney and his team at the Alpha-1 clinic in Beaumont Hospital to follow up on the lung aspect of my condition. I attended this clinic every six months for pulmonary tests and other required tests. My only period of hospitalisation before the liver transplant was in 2015 in St Vincent's Hospital for a TACE procedure as tumours had formed on my liver.

On the 4th May 2016, I received a call from the liver unit at St Vincent's Hospital where a suitable donor liver was available for my transplant operation. From that day onwards, a life changing experience occurred which has impacted on every aspect of my life, both physical and psychologically ever since. Fortunately my health in the preceding years had been stable and I was reasonably fit to undergo a major operation. In the years following the liver transplant, my health and fitness have remained at a positive level.

I attend the liver clinic every six months for blood tests. I attend the Alpha-1 clinic in Beaumont Hospital every year for pulmonary tests. Last year I started to attend the local COPD support group in Mullingar, we do weekly exercise classes under supervision from a physiotherapy coach. Dr Tomás Carroll from Alpha-1 Foundation Ireland kindly came to our group last October and gave a very comprehensive talk on Alpha-1. The talk was well received as many of our group were unaware of the link between COPD and Alpha-1 Antitrypsin Deficiency.

I hope the story of my journey with AATD will give others with a similar diagnosis and the possibility of a future transplant a greater degree of positivity and confidence to travel their journey with the hope and belief that all will be well.

I am forever grateful to my GP, now retired, and all of the medical and surgical teams, especially St Vincent's liver unit and their nurse coordinators, the team at Beaumont Hospital Alpha-1 clinic and the pulmonary unit. My deepest and heartfelt gratitude to the family of my liver donor. For the liver I received in the circumstances which are unknown to me, I owe my life to that person and I treasure that gift in my body every day I live.

5 Recent Events

Marathon Challenge

In February family and friends of one of the original Alpha-1 warriors, Josephine McGuirk, completed yet another marathon challenge. The goal was to raise awareness of Alpha-1 and to fundraise for Alpha-1 Foundation Ireland. The challenge took place across Dublin, Meath and Kildare. A huge thank you to the McGuirk family, friends and everyone who supported them.

St. Patrick's Day Gala Ball for Alpha-1 in Madrid

In March, the Spanish Irish Business Network (SIBN) held a wonderful St Patrick's Day Gala Event in Madrid. The proceeds raised went to Alfa España and Alpha-1 Foundation Ireland to help continue their work raising #Alpha1Awareness in Spain and Ireland.

Global Alpha-1 Congress Hosted in Dublin

In April we co-hosted the Global Alpha-1 Patient Congress with our colleagues in the US Alpha-1 Foundation. Over 300 patient leaders, physicians and scientists from around the world visited Dublin to discuss the latest developments in patient advocacy, clinical care, research, and new treatments in Alpha-1. See Chapter 6 for more on this congress.

OSPIDÉAL SAN SÉAMAS
ST JAMES'S HOSPITAL

Alpha-1 Foundation Ireland Visits St. James's Hospital

In May Alpha-1 Foundation Ireland was invited to meet respiratory nurse and physiotherapy staff in St. James's Hospital Dublin. We discussed how Alpha-1 can cause lung and liver disease, how this risk can be reduced, how to get tested, and the high quit smoking rates seen in people with Alpha-1.

Irish Alpha-1 Research Published

In June a team of researchers from RCSI published the first review of physical activity and exercise capacity in people with Alpha-1 in the International Journal of COPD. We know that physical activity is important as it allows people to stay healthy. This is even more important for people with Alpha-1 who are susceptible to lung disease, particularly if they have ever smoked.

Alpha-1 Visits Wexford

In July we visited the Wexford COPD Support Group to talk about all things Alpha-1. Thanks to Lanie, Richard and colleagues for the warm welcome and excellent questions.

Alpha-1 Visits Mayo

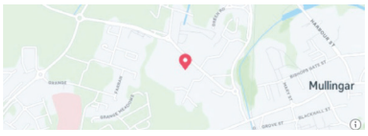
In September Alpha-1 Foundation Ireland was delighted to visit Mayo University Hospital for the first time to raise #alpha1awareness. Thanks to Rita Corcoran and Dr. Cyril Rooney for the warm Mayo welcome.

Nursing Lecture on Alpha-1 in DCU

In September Professor Ciara White, School of Nursing at DCU, gave a huge boost to #Alpha1Awareness by including content on Alpha-1 in the respiratory module taught to 2nd year undergraduate nurses.

World Lung Day Webinar

On September 25th Alpha-1 Foundation Ireland took part in a webinar for respiratory healthcare professionals. Along with colleagues from the HSE National Clinical Programme for Respiratory, the Asthma Society and COPD Support Ireland, we spoke about how patient organisations partner with healthcare professionals to provide valuable information, support, and advice as part of holistic care for people with lung diseases.



Alpha-1 Foundation Ireland Visits Mullingar COPD Group

In late October Alpha-1 Foundation Ireland visited the Mullingar COPD Support Group to talk about all things Alpha-1. Thanks to Declan and friends for the warm midlands welcome with lots of excellent questions.

Irish Alpha-1 Research Published in Top Scientific Journal

In November, an Irish study showed augmentation therapy is an effective treatment for people with lung disease caused by severe AATD (for example the ZZ genotype). The project examined over 600 people with severe Alpha-1 taking part in national registries in Ireland, Austria and Switzerland. A huge thank you to everyone who took part. Without your help this kind of valuable research cannot happen. Lead researcher & Tipperary man Dr. Dan Fraughen featured in the emerging investigator section of the issue (below) and received the best abstract award at the European Respiratory Society conference for his work.

Daniel D. Fraughen, M.B., is a respiratory specialist trainee and is currently undertaking his Ph.D. in the Royal College of Surgeons in Ireland, under the supervision of Prof. Gerry McElvaney and Dr. Tomás Carroll. His Ph.D. focuses on alpha-1 antitrypsin deficiency (AATD), which is the most common genetic cause of COPD. His most recent publication explores the effects of augmentation therapy on FEV_1 decline and survival in those with severe AATD, using a collaborative multinational approach

Augmentation Therapy for Severe Alpha-1 Antitrypsin Deficiency Improves Survival and Is Decoupled from Spirometric Decline—A Multinational Registry Analysis Pathology (page 964)

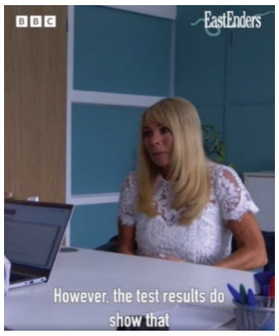
Alpha-1 Foundation Ireland Attends National Meeting

In early November Alpha-1 Foundation Ireland attended the Irish Thoracic Society annual conference in Limerick. Over 500 nurses, doctors, physiotherapists, and scientists who work in the field of respiratory medicine attend the conference. Two RCSI medical students, Mariam Ghoneem and Mohamed Abdulkadir, who worked on Alpha-1 projects earlier in 2023, presented their research.

BEAUMONT HOSPITAL

World COPD Day

November 15th was World COPD Day and Alpha-1 Foundation Ireland was invited to meet respiratory nurses and respiratory physiotherapists working in the HSE CHO9 (Beaumont) area.



Alpha-1 on the BBC - Eastenders Spoiler Alert!

Also in November Alpha-1 featured in the biggest TV show on the BBC. No surprise that a “who is the Daddy” mystery involved a certain Phil Mitchell – this might seem trivial but it was a great awareness boost. Thousands of people were Googling Alpha-1 after watching the show – even if the show writers mistakenly called the condition “AADT”.

Alpha-1 in the European Parliament

At the end of November, a delegation of Alpha-1 advocates from many different countries spoke at the European Parliament in Brussels to highlight Alpha-1 Awareness Month and the efforts of patients and policymakers as they strive for a better quality of life and greater treatment accessibility for alphas worldwide. Professor Gerry McElvaney represented Ireland at the meeting.

Alpha-1 Europe Alliance

In December Anne Marie O’Dowd represented Ireland at the inaugural meeting of the Alpha-1 Europe Alliance in Barcelona.

6 The Global Alpha-1 Congress Comes to Ireland

In November 2022 it was an immense honour for Alpha-1 Foundation Ireland to be invited to host the Global Alpha-1 5th International Research Conference and 8th Patient Congress. The event took place over three days in Dublin from 13–15 April.

Planning and preparation started in the latter part of 2022 with decisions being made on the location for the conference, the agenda, topics for discussion and potential presenters and speakers. Myself, Professor McElvaney and Dr. Tomás Carroll collaborated closely with our colleagues in the Alpha-1 Foundation in the US. It was a strong and very successful partnership. The anticipated attendance of over 350 delegates included doctors, scientists, researchers, patient leaders and patient representatives from over 25 countries. Presentation topics were decided and meetings were organised with potential speakers/presenters to discuss their valued contributions and agree timelines for submission of conference material. Patient leaders and patients were invited to attend with some limitations on numbers due to a last-minute decision by the US President, Joe Biden to visit Dublin over the same couple of days, creating a shortage of hotel rooms across the city. All decisions were made swiftly and in consultation with the team in Ireland making good use of local knowledge.

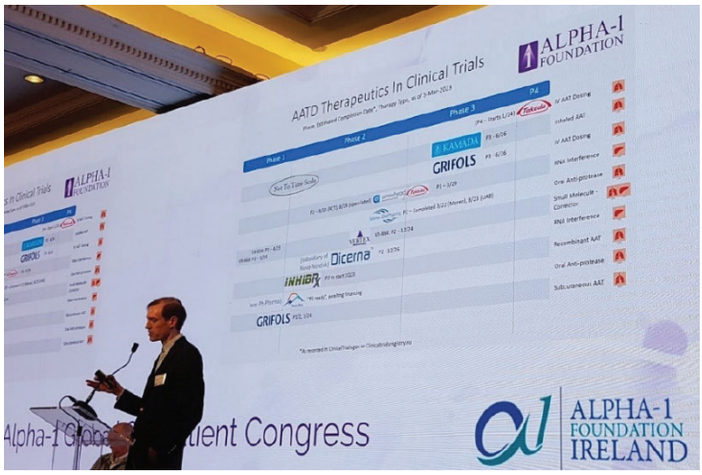
Scott Santarella, President & CEO, Alpha-1 Foundation kicks off the 8th Patient Congress.

The goal of the Research Conference is to bring the global research community together to help build partnerships with a view to sharing and improving our knowledge of Alpha-1, to share information on new treatments and ultimately to find a cure for this genetic condition. Friday was the Research Conference and it started with a welcome and introduction from Scott Santarella, President and CEO, US Alpha-1 Foundation and Professor Gerry McElvaney.

Professor Gerry McElvaney from RCSI talks about the latest Irish research on Alpha-1.

The day continued with presentations from industry sponsors, presentations on treatments for AATD associated lung disease and liver disease. The Pros and Cons of Inhaled Therapies raised a great deal of interest from the audience particularly the patients. It was great to see presentations being followed by strong audience participation in Q&A sessions.

Dr. Andrew Wilson from Boston University talks about some of the exciting new therapies being developed for Alpha-1.



The aim of the 8th Patient Congress on Saturday was to provide a platform for education, discussion and networking. There were therapeutic updates provide by many of the doctors, stories on how some countries approached their battle for augmentation therapy and their successes and challenges. There were great discussions on patient involvement in research, participation in patient registries and access to clinical trials. An excellent session focused on the importance of mental and physical wellness when dealing with the effects of Alpha-1.

Professor Frank Doyle from RCSI discusses tips for dealing with stress.

Upcoming research was discussed in great detail and it was followed by a research panel Q&A made up of nine leading AATD specialists from across the world.

Professor McElvaney chairs the panel discussion with nine leading Alpha-1 experts.

A second panel of nine patient leaders from around the world talked about the challenges faced by people living with Alpha-1 in each country, and some of the exciting new treatments being developed.

A panel of global Alpha-1 patient leaders discusses the challenges and opportunities for each country.

The newly formed European Alpha-1 Alliance presented its mission and goals and their intention to build a strong and lasting partnership with the Alpha-1 Foundation in the US, while at the same time focusing on the needs of Alpha-1 patients across Europe. Irish patients were very engaged throughout the two days, asking very relevant questions and providing strong and pertinent contributions to discussion.

Angela McBride of the US Alpha-1 Foundation and a proud Meath woman with two Irish Alpha-1 leaders, Josephine McGuirk and Orla Keane.

The Conference was a great opportunity to meet old friends and make new ones in the Alpha-1 community. It was a huge success and on behalf of Professor Gerry McElvaney, Dr. Tomás Carroll and myself I would like to thank the US Alpha-1 Foundation for choosing Ireland in 2023 and for giving us the opportunity to showcase the great work carried out by the medical team, the research team, and Alpha-1 Foundation Ireland in support of all Alpha-1 patients and their families.

Some of the Irish Alpha-1 Delegation at the Global Alpha-1 Congress.

7 Alpha-1 Research Highlights in 2023

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, questionnaires, and some blood tests. In this study we hope clarify to what extent lung disease is present in the siblings, parents and children of those 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.

Emma Farrell, MD Researcher on ZZ Family Study

If you have been diagnosed with ZZ AATD and you think your family would be interested in this study, email Dr. Emma Farrell at *farrellemma@rcsi.ie* to find out more.

Irish Alpha-1 Research Published in 2023

1. Alpha-1 antitrypsin deficiency: current therapy and emerging targets. McElvaney OF, Fraughen DD, McElvaney OJ, Carroll TP, McElvaney NG. *Expert Rev Respir Med.* 2023 Mar;17(3):191–202. PMID: 36896570
2. The effect of exacerbations on lung density in α1-antitrypsin deficiency. Strange C, McElvaney NG, et al. *ERJ Open Res.* 2023 Mar 13;9(2):00457–2022. eCollection 2023 Mar. PMID: 36923570
3. Alpha-1 Antitrypsin Deficiency and Smoking Cessation: Tackling the Burden of COPD One Test at a Time? Roche SM, Carroll TP, Fraughen DD, McElvaney NG. Chest. 2023 Apr;163(4):e197. PMID: 37031997
4. Physical Activity, Exercise Capacity and Sedentary Behavior in People with Alpha-1 Antitrypsin Deficiency: A Scoping Review. O'Shea O, et al. *Int J Chron Obstruct Pulmon Dis.* 2023 Jun 16;18:1231–1250. PMID: 37346078
5. Comprehensive Clinical Diagnostic Pipelines Reveal New Variants in Alpha-1 Antitrypsin Deficiency. Ottaviani S, Bartoli G, Carroll TP, et al. *Am J Respir Cell Mol Biol.* 2023 Sep;69(3):355–366. PMID: 37071847
6. Augmentation Therapy for Severe Alpha-1 Antitrypsin Deficiency Improves Survival and Is Decoupled from Spirometric Decline – A Multinational Registry Analysis. Fraughen DD, Ghosh AJ, et al. *Am J Respir Crit Care Med.* 2023 Nov 1;208(9):964–974. PMID: 37624745
7. Provider Education in Alpha 1 Antitrypsin Deficiency: Try Again, Fail Again, Fail Better. Roche S, Carroll TP, Mcelvaney NG. *ATS Sch.* 2023 Dec 28;4(4):396–399. PMID: 38196687
8. Altered Serum Alpha1-Antitrypsin Protease Inhibition before and after Clinical Hematopoietic Stem Cell Transplantation: Association with Risk for Non-Relapse Mortality. Brami I, et al. *Int J Mol Sci.* 2023 Dec 28;25(1):422. PMID: 38203593
9. Alpha-1 Antitrypsin Augmentation and the Liver Phenotype of Adults With Alpha-1 Antitrypsin Deficiency (Genotype Pi*ZZ). Fromme M, et al. *Clin Gastroenterol Hepatol.* 2024 Feb;22(2):283–294.e5. Epub 2023 Sep 15. PMID: 37716616
10. Testing Alpha-1 Antitrypsin Deficiency in Black Populations. Lafortune P, et al. *Adv Respir Med.* 2023 Dec 19;92(1):1–12. PMID: 38392031

Financial Report

Alpha-1 Foundation Ireland
(A Company Limited by Guarantee and not having Share Capital)
Financial Statement
Financial year ended 31 December 2023

	2023	2022
TURNOVER	**€**	**€**
Northern Area HSE	119,568	119,565
Donations	22,426	9,474
Fundraising	15,000	-
Other funding	5,189	-
Charity VAT Compensation Scheme	108	-
	162,291	129,039
Gross profit	162,291	129,039
Gross profit percentage	100.00%	100.00%
OVERHEADS		
Adminsitrative Expenses	(159,881)	(107,925)
Operating profit	2,410	21,114
Operating profit percentage	1.50%	16.40%
Profit before taxation	2,410	21,114
Overheads		
Administrative expenses		
Wages and salaries	(74,881)	(76,911)
Lab costs	(9,189)	(7,220)
Conference costs	(1,285)	-
Printing, postage and stationery	(2,698)	(1,132)
Annual report	(2,773)	(2,773)
Telephone	(284)	-
Computer cost and system maintenance	(44,883)	(9,192)
Travel	(3,060)	-
Consultancy fees	(6,458)	-
Accountancy fees	(6,150)	(6,150)
Bank charges	(114)	(107)
General expenses	(114)	(1)
Charitable donations – type 2	(5)	(371)
Subscriptions	(3,964)	(1,103)
Depreciation of tangible assets	(4,063)	(3,007)
	(159,881)	(107,925)
Profit before taxation	2,420	21,114
Tax on profit	-	-
Profit for the financial year	2,420	21,114

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

9 Acknowledgements

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- Orla Cahalane, Ella Howard, Bríd Holohan, Rabelani Kaela, Dr. Bill Tormey and the Beaumont Hospital Chemical Pathology Department for their continued support and assistance
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- 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 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

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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

23,500+ people tested for Alpha-1 to date in a National Targeted Detection Programme

900+ 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