**Supplementary Online Content**

Vanderpool RR, Saul M, Nouraie M, Gladwin MT, Simon MA. Association between hemodynamic markers of pulmonary hypertension and outcomes in heart failure with preserved ejection fraction. *JAMA Cardiol*. Published online March 14, 2018. doi:10.1001/jamacardio.2018.0128



This supplementary material has been provided by the authors to give readers additional information about their work.

**eAppendix 1.** eMethods

***Patient Linked Data Sources***

The administrative file is the medical record discharge abstract file and includes every in-network visit for the subject, admission date, discharge date, date of birth, discharge disposition, sex, race, patient type, visit type, primary diagnosis code, 24 secondary diagnosis codes, primary procedure code and date of procedure, and 24 secondary procedure codes and date of procedure (**eFigure 1**). Left ventricular ejection fraction (LVEF) was extracted from full text search of the clinical data repository (CDR) sources including echocardiography (echo-derived) and nuclear (volumetric-derived) data sources. Volumetric EF data was available from subjects who had undergone a nuclear cardiology test between 3/13/1992 – 8/18/2015 at any UPMC hospital (**eFigure 2)**. Echocardiography data was available from subjects who had undergone an echocardiogram between 11/1/1993 and 7/6/2015 at any UPMC hospital. Standard echocardiography data available includes: Systolic LV diameter, diastolic LV diameter, posterior wall thickness, septal wall thickness, aortic root diameter, left atrium diameter, estimated LV ejection fraction. The EF closest to the indexed RHC was used unless the subject had both an echocardiographic-derived and a volumetric-derived EF within 7 days of the RHC, in which case priority was then given to the volumetric derived EF. A preserved ejection fraction was defined as ≥45% based on the ACC/AHA 2014 heart failure guidelines.

A RHC visit was included in the analysis if there was follow-up data (administrative, nuclear, echocardiography, laboratory, or pulmonary function test) and included recorded values for pulmonary artery pressure (systolic, diastolic and mean), cardiac output (thermodilution or Fick) and pulmonary artery wedge pressure (PAWP). In the case of a subject with both a thermodilution and a Fick measure of cardiac output, the thermodilution measure was used.

***Outcomes: Mortality, acute hospitalizations and cardiac hospitalizations***

The primary outcome was time to all-cause mortality which was assessed via the social security death index (SSDI). Secondary outcomes were time to acute hospitalization and cardiovascular hospitalization post index procedure. An acute hospitalization was defined as the first acute inpatient visit or observational visit (direct observation visit or emergency visit and a length of stay > 1 day) to occur after the date of discharge (for inpatients) or date of procedure (for outpatients). International Classification of Diseases, Ninth Revision (ICD-9) was used to identify cardiac hospitalizations which include: hypertension (401-405), ischemic heart disease (410-414), disease of pulmonary circulation (415-417) and other forms of heart disease (420-429) including heart failure (428). For each hospitalization, only the principal diagnosis code was used to identify a cardiovascular event. In all hospitalizations (all-cause and cardiac), time 0 was defined as the date of the index RHC.

**eAppendix 2.** eResults

***Identification of LVEF***

LVEF was identified in 9427 subjects (94.1% of the population with right heart catheterization hemodynamics). Of the LVEF data identified, 67.3% was obtained from echocardiography data and 26.8% was obtained from nuclear imaging (**eFigure 2**).

***Association between PH classifications and adverse outcomes***

The survival table for patients classified hemodynamically as No PH, PAH, PH-LHD, PH-HFrEF, and PH-HFpEF is presented in **eTable 1**. The corresponding table for freedom from cardiac hospitalization is presented in **eTable 2**. These data correspond to **Figures 2A-D** of the primary manuscript.

***Association between hemodynamic markers of pre-capillary involvement and outcomes in PH-HFpEF***

Stratifying the PH-HFpEF cohort by the three hemodynamic markers of pre-capillary involvement identified different phenotypes (**eFigure 2 and 3**, **eTable 3 and 4**). Detailed survival tables for PH-HFpEF patients stratified by TPG, PVR or DPG are presented in **eTables 5-7**. Detailed tables for cardiac hospitalization stratified by TPG, PVR or DPG are presented in **eTables 8-10**.

**eTable 1.** Table of the Survival Probability and the Number of Participants at Risk

| | No PH | | PAH | | PH-LHD | | PH-HFrEF | | PH-HFpEF | |
|---|---|---|---|---|---|---|---|---|---|---|
| Time (years) | Survival | # at risk | Survival | # at risk | Survival | # at risk | Survival | # at risk | Survival | # at risk |
| 0.0 | 100.0 | 3792 | 100.0 | 1595 | 100.0 | 4603 | 100.0 | 1813 | 100.0 | 2577 |
| 0.5 | 92.1 | 3493 | 83.9 | 1339 | 78.1 | 3595 | 71.6 | 1299 | 82.5 | 2127 |
| 1.0 | 88.6 | 3361 | 77.5 | 1236 | 71.7 | 3304 | 64.8 | 1175 | 76.4 | 1969 |
| 1.5 | 86.1 | 3265 | 72.2 | 1152 | 67.1 | 3087 | 60.5 | 1097 | 71.4 | 1841 |
| 2.0 | 83.8 | 3176 | 68.2 | 1088 | 63.2 | 2909 | 56.7 | 1028 | 67.3 | 1735 |
| 2.5 | 81.8 | 3102 | 64.0 | 1021 | 60.4 | 2781 | 54.0 | 979 | 64.4 | 1659 |
| 3.0 | 79.5 | 3016 | 60.9 | 972 | 57.7 | 2655 | 51.6 | 937 | 61.4 | 1582 |
| 3.5 | 77.3 | 2792 | 58.2 | 867 | 54.6 | 2355 | 48.2 | 824 | 58.6 | 1405 |
| 4.0 | 75.4 | 2569 | 55.8 | 768 | 52.0 | 2059 | 46.2 | 727 | 55.7 | 1226 |
| 4.5 | 73.2 | 2295 | 52.4 | 654 | 50.0 | 1824 | 44.4 | 639 | 53.5 | 1085 |
| 5.0 | 71.2 | 2062 | 50.3 | 579 | 48.0 | 1640 | 42.4 | 569 | 51.8 | 978 |
| 5.5 | 69.3 | 1824 | 48.0 | 489 | 45.9 | 1426 | 40.6 | 490 | 49.4 | 850 |
| 6.0 | 66.9 | 1608 | 46.1 | 416 | 43.8 | 1237 | 38.7 | 424 | 47.5 | 740 |
| 6.5 | 65.1 | 1431 | 44.2 | 354 | 41.7 | 1053 | 37.1 | 356 | 45.1 | 632 |
| 7.0 | 63.1 | 1243 | 42.9 | 295 | 40.4 | 868 | 35.8 | 289 | 43.8 | 523 |
| 7.5 | 61.5 | 1072 | 40.8 | 244 | 38.7 | 705 | 34.5 | 220 | 42.0 | 437 |
| 8.0 | 59.9 | 908 | 39.7 | 194 | 37.0 | 571 | 32.9 | 176 | 40.1 | 356 |
| 8.5 | 58.1 | 728 | 38.8 | 160 | 35.7 | 447 | 32.1 | 141 | 38.6 | 280 |
| 9.0 | 56.7 | 566 | 37.0 | 119 | 34.8 | 311 | 31.3 | 91 | 37.5 | 200 |
| 9.5 | 55.0 | 391 | 35.0 | 85 | 33.5 | 212 | 29.5 | 66 | 36.6 | 132 |
| 10.0 | 53.7 | 252 | 33.4 | 56 | 31.7 | 121 | 27.8 | 32 | 34.7 | 79 |

**eTable 2.** Freedom from Cardiac Hospitalization and the Number of Participants at Risk

| | No PH | | PAH | | PH-LHD | | PH-HFrEF | | PH-HFpEF | |
|---|---|---|---|---|---|---|---|---|---|---|
| Time (years) | % | # at risk | % | # at risk | % | # at risk | % | # at risk | % | # at risk |
| 0.0 | 100.0 | 3801 | 100.0 | 1600 | 100.0 | 4621 | 100.0 | 1819 | 100.0 | 2587 |
| 0.5 | 85.0 | 2632 | 84.5 | 972 | 72.9 | 2249 | 64.5 | 731 | 77.3 | 1433 |
| 1.0 | 81.6 | 2362 | 79.6 | 828 | 66.7 | 1864 | 56.4 | 572 | 71.9 | 1219 |
| 1.5 | 79.2 | 2168 | 75.6 | 730 | 62.2 | 1594 | 50.2 | 469 | 68.2 | 1058 |
| 2.0 | 77.4 | 2007 | 72.7 | 650 | 59.1 | 1390 | 47.0 | 390 | 65.1 | 939 |
| 2.5 | 75.3 | 1773 | 69.9 | 523 | 56.5 | 1167 | 44.8 | 336 | 62.3 | 782 |
| 3.0 | 73.4 | 1583 | 67.7 | 449 | 54.5 | 971 | 42.1 | 282 | 60.5 | 651 |
| 3.5 | 71.9 | 1379 | 64.5 | 366 | 52.0 | 802 | 39.1 | 225 | 58.4 | 544 |
| 4.0 | 70.8 | 1225 | 62.7 | 314 | 50.1 | 674 | 37.4 | 184 | 56.3 | 460 |
| 4.5 | 69.8 | 1045 | 61.2 | 259 | 48.3 | 569 | 35.5 | 149 | 54.6 | 396 |
| 5.0 | 68.4 | 894 | 59.4 | 205 | 46.4 | 475 | 33.7 | 126 | 52.6 | 326 |
| 5.5 | 66.5 | 767 | 57.2 | 166 | 44.6 | 375 | 32.0 | 96 | 50.5 | 258 |
| 6.0 | 65.4 | 637 | 55.5 | 128 | 42.6 | 301 | 29.4 | 70 | 49.1 | 213 |
| 6.5 | 64.0 | 526 | 53.6 | 98 | 40.1 | 231 | 26.8 | 45 | 46.2 | 170 |
| 7.0 | 62.9 | 426 | 51.2 | 69 | 38.7 | 181 | 24.8 | 36 | 45.0 | 135 |
| 7.5 | 61.4 | 328 | 51.2 | 54 | 37.4 | 128 | 23.0 | 22 | 44.6 | 99 |
| 8.0 | 60.5 | 253 | 47.8 | 32 | 36.3 | 87 | 23.0 | 14 | 43.4 | 68 |
| 8.5 | 59.1 | 176 | 47.8 | 21 | 34.8 | 49 | 21.2 | 10 | 41.9 | 38 |
| 9.0 | 57.3 | 96 | 44.8 | 10 | 32.8 | 25 | 21.2 | 5 | 39.0 | 20 |

**eTable 3.** Overlap of Hemodynamic Markers Quantifying Precapillary Involvement in PH-LHD and PH-HFpEF

| **Overlap of markers** | TPG >12 | PVR ≥3 | DPG ≥ 7 | TPG >12 & PVR ≥3 | TPG >12 & DPG ≥ 7 | PVR ≥3 & DPG ≥ 7 | TPG >12 & PVR ≥3 & DPG ≥ 7 |
|---|---|---|---|---|---|---|---|
| PH-LHD | 239 | 635 | 5 | 953 | 3 | 55 | 476 |
| PH-HFpEF | 424 | 81 | 4 | 491 | 38 | 0 | 312 |

**eTable 4.** Characteristics of the Pulmonary Hypertension Associated With Heart Failure With Preserved Ejection Fraction (PH-HFpEF) Cohort Stratified by Clinically Defined Hemodynamic Cutoffs

| PH-HFpEF | All | TPG ≤ 12 | TPG > 12 | | PVR < 3 | PVR ≥ 3 | | DPG < 7 | DPG ≥ 7 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | (n = 2587) | (n = 1322) | (n = 1265) | P | (n = 1703) | (n = 884) | P | (n = 2233) | (n = 354) | P |
| Sex (F/M/NA) | 1298/1287/2 | 591/613/ | 707/557/1 | | 759/942/2 | 539/345/0 | | 1097/1134/2 | 201/153/0 | |
| Age (years) | 65 ± 38 | 65 ± 51 | 64 ± 13 | 0.5 | 64 ± 46 | 65 ± 14 | 0.4 | 65 ± 40 | 60 ± 13 | <0.001 |
| Heart Rate (beats/min) | 77 ± 18 | 77 ± 18 | 77 ± 17 | 1.0 | 76 ± 18 | 77 ± 18 | 0.7 | 76 ± 18 | 80 ± 18 | <0.001 |
| BMI ($kg/m^2$) | 31 ± 9 | 31 ± 8 | 32 ± 9 | <0.001 | 32 ± 9 | 30 ± 8 | <0.001 | 31 ± 9 | 32 ± 9 | 0.1 |
| BSA ($m^2$) | 2 ± 0.3 | 2 ± 0.3 | 2 ± 0.3 | 0.3 | 2 ± 0.3 | 1.9 ± 0.3 | <0.001 | 2 ± 0.3 | 2 ± 0.3 | 0.5 |
| LVEF (%) | 60 ± 7 | 60 ± 8 | 60 ± 7 | 0.09 | 60 ± 7 | 60 ± 7 | 0.2 | 60 ± 7 | 61 ± 7 | 0.003 |
| LA size | 4.5 ± 0.9 | 4.5 ± 0.9 | 4.6 ± 0.9 | 0.002 | 4.5 ± 0.9 | 4.6 ± 0.9 | 0.07 | 4.5 ± 0.9 | 4.5 ± 1 | 0.7 |
| RAP (mm Hg) | 14 ± 7 | 14 ± 8 | 14 ± 7 | 0.03 | 13 ± 8 | 15 ± 7 | <0.001 | 14 ± 7 | 16 ± 7 | <0.001 |
| sPAP (mm Hg) | 58 ± 18 | 48 ± 10 | 69 ± 18 | <0.001 | 51 ± 12 | 73 ± 19 | <0.001 | 55 ± 14 | 80 ± 22 | <0.001 |
| dPAP (mm Hg) | 23 ± 8 | 20 ± 6 | 27 ± 8 | <0.001 | 20 ± 6 | 29 ± 9 | <0.001 | 21 ± 7 | 34 ± 8 | <0.001 |
| mPAP (mm Hg) | 38 ± 10 | 32 ± 6 | 44 ± 10 | <0.001 | 34 ± 7 | 46 ± 11 | <0.001 | 36 ± 8 | 52 ± 13 | <0.001 |
| PAWP (mm Hg) | 24 ± 15 | 24 ± 20 | 23 ± 6 | 0.02 | 24 ± 18 | 23 ± 6 | 0.3 | 24 ± 16 | 21 ± 5 | <0.001 |
| Cardiac Output (L/min) | 5.7 ± 2.1 | 5.7 ± 2.2 | 5.6 ± 2.1 | 0.3 | 6.3 ± 2.2 | 4.5 ± 1.4 | <0.001 | 5.8 ± 2.1 | 5.3 ± 2 | <0.001 |
| Cardiac Index ($L/min/m^2$) | 2.9 ± 1 | 2.9 ± 1 | 2.9 ± 0.9 | 0.3 | 3.1 ± 1 | 2.4 ± 0.7 | <0.001 | 2.9 ± 1 | 2.7 ± 0.9 | <0.001 |
| TPG (mm Hg) | 14 ± 16 | 8 ± 19 | 21 ± 9 | NA | 10 ± 17 | 23 ± 10 | <0.001 | 12 ± 15 | 30 ± 11 | <0.001 |
| PVR (Woods units) | 2.9 ± 3.3 | 1.5 ± 2.9 | 4.4 ± 3 | <0.001 | 1.6 ± 2.6 | 5.4 ± 3.1 | NA | 2.3 ± 2.6 | 6.7 ± 4.3 | <0.001 |
| DPG (mm Hg) | -1 ± 15 | -5 ± 19 | 4 ± 8 | <0.001 | -4 ± 17 | 5 ± 9 | <0.001 | -3 ± 15 | 13 ± 7 | NA |
| PA PP (mm Hg) | 35 ± 13 | 28 ± 9 | 42 ± 13 | <0.001 | 30 ± 10 | 44 ± 14 | <0.001 | 33 ± 12 | 46 ± 17 | <0.001 |
| Stroke Volume (mL) | 79 ± 36 | 80 ± 37 | 78 ± 35 | 0.2 | 87 ± 38 | 63 ± 26 | <0.001 | 80 ± 37 | 70 ± 29 | <0.001 |
| PA compliance (mL/mm Hg) | 2.6 ± 1.6 | 3.1 ± 1.6 | 2 ± 1.3 | <0.001 | 3.1 ± 1.6 | 1.5 ± 0.7 | <0.001 | 2.7 ± 1.5 | 1.9 ± 1.7 | <0.001 |
| RV Stroke Work (mmHg*ml) | 1884 ± 1138 | 1485 ± 986 | 2284 ± 1140 | <0.001 | 1811 ± 1157 | 2022 ± 1089 | <0.001 | 1794 ± 1107 | 2440 ± 1173 | <0.001 |
| RV Ea (mmHg/ml) | 0.9 ± 0.6 | 0.7 ± 0.4 | 1.1 ± 0.7 | <0.001 | 0.7 ± 0.3 | 1.3 ± 0.7 | <0.001 | 0.8 ± 0.5 | 1.4 ± 0.9 | <0.001 |

Values are mean ± SD. BMI: body mass index, BSA: body surface area, RAP: right atrial pressure, sPAP: systolic PA pressure, dPAP: diastolic PA pressure, mPAP: mean PA pressure, PAWP: mean pulmonary artery wedge pressure, CO: cardiac output, CI: cardiac index, TPG:

transpulmonary gradient, PVR: pulmonary vascular resistance, DPG: diastolic pulmonary gradient, PA PP: pulmonary artery pulse pressure, RV Ea: RV arterial elastance.

**eTable 5.** Survival Probability and the Number of PH-HFpEF Participants at Risk Stratified by Transpulmonary Gradient

| | TPG ≤ 6 | | TPG > 6 & TPG ≤ 9 | | TPG > 9 & TPG ≤ 12 | | TPG > 12 & TPG ≤ 15 | | TPG >15 | |
|---|---|---|---|---|---|---|---|---|---|---|
| Time (years) | Survival | # at risk | Survival | # at risk | Survival | # at risk | Survival | # at risk | Survival | # at risk |
| 0.0 | 100.0 | 305 | 100.0 | 464 | 100.0 | 547 | 100.0 | 379 | 100.0 | 882 |
| 0.5 | 82.3 | 251 | 83.0 | 385 | 85.2 | 466 | 84.7 | 321 | 79.8 | 704 |
| 1.0 | 77.4 | 236 | 76.7 | 356 | 80.6 | 441 | 79.9 | 304 | 71.7 | 632 |
| 1.5 | 73.4 | 224 | 72.4 | 336 | 77.1 | 422 | 74.7 | 283 | 65.3 | 576 |
| 2.0 | 70.5 | 215 | 69.4 | 322 | 74.0 | 406 | 71.2 | 270 | 59.2 | 522 |
| 2.5 | 67.5 | 206 | 67.5 | 313 | 72.4 | 396 | 66.8 | 253 | 55.7 | 491 |
| 3.0 | 65.6 | 200 | 64.9 | 301 | 69.8 | 382 | 62.8 | 238 | 52.3 | 461 |
| 3.5 | 63.2 | 178 | 62.9 | 274 | 66.3 | 337 | 59.5 | 211 | 49.6 | 405 |
| 4.0 | 61.3 | 161 | 60.7 | 245 | 64.0 | 295 | 56.6 | 184 | 45.7 | 341 |
| 4.5 | 58.6 | 149 | 59.4 | 217 | 60.6 | 258 | 54.7 | 165 | 43.8 | 296 |
| 5.0 | 57.4 | 136 | 57.4 | 197 | 58.9 | 237 | 52.6 | 148 | 42.1 | 260 |
| 5.5 | 54.8 | 125 | 55.3 | 178 | 56.9 | 203 | 49.3 | 128 | 39.7 | 216 |
| 6.0 | 54.4 | 114 | 53.1 | 156 | 55.8 | 185 | 46.9 | 114 | 37.1 | 171 |
| 6.5 | 52.4 | 100 | 49.2 | 132 | 52.9 | 159 | 44.3 | 95 | 35.8 | 146 |
| 7.0 | 51.2 | 81 | 48.3 | 107 | 51.8 | 137 | 42.4 | 80 | 34.2 | 118 |
| 7.5 | 50.6 | 70 | 45.8 | 85 | 49.8 | 116 | 40.1 | 65 | 32.6 | 101 |
| 8.0 | 48.2 | 60 | 44.7 | 74 | 47.1 | 91 | 37.3 | 51 | 31.6 | 80 |
| 8.5 | 45.4 | 44 | 42.0 | 59 | 44.9 | 74 | 37.3 | 39 | 31.1 | 64 |
| 9.0 | 43.1 | 28 | 41.2 | 50 | 43.4 | 49 | 36.3 | 26 | 30.6 | 47 |
| 9.5 | 43.1 | 19 | 41.2 | 32 | 40.3 | 32 | 36.3 | 17 | 29.9 | 32 |
| 10.0 | 43.1 | 11 | 39.5 | 17 | 39.0 | 21 | 34.1 | 10 | 26.6 | 20 |

**eTable 6.** Survival Probability and the Number of PH-HFpEF Participants at Risk Stratified by Pulmonary Vascular Resistance

| | PVR < 1 | | PVR ≥ 1 & PVR < 2 | | PVR ≥ 2 & PVR < 3 | | PVR ≥ 3 & PVR < 4 | | PVR ≥ 4 | |
|---|---|---|---|---|---|---|---|---|---|---|
| Time (years) | Survival | # at risk | Survival | # at risk | Survival | # at risk | Survival | # at risk | Survival | # at risk |
| 0.0 | 100.0 | 249 | 100.0 | 839 | 100.0 | 607 | 100.0 | 344 | 100.0 | 538 |
| 0.5 | 80.7 | 201 | 86.5 | 726 | 82.7 | 502 | 81.4 | 280 | 77.7 | 418 |
| 1.0 | 73.9 | 184 | 80.8 | 678 | 78.6 | 478 | 75.6 | 260 | 68.6 | 369 |
| 1.5 | 67.9 | 169 | 78.1 | 655 | 73.8 | 448 | 68.9 | 237 | 61.7 | 332 |
| 2.0 | 65.5 | 163 | 74.3 | 624 | 71.0 | 431 | 65.4 | 225 | 54.3 | 292 |
| 2.5 | 63.5 | 158 | 71.8 | 602 | 68.2 | 414 | 61.9 | 213 | 50.6 | 272 |
| 3.0 | 62.2 | 155 | 69.2 | 581 | 64.7 | 393 | 57.6 | 198 | 47.4 | 255 |
| 3.5 | 59.3 | 138 | 66.8 | 518 | 61.2 | 353 | 55.2 | 180 | 44.7 | 216 |
| 4.0 | 58.0 | 129 | 64.2 | 454 | 58.7 | 311 | 51.3 | 149 | 40.9 | 183 |
| 4.5 | 55.7 | 119 | 61.4 | 399 | 56.7 | 266 | 49.6 | 132 | 39.3 | 169 |
| 5.0 | 54.7 | 104 | 58.9 | 361 | 55.5 | 245 | 48.0 | 119 | 37.6 | 149 |
| 5.5 | 52.1 | 95 | 56.5 | 325 | 53.9 | 210 | 43.2 | 93 | 35.7 | 127 |
| 6.0 | 51.5 | 87 | 54.7 | 292 | 52.3 | 184 | 38.9 | 76 | 34.2 | 101 |
| 6.5 | 49.7 | 76 | 51.8 | 249 | 48.9 | 149 | 36.3 | 66 | 33.5 | 92 |
| 7.0 | 49.7 | 60 | 50.0 | 207 | 48.3 | 129 | 35.7 | 59 | 31.1 | 68 |
| 7.5 | 49.7 | 51 | 47.9 | 169 | 45.9 | 110 | 33.1 | 47 | 30.1 | 60 |
| 8.0 | 48.6 | 44 | 45.8 | 139 | 43.7 | 89 | 30.5 | 34 | 29.1 | 50 |
| 8.5 | 46.1 | 34 | 44.3 | 110 | 41.0 | 71 | 30.5 | 28 | 28.4 | 37 |
| 9.0 | 46.1 | 22 | 42.0 | 77 | 40.4 | 54 | 30.5 | 24 | 27.4 | 23 |
| 9.5 | 46.1 | 15 | 42.0 | 52 | 38.7 | 31 | 27.7 | 17 | 27.4 | 17 |
| 10.0 | 46.1 | 9 | 40.9 | 32 | 36.0 | 17 | 26.0 | 10 | 23.7 | 11 |

**eTable 7.** Survival Probability and the Number of PH-HFpEF Participants at Risk Stratified by Diastolic Pulmonary Gradient

| | DPG < 1 | | DPG ≥ 1 & DPG < 3 | | DPG ≥ 3 & DPG < 5 | | DPG ≥ 5 & DPG < 7 | | DPG ≥ 7 | |
|---|---|---|---|---|---|---|---|---|---|---|
| Time (years) | Survival | # at risk | Survival | # at risk | Survival | # at risk | Survival | # at risk | Survival | # at risk |
| 0.0 | 100.0 | 1520 | 100.0 | 312 | 100.0 | 234 | 100.0 | 157 | 100.0 | 354 |
| 0.5 | 83.6 | 1270 | 84.3 | 263 | 82.5 | 193 | 80.9 | 127 | 77.4 | 274 |
| 1.0 | 78.0 | 1186 | 78.5 | 245 | 77.4 | 181 | 72.0 | 113 | 68.6 | 244 |
| 1.5 | 73.6 | 1118 | 75.0 | 234 | 72.2 | 169 | 66.2 | 104 | 61.0 | 216 |
| 2.0 | 70.4 | 1071 | 70.2 | 219 | 67.9 | 159 | 58.6 | 92 | 54.8 | 194 |
| 2.5 | 67.6 | 1028 | 67.6 | 211 | 63.2 | 148 | 57.3 | 90 | 51.4 | 182 |
| 3.0 | 65.2 | 991 | 62.2 | 194 | 60.3 | 141 | 54.1 | 85 | 48.3 | 171 |
| 3.5 | 62.1 | 885 | 60.9 | 177 | 58.5 | 126 | 50.3 | 76 | 45.1 | 141 |
| 4.0 | 59.5 | 780 | 58.3 | 147 | 53.8 | 111 | 48.9 | 66 | 41.8 | 122 |
| 4.5 | 56.6 | 682 | 57.5 | 132 | 52.3 | 102 | 48.1 | 56 | 40.3 | 113 |
| 5.0 | 54.6 | 611 | 55.2 | 121 | 50.7 | 90 | 45.3 | 48 | 40.3 | 108 |
| 5.5 | 52.1 | 531 | 52.8 | 103 | 49.0 | 85 | 42.3 | 40 | 38.0 | 91 |
| 6.0 | 50.1 | 463 | 50.3 | 98 | 49.0 | 77 | 37.5 | 30 | 37.1 | 72 |
| 6.5 | 47.5 | 392 | 48.7 | 88 | 44.4 | 64 | 36.2 | 26 | 36.0 | 62 |
| 7.0 | 46.8 | 330 | 45.6 | 71 | 43.0 | 55 | 36.2 | 19 | 32.9 | 48 |
| 7.5 | 44.5 | 271 | 44.3 | 62 | 42.1 | 47 | 34.2 | 16 | 32.2 | 41 |
| 8.0 | 42.6 | 225 | 42.7 | 50 | 40.3 | 35 | 31.1 | 11 | 30.5 | 35 |
| 8.5 | 40.7 | 180 | 40.9 | 41 | 40.3 | 27 | 31.1 | 7 | 29.5 | 25 |
| 9.0 | 39.6 | 129 | 37.8 | 33 | 40.3 | 16 | 31.1 | 5 | 29.5 | 17 |
| 9.5 | 38.6 | 81 | 36.6 | 23 | 40.3 | 14 | 31.1 | 3 | 29.5 | 11 |
| 10.0 | 37.0 | 48 | 33.7 | 11 | 37.4 | 11 | 31.1 | 2 | 26.8 | 7 |

**eTable 8.** Freedom From Cardiac Hospitalization and the Number of PH-HFpEF Individuals at Risk Stratified by Transpulmonary Gradient

| | TPG ≤ 6 | | TPG > 6 & TPG ≤ 9 | | TPG > 9 & TPG ≤ 12 | | TPG > 12 & TPG ≤ 15 | | TPG >15 | |
|---|---|---|---|---|---|---|---|---|---|---|
| Time (years) | % | # at risk | % | # at risk | % | # at risk | % | # at risk | % | # at risk |
| 0.0 | 100.0 | 306 | 100.0 | 467 | 100.0 | 549 | 100.0 | 381 | 100.0 | 884 |
| 0.5 | 77.8 | 162 | 82.3 | 288 | 78.4 | 314 | 75.0 | 209 | 74.8 | 460 |
| 1.0 | 73.8 | 144 | 77.4 | 243 | 75.0 | 283 | 69.4 | 181 | 67.4 | 368 |
| 1.5 | 71.0 | 123 | 74.7 | 214 | 71.2 | 255 | 65.3 | 154 | 63.0 | 312 |
| 2.0 | 69.2 | 111 | 71.5 | 192 | 68.4 | 235 | 61.8 | 139 | 59.5 | 262 |
| 2.5 | 65.0 | 90 | 69.9 | 169 | 65.5 | 201 | 59.3 | 112 | 56.0 | 210 |
| 3.0 | 63.4 | 77 | 68.5 | 140 | 64.5 | 172 | 54.9 | 87 | 54.5 | 175 |
| 3.5 | 62.6 | 71 | 67.5 | 124 | 62.1 | 144 | 51.5 | 69 | 52.1 | 136 |
| 4.0 | 61.6 | 62 | 65.2 | 106 | 59.4 | 124 | 49.1 | 58 | 50.4 | 110 |
| 4.5 | 58.5 | 53 | 64.5 | 96 | 58.4 | 108 | 45.3 | 48 | 49.0 | 91 |
| 5.0 | 57.3 | 45 | 60.8 | 77 | 57.3 | 95 | 43.4 | 40 | 46.7 | 69 |
| 5.5 | 54.6 | 33 | 59.1 | 63 | 54.7 | 80 | 43.4 | 31 | 43.8 | 51 |
| 6.0 | 52.9 | 30 | 57.1 | 51 | 54.7 | 69 | 42.0 | 27 | 41.0 | 36 |
| 6.5 | 43.3 | 22 | 55.8 | 39 | 51.2 | 55 | 42.0 | 22 | 39.9 | 32 |
| 7.0 | 43.3 | 15 | 54.3 | 34 | 50.0 | 44 | 37.8 | 17 | 39.9 | 25 |
| 7.5 | 43.3 | 11 | 54.3 | 27 | 48.8 | 31 | 37.8 | 12 | 39.9 | 18 |
| 8.0 | 43.3 | 9 | 54.3 | 23 | 46.5 | 19 | 33.1 | 7 | 39.9 | 10 |
| 8.5 | 43.3 | 7 | 51.9 | 11 | 43.8 | 12 | 33.1 | 3 | 39.9 | 5 |
| 9.0 | 32.4 | 3 | 51.9 | 3 | 40.2 | 8 | 33.1 | 2 | 39.9 | 4 |

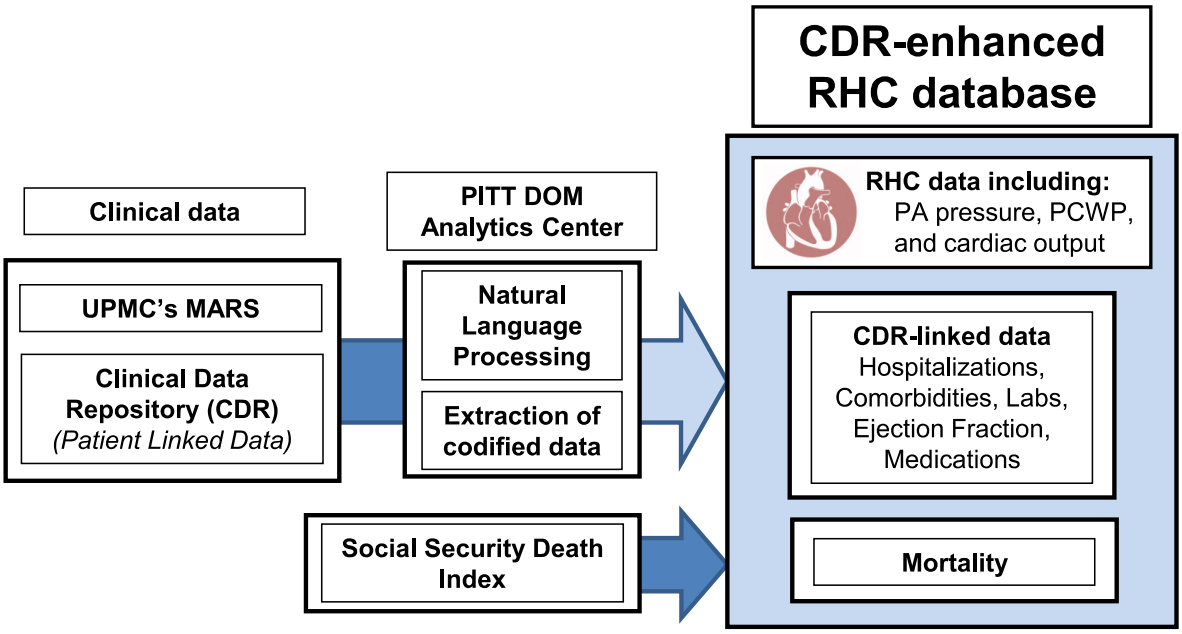
**eTable 9.** Freedom From Cardiac Hospitalization and the Number of PH-HFpEF Individuals at Risk Stratified by Pulmonary Vascular Resistance

| | PVR < 1 | | PVR ≥ 1 & PVR < 2 | | PVR ≥ 2 & PVR < 3 | | PVR ≥ 3 & PVR < 4 | | PVR ≥ 4 | |
|---|---|---|---|---|---|---|---|---|---|---|
| Time (years) | % | # at risk | % | # at risk | % | # at risk | % | # at risk | % | # at risk |
| 0.0 | 100.0 | 251 | 100.0 | 843 | 100.0 | 609 | 100.0 | 345 | 100.0 | 539 |
| 0.5 | 81.2 | 141 | 79.9 | 510 | 79.2 | 342 | 76.0 | 186 | 70.0 | 254 |
| 1.0 | 76.9 | 120 | 76.5 | 448 | 74.2 | 301 | 69.6 | 156 | 60.9 | 194 |
| 1.5 | 73.5 | 102 | 72.5 | 392 | 70.8 | 265 | 65.4 | 137 | 57.2 | 162 |
| 2.0 | 72.7 | 92 | 70.2 | 360 | 66.4 | 236 | 61.5 | 120 | 53.7 | 131 |
| 2.5 | 70.1 | 79 | 67.7 | 300 | 63.9 | 200 | 58.2 | 102 | 49.6 | 101 |
| 3.0 | 68.2 | 67 | 66.5 | 254 | 62.3 | 158 | 55.2 | 84 | 47.5 | 88 |
| 3.5 | 68.2 | 61 | 64.2 | 216 | 60.5 | 130 | 51.7 | 66 | 45.2 | 71 |
| 4.0 | 66.9 | 49 | 62.1 | 194 | 58.0 | 110 | 50.1 | 50 | 43.1 | 57 |
| 4.5 | 64.1 | 41 | 61.1 | 174 | 55.2 | 92 | 47.9 | 42 | 42.3 | 47 |
| 5.0 | 64.1 | 35 | 58.5 | 145 | 52.8 | 74 | 46.6 | 36 | 40.2 | 36 |
| 5.5 | 64.1 | 23 | 55.5 | 120 | 51.2 | 60 | 46.6 | 27 | 36.7 | 28 |
| 6.0 | 61.1 | 19 | 55.0 | 103 | 48.6 | 49 | 46.6 | 25 | 33.6 | 17 |
| 6.5 | 53.2 | 13 | 50.7 | 79 | 47.5 | 43 | 44.7 | 19 | 33.6 | 16 |
| 7.0 | 53.2 | 10 | 49.3 | 62 | 45.1 | 35 | 44.7 | 16 | 33.6 | 12 |
| 7.5 | 53.2 | 6 | 49.3 | 46 | 43.6 | 26 | 44.7 | 13 | 33.6 | 8 |
| 8.0 | 53.2 | 5 | 48.0 | 33 | 43.6 | 18 | 39.7 | 8 | 33.6 | 4 |
| 8.5 | 53.2 | 4 | 46.5 | 18 | 40.5 | 8 | 39.7 | 5 | 33.6 | 3 |
| 9.0 | 53.2 | 2 | 41.8 | 8 | 35.4 | 4 | 39.7 | 4 | 33.6 | 2 |

**eTable 10.** Freedom From Cardiac Hospitalization and the Number of PH-HFpEF Individuals at Risk Stratified by Diastolic Pulmonary Gradient

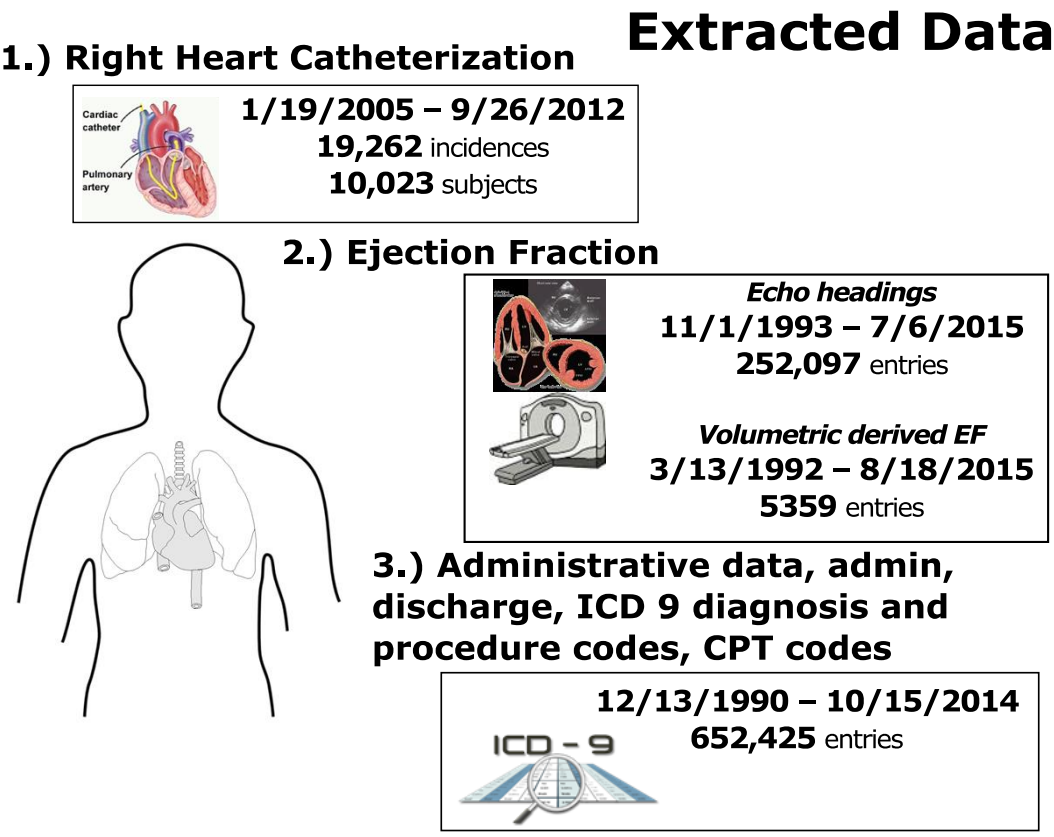
| | DPG < 1 | | DPG ≥ 1 & DPG < 3 | | DPG ≥ 3 & DPG < 5 | | DPG ≥ 5 & DPG < 7 | | DPG ≥ 7 | |
|---|---|---|---|---|---|---|---|---|---|---|
| Time (years) | % | # at risk | % | # at risk | % | # at risk | % | # at risk | % | # at risk |
| 0.0 | 100.0 | 1527 | 100.0 | 313 | 100.0 | 236 | 100.0 | 157 | 100.0 | 354 |
| 0.5 | 78.9 | 881 | 76.0 | 181 | 77.0 | 124 | 72.6 | 77 | 73.9 | 170 |
| 1.0 | 74.4 | 775 | 70.2 | 145 | 69.2 | 102 | 69.7 | 68 | 64.9 | 129 |
| 1.5 | 70.9 | 676 | 68.6 | 132 | 63.5 | 86 | 66.5 | 60 | 59.1 | 104 |
| 2.0 | 67.9 | 609 | 65.4 | 118 | 59.6 | 74 | 63.1 | 52 | 56.0 | 86 |
| 2.5 | 65.0 | 515 | 63.6 | 98 | 54.1 | 55 | 61.7 | 45 | 53.1 | 69 |
| 3.0 | 63.3 | 432 | 60.5 | 72 | 54.1 | 47 | 57.5 | 39 | 52.2 | 61 |
| 3.5 | 61.1 | 362 | 57.7 | 61 | 51.6 | 41 | 55.9 | 29 | 51.3 | 51 |
| 4.0 | 59.0 | 304 | 55.7 | 56 | 47.7 | 35 | 53.4 | 22 | 51.3 | 43 |
| 4.5 | 57.4 | 266 | 53.5 | 46 | 44.8 | 30 | 50.9 | 18 | 51.3 | 36 |
| 5.0 | 55.1 | 217 | 52.2 | 38 | 44.8 | 29 | 50.9 | 15 | 46.7 | 27 |
| 5.5 | 52.3 | 169 | 52.2 | 33 | 43.2 | 24 | 47.3 | 10 | 46.7 | 22 |
| 6.0 | 51.0 | 142 | 52.2 | 26 | 37.8 | 20 | 47.3 | 8 | 46.7 | 17 |
| 6.5 | 47.4 | 110 | 50.1 | 22 | 37.8 | 17 | 40.5 | 5 | 46.7 | 16 |
| 7.0 | 46.4 | 88 | 47.4 | 17 | 35.3 | 13 | 40.5 | 4 | 46.7 | 13 |
| 7.5 | 45.8 | 64 | 47.4 | 13 | 35.3 | 10 | 40.5 | 3 | 46.7 | 9 |
| 8.0 | 44.9 | 48 | 43.1 | 9 | 35.3 | 6 | 40.5 | 1 | 46.7 | 4 |
| 8.5 | 42.6 | 24 | 43.1 | 6 | 35.3 | 6 | | | 46.7 | 2 |
| 9.0 | 37.3 | 10 | 43.1 | 4 | 35.3 | 4 | | | 46.7 | 2 |

**eFigure 1.** Development of the Clinical Data Repository Enhanced Right Heart Catheterization Database (CDR-Enhanced RHC Database) and Association of PH Groups With Mortality



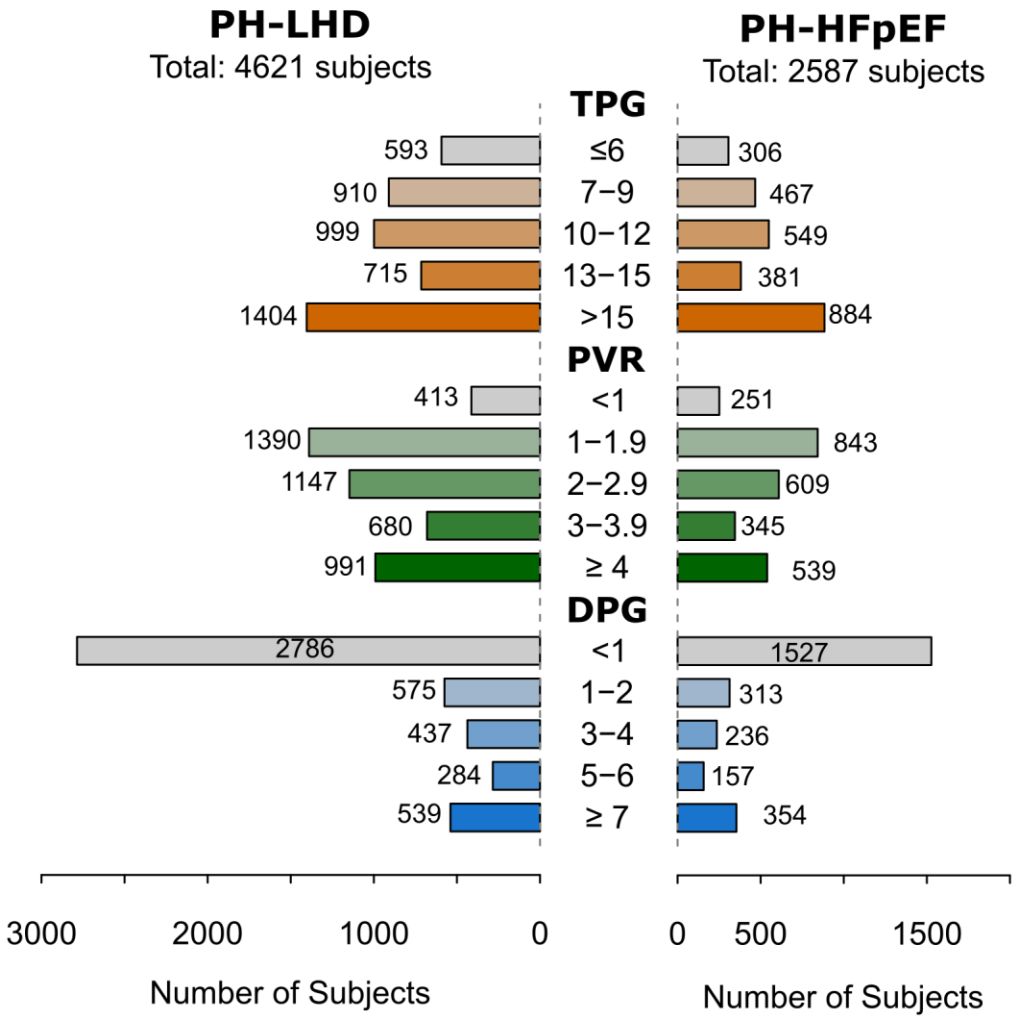

Through a collaboration with the University of Pittsburgh Department of Medicine (PITT DOM) Analytics center, codified clinical data was extracted from the clinical data repository. Natural language processing was used to extract non-codified data from source documentation archived in the UMPC's MARS system.

**eFigure 2.** Descriptive Information on the Extracted Data in the CDR-Enhanced RHC Database



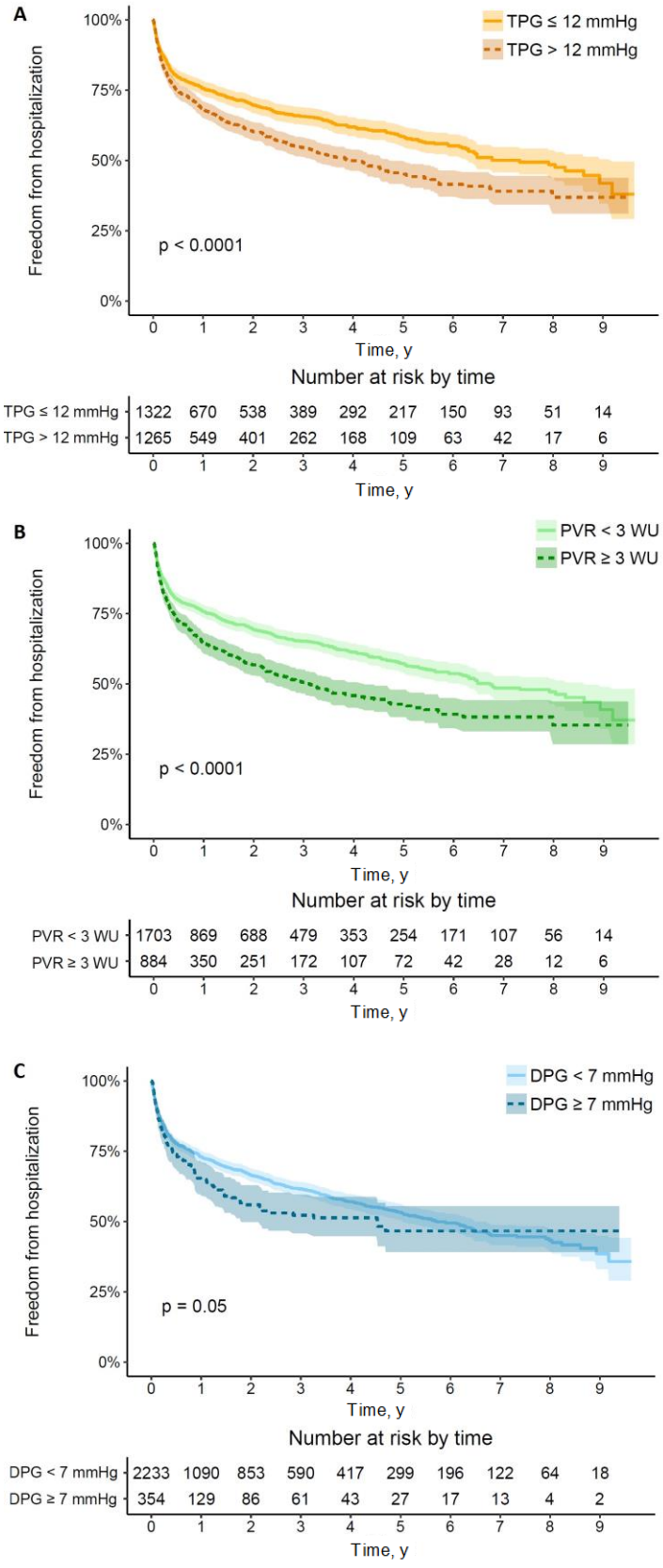

The database includes 1.) right heart catheterization data (years: 2005 to 2012), 2.) left ventricular ejection fractions (LVEFs) (years: 1992-2015), and 3) structured administrative data (years (1990 – 2014). Data on LVEF was available on 9427 subjects (94.1% of the population with right heart catheterization hemodynamics) where 67.3% was obtained from echocardiography data and 26.8% was obtained from nuclear imaging.

**eFigure 3.** Prevalence of precapillary Pulmonary Vascular Disease in PH-LHD and PH-HFpEF Based on Hemodynamic Definitions




Breakdown of the number of PH-LHD and PH-HFpEF subjects with varying values of transpumonary gradient (TPG), pulmonary vascular resistance (PVR) and diastolic pulmonary gradient (DPG). The prevalence of pre-capillary involvement is a function of the selected hemodynamic marker in both the PH-LHD and PH-HFpEF cohorts. More subjects have an elevated TPG (> 12 mmHg) than PVR (≥ 3WU) and DPG (≥ 7 mmHg). Over half of the PH-LHD cohort and PH-HFpEF cohort meet the criteria for at least one hemodynamic marker of pre-capillary pulmonary vascular disease. There is significant overlap in the markers in both groups where DPG is the more selective marker.

**eFigure 4.** Elevated TPG, PVR, and DPG are Associated With Increased Cardiac Hospitalizations in the PH-HFpEF Cohort




TPG (panel A), PVR (panel B) and DPG (panel C) are associated with cardiac hospitalizations. TPG indicates transpulmonary gradient; PVR, pulmonary vascular resistance; DPG, diastolic pulmonary gradient.