Risk assessment and real-world outcomes in chronic thromboembolic pulmonary hypertension: insights from a UK pulmonary hypertension referral service

## Supplementary tables

Supplementary Table 1. Average HCRU and associated costs per year at 1- and 3-years' follow-up post-diagnosis, by cohort

| | **Operated patients** | | **Not-operated patients** | |
|---|---|---|---|---|
| | **1-year follow-up (n=237)** | **3-year follow-up* (n=134)** | **1-year follow-up (n=292)** | **3-year follow-up* (n=149)** |
| **HCRU, per patient per year of follow-up, n** | | | | |
| Inpatient hospitalisations (>1 day) | | | | |
| Mean (SD) | 2.5 (1.8) | 1.7 (1.1) | 1.2 (1.5) | 0.8 (1.2) |
| Median (Q1, Q3) | 2.0 (1.0, 3.0) | 1.7 (1.0, 2.0) | 1.0 (0.0, 2.0) | 0.3 (0.3, 1.0) |
| Duration (>1 day) inpatient hospitalisations, days | | | | |
| Mean (SD) | 10.2 (8.0) | 7.8 (5.7) | 6.8 (10.0) | 6.1 (7.0) |
| Median (Q1, Q3) | 8.7 (6.0, 12.0) | 6.3 (5.3, 8.7) | 3.0 (2.0, 8.0) | 3.5 (2.0, 6.8) |
| Same-day visits | | | | |
| Mean (SD) | 2.1 (1.5) | 2.0 (2.6) | 2.4 (1.9) | 1.9 (1.2) |
| Median (Q1, Q3) | 2.0 (1.0, 3.0) | 1.7 (1.3, 2.3) | 2.0 (1.0, 3.0) | 1.7 (1.3, 2.7) |
| Outpatient consultations | | | | |
| Mean (SD) | 9.7 (10.5) | 8.6 (8.1) | 10.8 (10.3) | 9.0 (7.1) |
| Median (Q1, Q3) | 5.0 (3.0, 12.0) | 5.7 (3.3, 10.7) | 7.0 (4.0, 15.0) | 7.0 (4.0, 11.7) |
| A&E visits | | | | |
| Mean (SD) | 1.0 (2.1) | 0.8 (1.4) | 0.9 (1.5) | 0.7 (1.2) |
| Median (Q1, Q3) | 0.0 (0.0, 1.0) | 0.3 (0.0, 1.0) | 0.0 (0.0, 1.0) | 0.3 (0.0, 1.0) |

| | Operated patients | | Not-operated patients | |
|---|---|---|---|---|
| **Costs (GBP), per patient per year of follow-up** | | | | |
| Inpatient hospitalisations (>1 day) | | | | |
| Mean (SD) | 4215 (4693) | 2539 (2813) | 3101 (4718) | 1901 (2951) |
| Median (Q1, Q3) | 2836 (0, 6941) | 1862 (828, 3474) | 1527 (0, 3681) | 1015 (176, 2279) |
| Same-day spells | | | | |
| Mean (SD) | 1971 (1483) | 1855 (3911) | 2247 (2767) | 1704 (1410) |
| Median (Q1, Q3) | 1838 (989, 2813) | 1407 (871, 1897) | 1992 (1002, 2899) | 1580 (1012, 2191) |
| Outpatient consultations | | | | |
| Mean (SD) | 1448 (1361) | 1173 (1046) | 1476 (1447) | 1212 (954) |
| Median (Q1, Q3) | 935 (604, 1705) | 849 (543, 1368) | 1043 (592, 1825) | 983 (578, 1544) |
| A&E visits | | | | |
| Mean (SD) | 112 (200) | 86 (143) | 115 (222) | 94 (184) |
| Median (Q1, Q3) | 0 (0, 169) | 47 (0, 104) | 0 (0, 148) | 40 (0, 114) |
| **Total mean costs per patient** | 7746 | 5653 | 6939 | 4911 |

*HCRU and costs 3 years post-diagnosis represent the mean and median per year for patients with 3 years of follow-up data, not during the third year. Total costs represent the sum of means for the four types of HCRU.

A&E, accident and emergency; GBP, British Pound Sterling; HCRU, healthcare resource utilisation; SD standard deviation

Supplementary Table 2. Survival probabilities by cohort and risk group

| | **Survival probability (95% CI)** | | |
|---|---|---|---|
| | **1 year** | **3 year** | **5 year** |
| **Not operated patients** | 0.85 (0.82, 0.89) | 0.63 (0.58, 0.69) | 0.49 (0.43, 0.56) |
| Low-risk | 0.91 (0.81, 1.00) | 0.91 (0.81, 1.00) | 0.91 (0.81, 1.00) |
| Intermediate-risk | 0.91 (0.87, 0.95) | 0.70 (0.64, 0.78) | 0.59 (0.50, 0.68) |
| High-risk | 0.76 (0.68, 0.84) | 0.48 (0.39, 0.58) | 0.29 (0.20, 0.41) |
| **Operated patients** | 0.98 (0.96, 1.00) | 0.91 (0.87, 0.95) | 0.83 (0.78, 0.90) |
| Low-risk | 1.00 (1.00, 1.00) | 0.94 (0.84, 1.00) | 0.94 (0.84, 1.00) |
| Intermediate-risk | 0.98 (0.95, 1.00) | 0.92 (0.88, 0.97) | 0.83 (0.75, 0.92) |
| High-risk | 0.97 (0.92, 1.00) | 0.85 (0.76, 0.95) | 0.79 (0.67, 0.92) |

Supplementary Table 3. Patient characteristics included in the Kylhammar risk assessment tool [32]

| **Determinants of prognosis** | **Low risk** | **Intermediate risk** | **High risk** |
|---|---|---|---|
| WHO FC | I, II | III | IV |
| 6MWD | >440 m | 165–440 m | <165 m |
| NT-proBNP levels | <300 ng/L | 300–1400 ng/L | >1400 ng/L |
| Imaging (echocardiography) | RA area <18 $cm^2$<br>No pericardial effusion | RA area 18–26 $cm^2$<br>No or minimal pericardial effusion | RA area >26 $cm^2$<br>Pericardial effusion |
| Haemodynamics | RAP <8 mmHg<br>CI ≥2.5 L/min/$m^2$<br>$SvO_2$ >65% | RAP 8–14 mmHg<br>CI 2.0–2.4 L/min/$m^2$<br>$SvO_2$ 60–65% | RAP >14 mmHg<br>CI <2.0 L/min/$m^2$<br>$SvO_2$ <60% |

Source: Kylhammar et al. 2018 [32]

6MWD, 6-minute walking distance; CI, cardiac index; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; RA, right atrium; RAP, right atrial pressure; $SvO_2$, mixed venous oxygen saturation; WHO FC, World Health Organization functional class

Supplementary Table 4. Final risk category assessment strategy

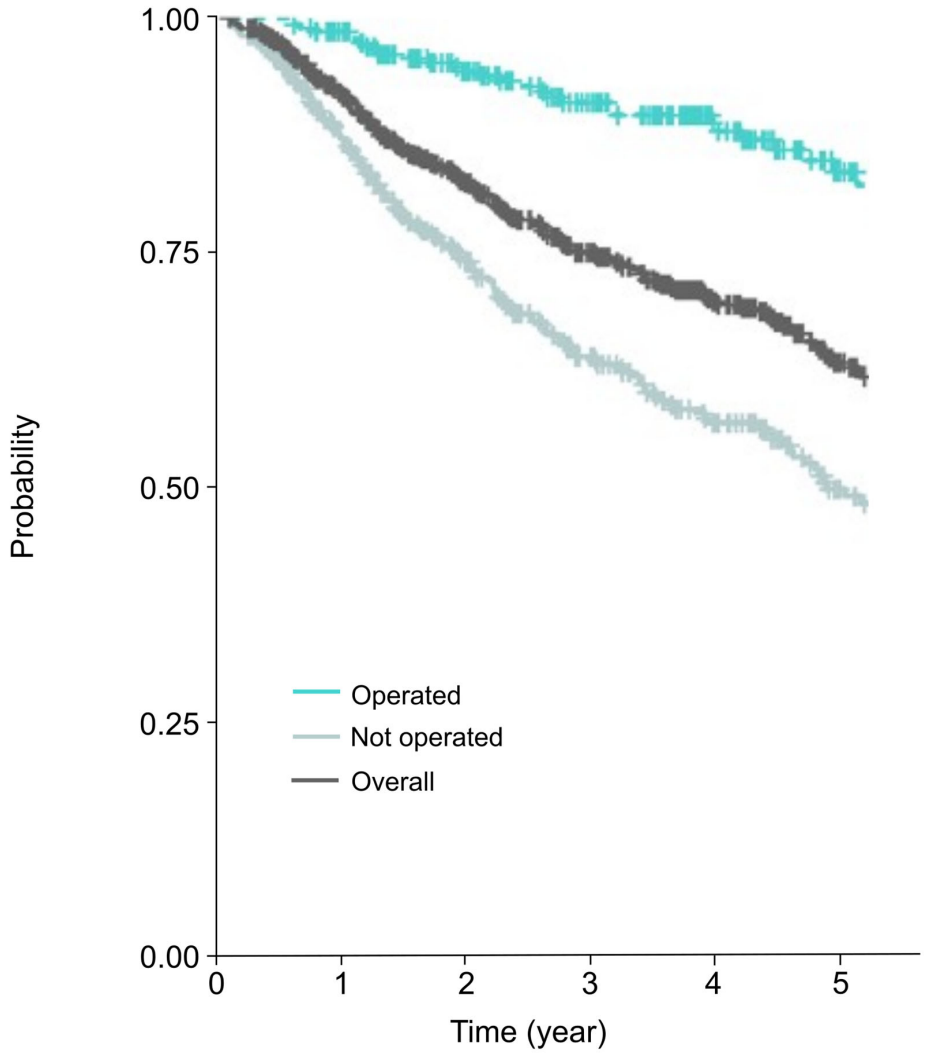
| **Variables included in risk score at each assessment point** | **Risk score methodology** |
|---|---|
| 1. WHO FC<br>2. ISWT or 6MWD<br>• ISWT thresholds were: ≥340 m (low risk), 190–330 m (intermediate risk), ≤180 m (high risk)<br>3. RVEF where available<br>4. RAP where available<br>5. Cardiac index where available<br>6. $SvO_2$ where available | 1. A minimum of ISWT and WHO FC were used to define a patient risk score at any risk assessment<br>2. Each variable was graded from 1 to 3 based on the ESC/ERS guidelines and cardiovascular magnetic resonance imaging<br>3. 1= 'Low risk', 2= 'Intermediate risk', and 3= 'High risk'<br>4. A mean grade (sum of all grades/the number of parameters for each patient) was calculated and rounded off to the nearest integer, which was used to define the patient's risk stratum |

ISWT was used if 6MWD was not available, as ISWT is more commonly used at Sheffield Pulmonary Vascular Disease Unit. Both WHO FC and ISWT/6MWD were required to calculate a score as a minimum; if either were not available, the risk score was defined as 'missing/undetermined'.

6MWD, 6-minute walk distance; ESC/ERS, European Society of Cardiology/European Respiratory Society; ISWT, incremental shuttle walk test; RAP, right atrial pressure; RVEF, right ventricular ejection fraction; $SvO_2$, mixed venous oxygen saturation; WHO FC, World Health Organization functional class

## Supplementary figure

Figure 1. Survival in patients after diagnosis with CTEPH




Number of patients at risk

| | | | | | | |
|---|---|---|---|---|---|---|
| Operated | 268 | 246 | 191 | 139 | 99 | 61 |
| Not operated | 415 | 295 | 208 | 154 | 112 | 64 |
| Overall | 683 | 541 | 399 | 293 | 211 | 125 |

Small numbers were suppressed in line with data protection requirements. A result of '<7' substitutes any patient count that is below 7 unique patients and therefore masked for data privacy reasons. 'S*' means that a number that has been 'Suppressed'. Values of zero or missing do not require suppression.

CTEPH, chronic thromboembolic pulmonary hypertension