

Supplementary Material

Supplementary Table 1. Codes used to identify patient diagnoses, drugs, and healthcare resource utilisation.

Description	Code
<i>Inclusion diagnoses</i>	<i>ICD-10</i>
Primary pulmonary hypertension	I27.0
Other secondary pulmonary hypertension	I27.2
<i>Right heart catheterisation</i>	<i>OPCS</i>
Catheterisation of right side of heart NEC	K65.2
Other specified catheterisation of heart	K65.8
Unspecified catheterisation of heart	K65.9
<i>Specialist referral centres for PAH in England</i>	<i>Trust code</i>
Great Ormond Street Hospital for Children part of Great Ormond Street Hospital for Children NHS Foundation Trust	RP4
Hammersmith Hospital part of Imperial College Healthcare NHS Trust	RYJ
Royal Brompton Hospital part of Royal Brompton and Harefield NHS Foundation Trust	RT3
Royal Free Hospital part of Royal Free London NHS Foundation Trust	RAL
Papworth Hospital part of Papworth Hospital NHS Foundation Trust	RGM
Royal Hallamshire Hospital part of Sheffield Teaching Hospitals NHS Foundation Trust	RHQ
Freeman Hospital part of The Newcastle Upon Tyne Hospitals NHS Foundation Trust	RTD
<i>Cardiology specialty</i>	<i>Specialty code</i>
Surgical specialties	
Cardiothoracic surgery	170
Medical specialties	
Cardiology	320
Paediatric cardiology	321
Respiratory medicine (also known as thoracic medicine)	340
Rheumatology	410
<i>PAH-specific drugs</i>	<i>OPCS</i>
Ambrisentan	X82.1
Bosentan	X82.2
Epoprostenol	X82.4
Iloprost	X82.3
Macitentan	X82.1
Riociguat ^a	X82.1
Selexipag	X82.1
Sildenafil ^a	X82.1
Tadalafil ^a	X82.1
Treprostinil sodium	X82.1
<i>Non-PAH forms of PH</i>	<i>ICD-10</i>
WSPH Group 2: left heart disease	
Left ventricular failure	I50.1
Non-rheumatic mitral valve disorders	I34
Non-rheumatic aortic valve disorders	I35
Angina pectoris	I20
STEMI and NSTEMI	I21
Subsequent STEMI and NSTEMI	I22
Certain current complications following STEMI and NSTEMI (within 28-day period)	I23
Other acute ischaemic heart diseases	I24
Chronic ischaemic heart disease	I25
WSPH Group 3: lung disease and/or hypoxaemia	
Bronchitis, not specified as acute or chronic	J40
Simple and mucopurulent chronic bronchitis	J41
Unspecified chronic bronchitis	J42
Emphysema	J43
Other chronic obstructive pulmonary disease	J44
Asthma	J45

Description	Code
Bronchiectasis	J47
Other interstitial pulmonary diseases	J84
Sleep apnoea	G47.3
Exposure to high and low air pressure and changes in air pressure	W94
WSPH Group 4: CTEPH	
Pulmonary thromboembolism	I26
<i>Congenital heart disease</i>	<i>ICD-10</i>
Congenital malformations of cardiac chambers and connections	Q20
Congenital malformations of cardiac septa	Q21
Congenital malformations of pulmonary and tricuspid valves	Q22
Congenital malformations of aortic and mitral valves	Q23
Other congenital malformations of heart	Q24
Congenital malformations of great arteries	Q25
Congenital malformations of great veins	Q26
Other congenital malformations of peripheral vascular system	Q27
Other congenital malformations of circulatory system	Q28
<i>Renal failure</i>	<i>ICD-10</i>
Acute kidney failure	N17
CKD	N18
Unspecified kidney failure	N19
<i>Digital ulcers</i>	
Non-pressure chronic ulcer of lower limb, not elsewhere classified	L97
Other disorders of skin and subcutaneous tissue, not elsewhere classified	L98
<i>Erectile dysfunction</i>	<i>ICD-10</i>
Failure of genital response	F52.2
Impotence of organic origin	N48.4

CKD, chronic kidney disease; CTEPH, chronic thromboembolic pulmonary hypertension; ICD-10, International Classification of Diseases; Tenth Revision; NEC, not elsewhere classified; NHS, National Health Service; NSTEMI, non-ST-elevation myocardial infarction; OPCS, Office of Population Censuses and Surveys [defunct] Classification of Interventions and Procedures; PAH, pulmonary arterial hypertension; PH, pulmonary hypertension; STEMI, ST-elevation myocardial infarction; WSPH, World Symposium on Pulmonary Hypertension.

^aAlthough these drugs have additional indications, it is assumed that when coded under X82.1–4 their use is specific to patients with PAH.

Supplementary Table 2. Proportion of patients in the overall PAH cohort with inpatient admissions, outpatient visits and A&E attendances.

Percentage of patients with:		2013 (n=1370)	2014 (n=1605)	2015 (n=1774)	2016 (n=1850)	2017 (n=1825)
Inpatient admissions	Total	83.6%	83.1%	82.0%	81.0%	79.9%
	PAH-related	72.1%	70.8%	72.7%	71.2%	71.8%
	Non-PAH-related	33.8%	33.8%	31.2%	30.2%	28.4%
Outpatient visits	Total	96.3%	96.0%	97.4%	97.0%	98.0%
A&E attendance	Total	39.1%	32.2%	35.2%	41.0%	39.9%
	PAH-related	19.3%	19.0%	20.3%	20.9%	20.3%
	Non-PAH-related	26.6%	29.3%	28.4%	29.0%	29.3%

A&E, Accident and Emergency; PAH, pulmonary arterial hypertension.

Supplementary Table 3. Inpatient, outpatient and A&E hospital events in incident patients with PAH, by year following index date.

		Year 1 (n=1410)		Year 2 (n=1045)		Year 3 (n=765)	
		Mean	SD	Mean	SD	Mean	SD
Inpatient admissions	Total	4.4	3.8	2.6	3.9	2.3	3.8
	PAH-related	3.2	2.8	1.8	0.8	1.6	2.1
	Non-PAH-related	1.2	4.3	0.8	5.1	0.7	4.9
Outpatient visits	Total	10.9	7.7	9.1	7.5	8.2	6.2
A&E attendances	Total	1.1	1.1	0.8	1.0	0.8	0.9
	PAH-related	0.6	1.0	0.3	0.9	0.3	0.9
	Non-PAH-related	0.5	1.1	0.5	1.1	0.5	1.0

A&E, Accident and Emergency; PAH, pulmonary arterial hypertension; SD, standard deviation.

Supplementary Table 4. Frequency distribution of inpatient admissions in the overall PAH cohort, by year.

Admissions, n (%)	2013 (n=1143)	2014 (n=1328)	2015 (n=1448)	2016 (n=1495)	2017 (n=1454)
1	278 (24%)	352 (27%)	369 (25%)	414 (28%)	429 (30%)
2	244 (21%)	315 (24%)	339 (23%)	350 (23%)	342 (24%)
3	209 (18%)	226 (17%)	226 (16%)	231 (15%)	228 (16%)
4	126 (11%)	127 (10%)	154 (11%)	162 (11%)	155 (11%)
5	88 (8%)	99 (7%)	99 (7%)	104 (7%)	116 (8%)
6	51 (4%)	56 (4%)	65 (4%)	74 (5%)	44 (3%)
7	34 (3%)	43 (3%)	42 (3%)	40 (3%)	29 (2%)
8	32 (3%)	34 (3%)	29 (2%)	22 (1%)	33 (2%)
9	12 (1%)	19 (1%)	23 (2%)	16 (1%)	10 (1%)
10	16 (1%)	11 (1%)	9 (1%)	23 (2%)	16 (1%)
11–13	22 (2%)	13 (1%)	20 (1%)	24 (2%)	23 (2%)
14–16	14 (1%)	13 (1%)	11 (1%)	7 (0%)	10 (1%)
≥17	17 (1%)	31 (2%)	22 (2%)	28 (2%)	19 (1%)
Total	1143 (100%)	1328 (100%)	1448 (100%)	1495 (100%)	1454 (100%)

PAH, pulmonary arterial hypertension.

Supplementary Table 5. Length of hospital stays in incident patients with PAH, by year following index date.

Days per inpatient spell^a	Year 1 (n=1410)		Year 2 (n=1045)		Year 3 (n=765)	
	Mean	SD	Mean	SD	Mean	SD
Total	4.6	9.2	4.0	8.5	3.6	7.6
PAH-related	5.3	10.3	4.6	9.5	4.1	8.2
Non-PAH-related	2.4	4.2	2.7	5.1	2.4	5.8

PAH, pulmonary arterial hypertension, SD, standard deviation.

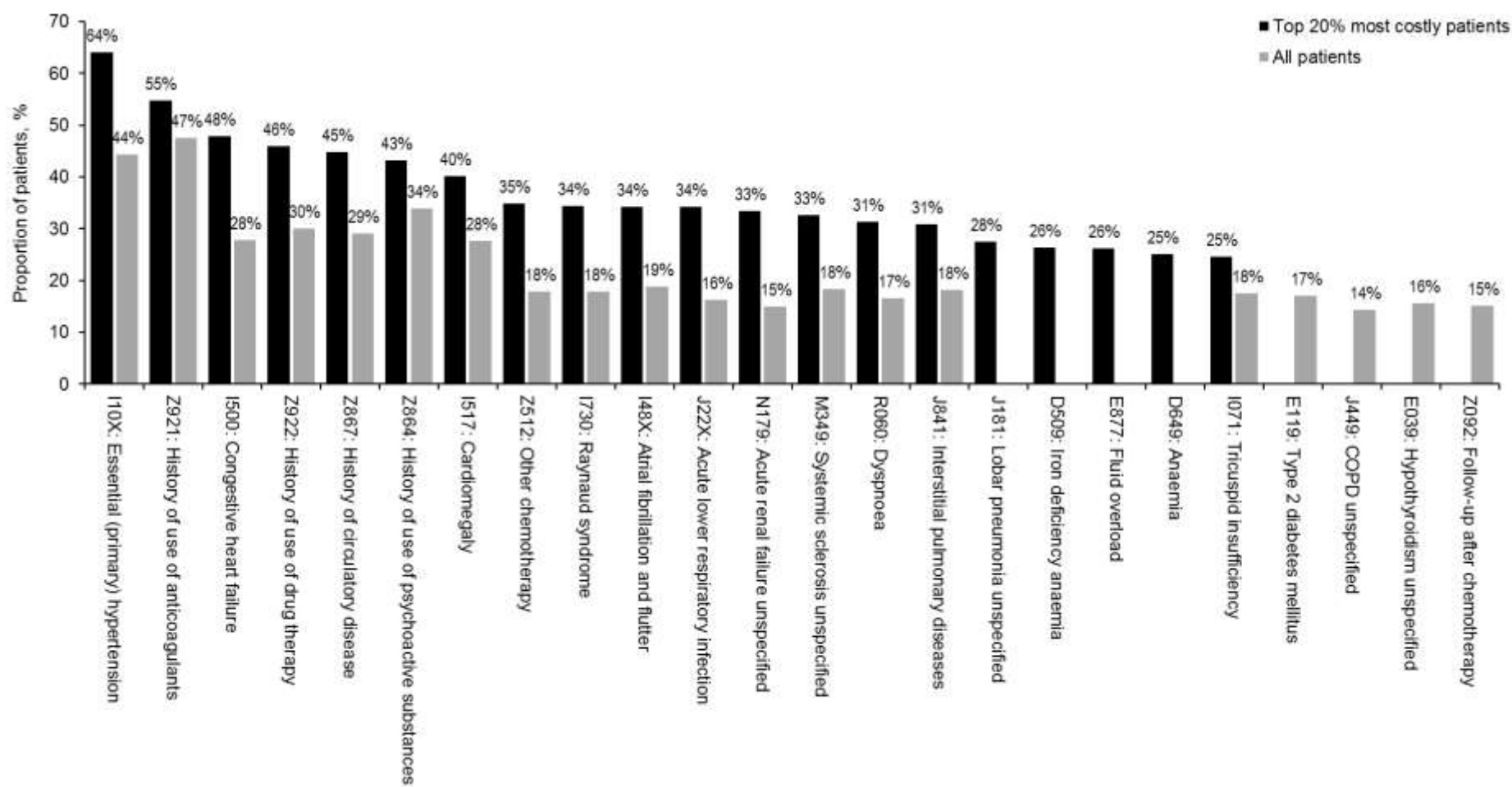
^aDefined as a continuous period spent as an inpatient, from admission until the earlier of discharge or study exit, plus any linked A&E attendance 24 hours prior to the inpatient admission.

Supplementary Table 6. Inpatient, outpatient and A&E hospital events in the top 20% of all patients with PAH in terms of healthcare expenditure, by year, 2013–2017.

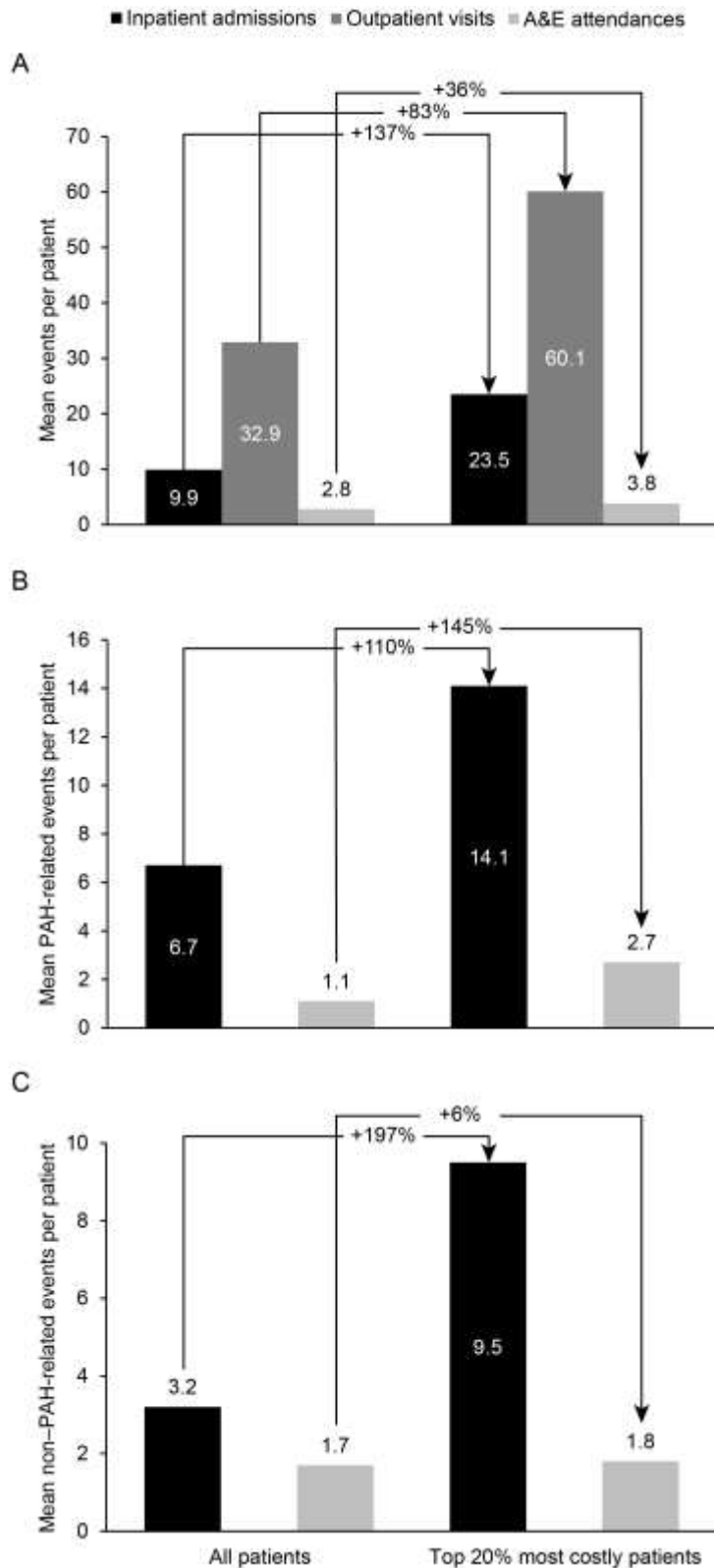
		2013 (n=374)		2014 (n=434)		2015 (n=451)		2016 (n=430)		2017 (n=369)	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Inpatient admissions	Total	5.6	3.9	5.5	4.1	5.5	4.1	6.1	6.9	6.3	8.9
	PAH-related	3.3	3.7	3.2	3.4	3.4	3.9	3.6	3.9	3.8	5.7
	Non-PAH-related	2.3	4.1	2.3	4.6	2.0	4.3	2.5	8.9	2.5	11.1
Outpatient visits	Total	13.9	9.9	14.2	9.7	15.0	10.1	15.9	10.5	14.8	10.3
A&E attendances	Total	1.4	2.0	1.5	2.0	1.6	2.4	1.7	2.0	1.6	1.6
	PAH-related	0.6	1.2	0.6	1.2	0.6	1.2	0.7	1.2	0.8	1.7
	Non-PAH-related	0.8	2.6	0.9	2.5	1.0	3.1	1.0	2.6	0.9	1.6

A&E, Accident and Emergency; PAH, pulmonary arterial hypertension; SD, standard deviation.

Supplementary Figure 1. Top 20 most common comorbidities in patients with pulmonary arterial hypertension, 2013–2017: comparison of the top 20% of patients in terms of healthcare expenditure *versus* the overall cohort. *COPD* chronic obstructive pulmonary disease.



Supplementary Figure 2. Mean number of A) total, B) PAH-related, and C) non-PAH-related inpatient, outpatient and Accident and Emergency (A&E) hospital events in patients with pulmonary arterial hypertension, 2013–2017: comparison of the top 20% of patients in terms of healthcare expenditure *versus* the overall cohort.



Supplementary Figure 3. Mean cost per event of A) total, B) PAH-related, and C) non-PAH-related inpatient, outpatient and Accident and Emergency (A&E) hospital events in patients with pulmonary arterial hypertension, 2013–2017: comparison of the top 20% of patients in terms of healthcare expenditure *versus* the overall cohort.

