

Incidence and outcomes of pulmonary hypertension in the Ireland

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ABSTRACT

Introduction Pulmonary hypertension (PH) is a progressive disease of the pulmonary vasculature, which is characterised by premature morbidity and mortality. The aim of this study is to define the characteristics of PH in the national PH unit (NPHU) in Ireland between 2010 and 2020.

Methods Cases of PH which were referred to the NPHU between 2010 and 2020 were included. PH was defined as a mean pulmonary artery pressure ≥ 25 mm Hg at right heart catheterisation.

Results Four hundred and fifteen cases of PH were identified during the study period. Group 1 pulmonary arterial hypertension (PAH) accounted for 39% (n=163) of cases, with a calculated annual incidence of 3.11 per million population (95% CI 1.53 to 4.70). The leading PAH subgroup was connective tissue disease-associated PAH (CTD-PAH), which was responsible for 49% of PAH referrals. This was followed by idiopathic PAH, with an estimated annual incidence of 0.63 cases per million population. The mean age at PAH diagnosis was 56 ± 15 years and 86% (n=111) received double-combination or triple-combination therapy within the first 12 months of diagnosis. The 1-year, 3-year and 5-year transplant-free survival for PAH was 89%, 75% and 65%. This was significantly lower for individuals with CTD-PAH relative to other PAH subgroups ($p < 0.05$).

Discussion This study describes the incidence and outcomes of PH in Ireland. While the outcomes are comparable to other centres, the incidence of PAH and specific subgroups appears low, suggesting that improved disease awareness and case recognition are required. Furthermore, the survival of individuals with CTD-PAH is poor and requires additional exploration.

INTRODUCTION

Pulmonary hypertension (PH) is a heterogeneous disease of the pulmonary circulation, with an estimated prevalence of 1% of the global population.^{1 2} The clinical classification of PH categorises PH into five groups based on the underlying aetiology. These include group 1 pulmonary arterial hypertension (PAH), group 2 PH due to left heart disease, group 3 PH due to lung disease and/or hypoxia, group 4 PH caused by pulmonary vascular obstructions such as chronic thromboembolic PH (CTEPH) and group 5 PH with

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Pulmonary arterial hypertension (PAH) is a progressive disease of the pulmonary circulation, with an estimated annual incidence between 5.8 and 13.7 cases per million population.

WHAT THIS STUDY ADDS

⇒ This study addressed the paucity of data regarding the clinical characteristics of pulmonary hypertension (PH) in Ireland and provided insights into the incidence and outcomes of PH in the preceding decade.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The incidence of PAH and specific subgroups appears low, suggesting that improved disease awareness and case recognition are required. Furthermore, the survival of individuals with CTD-PAH remains poor and requires additional exploration.

unclear and/or multifactorial mechanisms.³ A diagnosis of PH requires right heart catheterisation (RHC) and evidence of an mean pulmonary artery pressure (MPAP) ≥ 25 mm Hg. However, the haemodynamic definition is evolving and this threshold will be reduced to >20 mm Hg in forthcoming guidelines.³

There is a paucity of information regarding the characteristics of PH in Ireland. A study of incident, treatment naïve subjects with idiopathic PAH (IPAH), hereditary PAH (HPAH) and anorexigen-associated PAH diagnosed in Ireland and the UK between 2001 and 2009 revealed an estimated annual incidence of 1.1 cases per million population.⁴ These individuals typically presented with severe functional and haemodynamic impairment. The median age at diagnosis was 50 years and the 1-year, 3-year and 5-year survival was 92.7%, 73.3% and 61.1%.⁴ Since then, there has been no published data regarding the characteristics of PAH in Ireland, despite considerable advances in the field. Our understanding of the pathobiology, pathophysiology and epidemiology of PAH has evolved in recent years.⁵ Similarly, treatment options have expanded



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and PH has become a paradigm for a successful approach to rare respiratory diseases.⁶ The transforming landscape of PH will have implications for disease incidence and patient outcomes.

In the UK and Ireland, PH care is centralised, and patients must be referred to one of nine centres to receive a diagnosis and treatment with PH-specific therapy. The eight specialist PH centres in the UK are audited annually, resulting in contemporary information on PH epidemiology and survival. However, this is not the case in Ireland, as there is no formal national registry. Therefore, the objective of this study is to determine the characteristics of PH attending the national PH unit (NPHU) in Ireland between 2010 and 2020, with special consideration of incidence and outcomes.

METHODS

Cases of PH which were referred to the NPHU between 2010 and 2020 were included in this study. The NPHU was established in Dublin, Ireland in 2003 and is one of nine specialised PH centres between Ireland and the UK. It is the only PH referral centre in the Ireland. As the prescription of PH-specific therapy is restricted, all suspected cases of group 1 PAH and group 4 PH that are potentially amenable to these therapies should be referred and reviewed in the national centre. However, not all cases of group 2 or group 3 PH are typically referred to the NPHU as the PH-directed interventions are limited.

For study inclusion, RHC and evidence of a MPAP ≥ 25 mm Hg were required. Exclusion criteria included prevalent PH cases and cases with inadequate information. Inadequate information was defined as the availability of less than 50% of key parameters including WHO functional class (WHO FC), B type natriuretic peptide (BNP), 6 min walk distance (6MWD), RHC data, treatment characteristics and survival information. Information was collected from hospital charts and the electronic IT system. Patient demographics and clinical characteristics including FC, BNP, RHC parameters and lung function represent those performed at the time of PH diagnosis. Treatment characteristics refer to prescriptions within the first 12 months following diagnosis. The annual incidence was derived using population estimates from the central statistics office and the national census of the Ireland, which reported a population of 4 757 976 persons in 2016.^{7,8} The European Society of Cardiology/European Respiratory Society 2015 guidelines and risk stratification table are used in clinical practice.⁹

Statistical analysis was performed using GraphPad online statistical software. Continuous variables were expressed as mean \pm SD and categorical variables as n (%). Median values and the IQR were used when the variables were not normally distributed. An unpaired t test was used to calculate the significance between means and a CI of 95% was chosen.¹⁰ A value less than 0.05 was considered statistically significant ($p < 0.05$). Survival estimates were

made using the Kaplan-Meier method, with comparisons performed by the log-rank test.

RESULTS

Study population

Four hundred and fifteen cases of PH were referred to the NPHU between 2010 and 2020 (online supplemental figure 1). The estimated annual incidence of PH during this period was 7.93 per million population (95% CI 5.40 to 10.46). Group 1 PAH accounted for 39% (n=163) of these cases. This was followed by group 2 PH (16%, n=69), group 4 (16%, n=67), group 3 (9%, n=39) and finally group 5 (6%, n=23). The remaining 13% (n=54) were defined as PH of mixed aetiology, as they could not be isolated to a single diagnostic group (table 1).

The calculated annual incidence of PAH was 3.11 per million population (95% CI 1.53 to 4.70). Within group 1, connective tissue disease-associated PAH (CTD-PAH) was the predominant subtype (49%, n=80), followed by IPAH (20%, n=33) and congenital heart disease-associated PAH (CHD-PAH) (13%, n=22) (table 2). The calculated annual incidence of PAH-CTD was 1.53 per million population (95% CI 0.42 to 2.64). The estimated annual incidence of IPAH was 0.63 per million population (95% CI -0.08 to -1.34), of drug-associated PAH was 0.06 per million population, of HPAH was 0.04 per million population and of CHD-associated PAH was 0.63 per million population (table 3).

Of the 80 subjects with CTD-PAH, 81% (n=65) had a diagnosis of systemic sclerosis, 15% (n=12) had mixed CTD, 3% (n=2) had systemic lupus erythematosus and 1 case was classified as undefined. The calculated incidence for CHD-PAH does not reflect the true incidence of this specific subgroup, as these patients are not consistently referred to the NPHU, and is typically managed separately in adult congenital cardiology clinics.

The mean age at PAH-CTD diagnosis was 64 \pm 11 (median 66) years and 56 \pm 17 years (median 61) for IPAH. Individuals with IPAH demonstrated a mean BNP of 268 ng/L (SD \pm 295), 6MWD of 392 m (SD \pm 137) and 73% were stratified as intermediate or high risk at diagnosis (table 2).

The pulmonary vascular resistance was significantly higher in patients with group 1 PAH relative to groups 2, 3, 5 PH and those with mixed disease ($p < 0.05$), but not group 4 PH ($p = 0.27$). Additional patient characteristics are described in table 1 and table 2. Reducing the diagnostic threshold of PH from a mPAP threshold of > 25 mm Hg to > 20 mm Hg identified an additional 18 cases (7 with group 2 PH, 5 with CTEPH and a further 6 with PH of mixed aetiology).

Treatment

Sixty-eight per cent (n=111) of subjects with PAH received combination therapy in the first 12 months following diagnosis. Triple combination therapy regimens included oral or nebulised prostacyclin and were prescribed in

Table 1 Overview of characteristics of individuals diagnosed with pulmonary hypertension in the NPHU between 2010 and 2020

	Group 1	Group 2	Group 3	Group 4	Group 5	Mixed
Subjects, n	163	69	39	67	23	54
Sex: female n (%)	125 (77)	45 (65)	20 (51)	29 (43)	9 (39)	26 (48)
Age (years): mean±SD	56±15	69±10	64±13	61±16	57±13	64±11
WHO functional class: % I/II/III/IV	1/29/56/14	1/26/49/22	0/15/56/28	1/28/64/7	0/22/74/4	0/22/61/17
BNP (ng/L): median (IQR)	172 (57–570)	366 (234–826)	117 (41–468)	128 (62–451)	90 (45–183)	225 (78–860)
Right heart catheterisation						
mRAP (mm Hg)	9±6	11±6	6±3	9±5	8±6	11±6
mPAP (mm Hg)	46±15	42±12	39±11	44±9	39±12	40±12
PAWP (mm Hg)	11±5	20±7	10±5	11±4	12±6	15±7
CO (L/min)	4±1	5±1	4±2	4±1	5±1	4±1
PVR (WU)	10±7	5±3	7±4	9±4	6±5	7±5
DLCO, % predicted	49±23	46±15	35±14	67±13	42±18	41±16
PH therapy within 12 months of diagnosis: n (%)	148 (91)	33 (48)	29 (74)	54 (81)	17 (74)	35 (65)
Monotherapy	37 (23)	29 (42)	23 (59)	38 (57)	8 (35)	26 (48)
Double combination therapy	88 (54)	4 (6)	5 (13)	15 (22)	7 (30)	7 (13)
Triple combination therapy	23 (14)	0	1 (3)	1 (1)	2 (9)	1 (2)
Balloon atrial septostomy	3 (2)	0	0	0	0	0
Lung transplantation	5 (3)	0	2 (5)	0	1 (4)	0
Survival*						
1-year, 3-year and 5-year survival, %	89, 75, 65	94, 88, 75	66, 33, 14	93, 79, 64	100, 75, 75	89, 71, 64
Median follow-up (IQR): years	3 (1–5)	2 (1–4)	1.5 (1–3)	3 (2–5)	2 (1–3)	3 (1–4)

FC, BNP, RHC parameters and lung function were collected at diagnosis. WHO FC was available for all 415 patients. Of note data were incomplete for the following parameters: BNP not available for 12%, mRAP in 39%, mPAP in 9%, PAWP in 19%, CO in 46%, PVR in 54% and DLCO in 52%.

Survival data were available for 19 (86%) individuals with CHD-PAH.

BNP, B-type natriuretic peptide; CO, cardiac output; DLCO, diffusion capacity for carbon monoxide; mPAP, mean pulmonary artery pressure; mRAP, mean right atrial pressure; PAWP, pulmonary artery wedge pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance.;

Table 2 Characteristics of pulmonary arterial hypertension subgroups at the time of diagnosis, with a specific focus on demographics and treatment patterns

	CTD-PAH	IPAH	CHD-PAH	PoPH	PVOD	DPAH	CCB	HPAH	HIV-PAH	HHT-PAH
Subjects, n	80 (49)	33 (20)	22 (13)	11 (7)	5 (3)	3 (2)	3 (2)	2 (1)	2 (1)	2 (1)
Sex: female n (%)	72 (90)	26 (79)	13 (59)	2 (18)	2 (40)	3 (100)	3 (100)	2 (100)	2 (100)	1 (50)
Age (years): mean±SD	64±11	56±17	55±21	47±9	69±9	58±15	34±13	46±14	45±1	47±29
WHO functional class: % I/II/III/IV	0/22/60/18	3/24/55/18	0/50/50/0	0/36/64/0	0/20/40/40	0/33/33/33	0/67/33/0	0/0/100/0	0/50/50/0	0/50/50/0
BNP (ng/L): mean±SD	611±795	268±295	271±348	63±40	417±675	1330±1800	53±41	298±87	---	187±127
Risk stratification: % Low/intermediate/high risk	8/61/31	27/45/28	27/55/18	9/91/0	20/60/20	33/33/33	33/67/0	0/50/50	50/50/0	0/100/0
Right heart catheterisation (mean, ±SD)										
mPAP (mm Hg)	43±11	50±12	51±25	51±17	38±14	43±25	38±1	49±0	44±6	46±0
PAWP (mm Hg)	11±4	8±3	13±5	12±7	12±10	7±0	7±2	8±0	12±0	---
CO (L/min)	4±1	4±2	4±1	5±1	4±0	3±0	5±1	2±0	4±0	9±0
PVR (WU)	9±4	12±7	12±13	6±3	8±0	13±0	6±1	18±0	15±0	---
DLCO, % predicted	35±14	69±20	73±21	50±6	43±13	19±0	88±0	---	---	---
PH therapy: n (%)	79 (99)	32 (97)	14 (64)	9 (82)	5 (100)	3 (100)	1 (33)	2 (100)	2 (100)	1 (50)
Monotherapy	20 (25)	4 (12)	4 (29)	4 (44)	2 (40)	1 (33)	1 (100)	0	1 (50)	0
PD5 inhib.	10 (50)	4 (100)	2 (50)	3 (75)	2 (100)	1	1 (100)	0	0	0
ERA	10 (50)	0	2 (50)	1 (25)	0	0	0	0	1 (100)	0
Double combination therapy	45 (56)	22 (67)	9 (64)	5 (56)	2 (40)	1 (33)	0	2 (100)	1 (50)	1 (100)
PD5 inhib. and ERA	44 (98)	21 (95)	9 (100)	5 (100)	2 (100)	1 (100)	0	2 (100)	1 (100)	1 (100)
sGCS+ERA	0	1 (5)	0	0	0	0	0	0	0	0
ERA+PGI2	1 (2)	0	0	0	0	0	0	0	0	0
Triple combination therapy	14 (18)	6 (18)	1 (7)	0	1 (20)	1 (33)	0	0	0	0
PD5 inhib.+ERA + neb PGI2	12 (86)	4 (67)	1 (100)	0	1 (100)	1 (100)	0	0	0	0
PD5 inhib.+ERA + oral PGI2	2 (14)	2 (33)	0	0	0	0	0	0	0	0

Data were incomplete for the following characteristics and parameters at the time of diagnosis: mPAP was missing for 22 (13%) subjects, PAWP for 22 (13%), CO for 85 (52%), PVR for 95 (58%) and DLCO was missing in 87 (53%) cases. Of note: While mPAP was unavailable at diagnosis for 13% of PAH subjects, a subsequent RHC with evidence of a mPAP >25 mm Hg was available for all subjects, but not included in this analysis. Inadequate data were omitted and replaced by '---'.

BNP, B-type natriuretic peptide; CCB, long-term responsive to calcium channel blockers PAH; CHD-PAH, congenital heart disease associated PAH; CO, cardiac output; CTD-PAH, connective tissue disease associated pulmonary arterial hypertension; DLCO, diffusion capacity for carbon monoxide; DPAH, drug-associated PAH; ERA, endothelin receptor antagonist; HHT-PAH, hereditary haemorrhagic telangiectasia associated PAH; HIV-PAH, HIV associated PAH; HPAH, hereditary PAH; PD5 inhib, phosphodiesterase type-5 inhibitor; IPAH, idiopathic pulmonary arterial hypertension; mPAP, mean pulmonary artery pressure; neb, nebulised; PAWP, pulmonary artery wedge pressure; PGI2, prostacyclin; PH, pulmonary hypertension; PoPH, portopulmonary hypertension; PVOD, pulmonary veno occlusive disease; PVR, pulmonary vascular resistance; sGCS, soluble guanylate cyclase stimulator.

Table 3 1-year, 3-year and 5-year survival of individuals with PAH, with a specific focus on CTD-PAH, IPAH, CHD-PAH and PoPH

	PAH	CTD-PAH	IPAH	CHD-PAH	PoPH
Subjects, n	160*	80	33	19*	11
Annual incidence	3.11	1.53	0.63	0.63*	0.21
Survival, %					
1 year	89	83	100	100	91
3 year	75	62	100	100	81
5 year	65	47	95	91	81
Median (IQR) follow-up, years	3 (1–5)	2.5 (1–4)	3 (2–7)	4 (3–7)	5 (3–6.5)

The median follow-up in years and IQR is also provided for each subgroup.

*The calculated incidence for CHD-PAH does not reflect the true incidence of this particular subgroup as these patients are an exception in that they are not consistently referred to the NPHU. Survival data were not available for three subjects with CHD-PAH. Annual incidence is reported per million population (pmp).

CHD-PAH, congenital heart disease PAH; CTD-PAH, connective tissue disease PAH; IPAH, idiopathic pulmonary arterial hypertension; PAH, pulmonary arterial hypertension; PoPH, portopulmonary pulmonary hypertension.

14% (n=24) of PAH cases (table 2). No parenteral proctacyclin therapy was prescribed in the first 12 months of diagnosis.

Of the 67 subjects with CTEPH, 31% (n=21) underwent pulmonary endarterectomy (PEA), 4% (n=3) underwent balloon pulmonary angioplasty and 1% (n=1) underwent both procedures.

Survival

The 1-year, 3-year and 5-year transplant-free survival for subjects with PAH was 89%, 75% and 65%, respectively. This was significantly lower for individuals with CTD-PAH, when compared with other PAH subgroups, including IPAH (p=0.0009) (table 3). This was most

notable for individuals with systemic sclerosis-associated PAH (SSc-PAH) as illustrated in figure 1. The 1-year, 3-year and 5-year survival for individuals with group 3 PH was significantly lower than all other groups, including PAH (p<0.0001) (online supplemental figure 2). Balloon atrial septostomy (BAS) was performed in a total of three subjects and eight (2%) individuals with PH underwent lung transplantation during the study period.

DISCUSSION

PH is a disease of the pulmonary circulation that encompasses a spectrum of conditions that differ in characteristics.¹² This study addressed the paucity of data regarding the clinical characteristics of PH in the Ireland and provide insights into the incidence and outcomes of PH in the preceding decade. This is particularly relevant given the transforming landscape of PH, with evolving patient demographics and expanding treatment options.¹¹

This study revealed an estimated annual incidence of PAH in Ireland of 3.11 cases per million population. While the true global incidence of PAH is unknown, data from national systematic registries in Europe suggest that the annual incidence is between 5.8 to 13.7 cases per million population (table 4).^{12–15} Epidemiological estimates derived from non-systematic sources typically report lower estimates¹⁶ and this may have contributed to the results in this study, which were derived from a local database. Interestingly, the estimated annual incidence of PAH in the UK is 6.1–7.6 cases per million population.^{14 16 17} As Ireland shares similar demographic characteristics with the UK, this may reflect the success of the national UK audit of PH, which is a current and authoritative source of epidemiological data.¹⁶ A national systematic registry in Ireland would be valuable to ensure structured and consistent data collection and to facilitate national and international comparisons. It is also plausible that the calculated incidence of PAH in Ireland may

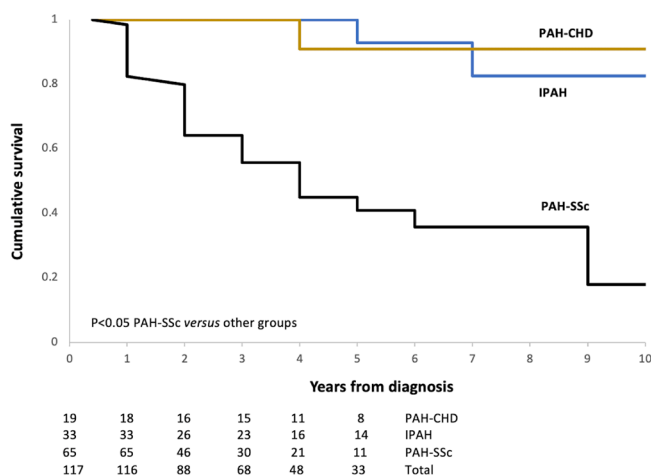


Figure 1 Kaplan-Meier curve illustrating the cumulative survival of patients with congenital heart disease-associated pulmonary arterial hypertension (PAH-CHD), idiopathic pulmonary arterial hypertension (IPAH) and systemic sclerosis-associated PAH (PAH-SSc). The cumulative 5-year survival was significantly lower in patients with PAH-SSc relative to IPAH and PAH-CHD (p<0.05).

Table 4 Incidence and survival of PAH in Ireland and other European countries

Country	Ireland	UK ¹⁴ (Scotland)	UK ¹⁷ (ASPIRE)	France ^{22,33}	Spain ²³	Sweden ^{12,16} (SPAHR)	Czech ¹⁵	Germany ²⁴ (Giessen)	Germany ²⁵ (COMPERA)	Latvia ¹³	Denmark ²⁶	Portugal ³⁴
Subjects with PAH, n	163	374	1344	674	866	457	191	685	263	130	134	46
Recruitment period	2010–2020	1997–2006	2001–2010	2002–2003	1998–2008	2000–2014	2000–2007	2008–2011	2014	2007–2016	2000–2012	2008–2010
Age (years), mean±SD	56±15	52±13*	59±17	50±15	45±17	67†	52±17	51±16	61±18	65†	50±21	43±16
Female, %	77%	70%		65.3%	71%	64%	65%	65%	67%	73%	58.2%	65.2%
Annual incidence												
PAH	3.11	7.6	6.1	2.4	3.7	-	10.7	-	3.9	13.7	-	1.5
IPAH	0.63	2.6	2.1	-	1.2	5†	6.2‡	-	2.4	7.6	-	-
CTD-PAH	1.53	2.8	2.4	-	-	-	-	-	1.0	-	-	-
Survival PAH, %												
1 year	89	-	88	87	87	85	89	88.2	-	88	86.4	93.5
3 year	75	-	68	67	75	71	74	72.2	-	73.3	72.9	-
5 year	65	-	-	-	65	59	-	59.4	-	58.1	65.4	-
Survival IPAH, %												
1 year	100	-	-	89§	89	-	85‡	89.7	-	-	-	-
3 year	100	-	63	69§	77	-	62‡	76.2	-	-	-	-
5 year	95	-	-	-	68	-	-	65.3	-	-	-	-
Survival CTD-PAH, %												
1 year	83	-	-	-	-	-	-	85.3	-	-	-	-
3 year	62	-	54	-	-	-	-	65.6	-	-	-	-
5 year	47	-	-	-	-	-	-	50.9	-	-	-	-

The annual incidence is calculated per million population. Age is displayed as mean and SD unless otherwise specified.

*Female mean age (SD).

†Median.

‡Incidence reflects IPAH and HPAH combined.

§Incidence reflects IPAH, HPAH and Anorexigen-associated PAH.

¶Incidence reflects tissue disease associated PAH; IPAH, idiopathic PAH; PAH, pulmonary arterial hypertension.

reflect suboptimal disease recognition and referral¹⁸ and this requires further exploration.

The characteristics of PAH subgroups in Ireland also differ from other centres. PH registries from Europe and the USA² generally report a predominance of IPAH within group 1 PAH, which is followed by PAH-CTD. In this study, the leading subgroup of PAH was PAH-CTD, which was responsible for 49% of PAH referrals (table 2). IPAH accounted for only 20% (n=33) of PAH cases, and the estimated annual incidence was low at 0.63 cases per million population. While it was the predominant subgroup, the incidence of PAH-CTD remained below UK estimates, at 1.53 versus 2.4 annual cases per million population.¹⁷ Therefore, rather than suggesting an abundance of PAH-CTD in Ireland, this data suggest suboptimal recognition of other PAH subgroups. Enhanced recognition of PAH-CTD may be attributed to screening tools such as the DETECT algorithm for SSc.¹⁹ However, as 82% of individuals with SSc-PAH reported FC III or IV symptoms at diagnosis and 32% had evidence of right heart failure, additional work is required to optimise the use of such screening tools in asymptomatic subjects.¹⁹ Ensuring adequate knowledge of CTD-PAH and access to RHC are additional important considerations.

The expansion of treatment options for PAH has been transformative for PAH care. Ninety-nine per cent of individuals with CTD-PAH and 97% of those with IPAH received PH-specific therapy within the first 12 months of diagnosis. Triple combination therapy for PAH comprised of oral or nebulised prostacyclin and there were no parenteral regimens commenced in this initial period. BAS was performed as a palliative procedure for three subjects with PAH and approximately 2% of subjects with PH underwent lung transplantation. Lung transplantation for this indication was somewhat below international statistics of 4.5%,²⁰ but above UK estimates of 1%.¹⁷

Outcomes have improved substantially for individuals with PAH²¹ and the 1-year, 3-year and 5-year survival was 89%, 75% and 65% in this study. This is comparable to other European centres^{17 22–26} and largely reflects the evolution of management strategies and advancements in therapeutics in the preceding decades (table 4).²⁷ Unfortunately, these improved outcomes did not translate to all PAH subgroups. Individuals with CTD-PAH and, in particular, SSc-PAH had distinctly worse survival when compared with those with IPAH. Notably, individuals with SSc-PAH were older at diagnosis (p<0.001) and had significantly higher BNP (p=0.0173) and PAWP (p<0.001) relative to those with IPAH. Furthermore, the diffusion capacity for carbon monoxide (DLCO) was markedly reduced in individuals with SSc-PAH at 35±14 (p<0.001). These characteristics may have contributed to the observed outcomes. In particular, older age has been associated with an attenuated response to PAH therapies^{28 29} and DLCO is an independent predictor of survival in PAH.^{30 31}

This study is limited by its retrospective nature and by missing data. Furthermore, only PH cases that were referred to the NPHU or attended the outpatient department were included in this study and, therefore, some cases may have been missed. Furthermore, patients with CHD-PAH are typically managed by congenital cardiology specialists and only select cases are referred to the NPHU. Therefore, the incidence of CHD-PAH reported in this article underestimates the incidence of PAH-CHD in Ireland. Irrespective, this study provides important insights into the incidence and outcomes of PH in Ireland. While the outcomes of PAH in Ireland are comparable to other centres,^{17 22–26} the incidence appears low.^{14 16 17 25 32} Furthermore, as previously described, the rate of PEA in subjects with CTEPH appears low and requires special attention and intervention.¹⁸ Improved disease awareness, increased case recognition and a national registry may be helpful to address this. Furthermore, while the outcomes of IPAH have improved,⁴ the survival of those with SSc-PAH is poor and requires exploration.

CONCLUSION

This study describes the incidence and outcomes of PH in Ireland and suggests that improved disease awareness and case recognition are required. The 1-year, 3-year and 5-year transplant-free survival for PAH was 89%, 75% and 65% during the study period. The outcomes of individuals with SSc-PAH and group 3 PH were poor and require additional attention and intervention.

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Patient consent for publication Not applicable.

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Data availability statement Data are available upon reasonable request. N/A.

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