

Supplementary Online Content

Filippatos G, Angermann CE, Cleland JGF, et al. Global differences in characteristics, precipitants, and initial management of patients presenting with acute heart failure. *JAMA Cardiol*. Published online January 8, 2020. doi:10.1001/jamacardio.2019.5108

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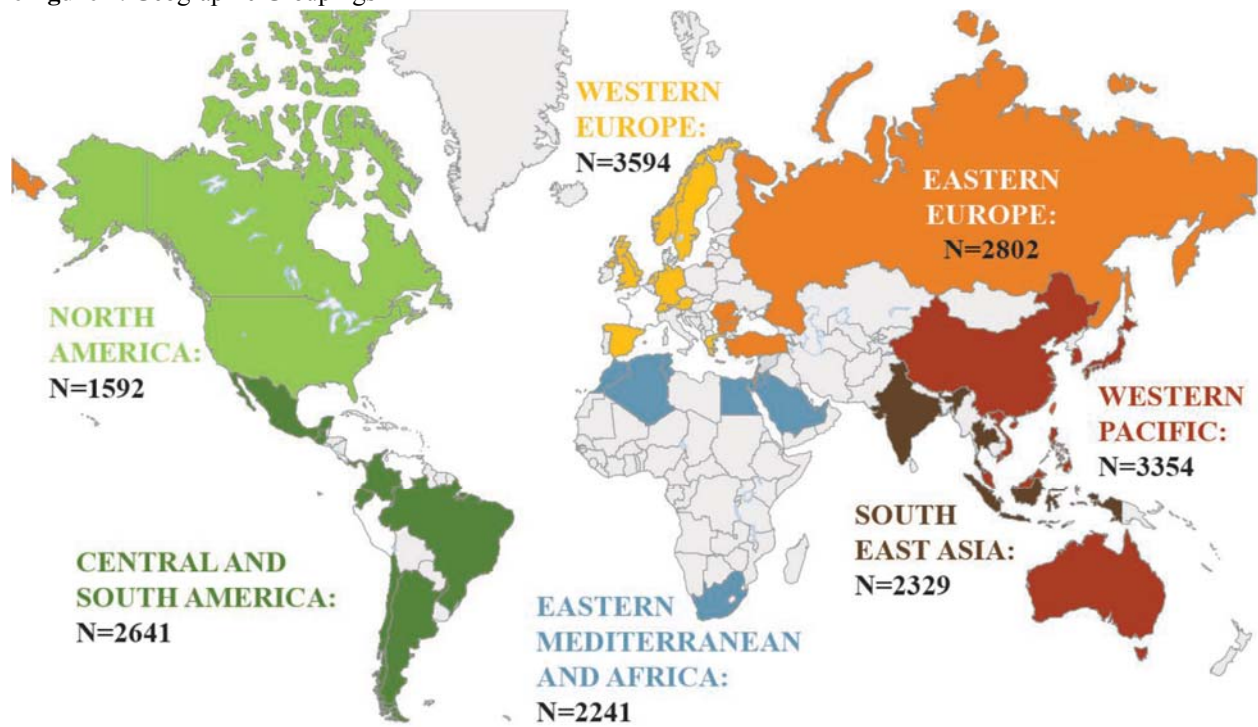
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This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. Geographic Groupings



Supplemental Table 1. HF Characteristics/history, AHF Precipitants and Prior Outpatient Cardiovascular Medication. Overall and Divided by Region of the World.

(All values reported as N (%) unless otherwise noted)

| | All N=18553 | Western Europe N=3594 | Eastern Europe N=2802 | Western Pacific N=3354 | South East Asia N=2329 | North America N=1592 | Central /So America N=2641 | East Med & Africa N=2241 | P- value |
|---|----------------------|-----------------------------|-----------------------------|------------------------------|---------------------------------|----------------------------|-------------------------------------|-----------------------------------|-------------|
| Heart Failure characteristics / history | | | | | | | | | |
| <i>HF Diagnosis</i> | 10651 (57.4%) | 2251 (62.6%) | 1867 (66.6%) | 1782 (53.1%) | 495 (21.3%) | 1275 (80.1%) | 1594 (60.4%) | 1387 (61.9%) | <0.001 |
| DCHF | 7902 (42.6%) | 1343 (37.4%) | 935 (33.4%) | 1572 (46.9%) | 1834 (78.7%) | 317 (19.9%) | 1047 (39.6%) | 854 (38.1%) | |
| <i>Etiology</i> | 6195 (33.4%) | 1139 (31.7%) | | | 724 (31.1%) | | 622 (23.6%) | | <0.001 |
| Ischemic | 2863 (15.4%) | 374 (10.4%) | 1165 (41.6%) | 1307 (39.0%) | 472 (20.3%) | 348 (21.9%) | 451 (17.1%) | 890 (39.7%) | |
| Hypertensive | 2905 (15.7%) | 510 (14.2%) | 558 (19.9%) | 361 (10.8%) | 455 (19.5%) | 302 (19.0%) | 342 (12.9%) | 345 (15.4%) | |
| Cardiomyopathy | 2006 (10.8%) | 513 (14.3%) | 302 (10.8%) | 305 (9.1%) | 135 (5.8%) | 369 (23.2%) | 342 (12.9%) | 273 (12.2%) | |
| Valvular | 1541 (8.3%) | 328 (9.1%) | 369 (13.2%) | 307 (9.2%) | 183 (7.9%) | 94 (5.9%) | 139 (8.7%) | 248 (11.1%) | |
| Other | 3043 (16.4%) | 730 (20.3%) | 187 (6.7%) | 420 (12.5%) | 360 (15.5%) | 139 (8.7%) | 296 (11.2%) | 101 (4.5%) | |
| Unknown/Unavailable | | | 221 (7.9%) | | | 340 (21.4%) | 588 (22.3%) | 384 (17.2%) | |
| <i>Prior HF-related Hospitalizations</i> | | | | | | | | | |
| DCHF: Hospitalized = yes | 7129 (66.9%) | 1487 (66.1%) | 1230 (65.9%) | 1343 (75.4%) | 328 (66.3%) | 921 (72.2%) | 917 (57.5%) | 903 (65.1%) | |
| # Hospitalizations within last 12 months | 6702 1.0 (1 - 2) | 1407 1.0 (0 - 2) | 1157 1.0 (0 - 2) | 1297 1.0 (1 - 2) | 302 1.0 (1 - 2) | 849 1.0 (1 - 2) | 837 1.0 (1 - 2) | 853 1.0 (1 - 2) | <0.001 |
| Median (IQR) | 1317 (12.4%) | 356 (15.8%) | 291 (15.6%) | 219 (12.3%) | 39 (7.9%) | 142 (11.1%) | 106 (6.6%) | 164 (11.8%) | |
| 0 | 3231 (30.3%) | 655 (29.1%) | 537 (28.8%) | 690 (38.7%) | 185 (37.4%) | 348 (27.3%) | 437 (27.4%) | 379 (27.3%) | |
| 1 | 1160 (10.9%) | 240 (10.7%) | 194 (10.4%) | 205 (11.5%) | 94 (5.3%) | 167 (13.1%) | 90 (7.1%) | 163 (11.8%) | |
| 2 | 496 (4.7%) | 87 (3.9%) | 80 (4.3%) | 41 (2.3%) | 39 (7.9%) | 90 (7.1%) | 152 (9.5%) | 70 (5.0%) | |
| 3 | 227 (2.1%) | 27 (1.2%) | 30 (1.6%) | 48 (2.7%) | 11 (2.2%) | 40 (3.1%) | 64 (4.0%) | 33 (2.4%) | |
| 4 | 271 (2.5%) | 42 (1.9%) | 25 (1.3%) | | 17 (3.4%) | 62 (4.9%) | 39 (2.4%) | 44 (3.2%) | |
| ≥ 5 | | | | | 11 (2.2%) | | 39 (2.4%) | | |
| <i>Ejection fraction (during or prior)</i> | 14709 40.3 (16.1) | 2473 39.5 (16.1) | 2389 45.2 (14.6) | 2907 41.5 (15.9) | 1944 38.4 (15.2) | 1035 38.1 (18.9) | 2215 38.9 (16.8) | 1746 38.2 (14.9) | <0.001 |
| Mean (SD) Median /IQR) | 39.0 (28-54) | 37.0 (26-53) | 48.0 (35-56) | 40.0 (29-55) | 35.0 (26-48) | 35.0 (20-55) | 35.0 (25-53) | 35.0 (27-50) | |
| <i>Ejection fraction (during or prior) < 40%</i> | 7443 (40.1%) | 1296 (36.1%) | 790 (28.2%) 649 (23.2%) | 1452 (43.3%) 571 (17.0%) | 1121 (48.1%) | 558 (35.1%) 140 (8.8%) | 1235 (46.8%) | 991 (44.2%) | |

| | All N=18553 | Western Europe N=3594 | Eastern Europe N=2802 | Western Pacific N=3354 | South East Asia N=2329 | North America N=1592 | Central /So America N=2641 | East Med & Africa N=2241 | P- valu e |
|------------------------|------------------|-----------------------------|-----------------------------|------------------------------|---------------------------------|----------------------------|-------------------------------------|-----------------------------------|-----------------|
| β-blockers | 9583 (51.7%) | 2299 (64.0%) | 1698 (60.6%) | 1235 (36.8%) | 580 (24.9%) | 1127 (70.8%) | 1480 (56.0%) | 1164 (51.9%) | <0.0001 |
| MRAs | 4673 (25.2%) | 955 (26.6%) | 841 (30.0%) | 913 (27.2%) | 260 (11.2%) | 376 (23.6%) | 845 (32.0%) | 483 (21.6%) | <0.0001 |
| Diuretics | 10025 (54.0%) | 2493 (69.4%) | 1604 (57.2%) | 1271 (37.9%) | 775 (33.3%) | 1119 (70.3%) | 1431 (54.2%) | 1332 (59.4%) | <0.0001 |
| Loop Diuretics | 9305 (50.2%) | 2347 (65.3%) | 1370 (48.9%) | 1193 (35.6%) | 734 (31.5%) | 1068 (67.1%) | 1313 (49.7%) | 1280 (57.1%) | <0.0001 |
| Ivabradine | 415 (2.2%) | 105 (2.9%) | 59 (2.1%) | 47 (1.4%) | 84 (3.6%) | 5 (0.3%) | 48 (1.8%) | 67 (3.0%) | <0.0001 |
| Digoxin | 2005 (10.8%) | 268 (7.5%) | 422 (15.1%) | 442 (13.2%) | 208 (8.9%) | 148 (9.3%) | 269 (10.2%) | 248 (11.1%) | <0.0001 |
| Nitrates | 2224 (12.0%) | 445 (12.4%) | 357 (12.7%) | 474 (14.1%) | 265 (11.4%) | 364 (22.9%) | 139 (5.3%) | 180 (8.0%) | <0.0001 |
| Ca channel blockers | 2649 (14.3%) | 669 (18.6%) | 441 (15.7%) | 429 (12.8%) | 235 (10.1%) | 311 (19.5%) | 265 (10.0%) | 299 (13.3%) | <0.0001 |
| Anti- thrombotics | 11249 (60.6%) | 2661 (74.0%) | 1777 (63.4) | 1725 (51.4%) | 914 (39.2%) | 1186 (74.5%) | 1425 (54.0%) | 1561 (69.7%) | <0.0001 |
| Anti-platelets | 7653 (41.2%) | 1304 (36.3%) | 1170 (41.8%) | 1366 (40.7%) | 770 (33.1%) | 890 (55.9%) | 956 (36.2%) | 1197 (53.4%) | <0.0001 |
| Anti- coagulant | 4717 (25.4%) | 1620 (45.1%) | 779 (27.8%) | 461 (13.7%) | 193 (8.3%) | 567 (35.6%) | 586 (22.2%) | 511 (22.8%) | <0.0001 |
| Amiodarone | 1273 (6.9%) | 286 (8.0%) | 219 (7.8%) | 102 (3.0%) | 71 (3.0%) | 162 (10.2%) | 257 (9.7%) | 176 (7.9%) | <0.0001 |
| Statins | 7045 (38.0%) | 1723 (47.9%) | 737 (26.3%) | 1103 (32.9%) | 789 (33.9%) | 892 (56.0%) | 862 (32.6%) | 939 (41.9%) | <0.0001 |

ACE inhibitor = angiotensin-converting-enzyme inhibitor; AHF = acute heart failure; ARB = angiotensin II receptor blockers; DCHF = decompensated chronic heart failure; HT = hypertension; med = medication; resp. = respiratory; WRF = worsening renal function

Supplemental Table 2. Presenting Vital Signs, signs and symptoms and laboratory values. Overall and Divided by Regions of the World

(All values reported as N (%) or median (IQR) unless otherwise noted)

| | All N=18553 | Western Europe N=3594 | Eastern Europe N=2802 | Western Pacific N=3354 | South East Asia N=2329 | North America N=1592 | Central/So America N=2641 | East Med & Africa N=2241 | P- value |
|---|------------------|-----------------------------|-----------------------------|------------------------------|---------------------------------|----------------------------|---------------------------------|-----------------------------------|-------------|
| Presenting characteristics / Clinical Exam | | | | | | | | | |
| SBP (mmHg) | 16995 | 3168 | 2479 | 3110 | 2162 | 1578 | 2363 | 2135 | <0.0001 |
| n | 133.3 | 135.1 | 137.3 | 132.6 | 132.0 | 138.1 | 128.2 | 130.6 | |
| Mean (SD) | (29.2) | (28.1) | (28.7) | (28.3) | (28.7) | (31.9) | (28.7) | (30.4) | |
| Median (IQR) | 130 (110-150) | 131 (115-150) | 133 (120-155) | 130 (110-149) | 130 (110-150) | 134 (115-156) | 125 (109-143) | 126 (110-148) | |
| DBP (mmHg) | 16975 | 3158 | 2479 | 3106 | 2160 | 1575 | 2363 | 2134 | <0.0001 |
| n | 79.2 | 78.3 | 81.2 | 79.8 | 80.2 | 81.3 | 77.4 (17.1) | 76.5 | |
| Mean (SD) | (17.3) | (17.3) | (15.1) | (17.3) | (16.4) | (20.8) | 77 (65-89) | (17.5) | |
| Median (IQR) | 80 (69-90) | 77 (66-90) | 80 (70-90) | 80 (70-90) | 80 (70-90) | 79 (67-93) | | 75 (65-86) | |
| Heart rate (b.p.m) | 16932 | 3135 | 2477 | 3096 | 2159 | 1578 | 2362 | 2125 | <0.0001 |
| n | 89.4 | 87.4 | 88.5 | 89.0 | 94.0 | 89.6 | 87.3 (23.2) | 91.7 | |
| Mean (SD) | (22.9) | (23.4) | (24.0) | (22.4) | (21.9) | (21.2) | 84 (71-100) | (22.3) | |
| Median (IQR) | 86 (73-102) | 84 (70-100) | 82 (70-100) | 86 (73-101) | 92 (80-107) | 87 (74-103) | | 90 (76-104) | |
| Rhythm | 9478 (51.1%) | 1503 (41.8%) | 1331 (47.5%) | 1879 (56.0%) | 1280 (55.0%) | 883 (55.5%) | 1378 (52.2%) | 1224 (54.6%) | <0.0001 |
| Sinus Rhythm | 4222 (22.8%) | 1108 (30.8%) | 979 (34.9%) | 732 (21.8%) | 198 (8.5%) | 281 (17.7%) | 463 (17.5%) | 461 (20.6%) | |
| Atrial fib/flutter | 769 (4.1%) | 235 (6.5%) | 96 (3.4%) | 70 (2.1%) | 18 (0.8%) | 146 (9.2%) | 157 (5.9%) | 47 (2.1%) | |
| Pacemaker rhythm | 176 (0.9%) | 27 (0.8%) | 8 (0.3%) | 31 (0.9%) | 9 (0.4%) | 29 (1.8%) | 32 (1.2%) | 40 (1.8%) | |
| Bradycardia/AV block | | | | | | | 113 (4.3%) | 147 (6.6%) | |
| Other | 925 (5.0%) | 106 (2.9%) | 17 (0.6%) | 154 (4.6%) | 253 (10.9%) | 135 (8.5%) | 498 (18.9%) | 322 (14.4%) | |
| Unavailable | 2983 (16.1%) | 615 (17.1%) | 371 (13.2%) | 488 (14.5%) | 571 (24.5%) | 118 (7.4%) | | | |
| Symptoms & Signs | 17943 (96.7%) | 3450 (96.0%) | 2781 (99.3%) | 3188 (95.1%) | 2249 (96.6%) | 1532 (96.2%) | 2548 (96.5%) | 2195 (97.9%) | |
| Symptoms assessed | 17289 (93.2%) | 3334 (92.8%) | 2768 (98.8%) | 2915 (86.9%) | 1991 (85.5%) | 1539 (96.7%) | 2547 (96.4%) | 2195 (97.9%) | |
| Dyspnea at rest | 13603 (73.3%) | 2518 (70.1%) | 2353 (84.0%) | 2530 (75.4%) | 1765 (75.8%) | 605 (38.0%) | 1924 (72.9%) | 1908 (85.1%) | |
| PND | 9100 (49.0%) | 1485 (41.3%) | 1705 (60.8%) | 1871 (55.8%) | 986 (42.3%) | 295 (18.5%) | 1162 (44.0%) | 1596 (71.2%) | |
| Peripheral Edema | 11400 (61.4%) | 2365 (65.8%) | 2107 (75.2%) | 1725 (51.4%) | 913 (39.2%) | 942 (59.2%) | 1899 (71.9%) | 1449 (64.7%) | |
| Pulmonary rales | 10278 (55.4%) | 1663 (46.3%) | 1983 (70.8%) | 1645 (49.0%) | 1148 (49.3%) | 381 (23.9%) | 1652 (62.6%) | 1806 (80.6%) | |
| JVP | | | | | | | 1159 | 1084 | |
| < 6 cm | 6311 (34.0%) | 820 (22.8%) | 907 (32.4%) | 724 (21.6%) | 1028 (44.1%) | 589 (37.0%) | 1159 (43.9%) | 1084 (48.4%) | |
| 6-10 cm | 2401 (12.9%) | 316 (8.8%) | 384 (13.7%) | 245 (7.3%) | 471 (20.2%) | 165 (10.4%) | 442 (16.7%) | 378 (16.9%) | |
| >10 cm | | | | | | | 498 | 449 | |
| S3 gallop | 2682 (14.5%) | 362 (10.1%) | 436 (15.6%) | 272 (8.1%) | 467 (20.1%) | 198 (12.4%) | 498 (18.9%) | 449 (20.0%) | |
| Pleural effusion | 1228 (6.6%) | 142 (4.0%) | 87 (3.1%) | 207 (6.2%) | 90 (3.9%) | 226 (14.2%) | 219 (8.3%) | 257 (11.5%) | |
| | 2190 (11.8%) | 264 (7.3%) | 791 (28.2%) | 337 (10.0%) | 244 (10.5%) | 122 (7.7%) | 523 (19.8%) | 635 (28.3%) | |

| | All N=18553 | Western Europe N=3594 | Eastern Europe N=2802 | Western Pacific N=3354 | South East Asia N=2329 | North America N=1592 | Central/So America N=2641 | East Med & Africa N=2241 | P- value |
|--|---|--|--|--|--|--|---|--|-------------|
| | 4787 (25.8%) | 1172 (32.6%) | | 986 (29.4%) | 284 (12.2%) | 416 (26.1%) | | 615 (27.4%) | |
| Chest X-ray Yes, taken Signs of congestion* | 15918 (85.8%) 11451 (61.7%) | 3216 (89.5%) 2375 (66.1%) | 2513 (89.7%) 1986 (70.9%) | 2708 (80.7%) 1791 (53.4%) | 1639 (70.4%) 1038 (44.6%) | 1521 (95.5%) 860 (54.0%) | 2287 (86.6%) 1676 (63.5%) | 2034 (90.8%) 1725 (77.0%) | <0.0001 |
| Cardiac biomarkers | | | | | | | | | |
| NT-proBNP (ng/L) n (%) Median (IQR) | 5648 (30.4%) 4392 (2072- 9174) | 1696 (47.2%) 4785 (2204- 9222) | 366 (13.1%) 4321 (1858- 11287) | 1715 (51.1%) 3837 (1889- 8220) | 520 (22.3%) 5180 (2310- 12850) | 490 (30.8%) 3825 (2034- 8414) | 542 (20.5%) 4439 (2047- 9206) | 319 (14.2%) 4942 (2400- 9462) | <0.0001 |
| BNP (ng/L) n (%) Median (IQR) | 3388 (18.3%) 915 (408- 1888) | 448 (12.5%) 847 (388- 1593) | 198 (7.1%) 970 (486- 1832) | 761 (22.7%) 1137 500-2340 | 150 (6.4%) 483 (163- 1220) | 957 (60.1%) 767 (392- 1545) | 294 (11.1%) 1225 (541-2458) | 580 (25.9%) 937 (382- 2206) | <0.0001 |
| Troponin-I (µg/L) n (%) Median (IQR) | 5470 (29.5%) 0.04 (0.02- 0.11) | 790 (22.0%) 0.04 (0.02- 0.10) | 565 (20.2%) 0.04 (0.01- 0.12) | 1531 (45.6%) 0.05 (0.02- 0.16) | 423 (18.2%) 0.05 (0.02- 0.23) | 1013 (63.6%) 0.04 (0.02- 0.08) | 526 (19.9%) 0.04 (0.01-0.10) | 622 (27.8%) 0.02 (0.01- 0.07) | 0.0333 |
| Troponin-T (µg/L) n (%) Median (IQR) | 3589 (19.3%) 0.04 (0.02- 0.08) | 898 (25.0%) 0.03 (0.02- 0.06) | 268 (9.6%) 0.05 (0.02- 0.16) | 496 (14.8%) 0.04 (0.02- 0.06) | 536 (23.0%) 0.05 (0.02- 0.20) | 245 (15.4%) 0.02 (0.01- 0.04) | 480 (18.2%) 0.04 (0.02-0.06) | 666 (29.7%) 0.04 (0.02- 0.09) | <0.0001 |
| Hs-cTNT (µg/L) n (%) Median (IQR) | 849 (4.6%) 0.04 (0.02- 0.08) | 404 (11.2%) 0.04 (0.02- 0.07) | 69 (2.5%) 0.02 (0.01- 0.06) | 149 (4.4%) 0.03 (0.02- 0.08) | 36 (1.5%) 0.07 (0.02- 0.21) | 3 (0.2%) 0.01 (0.00- 0.03) | 96 (3.6%) 0.04 (0.02-0.08) | 92 (4.1%) 0.05 (0.02- 0.21) | 0.0154 |
| Renal function test results | | | | | | | | | |
| BUN (mmol/L) n (%) Median (IQR) | 6390 (34.4%) 8.2 (5.8- 12.5) | 145 (4.0%) 10.0 (6.4- 15.7) | 336 (12.0%) 9.6 (6.4- 14.6) | 1909 (56.9%) 7.7 (5.6- 11.1) | 1003 (43.1%) 7.9 (5.6- 12.5) | 1326 (83.3%) 8.2 (5.7- 13.2) | 1128 (42.7%) 8.8 (6.4- 13.2) | 543 (24.2%) 8.2 (6.0- 13.6) | <0.0001 |
| Urea (mmol/L) n (%) Median (IQR) | 9763 (52.6%) 8.2 (6.0- 12.1) | 2848 (79.2%) 9.2 (6.7- 13.7) | 1604 (57.2%) 7.7 (5.8- 10.6) | 953 (28.4%) 7.1 (5.3- 9.8) | 1016 (43.6%) 6.2 (4.4- 8.8) | 266 (16.7%) 10.0 (6.9- 15.8) | 1490 (56.4%) 8.2 (6.0- 11.7) | 1586 (70.8%) 9.0 (6.2- 14.0) | <0.0001 |
| eGFR [MDRD] (mL/min/1.73 m ²) n (%) Median (IQR) | 11282 (60.8%) 64.4 (44.7- 87.1) | 2055 (57.2%) 63.8 (45.0- 85.5) | 820 (29.3%) 71.5 (50.4- 96.3) | 1150 (34.3%) 63.8 (41.7- 87.5) | 2129 (91.4%) 64.4 (45.3- 87.2) | 1441 (90.5%) 56.8 (37.9- 78.3) | 2280 (86.3%) 65.7 (46.2-86.6) | 1407 (62.8%) 67.1 (46.6- 91.5) | <0.0001 |
| Other labs | | | | | | | | | |
| Hemoglobin (g/L) n (%) Median (IQR) | 15934 (85.9%) 126.0 | 3122 (86.9%) 126.0 | 2496 (89.1%) 131.0 | 2738 (81.6%) 128.0 | 1995 (85.7%) 121.0 | 1567 (98.4%) 120.0 | 2144 (81.2%) 128.0 | 1872 (83.5%) 120.0 | <0.0001 |

| | All N=18553 | Western Europe N=3594 | Eastern Europe N=2802 | Western Pacific N=3354 | South East Asia N=2329 | North America N=1592 | Central/So America N=2641 | East Med & Africa N=2241 | P- value |
|--|------------------------|--------------------------------------|--------------------------------------|---------------------------------------|---|-------------------------------------|--|---|---------------------|
| | (110-140) | (110-141) | (116-144) | (111-143) | (105-136) | (103-134) | (112-143) | (106-135) | |

*JVP = Jugular venous pressure; PND= paroxysmal nocturnal dyspnea; *Signs of congestion = Cephalization/vascular engorgement, Interstitial edema, Pulmonary edema*

Supplemental Table 3. Hospital Point of Entry, Time to Initial AHF Treatment and Types of Initial AHF Therapy Administered, and In-hospital Outcomes. (All values reported as N (%) or median (IQR) unless otherwise noted)

| | All N=1855 3 | Wester n Europe N=3594 | Eastern Europe N=2802 | Wester n Pacific N=3354 | South East Asia N=2329 | North Americ a N=1592 | Central/ So America N=2641 | East Med & Africa N=2241 | P- val ue |
|--|----------------------------|---------------------------------|-----------------------------|----------------------------------|---------------------------------|--------------------------------|-------------------------------------|-----------------------------------|------------------|
| Hospital Point of Entry | | | | | | | | | |
| Emergency Room | 11636 (62.7%) | 2760 (76.8%) | 1048 (37.4%) | 1526 (45.5%) | 1447 (62.1%) | 1237 (77.7%) | 2085 (78.9%) | 1533 (68.4%) | <0.0 001 |
| Heart Failure Facilities | 923 (5.0%) | 125 (3.5%) | 271 (9.7%) | 211 (6.3%) | 84 (3.6%) | 63 (4.0%) | 135 (5.1%) | 34 (1.5%) | |
| Cardiac Ward | 3348 (18.0%) | 359 (10.0%) | 998 (35.6%) | 1113 (33.2%) | 210 (9.0%) | 222 (13.9%) | 145 (5.5%) | 301 (13.4%) | |
| Cardiac/ Coronary ICU | 1454 (7.8%) | 94 (2.6%) | 333 (11.9%) | 268 (8.0%) | 390 (16.7%) | 18 (1.1%) | 132 (5.0%) | 219 (9.8%) | |
| General/ Medical/ Surgical ICU | 482 (2.6%) | 114 (3.2%) | 23 (0.8%) | 85 (2.5%) | 116 (5.0%) | 6 (0.4%) | 55 (2.1%) | 83 (3.7%) | |
| Other | 698 (3.8%) | 138 (3.8%) | 129 (4.6%) | 150 (4.5%) | 82 (3.5%) | 40 (2.5%) | 89 (3.4%) | 70 (3.1%) | |
| Missing | 12 (0.1%) | 4 (0.1%) | 0 | 1 (0.0%) | 0 | 6 (0.4%) | 0 | 1 (0.0%) | |
| Patient Pathway while hospitalized | | | | | | | | | |
| ED + ICU/CCU | 2248 (12.1%) | 287 (8.0%) | 261 (9.3%) | 134 (4.0%) | 161 (6.9%) | 355 (22.3%) | 404 (15.3%) | 646 (28.8%) | * <0.0 001 |
| ED + General ward | 5900 (31.8%) | 1800 (50.1%) | 582 (20.8%) | 1003 (29.9%) | 648 (27.8%) | 696 (43.7%) | 845 (32.0%) | 326 (14.5%) | |
| ED + ICU/CCU + General ward | 2283 (12.3%) | 347 (9.7%) | 174 (6.2%) | 327 (9.7%) | 561 (24.1%) | 108 (6.8%) | 456 (17.3%) | 310 (13.8%) | |
| ACUTE HF-RELATED THERAPIES within 6 hours | | | | | | | | | |
| IV THERAPIES | | | | | | | | | |
| Loop diuretics | 14162 (76.3%) | 2529 (70.4%) | 2519 (89.9%) | 2192 (65.4%) | 1886 (81.0%) | 1091 (68.5%) | 2090 (79.1%) | 1855 (82.8%) | <0.0 001 |
| Vasodilators/ Nitrates | 2917 (15.7%) | 200 (5.6%) | 460 (16.4%) | 1026 (30.6%) | 304 (13.1%) | 86 (5.4%) | 593 (22.5%) | 248 (11.1%) | <0.0 001 |
| Inotropic agents | 1634 (8.8%) | 153 (4.3%) | 317 (11.3%) | 449 (13.4%) | 314 (13.5%) | 50 (3.1%) | 213 (8.1%) | 138 (6.2%) | <0.0 001 |
| OTHER THERAPIES | | | | | | | | | |
| Oral loop diuretics | 1119 (6.0%) | 228 (6.3%) | 162 (5.8%) | 454 (13.5%) | 119 (5.1%) | 26 (1.6%) | 75 (2.8%) | 55 (2.5%) | <0.0 001 |
| Other oral diuretics | 226 (1.2%) | 65 (1.8%) | 89 (3.2%) | 13 (0.4%) | 9 (0.4%) | 13 (0.8%) | 16 (0.6%) | 21 (0.9%) | <0.0 001 |
| MRAs | 2304 (12.4%) | 219 (6.1%) | 770 (27.5%) | 687 (20.5%) | 206 (8.8%) | 16 (1.0%) | 310 (11.7%) | 96 (4.3%) | <0.0 001 |
| Opiates | 81 (0.4%) | 21 (0.6%) | 26 (0.9%) | 11 (0.3%) | 0 | 18 (1.1%) | 5 (0.2%) | 0 | <0.0 001 |
| Oxygen | 3046 (16.4%) | 597 (16.6%) | 362 (12.9%) | 741 (22.1%) | 498 (21.4%) | 227 (14.3%) | 305 (11.5%) | 316 (14.1%) | <0.0 001 |
| Non-invasive ventilation | 220 (1.2%) | 62 (1.7%) | 15 (0.5%) | 21 (0.6%) | 23 (1.0%) | 40 (2.5%) | 18 (0.7%) | 41 (1.8%) | <0.0 001 |
| Time from admission to first initiation of AHF therapy: | | | | | | | | | |
| For any AHF therapy (hrs) n Median (IQR) | 18136 1.0 (0.2- 3.0) | 3469 1.2 (0.3- 4.3) | 2778 0.4 (0.0- 1.4) | 3264 1.0 (0.3- 2.6) | 2297 0.6 (0.1- 1.9) | 1578 3.0 (1.4- 5.6) | 2605 0.9 (0.2- 2.8) | 2145 1.0 (0.2- 2.5) | <0.0 001 |
| If 1 st treatment = IV loop diuretic (hrs) n Median (IQR) | 12793 1.0 (0.2- 3.0) | 2450 1.5 (0.4- 4.0) | 2260 0.4 (0.0- 1.5) | 1611 1.2 (0.4- 3.1) | 1629 0.7 (0.1- 2.1) | 1139 3.5 (2.0- 5.7) | 1933 0.9 (0.2- 2.7) | 1771 0.9 (0.2- 2.1) | <0.0 001 |
| If 1 st treatment = IV Vasodilators (hrs) | 766 | 43 | 67 | 321 | 51 | 44 | 195 | 45 | |

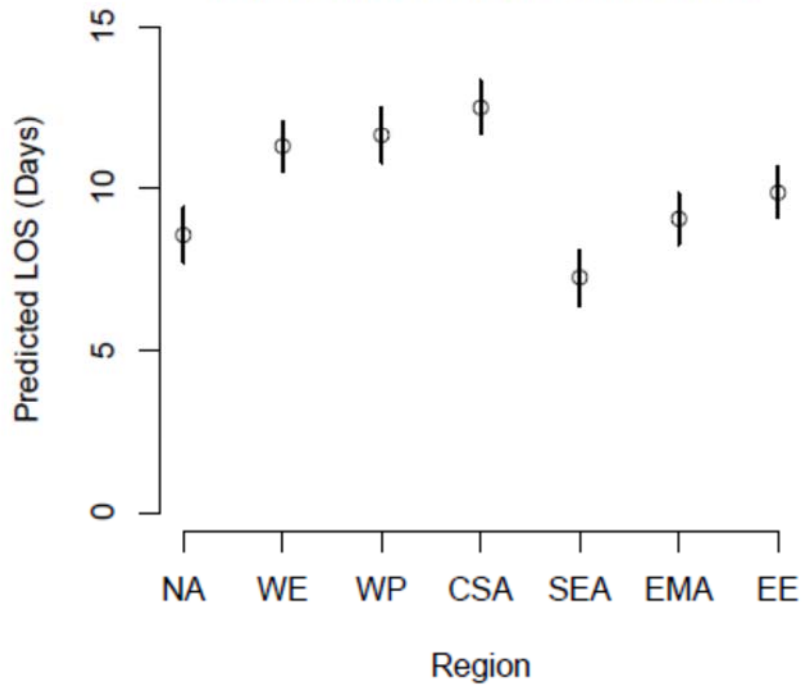
| | All N=18553 | Western Europe N=3594 | Eastern Europe N=2802 | Western Pacific N=3354 | South East Asia N=2329 | North America N=1592 | Central/ South America N=2641 | East Med & Africa N=2241 | P- value |
|--|--|--|--|--|---|--|---|--|-------------|
| n Median (IQR) | 0.9 (0.3- 2.2) | 1.0 (0.0- 2.3) | 0.4 (0.0- 0.9) | 1.0 (0.3- 1.9) | 0.8 (0.1- 1.8) | 1.3 (0.3- 4.0) | 1.1 (0.3- 3.1) | 0.9 (0.3- 2.6) | <0.0 001 |
| If 1 st treatment = IV Inotrope (hrs) n Median (IQR) | 1122 0.7 (0.0- 2.0) | 110 1.1 (0.2- 3.1) | 234 0.0 (0.0- 0.5) | 250 0.9 (0.3- 2.5) | 219 0.6 (0.07- 1.35) | 50 2.5 (0.7- 6.3) | 162 1.3 (0.3- 3.5) | 97 1.0 (0.3- 2.6) | <0.0 001 |
| Hospital LOS | | | | | | | | | |
| LOS (days) n Mean (SD) Median (IQR) | 18102 10.3 (10.21) 8.0 (5.0- 12.0) | 3489 11.1 (8.65) 9.0 (6.0- 13.0) | 2761 10.4 (8.27) 9.0 (6.0- 13.0) | 3298 11.5 (8.72) 9.0 (7.0- 14.0) | 2292 7.1 (5.51) 6.0 (4.0- 8.0) | 1565 8.8 (9.40) 6.0 (4.0- 10.0) | 2525 12.6 (15.68) 8.0 (5.0- 14.0) | 2172 8.8 (11.8) 6.0 (4.0- 10.0) | <0.0 001 |
| In-hospital Mortality | | | | | | | | | |
| Deaths during Index Hospitalization | 451 (2.4%) | 105 (2.9%) | 41 (1.5%) | 56 (1.7%) | 37 (1.6%) | 27 (1.7%) | 116 (4.4%) | 69 (3.1%) | <0.0 001 |

AHF = acute heart failure; ED = Emergency department; ICU/CCU = Intensive / Critical Care unit; HRS = hours; LOS = length of stay; * reflecting comparison of all possible pathways

Supplemental Table 4. Multivariable model evaluating the association of timeliness and type of IV therapy with in-hospital mortality and LOS adjusting for severity

| Variables | Higher Mortality (unadjusted) | Higher Mortality (adjusted) | Longer LOS (unadjusted) | Longer LOS (adjusted) |
|-----------------------------------|-------------------------------|---------------------------------------|-----------------------------------|---|
| Age | 1.01 (0.999 - 1.02) p=0.07 | 1.01 (1.00 - 1.02) p=0.006 (Older) | -0.05 (-0.06 - -0.03) p<0.0001 | -0.04 (-0.05 - -0.02) p<0.0001 (Younger) |
| SBP <115 mmHg | 1.24 (0.77 - 1.99) p=0.38 | 1.05 (0.63-1.74) p=0.86 | 2.45 (1.55 -3.36) p<0.0001 | 1.43 (0.51 - 2.36) p=0.002 |
| HF Etiology - Ischemia | 1.60 (1.10 - 2.32) p=0.014 | 1.65 (1.11-2.44) p=0.01 | 0.93 (0.42 - 1.44) p<0.0001 | 0.77 (0.26 - 1.29) p=0.003 |
| HF Etiology - Valvular | 2.10 (1.39 - 3.19) p=0.001 | 2.10 (1.36 - 3.25) p=0.001 | 2.40 (1.65 - 2.84) p<0.0001 | 2.01 (1.38 - 2.65) p=0.0001 |
| CXR signs of congestion | 1.89 (1.3 - 2.76) p=0.002 | 2.03 (1.39 - 2.97) p<0.0001 | 0.97 (0.52 -1.42) p<0.0001 | 1.02 (0.57 - 1.47) p<0.0001 |
| Creatinine >2.75 mg/dL | 0.64 (0.24 - 1.05) P=0.002 | 1.85 (1.20 - 2.85) p=0.005 | 1.55 (0.71 - 2.40) p = 0.001 | 1.16 (0.31 - 2.00) p=0.007 |
| Time to treatment | 1.00 (0.97 - 1.02) p=0.84 | 1.0 (0.97 - 1.02) p=0.75 | 0.035 (-0.001 - 0.071) p= 0.05 | 0.03 (-0.00 - 0.07) p=0.08 |
| | Treatment Type | | | |
| Diuretics alone | 2.08 (0.29 - 15.0) p=0.47 | 1.95 (0.27 - 14.2) p =0.51 | -1.14 (-2.87 -0.59) p=0.20 | -1.04 (-2.75 - 0.66) p=0.231 |
| Vasodilators/nitrates ± diuretics | 1.80 (0.24 - 13.2) p=0.56 | 1.89 (0.26 - 14.1) p = 0.53 | -2.13 (-3.90 - -0.37) p=0.02 | -1.79 (-3.53 - -0.04) p=0.05 (if not used) |
| Inotropes ± diuretics | 4.8 (0.66 - 35.3) p=0.12 | 3.70 (0.50 - 27.3) p = 0.20 | 0.08 (-1.73 - 1.89) p=0.93 | -0.60 (-2.40 - 1.19) p=0.51 |

Supplemental Figure 2
Predicted Length of Stay
With 95% Confidence Intervals



Supplemental Figure 3 Predicted Probability of Death With 95% Confidence Intervals

