

**α1** Alpha One  
Foundation

ANNUAL REPORT 2013

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The Alpha One Foundation is a charity dedicated to promoting awareness, increasing detection, and improving the diagnosis and treatment of Alpha-1 Antitrypsin Deficiency

#### CORE ACTIVITIES OF THE ALPHA ONE FOUNDATION



#### STAFF OF THE ALPHA ONE FOUNDATION

**Ms Kitty O'Connor**, CEO

**Dr Tomás Carroll**, Chief Scientist

**Ms Laura Fee**, Clinical Research Associate

**Professor N.G. McElvaney**, Chairman

# Alpha One Foundation Annual Report 2013

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## 1. Executive Summary

**This year marks the 50th anniversary of the discovery of Alpha-1 by Dr Sten Eriksson and Dr Carl-Bertil Laurell in Malmo, Sweden.** Their groundbreaking work led to the understanding of why lung disease develops in Alpha-1 deficient individuals. To highlight the 50<sup>th</sup> anniversary, the 4<sup>th</sup> International Alpha-1 Patient Congress took place in Barcelona in April. Four members of the Irish Alpha-1 support group attended this congress.

It is also fitting that this year the 10,000<sup>th</sup> Irish person was tested for Alpha-1 as part of the National Targeted Detection Programme, to date the only national screening programme in the world. This year there have been significant financial cutbacks to the national screening programme, however we endeavour to maintain our present level of service despite these constraints.

The 30<sup>th</sup> anniversary of the world's first successful single lung transplant also occurs this year. In 1983 Dr Joel Cooper transplanted a 58 year man suffering from pulmonary fibrosis in Toronto. In Ireland, the first single lung and first double lung transplants were both Alpha-1 recipients. With this in mind, we place a strong emphasis placed on organ donation awareness and the issue of organ donor consent. As members of the Irish Donor Network we support the move toward "soft opt out" as part of a package of measures to improve organ transplantation and donation in Ireland. This was discussed in a presentation by the Alpha One Foundation as part of the Irish Donor Network at the Oireachtas Health Committee meeting in April this year.

The Alpha One Foundation continues its active partnerships with the Medical Research

Charities Group, particularly its Rare Disease Taskforce, the Irish Donor Network, the Irish Platform for Patient Organisations, Science and Industry (IPPOSI), Irish Lung Health Alliance, the European Organisation for Rare Diseases (EURORDIS) and ALFA Europe.

The Alpha-1 support group held various fundraising events throughout the country this year. These were a tremendous success and raised much-needed funds for the Foundation. We held the Alpha-1 Chopin piano competition in the Mansion House in November 2012, with students from three universities competing for the award. We congratulate the winner Alexander Bernstein from the Royal Irish Academy of Music.

This brief overview may give you some idea of the work being done and the progress being made by the Alpha One Foundation. This work is collaborative and I wish to thank all my colleagues for their diligence and dedication throughout the year.

**Kitty O'Connor**  
CEO, Alpha One Foundation

## 2. An Update from the National Alpha-1 Antitrypsin Deficiency Targeted Detection Programme & Alpha-1 Antitrypsin Deficiency Patient Registry

### WHO SHOULD BE TESTED FOR ALPHA-1?

Guidelines from the World Health Organisation (WHO), American Thoracic Society (ATS), and European Respiratory Society (ERS) advocate targeted detection programmes for alpha-1 antitrypsin deficiency (AATD or more commonly called Alpha-1). Together these guidelines recommend targeted screening of patients with chronic obstructive pulmonary disease (COPD), nonresponsive asthma, cryptogenic liver disease and also first-degree relatives of known AATD individuals (Table 2.1).

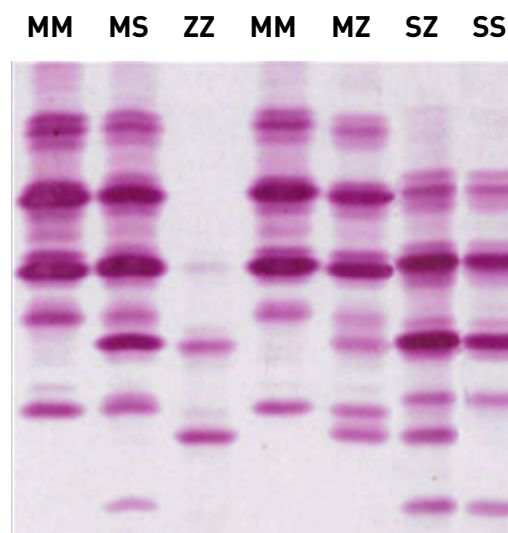
**TABLE 2.1:** ATS/ERS recommendations for diagnostic testing for AATD (type A recommendations)

ATS/ERS Recommendations for Diagnostic Testing
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 necrotising panniculitis
Siblings of individuals with AATD
Individuals with unexplained liver disease, including neonates, children, and adults, particularly the elderly

AATD can be diagnosed by a simple blood test, but unfortunately it remains vastly under-diagnosed in Ireland and worldwide. A diagnosis of AATD gives the clinician a unique opportunity for early medical intervention and the possible prevention of lung disease in both the affected individual and first-degree relatives. Unfortunately, despite huge strides in awareness and understanding of this condition, this opportunity is often missed. Large variability exists in the clinical course of lung disease in AATD and therefore all COPD patients should be tested for AATD, regardless of age or smoking history. In May 2004, a national targeted detection programme for AATD was launched by the Alpha One Foundation, based at the RCSI Education and Research Centre at Beaumont Hospital.

### HOW DO WE TEST FOR ALPHA-1?

Our principal diagnostic method analyses serum from suspected AATD individuals by isoelectric focusing (Sebia). This method, which identifies variants of alpha-1 antitrypsin (AAT) circulating in human blood, is known as "phenotyping" (Figure 2.2). It is the most accurate method of testing for AATD and identifies not only the most common but also rare AAT phenotypes.



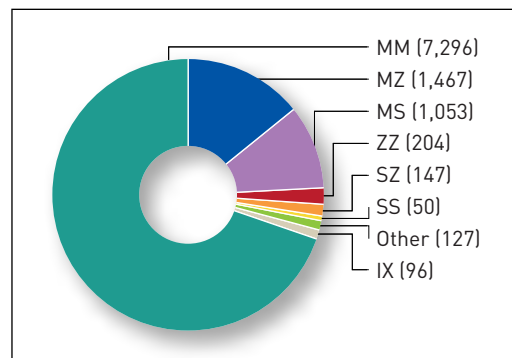
**FIGURE 2.2:** Typical isoelectric focusing gel for AAT phenotype identification with the most common phenotypes included

Since September 2010 the quantification of serum AAT by the Alpha One Foundation has been performed in collaboration with Dr Bill Tormey, Consultant Chemical Pathologist, Pat O'Brien and Emma Pentony of the Department of Chemical Pathology in Beaumont Hospital. Measurement of AAT levels is performed by immune turbidimetry on the Olympus AU4500 instrument, an automated system for plasma protein determinations. The Department of Chemical Pathology in Beaumont Hospital has attained CPA accreditation which means that AAT measurements are performed to the highest standards. In addition, the Alpha One Foundation has participated in the UKNEQAS quality assurance scheme for AAT phenotyping since 2007, achieving 100% compliance to date.

### WHAT HAVE WE FOUND IN IRELAND?

Over 10,000 individuals with COPD, asthma, and liver disease, as well as first-degree relatives of known AATD individuals have been screened in our national AATD targeted detection programme since 2004. A total of 204 ZZ (severe AATD) individuals have been identified, as well as 147 SZ (moderate AATD) individuals, who are also at risk of developing lung and liver disease (Figure 2.3). In addition, a large number of other clinically significant phenotypes have been detected including 50 SS, 1467 MZ, 14 IZ, and 8 IS phenotypes (IZ and IS are included in the IX category on the graph where X is any other variant). The percentage of deficiency variants (approximately 35%) detected has been high, even allowing for the targeted nature of screening. Rare AAT variants were also identified in the Irish population, including I, F, Z<sub>bristol</sub>, M<sub>malton</sub> and three Null variants. Further studies will reveal the risk of lung or liver disease associated with these rare variants.

**FIGURE 2.3:** AAT phenotypes identified in National Targeted Detection Programme



However, the primary outcome of the national screening programme is the opportunity to receive specialist care. Newly diagnosed individuals can avail of rapid referrals to our dedicated Alpha-1 clinic in Beaumont Hospital under the care of Professor Gerry McElvaney. In addition, family screening allows the identification of younger relatives with AATD in whom no significant lung damage has occurred. These individuals benefit from lifestyle changes such as smoking cessation and closer medical observation which can ultimately prevent or postpone the development of lung disease. In the 10 years since the screening programme began we have identified 142 new ZZ individuals. In addition, a further 62 ZZ individuals have been referred to Beaumont Hospital from other centres.

Blood samples for testing are received from over 25 hospitals in Ireland as well as from GP practices. In the Dublin area 39% of requests received are from Beaumont Hospital (Table 2.2). St Vincent's University Hospital is next, accounting for 29% of all Dublin requests.

Dublin	Requests
Beaumont Hospital	1992
St Vincent's University Hospital	1497
Bon Secours Dublin	471
Connolly Hospital Blanchardstown	382
St James's Hospital	314
Peamount Hospital	215
Mater Misericordiae University Hospital	122
The Adelaide and Meath Hospital, Dublin	114
Our Lady's Children's Hospital, Crumlin	96
St Columcille's Hospital	14
Temple St Children's University Hospital	18
Mount Carmel Hospital	3
Rotunda Hospital Dublin	3
Blackrock Clinic	3
National Maternity Hospital, Holles St	1

**TABLE 2.2:** Requests from Dublin Area Hospitals

Outside the Dublin area the largest participating centre is Cork University Hospital (CUH), responsible for 23% of test requests (Table 2.3). The second biggest centre outside of Dublin is Sligo General Hospital (20%), closely followed by Letterkenny General Hospital (18%).

Nationwide	Requests
Cork University Hospitals	948
Sligo General Hospital	819
Letterkenny General Hospital	786
Cavan General Hospital	454
Bon Secours Tralee	288
Galway University Hospitals	205
Midland Regional Hospital Mullingar	184
Our Lady of Lourdes Hospital Drogheda	104
Mid-Western Regional Hospital Limerick	100
Roscommon County Hospital	68
Midland Regional Hospital Tullamore	66
Naas General Hospital	65
Waterford Regional Hospital	60
Mayo General Hospital	17
Monaghan General Hospital	8
Louth County Hospital	3
Clane General Hospital	1
Bon Secours Galway	1

**TABLE 2.3:** Requests from Hospitals Nationwide (excluding Dublin)

In the past 12 months we have presented results from our screening programme to the respiratory and biochemistry departments in Waterford Regional Hospital and Peamount Hospital, and to third year medical students in UCD. The main aim of these presentations is to increase awareness of AATD amongst the respiratory and paramedical community.

While the respiratory teams are dealing with the patient populations most at risk due to AATD, Immunology, Biochemistry, and Clinical Chemistry Departments measure AAT levels as a routine test during normal blood investigations.

Furthermore, in an excellent example of joined-up thinking several laboratories have adopted a “red flag” system for AAT testing. This system means that if AAT concentrations are measured by a laboratory and found to be below a threshold of 1.0 g/L, an automatic “red flag” is included on the laboratory report to recommend testing for AATD (Figure 2.4). This value was found to achieve the greatest sensitivity, specificity, and cost-efficiency in the detection of deficient phenotypes in a large US study (Donato LJ et al Am J Clin Pathol. 2012). It is hoped that an electronic prompt system will lead to earlier diagnosis of AATD cases. The ultimate goal would be the adoption of this red flag system on AAT reports in every hospital in Ireland.

**FIGURE 2.4:** Example of an electronic prompt on a laboratory AAT report

Wex Western Regional Hospital BIOCHEMISTRY REPORT Tel: 061-482877/482679/482257			
PATIENT	FOUNDRY	LAB NO.	LAB NO.
		23/04/2013 u/k	23/04/2013 17:18
Serum			
Clinical Details:			
Total Protein	73	g/L	(61 - 79)
Albumin	41	g/L	(35 - 48)
Immunoglobulin-G	2.31	g/L	(5.4 - 16.1)
Immunoglobulin-A	2.32	g/L	(0.9 - 3.4)
Immunoglobulin-M	2.04	g/L	(0.5 - 2.0)
Protein electrophoresis:	See comment.		
Alpha-1-antitrypsin	0.80	g/L	(0.88 - 1.74)
(a) SPE: Decreased alpha-1 globulins.			
Serum alpha-1 antitrypsin of less than 1.00 g/L may be suggestive of alpha-1 antitrypsin deficiency and additional laboratory investigations may be undertaken in this regard. Further information on alpha-1 antitrypsin deficiency is available from the Alpha One Foundation, Beaumont Hospital, Tel 01 8093871 or www.alpha1.ie. NOTE: revised cut-off value effective January 2013.			
Alpha-1 antitrypsin is an acute phase reactant and its serum concentration will increase within days of trauma, acute infection or tissue necrosis.			

### NATIONAL ALPHA-1 ANTITRYPSIN DEFICIENCY PATIENT REGISTRY

The national Alpha-1 registry is a confidential database that records medical information from Alpha-1 individuals. Data including age, weight, gender, type of Alpha-1, lung function tests, liver function tests, lung and liver scans, and smoking history is stored on the registry.

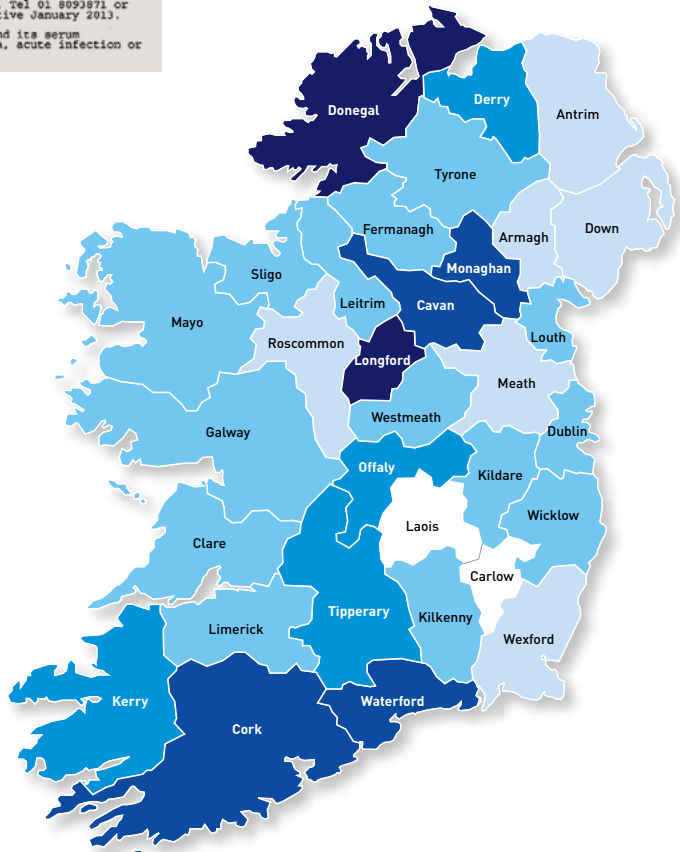
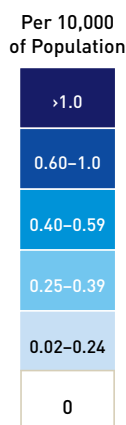
The registry is a vital research tool for studying Alpha-1. For example several questions remain unanswered. It is unknown why some Alpha-1's fare better than others, and why some Alpha-1's develop liver disease yet others do not. An active registry can help answer these questions. As well as improving our understanding of Alpha-1, an active registry can also facilitate clinical research and help to design effective clinical trials.

There are 246 Alpha-1 individuals from 29 counties in Ireland included on the registry to date. The process is ongoing and we would like to include as many Alpha-1 individuals as possible.

For queries related to the registry please contact:

**Laura Fee**, Clinical Research Associate,  
Alpha One Suite, Beaumont Hospital, Dublin 9.  
Telephone: 01-809 3702. Email: [alpha1@rcsi.ie](mailto:alpha1@rcsi.ie)

**FIGURE 2.5:** Geographical distribution of ZZ AATD cases detected per 10,000 of population (a bias may exist for some counties depending on the number of samples received for testing)



### 3. Research Studies

#### CLINICAL TRIALS

A new Alpha-1 antitrypsin intravenous augmentation therapy clinical trial will commence in the RCSI Clinical Research Centre at Beaumont Hospital in late 2013. This study will investigate the administration of different dosages of intravenous alpha-1 antitrypsin.

#### ALPHA-1 ANTITRYPSIN INHALED AUGMENTATION THERAPY CLINICAL TRIAL

Professor McElvaney and his team conducted a clinical trial looking at the safety and efficacy of inhaled alpha-1 antitrypsin (AAT) replacement therapy. This was a double-blinded study; therefore neither patients nor medical staff knows whether participants are receiving AAT (Kemada®) or placebo. **19 patients** were recruited onto this study. Recruitment for this study has now closed.

#### ALPHA-1 ANTITRYPSIN INTRAVENOUS AUGMENTATION THERAPY CLINICAL TRIAL

This study was conducted at Beaumont Hospital by Professor McElvaney and his team. This was a placebo-controlled, double-blinded, multicentre, phase III/IV study. The aim of this study is to assess the safety and efficacy of the drug Zemaira® in patients with emphysema due to Alpha-1 antitrypsin deficiency. The duration of this study is 2 years. **24 patients** were recruited onto this study. Recruitment for this study has now closed.

For further information on our clinical trials please contact the Alpha-1 research nurse, Emma Molloy on 01-8093864 or [emmamolloy@rcsi.ie](mailto:emmamolloy@rcsi.ie).

#### RESEARCH STUDIES

Emerging evidence suggests that the development of emphysema in alpha-1 antitrypsin (AAT) deficiency (AATD) is not only due to the disruption of the protease-antiprotease balance but is also caused by the absence of the important immuno-modulatory effects of AAT. For example, it is now recognised that AAT regulates the activity of white blood cells called neutrophils. Work by the RCSI Respiratory Research group has shown that AAT controls neutrophil degranulation, a process that releases toxins from compartments within the cell. Normally degranulation occurs to kill invading bacteria but if not tightly controlled by

AAT this can lead to harmful tissue damage. In addition, studies from the same group have shown that AAT can regulate the process of cell death. These results highlight the important role that AAT plays in regulating neutrophil biology.

This work is being carried out by an active and dynamic group of scientists and postgraduate PhD or MD students who have received a number of research awards over the last year. Dr Killian Hurley was awarded the William Stokes Award by the Royal College of Physicians. Ciara O'Dwyer was short-listed for the Donegan Medal competition at the Royal Academy of Medicine in Ireland annual meeting held at UCC. Dr Emmet O'Brien received the prestigious European Alpha-1 Antitrypsin Laurell Training Award (eALTA), supported by the healthcare company Grifols. This award supports basic and clinical research exploring new insights into AATD.

Another area of Alpha-1 research over the past twelve months has looked at the role of a family of regulators called 'microRNAs' and how they control AAT expression. MicroRNAs (miRNAs) are a recently discovered family of regulators that control most biological processes. Work by the RCSI Respiratory Research group has looked at how miRNAs can regulate AAT expression and have developed a new research tool to carry out these studies. This technology was filed as a PCT application in the European Patent Office in October 2012 (PCT/EP2012/070037) and was published in 'Nucleic Acids Research' in March 2013. We have used this technology specifically to understand the biology of AAT in more detail however, it can be used more widely in biological research. Based on its broader applications Science Foundation Ireland has funded a project to develop this technology via a Technology Innovation Development Award (12/TIDA/B2265).

We have been developing our expertise in studying miRNAs using cystic fibrosis as a model and have extended these studies into Alpha-1 by performing basic science and clinical research studies to investigate miRNA behaviour in monocytes from ZZ AATD individuals. This work has been presented in poster format and as an oral presentation at various local, national and international conferences (Irish Thoracic Society Meeting October 2012 and American Thoracic Society Conference May 2013 Philadelphia, U.S.A).



## 4. Organ Donation

### STEPHEN'S STORY

My name is Stephen Smith, I'm 34 years old. I've been married since 2009 and live with my wife Rachel in Cavan. I've been on the waiting list for a double lung transplant since 23 June 2010. I started to feel sick when I was just 25. At first I thought it was just asthma as I was suffering from shortness of breath playing Gaelic football initially. I spent the next few months going from my own GP, to various consultants before being diagnosed with emphysema. My emphysema was uncommon for someone my age considering I've never smoked in my life. The underlying cause of my illness was a mystery and eventually I was diagnosed with Alpha-1 Antitrypsin Deficiency. Of course I had no idea what it meant or how I'd gotten it until it was explained to me by Professor McElvaney and Kitty O'Connor of the Alpha One Foundation. Alpha-1 is a genetic condition that can affect the lungs and the liver. It is commonly referred to as genetic emphysema. 1 in 25 Irish people are carriers for Alpha-1, making it the second most common genetic lung disease after cystic fibrosis. The first single-lung and the first double-lung transplants in Ireland were in Alpha-1 patients.



Before I was diagnosed I worked 5 days a week driving patients to and from dialysis in Cavan, I played Gaelic and soccer and trained 3 or 4 days a week, I had a very active social life, and I could travel abroad on holidays. In the last 5 or 6 years I've had to give up work, give up playing all sport which I loved, and give up going out socially for fear of infection. This condition doesn't just affect me but it affects my whole family. I have received 8 transplant calls since 2010, the last one in July 2013. Each time the organs weren't usable and we were sent home to wait for the next call. Each time we hope that the next one is THE call which will hopefully give me back some quality of life.

Like all the hundreds of others awaiting transplants in Ireland, I need a donor and although nobody likes to think of a loved one becoming a donor, it is without a doubt the greatest gift you could give another person. I can personally speak of the selfless act of organ donation since my own aunt donated her organs in 2011 and saved 3 lives in the process. It was always her wish, in the event of such a tragedy, that her organs be donated and her family were happy to carry out her wish after she passed. Without brave people like her, people like me and others will not get the life saving gifts we so desperately need.

Thank You,  
Stephen

### A GUIDE TO SOME KEY TERMS

#### Organ Donor Consent

Transplantation is primarily an intervention that is made when other options are exhausted. In time, new therapies and treatment and improved health may reduce the need for transplantation,

but this is not likely to happen in the immediate future, and it is predicted that the pressure is set to increase for more kidney, lung, liver, heart and pancreas transplants. Transplantation can extend and significantly improve the quality of life, even when taking account of the risks and

possible adverse events always associated with such surgery. Transplantation can also in part be justified from an economic as well as an ethical/medical perspective.

About 30,000 transplant operations were carried out in Europe in 2012 as advances in medical treatment keep people alive who previously would have died at a much earlier age. However, the figures for organ donation are stark. Only 10 per cent of people who need a new organ in Europe will eventually get one.

### **Present Position in Ireland**

Ireland presently has an opt in/explicit consent position. If you wish to become an organ donor after your death, potential donors are advised to inform their next of kin of their intentions and to carry an organ donor card. In Ireland Next Of Kin (NOK) are always asked for consent in order for a donation to proceed. In Ireland, consent is not presumed, even if a donor card has been signed. The Irish Government is committed to introducing an opt-out approach as part of the forthcoming Human Tissue Bill.

### **Opt-out**

The person is considered to have consented to donate his or her organs after death, unless he or she has specified otherwise (see hard and soft approaches below).

### **Opt-in**

The person explicitly consents to donate his or her organs. Where the deceased has not made a decision his or her family may do so.

### **'Hard' and 'Soft' Presumed Consent**

In recent years the concept of 'hard' and 'soft' opt-out has entered into the discussion and practice on organ donation. In this context 'hard' and 'soft' indicates how much weight is placed on the views of Next of Kin (NOK).

'Hard' equals no consideration of NOK agreement to organ donation and 'soft' equals significant consideration of NOK views. There are very few countries that operate a 'hard' opt out approach, even those such as Austria that profess to do so. NOK are almost always consulted about organ donation.

### **What is the present rate of organ donation in Ireland?**

In recent years, Ireland has maintained a fairly positive but fluctuating rate of organ donation by international standards. In 2011 for example, there were 93 deceased organ donors in Ireland, representing a deceased organ donor rate of 20.67 per million of population. As a result, Ireland was in 10<sup>th</sup> place, out of a total of 31 European countries covered by the Council of

Europe organ donor table. However it should be noted that in the same year (2011) four countries: Spain, Croatia, Belgium and Malta had a deceased organ donor rate of around 30 per million population or more, a figure that should become a benchmark to which Ireland could aspire.

In short, the rate of organ donation in Ireland could be significantly higher than at present compared with other countries.

### **The Position in Ireland**

An external review of transplant services in Ireland commissioned by the National Organ Donation and Transplantation Office (NODTO) in 2011 identified systemic issues that need to be addressed in intensive care units throughout the country. They provided 10 recommendations including the need for an enhanced procurement organisation and the placement of key donation personnel (Donor Coordinators) in intensive care units throughout the country. The need for adequate resources and mandate for the NODTO and the need for a national organ donor registry has also been identified as an issue by patient groups in the Irish Donor Network.

The NODTO has indicated that the following targets are achievable for Ireland if the infrastructure is improved and soft opt-out is introduced;

- Increase deceased organ donation rates from 18ppm to 24ppm
- Increase living renal transplant rate to 30% of deceased donation
- Increase heart donation conversion rates from 13% to 25%
- Increase lung donation conversion rates from 16% to 35%
- Establish a deceased cardiac donation (DCD) programme

### **IN CONCLUSION:**

The Irish Donor Network (of which the Alpha One Foundation is a member) supports the move to soft opt out as part of a package of measures to improve lung transplantation and donation in Ireland. The package of measures would include for example:

- The appointment of organ donor coordinators in major ICU hospitals
- Setting a target for lung donation conversion rates
- A national donor registry to allow people to opt in and out of organ donation
- Better investment in organ donor awareness.

## 5. Recent Events

### ANNUAL ALPHA-1 PATIENT CONFERENCE OCTOBER 2012

The Annual Alpha-1 Patient Conference took place in October 2012 in the Marino Institute of Education. We were delighted to welcome Ronnie Delany, Olympic gold medallist and honorary RCSI fellow to open our meeting. Some of the speakers included Dr Frank Doyle, Lecturer in Psychology, RCSI; Eibhlín Mulroe, CEO, Irish Platform for Patients' Organisations, Science and Industry and Michelle O'Brien, Physiotherapist, Pulmonary Rehab St Michael's Hospital in Dun Laoghaire. The Alpha-1 Support Group presented a cheque for €7,500 to Asistec for the purchase of a -80 degree freezer for the storage of Alpha-1 samples.

*Alpha-1 Support Group  
presenting cheque*



*Ronnie Delany opening  
the Alpha-1 Conference*



### TABLE QUIZ IN TIPPERARY, NOVEMBER 2012

For the second time Harry English from Ballyporeen in County Tipperary held a very successful table quiz in November 2012. This event raised a staggering €3,400 for the Foundation. A big thanks to Harry and all the organisers of this event.

*John O'Brien (organiser),  
Harry English & Billy  
Macken (Quizmaster)*



### CHRISTMAS CARDS, DECEMBER 2013

We had another successful year with our special Alpha One Foundation Christmas cards. Thanks to everyone who bought the cards. This year more Christmas cards will be on sale, please contact the Alpha One Foundation or check our website for details.



### ALPHA-1 CHOPIN AWARDS NOVEMBER 2012

The Annual Alpha-1 Chopin Awards took place in the Mansion House in November of last year. Three students competed for a bursary of €1,000, Alexander Bernstein from the Irish Royal Academy of Music; Adam McDonagh from Dublin Institute of Technology; and Michelle Cooke from Cork Institute of Technology. Alexander Bernstein was a deserving winner of the prestigious award. The competition judges were Anthony Long, General Manager of the RTE Concert Orchestra and Florence Ryan pianist and teacher, who has frequently performed with the National Symphony Orchestra.



*Anthony Long, Florence Ryan, Prof. Gerry McElvaney,  
Alexander Bernstein (winner), Deputy Lord Mayor  
Councillor Clare Byrne & Kitty O'Connor*

### ORGAN DONOR AWARENESS WEEK, MANSION HOUSE, MARCH 2013

The launch of Organ Donor Awareness week took place in March this year. Two Alpha-1 patients Stephen Smith and Harry English attended this event in the Mansion House. Stephen spoke about his experience of waiting on a transplant list for the past 3 years.

*Stephen Smith at the launch of Organ Donor Awareness Week*



*Megan English, Joe Duffy, Harry English and Mary-Pat English*



*Mary Keane, Orla Keane, & Kitty O'Connor*

### **WEDDING FAVOURS AND COFFEE MORNING IN MAYNOOTH, JUNE 2013**

Many thanks to a newlywed couple from the west of Ireland who kindly gave a donation from their wedding favours to the Alpha One Foundation. Also congratulations to Orla Keane who organized a coffee morning in Maynooth and raised €700 for the patient support group.

### **FEDERATION OF EUROPEAN ACADEMIES OF MEDICINE, SPRING CONFERENCE, MAY 2013**

Orla Keane an Alpha-1 patient spoke at the FEAM meeting and gave the patients' perspective of personalized medicine and her personal experience of participating in a clinical trial.

*Dr Tomás Carroll and Orla Keane*



*Orla Keane and friends attending a coffee morning for Alpha-1 in Maynooth*

### **A FOCUS ON PATIENT COMPLIANCE AND ADHERENCE - IPPOSI ROUNDTABLE MEETING, JUNE 2013**

IPPOSI held a roundtable meeting entitled 'A Focus on Patient Compliance & Adherence in 2013'. This meeting highlighted the background psychology of non-compliance, the economic and health risk of prescribing therapies that are taken sub-therapeutically, the payers perspective and how future technologies might address these issues. The meeting was attended by the Secretary General of the Department of Health, Dr Ambrose McLoughlin. Kitty O'Connor from the Alpha One Foundation highlighted the patients' perspective on compliance and adherence. There was a broad consensus that the issue was extremely complex but that if tackled from different angles there were wider benefits for the health of the nation.

### **SCOIL NAISIÚNTA NA SRONAILLE, CO. TIPPERARY, JUNE 2013**

The 5<sup>th</sup> and 6<sup>th</sup> class of Shronell National School in Co. Tipperary made their confirmation in May 2013 and kindly donated €75 to the Alpha One Foundation. This was a very generous and thoughtful gesture by the students.

### **FLORA WOMAN'S MINI MARATHON, JUNE 2013**

A big thank you to all ladies who participated in the Flora Women's Mini Marathon this year. This was a great day out and raised valuable funds for the Foundation and the screening programme. If you wish to participate in next year's mini marathon, t-shirts and sponsorship cards are available from the Foundation, just call 01-8093871 or email [alpha1@rcsi.ie](mailto:alpha1@rcsi.ie).

## 6. Delegate Report from the 4<sup>th</sup> International Alpha-1 Patient Congress, Barcelona, April 2013

The 4<sup>th</sup> International Alpha-1 Patient Congress and International Research Conference on Alpha-1 Antitrypsin Deficiency took place in Barcelona in April this year. We were privileged to be asked to attend as Country delegate and patient representing the Alpha One Foundation in Ireland. This gave us the opportunity to mingle with patients, doctors and scientists with expertise in Alpha-1 Antitrypsin Deficiency.

The Research Conference focussed on the Alpha-1-related liver disease and invited expert scientists from some 20 countries worldwide to update and discuss their ongoing research. It was evident that much research is taking place in each country and the conference offered us the opportunity to hear about observations and findings through the various country representatives. In future, the conference will act as a forum for the exchange of ideas between researchers worldwide.

As you are already aware, 2013 is the year in which the Alpha One Foundation celebrates 50 years since the discovery of Alpha-1 by scientist Sten Eriksson who was also present at the conference. Over the two days, we heard about the research carried out since its discovery and had some valuable feedback and perspective from patients on the various interventions and treatments they have undergone and the benefits they have derived from them. It was also clear that the Patient Groups in each country shared common goals and each had five key objectives, namely: 1. Raising Awareness, 2. Support and Information for Patients and Families, 3. Augmentation Therapy (clinical trial results and lobbying), 4. Early Diagnosis of Alpha-1, and 5. Scientific Research

For the purposes of this report, we would like to share with you a number of topics or messages that particularly resonated with us during the conference, namely Augmentation Therapy, Registries, and Alpha - Self Care.

### **Augmentation or Replacement Therapy:**

Consists of weekly infusions of a human plasma based product. In the United States replacement therapy became available in 1986 following small limited research studies. The biochemical efficacy of replacement therapy is still being investigated by European countries. It was also reassuring to learn that there are many more

therapies being researched including Gene Therapy, Gene Correction, Cell Therapy and Inhaled and Intravenous Replacement therapy.

**Registries:** The challenge facing the Alpha One Foundation is to gather data to support the effectiveness of this expensive therapy and to lobby the various country Health representatives to gain support for the treatment. This is an on-going process. Trials and studies are taking place but take time. Countries also need to build up their registries of Alphas to be able to provide data on numbers of Alphas and demonstrate the occurrence of the disease within each country. Alpha One Foundation in Ireland is doing well in this area and has specifically targeted health providers to educate them on the importance of testing patients presenting with certain symptoms and in addition have encouraged Alphas to have family members tested which has added considerably to the registry.

**Alpha – Self Care:** Doctors at the conference provided some practical advice around patient self-care and nutrition. One of the key messages to all Alphas who currently smoke or passively smoke was to quit smoking and ensure that your living environment is free from smoke. They also highlighted the importance of exercise to maintain fitness, muscle strength and conditioning. This in turn contributes to improved breathing, positive mental health and quality of life.

We were also inspired by Dr Fedon Lindberg's talk on nutrition. He advocates the Mediterranean diet which is rich in vegetables, fruit, beans, nuts, seeds, healthy fats such as olive oil, while low in salt and sugar (the main culprits which cause inflammation in the body).

We hope this short report serves to provide you with a brief insight into the conference this year. This conference was a wonderful opportunity for patients, doctors and scientists to come together to share first hand health experiences, observations, expertise and research about a disease close to their hearts and was a very definite step closer to achieving our common goal to discover a cure for Alpha-1 Antitrypsin Deficiency.

*Report by: Fidelma Furey (Country Delegate), Martin Furey (Alpha-1 Patient). Also attended by Orla Keane and Josephine McGuirk (Alpha-1 patients).*

## 7. Acknowledgements

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- Galway University Hospitals
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- Letterkenny General Hospital
- Louth County Hospital, Dundalk
- Mayo General Hospital
- Monaghan General Hospital
- Midland Regional Hospital, Mullingar
- Midland Regional Hospital, Portlaoise
- Midland Regional Hospital, Tullamore
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- Peamount Hospital, Dublin
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- Rotunda Hospital, Dublin
- St Columcille's Hospital, Loughlinstown
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- St Vincent's University Hospital, Dublin
- Sligo General Hospital
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- Waterford Regional Hospital

## TIMELINE: 50 YEARS OF ALPHA-1

- 1963** Alpha-1 Antitrypsin Deficiency discovered by Swedish researchers Dr Carl Bertil-Laurell and Dr Sten Eriksson
- 1967** Enzyme called neutrophil elastase emerges a likely cause of emphysema in humans
- 1969** First description of liver disease associated with Alpha-1
- 1970's** Alpha-1 shown to block lung destruction caused by neutrophil elastase; finding that cigarette smoke renders alpha-1 protein inactive
- 1982** Z and S mutations in Alpha-1 gene discovered
- 1983** First successful single lung transplant
- 1986** First successful double lung transplant / First Alpha-1 lung transplant
- 1989** US National Heart, Lung, and Blood Institute (NHLBI) begins 7 year longitudinal study to understand the natural history of Alpha-1
- 1991–1995** Alpha-1 Association; Alpha-1 Foundation and Alpha Net are established in the United States
- 1993** Ireland's first liver transplant
- 2001** The Alpha One Foundation Ireland is established
- 2003** American Thoracic Society/European Respiratory Society 'Standards for the Diagnosis and Management of Individuals with Alpha-1' published
- 2004** Irish National Screening Programme for Alpha-1 Antitrypsin Deficiency commenced
- 2004** Ireland is the first country in the world to ban smoking in the workplace
- 2004** 2nd International Alpha-1 Patient Congress takes place in Dublin
- 2005** Irish Government introduces Disability Act – provides protection against genetic discrimination in Ireland
- 2005** First Irish single lung transplant (performed in Alpha-1 patient)
- 2005** Clinical trial for intravenous replacement therapy commenced in Alpha-1 Centre in RCSI Beaumont
- 2006** First Irish double lung transplant (performed in Alpha-1 patient)
- 2009** First national Alpha-1 clinic commenced on weekly basis in Beaumont Hospital
- 2011** Clinical trial for inhaled replacement therapy in Alpha-1 commenced in Alpha-1 Centre in RCSI Beaumont
- 2012** Irish research demonstrates Alpha-1 has anti-inflammatory properties
- 2012** Two new Null mutations discovered in Ireland
- 2013** 50th anniversary of the discovery of Alpha-1

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