

Supplementary Material

Healthcare resource utilization and medical costs in pulmonary arterial hypertension management in Japan: a retrospective study using a claims database

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Table S1 Diagnoses of PAH (extracted by the standard disease name)

ICD-10 level 4 code	ICD-10 level 4 name	Standard disease name
I270	Primary pulmonary hypertension	pulmonary arterial hypertension
I270	Primary pulmonary hypertension	idiopathic pulmonary arterial hypertension

PAH, pulmonary arterial hypertension; ICD-10, International Statistical Classification of Diseases and Related Health Problems

Table S2 PAH-targeted drugs (extracted by the general name)

Category	Form	ATC level 4 code	ATC level 4 name	General name	Brand name
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Bosentan	Tracleer
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Ambrisentan	Volibris
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Macitentan	Opsumit
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Bosentan	Bosentan [MOCHIDA]
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Bosentan	Bosentan [DSEP]
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Bosentan	Bosentan [JG]
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Bosentan	Bosentan [KN]
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Bosentan	Bosentan [MOCHIDA]
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Bosentan	Bosentan [TANABE]
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Bosentan	Bosentan [PFIZER]
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Bosentan	Bosentan [SAWAI]
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Bosentan	Unknown Brand Name in English
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Ambrisentan	Ambrisentan [SAWAI]
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Ambrisentan	Ambrisentan [KMP]
ERA	Oral	C06B1	Endothelin receptor antagonist PAH products	Bosentan	Bosentan [VTRS]
NO signaling	Oral	C06B2	PDE5 inhibitor PAH products	Sildenafil Citrate	Revatio
NO signaling	Oral	C06B2	PDE5 inhibitor PAH products	Tadalafil	Adcirca
NO signaling	Oral	C06B2	PDE5 inhibitor PAH products	Sildenafil Citrate	Revatio
NO signaling	Oral	C06B2	PDE5 inhibitor PAH products	Tadalafil	Tadalafil [TE]
NO signaling	Oral	C06B2	PDE5 inhibitor PAH products	Tadalafil	Tadalafil [JG]
NO signaling	Oral	C06B2	PDE5 inhibitor PAH products	Tadalafil	Tadalafil [SAWAI]

NO signaling	Oral	C06B2	PDE5 inhibitor PAH products	Tadalafil	Tadalafil [KYORIN]
PPA	Inhaled	C06B3	Prostacyclin agonist PAH products	Iloprost	Ventavis
PPA	Inhaled	C06B3	Prostacyclin agonist PAH products	Treprostinil	Treprost
PPA	Oral	C06B3	Prostacyclin agonist PAH products	Beraprost Sodium	Careload
PPA	Oral	C06B3	Prostacyclin agonist PAH products	Beraprost Sodium	Berasus
PPA	Oral	C06B3	Prostacyclin agonist PAH products	Selexipag	Uptravi
PPA	Parenteral	C06B3	Prostacyclin agonist PAH products	Epoprostenol Sodium	Flolan
PPA	Parenteral	C06B3	Prostacyclin agonist PAH products	Epoprostenol Sodium	Epoprostenol [F]
PPA	Parenteral	C06B3	Prostacyclin agonist PAH products	Epoprostenol Sodium	Epoprostenol [ACT]
PPA	Parenteral	C06B3	Prostacyclin agonist PAH products	Treprostinil	Treprost
PPA	Parenteral	C06B3	Prostacyclin agonist PAH products	Epoprostenol Sodium	Epoprostenol [TEVA]
PPA	Parenteral	C06B3	Prostacyclin agonist PAH products	Epoprostenol Sodium	Epoprostenol [JANSSEN]
PPA	Parenteral	C06B3	Prostacyclin agonist PAH products	Epoprostenol Sodium	Epoprostenol [NIG]
NO signaling	Oral	C06B9	Pulmonary arterial hypertension (PAH) products, other	Riociguat	Adempas

PAH, pulmonary arterial hypertension; ATC, Anatomical Therapeutic Chemical Classification; ERA, endothelin receptor antagonist; PDE5, phosphodiesterase 5; PPA, prostacyclin agonist

Table S3 Exclusion criteria (diseases)

Human immunodeficiency virus infection (extracted by ICD-10 code)

ICD-10 level 3 code	ICD-10 level 3 name
B20	Human immunodeficiency virus [HIV] disease
B21	Human immunodeficiency virus [HIV] disease
B22	Human immunodeficiency virus [HIV] disease
B23	Human immunodeficiency virus [HIV] disease
B24	Human immunodeficiency virus [HIV] disease

Portal hypertension (extracted by the ICD-10 code)

ICD-10 level 4 code	ICD-10 level 4 name
K766	Portal hypertension

Schistosomiasis (extracted by the ICD-10 code)

ICD-10 level 3 code	ICD-10 level 3 name
B65	Schistosomiasis [bilharziasis]

Chronic thromboembolic pulmonary hypertension (extracted by the standard disease name)

Disease code	Standard disease name
8841669 (ICD-10: I272)	chronic thromboembolic pulmonary hypertension

Persistent pulmonary hypertension of newborn (extracted by the standard disease name)

Disease code	Standard disease name
8844234 (ICD-10: P293)	persistent pulmonary hypertension of newborn

Table S4 Exclusion criteria (lung transplantation surgery)

Lung transplantation surgery (extracted by the standardized procedure code)

Procedure code	Standardized procedure code	Standardized procedure name
K514	150317510	lung allotransplantation from cadaver donor
K514	150336610	living-donor partial lung transplantation
K605	150322610	heart-lung allotransplantation

Table S5 Right heart catheterization (extracted by the standardized procedure code)

Procedure code	Standardized procedure code	Standardized procedure name
D206	160064610	right cardiac catheterization

Table S6 Cardiopulmonary comorbidities

Hypertension (extracted by ICD-10 code)

ICD-10 level2 code	ICD-10 level 2 name
I10-I15	Hypertensive diseases

Coronary heart disease (extracted by ICD-10 code + ATC code; diagnosed and prescribed at the same site in the same month)

ICD-10 level2 code	ICD-10 level 2 name
I20-I25	Ischaemic heart diseases

EphMRA-ATC code	ATC level 3 or 4 name
C09A	ACE INHIBITORS, PLAIN
C09C	ANGIOTENSIN-II ANTAGONISTS, PLAIN
C09D1	Angiotensin-II antagonist combinations with antihypertensives (C2) and/or diuretics
C09D3	Angiotensin-II antagonist combinations with calcium antagonists
C09D9	Angiotensin-II antagonist combinations with other drugs
C09X	OTHER AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM
C07A	BETA-BLOCKING AGENTS, PLAIN
C08A	CALCIUM ANTAGONISTS, PLAIN
C02A1	Antihypertensives plain, mainly centrally acting
C02A2	Antihypertensives plain, mainly peripherally acting
C02B2	Antihypertensive-diuretic combinations, mainly peripherally acting
C02C	RAUWOLFIA ALKALOIDS AND OTHER ANTIHYPERTENSIVES OF HERBAL ORIGIN
C02D	RAUWOLFIA ALKALOIDS AND OTHER ANTIHYPERTENSIVES OF HERBAL ORIGIN IN COMBINATION WITH DIURETICS
C03A1	Potassium-sparing agents plain
C03A2	Loop diuretics plain
C03A3	Thiazides and analogues plain
C03A7	Vasopressin receptor antagonist diuretics
C03A9	Other diuretics
C01E	NITRITES AND NITRATES
C01D	CORONARY THERAPY EXCLUDING CALCIUM ANTAGONISTS AND NITRITES

Atrial fibrillation (extracted by ICD-10 code)

ICD-10 level 3 code	ICD-10 level 3 name
I48	Atrial fibrillation and flutter

Diabetes mellitus (extracted by ICD-10 code)

ICD-10 level 3 code	ICD-10 level 3 name
E10	Type 1 diabetes mellitus
E11	Type 2 diabetes mellitus
E14	Unspecified diabetes mellitus

Obesity (extracted by ICD-10 code)

ICD-10 level 3 code	ICD-10 level 3 name
E66	Obesity

Mild parenchymal lung disease (extracted by ICD-10 code)

ICD-10 level 4 code	ICD-10 level 4 name
J840	Alveolar and parietoalveolar conditions
J841	Other interstitial pulmonary diseases with fibrosis
J849	Interstitial pulmonary disease, unspecified

Chronic obstructive pulmonary disease (extracted by ICD-10 code)

ICD-10 level 3 code	ICD-10 level 3 name
J42	Unspecified chronic bronchitis
J43	Emphysema
J44	Other chronic obstructive pulmonary disease

Table S7 Comorbidity disease

Cardiopulmonary comorbidities (i.e, hypertension, coronary heart disease, atrial fibrillation, diabetes mellitus, obesity, mild parenchymal lung disease and chronic obstructive pulmonary disease) indicated in the Supplementary Material Table S6 and follows:

Anxiety (extracted by ICD-10 code)

ICD-10 level 3 code	ICD-10 level 3 name
F40	Phobic anxiety disorders
F41	Other anxiety disorders

Depression (extracted by ICD-10 code)

ICD-10 level 4 code	ICD-10 level 3 name
F32	Depressive episode
F33	Recurrent depressive disorder

Table S8 Diagnostic procedure

Right heart catheterization (extracted by standardized procedure code)

Procedure code	Standardized procedure code	Standardized procedure name
D206	160064610	right cardiac catheterization

Echocardiography (extracted by standardized procedure code)

Procedure code	Standardized procedure code	Standardized procedure name
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D215	160072510	ultrasonography, echocardiography (transthoracic echocardiography)
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Electrocardiogram (extracted by standardized procedure code)

Procedure code	Standardized procedure code	Standardized procedure name
D208	160068410	electrocardiography (ECG, at least 12 leads including unipolar limb lead and precordial lead)
D208	160068510	electrocardiography (ECG, 6 leads or more)
D208	160068610	electrocardiographic diagnosis (description from another medical institution)
D208	160068750	electrocardiography (body surface His bundle electrocardiography)
D208	160068850	vectorcardiography (VCG)
D208	160150650	electrocardiography, using portable cardiac event recorder and transmitter
D208	160198510	electrocardiography, ventricular late potentials measurement with signal averaged electrocardiogram

Chest X-ray (extracted by standardized procedure code)

Procedure code	Standardized procedure code	Standardized procedure name
E002	170001910	plain radiography (analog radiography)
E002	170002410	plain indirect radiography (analog radiography)
E002	170021750	plain radiography, analog radiography <preoperative management fee, 2 images or more>
E002	170021850	plain indirect radiography, analog radiography <preoperative management fee, 2 images or more>
E002	170023950	plain radiography, analog radiography <short stay surgery etc. basic fee, 2 images or more>
E002	170024050	plain indirect radiography, analog radiography <short stay surgery etc. basic fee, 2 images or more>
E002	170027910	plain radiography (digital radiography)
E002	170028310	plain indirect radiography (digital radiography)
E002	170031350	plain radiography, digital radiography <preoperative management fee, 2 images or more>
E002	170031450	plain indirect radiography, digital radiography <preoperative management fee, 2 images or more>
E002	170031550	plain radiography, digital radiography <short stay surgery etc. basic fee, 2 images or more>
E002	170031650	plain indirect radiography, digital radiography <short stay surgery etc. basic fee, 2 images or more>
E002	170032050	plain radiography (simultaneously with digital) (analog radiography)
E002	170032150	plain radiography (simultaneously with analog) (digital radiography)

E002	170032450	plain indirect radiography (simultaneously with digital) (analog radiography)
E002	170032550	plain indirect radiography (simultaneously with analog) (digital radiography)

Blood gas tests (extracted by standardized procedure code)

Procedure code	Standardized procedure code	Standardized procedure name
D007	160027710	blood gas analysis

Pulmonary function tests (extracted by standardized procedure code)

Procedure code	Standardized procedure code	Standardized procedure name
D200	160062470	load test
D200	160062570	provocation test for asthma
D200	160062610	lung volume fraction measurement
D200	160062710	flow volume curve
D200	160062810	functional residual capacity
D200	160062810	functional residual capacity measurement
D200	160063010	expiratory gas analysis
D200	160063110	bronchspirometry
D200	160063110	bronchspirometry test
D201	160063310	lung compliance
D201	160063310	lung compliance measurement
D201	160063410	airway resistance
D201	160063410	airway resistance measurement
D201	160063550	pulmonary viscous resistance
D201	160063550	pulmonary viscous resistance measurement
D201	160063750	inspired air distribution test
D201	160198210	respiratory resistance measurement (multi-frequency forced oscillation technique)
D201	160198310	respiratory resistance measurement (other)
D202	160063810	indicator gas detection (pulmonary gas distribution)
D202	160063810	indicator gas detection test (pulmonary gas distribution)
D202	160063910	closing volume measurement
D203	160064010	pulmonary diffusing capacity test
D203	160064110	dead space volume measurement
D203	160064210	intrapulmonary shunt test
D204	160064310	basal metabolic rate (BMR)
D205	160146910	test results interpretation fee of respiratory function test

High-resolution computed tomography (extracted by standardized procedure code)

Procedure code	Standardized procedure code	Standardized procedure name
E200	170011810	CT imaging, with multislice device with 16-63 rows
E200	170033410	CT imaging, with multislice device with 64 rows or more (other)
E200	170034910	CT imaging, with multislice device with 64 rows or more, at shared facility
E200	170034910	CT imaging, with multislice device with 64 or more rows, at shared facility
E200	170040210	CT imaging, with multislice device with 64 or more rows, at shared facility (joint diagnostic imaging)
E200	170040410	CT imaging, with multislice device with 64 rows or more (other) (Joint Diagnostic Imaging)
E200	170040610	CT imaging, with multislice device with 16-63 rows (Joint Diagnostic Imaging)

CT, computed tomography

Ventilation/perfusion lung scan (extracted by standardized procedure code)

Procedure code	Standardized procedure code	Standardized procedure name
E100	170024510	scintigraphy (partial-body, static imaging)
E100	170024610	scintigraphy (partial-body, dynamic imaging)

Contrast-enhanced chest CT (extracted by standardized procedure code)

Procedure code	Standardized procedure code	Standardized procedure name
E200	170011810	CT imaging, with multislice device with 16-63 rows
E200	170033410	CT imaging, with multislice device with 64 rows or more (other)
E200	170034910	CT imaging, with multislice device with 64 rows or more, at shared facility
E200	170034910	CT imaging, with multislice device with 64 or more rows, at shared facility
E200	170040210	CT imaging, with multislice device with 64 or more rows, at shared facility (joint diagnostic imaging)
E200	170040410	CT imaging, with multislice device with 64 rows or more (other) (Joint Diagnostic Imaging)
E200	170040610	CT imaging, with multislice device with 16-63 rows (Joint Diagnostic Imaging)
E200	170012070	additional fee for contrast medium use <CT imaging>

CT, computed tomography

Blood test: brain natriuretic peptide and N-terminal pro-brain natriuretic peptide (extracted by standardized procedure code)

Procedure code	Standardized procedure code	Standardized procedure name
D008	160162350	brain natriuretic peptide (BNP)
D008	160181250	N-terminal pro-brain natriuretic peptide (NT-proBNP)

Table S9 Intravenous prostacyclin (extracted by the general name)

ATC level 4 code	General name	Drug name
C06B3	Epoprostenol Sodium	Flolan 0.5mg for I.V.Injection
C06B3	Epoprostenol Sodium	Flolan 1.5mg for I.V.Injection
C06B3	Epoprostenol Sodium	Epoprostenol for I.V.Injection 0.5mg [F]
C06B3	Epoprostenol Sodium	Epoprostenol for I.V.Injection 1.5mg [F]
C06B3	Epoprostenol Sodium	Epoprostenol for I.V.Injection 0.5mg [ACT]
C06B3	Epoprostenol Sodium	Epoprostenol for I.V.Injection 1.5mg [ACT]
C06B3	Epoprostenol Sodium	Epoprostenol for I.V.Injection [ACT] Unspecified
C06B3	Epoprostenol Sodium	Epoprostenol for I.V.Injection 0.5mg [TEVA]
C06B3	Epoprostenol Sodium	Epoprostenol for I.V.Injection 1.5mg [TEVA]
C06B3	Epoprostenol Sodium	Epoprostenol for I.V.Injection [TEVA] Unspecified
C06B3	Epoprostenol Sodium	Epoprostenol for I.V.Injection [JANSSEN] Unspecified
C06B3	Epoprostenol Sodium	Epoprostenol for I.V.Injection 0.5mg [JANSSEN]
C06B3	Epoprostenol Sodium	Epoprostenol for I.V.Injection 1.5mg [JANSSEN]
C06B3	Epoprostenol Sodium	Epoprostenol for I.V.Injection 1.5mg [NIG]
C06B3	Epoprostenol Sodium	Epoprostenol for I.V.Injection 0.5mg [NIG]

Table S10 Intensive care unit and emergency department

Intensive care unit (extracted by procedure category subclassification name)

procedure code	standardized procedure code	standardized procedure name
A301	190175010	inpatient management fee in high care unit [1]
A301	193010810	inpatient management fee in high care unit [1] (within 14 days) (advanced treatment hospital)
A301	193311010	inpatient management fee in high care unit [1] (within 14 days) (specialty hospital)
A301	193512510	inpatient management fee in high care unit [1], within 14 days (DPC)
A301	193010910	inpatient management fee in high care unit [1] (for 15-21 days) (advanced treatment hospital)
A301	193311110	inpatient management fee in high care unit [1] (for 15-21 days) (specialty hospital)
A301	193512610	inpatient management fee in high care unit [1], for 15-21 days (DPC)
A301	190175110	inpatient management fee in high care unit [2]
A301	193011010	inpatient management fee in high care unit [2] (within 14 days) (advanced treatment hospital)
A301	193311210	inpatient management fee in high care unit [2] (within 14 days) (specialty hospital)
A301	193512710	inpatient management fee in high care unit [2], within 14 days (DPC)

A301	193011110	inpatient management fee in high care unit [2] (for 15-21 days) (advanced treatment hospital)
A301	193311310	inpatient management fee in high care unit [2] (for 15-21 days) (specialty hospital)
A301	193512810	inpatient management fee in high care unit [2], for 15-21 days (DPC)
A301	193014110	specific intensive care unit management fee [1], for 15-30 days (advanced treatment hospital)
A301	193317210	specific intensive care unit management fee [1], for 15-30 days (specialty hospital)
A301	193588110	specific intensive care unit management fee [1], for 15-30 days (DPC)
A301	193014210	specific intensive care unit management fee [1], for 31 days or more (advanced treatment hospital)
A301	193317310	specific intensive care unit management fee [1], for 31 days or more (specialty hospital)
A301	193588210	specific intensive care unit management fee [1], for 31 days or more (DPC)
A301	190174410	specific intensive care unit management fee [1], within 7 days
A301	193010010	specific intensive care unit management fee [1], within 7 days (advanced treatment hospital)
A301	193310210	specific intensive care unit management fee [1], within 7 days (specialty hospital)
A301	193511710	specific intensive care unit management fee [1], within 7 days (DPC)
A301	190246510	specific intensive care unit management fee [1], within 7 days (acute blood purification or ECMO, organ transplantation)
A301	190174510	specific intensive care unit management fee [1], for 8 days or more
A301	190246610	specific intensive care unit management fee [1], for 8 days or more (acute blood purification or ECMO, organ transplantation)
A301	190174510	specific intensive care unit management fee [1], for 8-14 days
A301	193010110	specific intensive care unit management fee [1], for 8-14 days (advanced treatment hospital)
A301	193310310	specific intensive care unit management fee [1], for 8-14 days (specialty hospital)
A301	193511810	specific intensive care unit management fee [1], for 8-14 days (DPC)
A301	190174710	specific intensive care unit management fee [2], for 8 days or more
A301	193014310	specific intensive care unit management fee [2], for 15-30 days (specific intensive care unit management fee) (advanced treatment hospital)
A301	193317410	specific intensive care unit management fee [2], for 15-30 days (specific intensive care unit management fee) (specialty hospital)
A301	193588310	specific intensive care unit management fee [2], for 15-30 days (specific intensive care unit management fee) (DPC)
A301	193014410	specific intensive care unit management fee [2], for 31 days or more (specific intensive care unit management fee) (advanced treatment hospital)
A301	193317510	specific intensive care unit management fee [2], for 31 days or more (specific intensive care unit management fee) (specialty hospital)

A301	193588410	specific intensive care unit management fee [2], for 31 days or more (specific intensive care unit management fee) (DPC)
A301	190174610	specific intensive care unit management fee [2], within 7 days
A301	193010210	specific intensive care unit management fee [2], within 7 days (advanced treatment hospital)
A301	193310410	specific intensive care unit management fee [2], within 7 days (specialty hospital)
A301	193511910	specific intensive care unit management fee [2], within 7 days (DPC)
A301	190174710	specific intensive care unit management fee [2] (specific intensive care unit management fee) (for 8-14 days)
A301	193010310	specific intensive care unit management fee [2] (specific intensive care unit management fee) (for 8-14 days) (advanced treatment hospital)
A301	193310510	specific intensive care unit management fee [2] (specific intensive care unit management fee) (for 8-14 days) (specialty hospital)
A301	193512010	specific intensive care unit management fee [2] (specific intensive care unit management fee) (for 8-14 days) (DPC)
A301	193512010	specific intensive care unit management fee [2], for 8-14 days (DPC)
A301	193014510	specific intensive care unit management fee [3], for 15-30 days (advanced treatment hospital)
A301	193317610	specific intensive care unit management fee [3], for 15-30 days (specialty hospital)
A301	193588510	specific intensive care unit management fee [3], for 15-30 days (DPC)
A301	193014610	specific intensive care unit management fee [3], for 31 days or more (advanced treatment hospital)
A301	193317710	specific intensive care unit management fee [3], for 31 days or more (specialty hospital)
A301	193588610	specific intensive care unit management fee [3], for 31 days or more (DPC)
A301	190116310	specific intensive care unit management fee [3], within 7 days
A301	193001610	specific intensive care unit management fee [3], within 7 days (advanced treatment hospital)
A301	193301410	specific intensive care unit management fee [3], within 7 days (specialty hospital)
A301	193501610	specific intensive care unit management fee [3], within 7 days (DPC)
A301	190246910	specific intensive care unit management fee [3], within 7 days (acute blood purification or ECMO, organ transplantation)
A301	190116410	specific intensive care unit management fee [3], for 8 days or more
A301	190247010	specific intensive care unit management fee [3], for 8 days or more (acute blood purification or ECMO, organ transplantation)
A301	190116410	specific intensive care unit management fee [3], for 8-14 days
A301	193001710	specific intensive care unit management fee [3], for 8-14 days (advanced treatment hospital)
A301	193301510	specific intensive care unit management fee [3], for 8-14 days (specialty hospital)

A301	193501710	specific intensive care unit management fee [3], for 8-14 days (DPC)
A301	190139910	specific intensive care unit management fee [4], for 8 days or more
A301	193014710	specific intensive care unit management fee [4], for 15-30 days (specific intensive care unit management fee) (advanced treatment hospital)
A301	193317810	specific intensive care unit management fee [4], for 15-30 days (specific intensive care unit management fee) (specialty hospital)
A301	193588710	specific intensive care unit management fee [4], for 15-30 days (specific intensive care unit management fee) (DPC)
A301	193014810	specific intensive care unit management fee [4], for 31 days or more (specific intensive care unit management fee) (advanced treatment hospital)
A301	193317910	specific intensive care unit management fee [4], for 31 days or more (specific intensive care unit management fee) (specialty hospital)
A301	193588810	specific intensive care unit management fee [4], for 31 days or more (specific intensive care unit management fee) (DPC)
A301	190139810	specific intensive care unit management fee [4], within 7 days
A301	193005910	specific intensive care unit management fee [4], within 7 days (advanced treatment hospital)
A301	193307210	specific intensive care unit management fee [4], within 7 days (specialty hospital)
A301	193507510	specific intensive care unit management fee [4], within 7 days (DPC)
A301	190139910	specific intensive care unit management fee [4] (specific intensive care unit management fee) (for 8-14 days)
A301	193006010	specific intensive care unit management fee [4] (specific intensive care unit management fee) (for 8-14 days) (advanced treatment hospital)
A301	193307310	specific intensive care unit management fee [4] (specific intensive care unit management fee) (for 8-14 days) (specialty hospital)
A301	193507610	specific intensive care unit management fee [4] (specific intensive care unit management fee) (for 8-14 days) (DPC)
A301	193507610	specific intensive care unit management fee [4], for 8-14 days (DPC)

Emergency department (extracted by standardized procedure code)

procedure code	standardized procedure code	standardized procedure name
A205	190171910	emergency hospitalization management fee [1] (per day)
A205	190172010	emergency hospitalization management fee [2] (per day)
B001	113013810	management fee for emergency transportation at night or on holiday
C004	114003010	critical care in transportation fee
A000	112017790	first visit fee
A000	112017890	first visit fee

A000	112017990	first visit fee
A000	112018390	first visit fee
A000	112018890	first visit fee
A000	112018990	first visit fee
A000	112019090	first visit fee
A000	112019390	first visit fee
A000	111000570	first visit fee
A000	111000670	first visit fee
A000	111000770	first visit fee
A000	111000870	first visit fee
A000	111012470	first visit fee
A001	112001110	return visit
A001	112001210	return visit
A001	112001310	return visit
A001	112001410	return visit
A001	112015570	return visit
A001	112016070	return visit
A001	112015670	return visit
A001	112016170	return visit
A002	112006470	outpatient care fee
A002	112006570	outpatient care fee
A002	112006670	outpatient care fee
A002	112006770	outpatient care fee
B006	113002610	emergency management fee

Table S11 Demographic and clinical characteristics of patients

	RHC(-) cohort, N=298			RHC(+) cohort, N=107		
	Oral/Inhaled Monotherapy N= 209	Oral/Inhaled Combination N= 84	PPA Combination N= 5	Oral/Inhaled Monotherapy N= 31	Oral/Inhaled Combination N= 59	PPA Combination N= 17
Demographics						
Age at index date						
Mean (SD)	48.9 (13.4)	47.3 (12.9)	30.0 (6.4)	48.2 (13.5)	45.5 (12.6)	37.9 (9.7)
Median (IQR)	50.0 (40.0 - 58.0)	49.5 (38.0 - 56.0)	29.0 (29.0 - 30.0)	50.0 (36.0 - 58.0)	46.0 (35.0 - 55.0)	37.0 (30.0 - 48.0)
Sex, n (%)						
Female	163 (78.0)	68 (81.0)	3 (60.0)	17 (54.8)	45 (76.3)	12 (70.6)
Time to end of follow up, months						
Mean (SD)	40.9 (17.3)	45.0 (17.5)	49.6 (19.6)	38.5 (15.3)	40.1 (18.8)	50.6 (14.4)
Median (IQR)	42.0 (27.0 - 59.0)	54.0 (30.0 - 60.0)	60.0 (53.0 - 60.0)	39.0 (25.0 - 49.0)	41.0 (22.0 - 60.0)	60.0 (46.0 - 60.0)
Clinical characteristics						
Department at index date, n (%)						
General Internal Medicine	40 (19.1)	17 (20.2)	0 (0.0)	8 (25.8)	9 (15.3)	2 (11.8)
Respiratory	7 (3.3)	2 (2.4)	0 (0.0)	0 (0.0)	3 (5.1)	0 (0.0)
Cardiology	19 (9.1)	20 (23.8)	1 (20.0)	17 (54.8)	32 (54.2)	13 (76.5)
Rheumatology	52 (24.9)	14 (16.7)	0 (0.0)	1 (3.2)	6 (10.2)	0 (0.0)
Dermatology	21 (10.0)	6 (7.1)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)
Pediatrics	15 (7.2)	8 (9.5)	2 (40.0)	2 (6.5)	3 (5.1)	0 (0.0)
Other	15 (7.2)	5 (6.0)	0 (0.0)	3 (9.7)	5 (8.5)	1 (5.9)

Null	44 (21.1)	17 (20.2)	2 (40.0)	1 (3.2)	8 (13.6)	3 (17.6)
Facility at index date, n (%)						
Facilities specialized for cardiology	160 (76.6)	71 (84.5)	4 (80.0)	30 (96.8)	56 (94.9)	15 (88.2)
Facilities specialized for PAH	56 (26.8)	32 (38.1)	3 (60.0)	18 (58.1)	32 (54.2)	13 (76.5)
Facilities not specialized for PAH treatment	105 (50.2)	39 (46.4)	1 (20.0)	13 (41.9)	28 (47.5)	2 (11.8)
Comorbidity in baseline period, n (%)						
CPC						
Hypertension	98 (46.9)	45 (53.6)	1 (20.0)	23 (74.2)	28 (47.5)	6 (35.3)
Coronary heart disease	35 (16.7)	11 (13.1)	0 (0.0)	8 (25.8)	15 (25.4)	3 (17.6)
Atrial fibrillation	18 (8.6)	2 (2.4)	0 (0.0)	8 (25.8)	8 (13.6)	1 (5.9)
Diabetes mellitus	76 (36.4)	35 (41.7)	1 (20.0)	9 (29.0)	16 (27.1)	5 (29.4)
Obesity	1 (0.5)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mild parenchymal lung disease	94 (45.0)	32 (38.1)	0 (0.0)	5 (16.1)	15 (25.4)	3 (17.6)
COPD	37 (17.7)	16 (19.0)	1 (20.0)	6 (19.4)	8 (13.6)	4 (23.5)
Non-CPC						
Anxiety	16 (7.7)	5 (6.0)	0 (0.0)	3 (9.7)	2 (3.4)	0 (0.0)
Depression	17 (8.1)	4 (4.8)	0 (0.0)	3 (9.7)	5 (8.5)	2 (11.8)
Diagnostic procedure, n (%)						
RHC	0 (0.0)	0 (0.0)	0 (0.0)	31 (100.0)	59 (100.0)	17 (100.0)
Non-RHC						
Echocardiography	114 (54.5)	62 (73.8)	5 (100.0)	31 (100.0)	57 (96.6)	16 (94.1)

Other diagnostic tests						
Electrocardiogram	106 (50.7)	56 (66.7)	5 (100.0)	30 (96.8)	57 (96.6)	17 (100.0)
Chest X-ray	164 (78.5)	71 (84.5)	5 (100.0)	31 (100.0)	58 (98.3)	17 (100.0)
Blood gas tests	25 (12.0)	7 (8.3)	1 (20.0)	18 (58.1)	36 (61.0)	7 (41.2)
Pulmonary function tests	57 (27.3)	20 (23.8)	1 (20.0)	21 (67.7)	41 (69.5)	14 (82.4)
HRCT	96 (45.9)	28 (33.3)	3 (60.0)	26 (83.9)	46 (78.0)	11 (64.7)
V/Q lung scan	0 (0.0)	0 (0.0)	0 (0.0)	4 (12.9)	12 (20.3)	2 (11.8)
Contrast-enhanced chest CT	96 (45.9)	28 (33.3)	3 (60.0)	26 (83.9)	46 (78.0)	11 (64.7)
Blood test: BNP, NT-proBNP	130 (62.2)	65 (77.4)	5 (100.0)	29 (93.5)	58 (98.3)	17 (100.0)

RHC, right heart catheterization; BL, baseline; SD, standard deviation; IQR, interquartile range; PAH, pulmonary arterial hypertension; CPC, cardiopulmonary comorbidities; COPD, chronic obstructive pulmonary disease; RHC, right cardiac catheterization; HRCT, high-resolution computed tomography; CT, computed tomography; V/Q, ventilation/perfusion; BNP, brain natriuretic peptide; NT-proBNP, N-terminal pro-brain natriuretic peptide; PPA, prostacyclin pathway agents

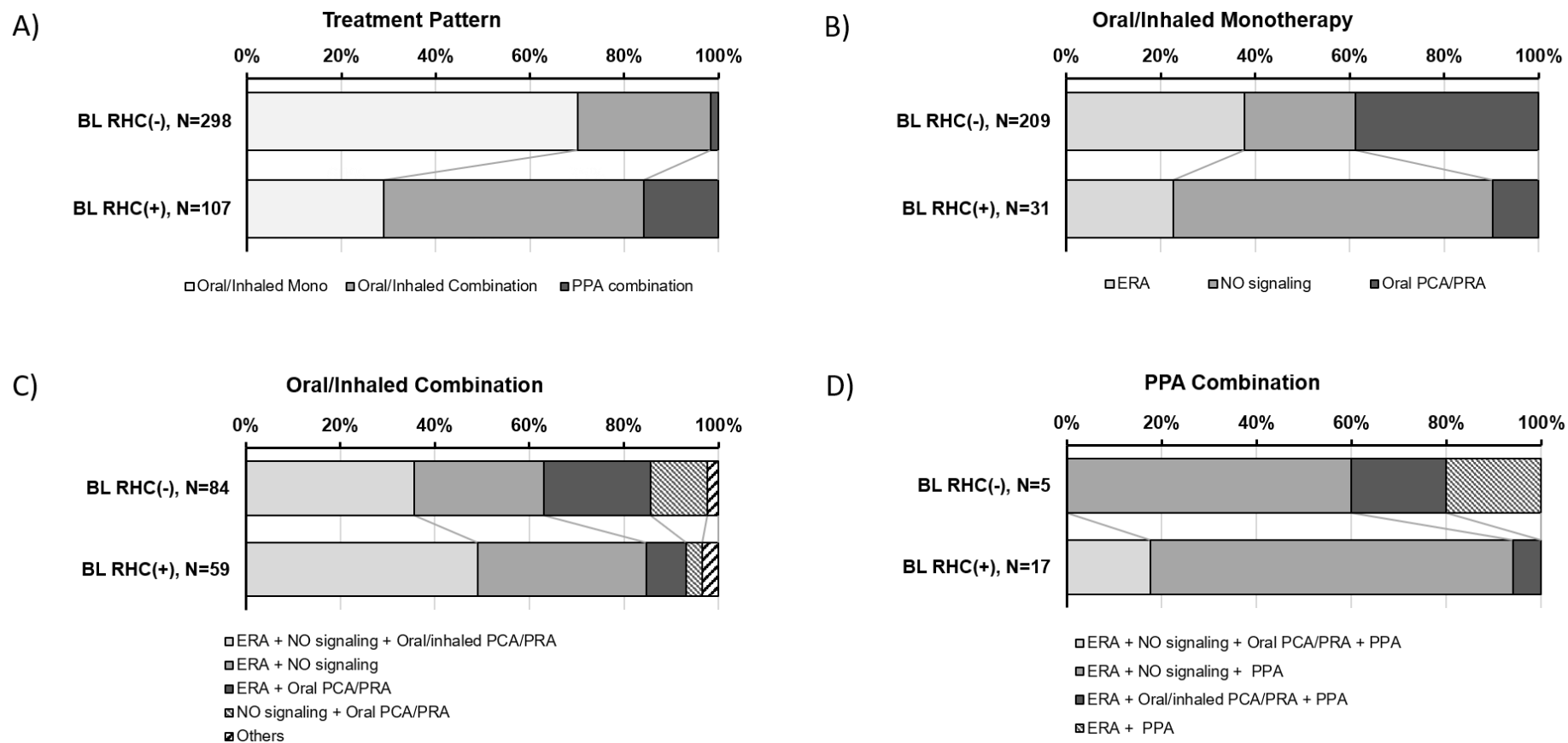
Table S12 Mean hospitalization costs per episode (adjusted by National Healthcare Insurance unit price in 2022)

	Overall	RHC(-) cohort	Oral/Inhaled Monotherapy	Oral/Inhaled Combination	PPA Combination	RHC(+) cohort	Oral/Inhaled Monotherapy	Oral/Inhaled Combination	PPA Combination
	N= 405	N= 298	N= 209	N= 84	N= 5	N= 107	N= 31	N= 59	N= 17
All-cause hospitalization costs/episode									
Overall									
Number of patients, n (%)	247 (61)	161 (54.0)	103 (49.3)	54 (64.3)	4 (80)	86 (80.4)	21 (67.7)	48 (81.4)	17 (100)
Mean, JPY	¥780,038	¥797,662	¥745,979	¥876,786	¥1,060,303	¥747,045	¥786,020	¥719,940	¥775,434
SD	1,573,266	1,762,834	1,846,580	1,659,596	920,667	1,145,498	1,004,630	1,296,601	875,088
Without ICU admission									
Number of patients, n (%)	245 (60.5)	161 (54.0)	103 (49.3)	54 (64.3)	4 (80)	84 (78.5)	20 (64.5)	47 (79.7)	17 (100)
Mean, JPY	¥559,634	¥662,445	¥668,277	¥658,650	¥563,498	¥362,581	¥385,930	¥333,672	¥415,035
SD	1,373,354	1,669,660	1,822,721	1,417,996	430,138	332,983	284,680	348,495	351,731
With ICU admission									
Number of patients, n (%)	47 (11.6)	23 (7.7)	11 (5.3)	9 (10.7)	3 (60)	24 (22.4)	6 (19.4)	12 (20.3)	6 (35.3)
Mean, JPY	¥4,913,873	¥4,383,989	¥3,532,658	¥5,615,267	¥3,811,706	¥5,421,678	¥5,257,095	¥4,804,151	¥6,821,314
SD	5,250,711	5,667,448	3,632,675	8,049,404	4,106,903	4,885,349	3,477,968	4,982,340	6,307,106

PAH-related hospitalization costs/episode									
Overall									
Number of patients, n (%)	176 (43.5)	97 (32.6)	50 (23.9)	43 (51.2)	4 (80)	79 (73.8)	18 (58.1)	44 (74.6)	17 (100)
Mean, JPY	¥858,910	¥841,325	¥801,026	¥863,645	¥1,105,116	¥880,502	¥1,173,506	¥783,212	¥822,075
SD	1,692,317	1,828,079	1,883,126	1,853,636	888,157	1,520,384	1,622,245	1,660,914	965,740
Without ICU admission									
Number of patients, n (%)	173 (42.7)	96 (32.2)	50 (23.9)	42 (50)	4 (80)	77 (72.0)	17 (54.8)	43 (72.9)	17 (100)
Mean, JPY	¥542,069	¥671,054	¥645,748	¥708,852	¥590,488	¥381,257	¥393,169	¥365,605	¥408,937
SD	1,292,006	1,681,210	1,790,253	1,644,353	404,627	444,463	315,111	520,857	353,962
With ICU admission									
Number of patients, n (%)	32 (7.9)	12 (4.0)	5 (2.4)	4 (4.8)	3 (60)	20 (18.7)	5 (16.1)	9 (15.3)	6 (35.3)
Mean, JPY	¥5,186,509	¥4,047,937	¥5,605,092	¥2,278,667	¥3,811,706	¥5,869,652	¥6,639,605	¥4,809,567	¥6,818,150
SD	4,685,660	3,863,282	4,484,139	2,898,206	4,106,903	5,086,377	2,788,523	5,509,915	6,310,320

RHC, right heart catheterization; JPY, Japanese yen; ICU, intensive care unit; PAH, pulmonary arterial hypertension; PPA, prostacyclin pathway agents

Figure S1 Distribution of the therapy



BL, baseline; RHC, right heart catheterization; ERA, endothelin receptor antagonists; NO signaling, nitric oxide signaling; PCA, prostacyclin analogue; PRA, prostacyclin receptor agonist; PPA, prostacyclin pathway agents