**Table S1. Baseline Patient Demographic Characteristics, EM vs. EC**

|  |  |  |  |
| --- | --- | --- | --- |
| ***Index Treatment Type*** | **EM** | **EC** |  **P-value\*** |
| **Characteristic**  | **N=354** | **N=1,270** |
| **Mean (SD) (years)** | 49.7 (12.3) | 50.5 (12.0) | 0.3154 |
| **Age group (%)** |  |  | 0.3610 |
| 18-34 years | 14.7% | 12.8% |  |
| 35-44 years | 13.8% | 13.6% |  |
| 45-54 years | 25.7% | 27.6% |  |
| 55-64 years | 44.6% | 43.2% |  |
| ≥65 years | 1.1% | 2.8% |  |
| **Female (%)** | 57.6% | 51.5% | 0.0410 |
| **Geographic region (%)** |  |  |  |
| Northeast | 12.1% | 16.0% | <0.0001  |
| Midwest | 23.7% | 14.4% |  |
| South | 56.5% | 54.6% |  |
| West | 7.6% | 15.0% |  |
| **Health plan type (%)** |  |  | 0. 2917 |
| PPO | 76.3% | 73.4% |  |
| HMO | 19.5% | 20.2% |  |
| POS | 3.4% | 4.6% |  |
| Consumer directed health care | 0.0% | 0.2% |  |
| Indemnity | 0.3% | 1.4% |  |
| Other/Unknown | 0.6% | 0.2% |  |
| **Payer type (%)** |  |  |  |
| Commercial | 54.0% | 48.0% | 0.0387 |
| Medicaid | 10.2% | 10.6% |  |
| Medicare Risk | 1.4% | 4.1% |  |
| Self-insured | 34.5% | 37.4% |  |
| **Index year (%)** |  |  |  |
| 2012 | 27.4% | 25.0% | 0.7075 |
| 2013 | 22.0% | 20.5% |  |
| 2014 | 20.1% | 20.2% |  |
| 2015 | 16.1% | 17.9% |  |
| 2016 | 14.4% | 16.5% |  |

\*Parametric t-test for continuous variables and the Chi-square test for categorical variables.

Abbreviations. EC, empiric combination therapy; EM, empiric monotherapy; HMO, health maintenance organization; POS, point-of-service; PPO, preferred provider organization.

**Table S2. Baseline Patient Clinical Characteristics, EM vs. EC**

| ***Index Treatment Type*** | **EM** | **EC** | **P-value** |
| --- | --- | --- | --- |
| **Characteristic**  | **N=354** | **N=1,270** |
| **Mean (SD) CCI score** | 1.2 (1.7) | 1.4 (2.0) | 0.0353 |
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| **Respiratory conditions (%)** |   |   |   |
| Respiratory failure | 3.4% | 3.6% | 0.8351 |
| Respiratory acute infection | 39.0% | 28.1% | <0.0001  |
| Respiratory (other disease) | 16.7% | 12.1% | 0.0252 |
| Respiratory (chronic condition) | 27.4% | 26.6% | 0.7675 |
| **Pre-index comorbid conditions (≥5%)** |   |   |   |
| Asthma | 13.6% | 13.5% | 0.9632 |
| Cardiac arrhythmia | 10.2% | 14.2% | 0.0498 |
| Cardiac valvular disease | 5.1% | 6.5% | 0.3423 |
| Cerebrovascular disease | 3.7% | 5.5% | 0.1646 |
| Chronic kidney disease | 4.5% | 7.2% | 0.0689 |
| Chronic pain/fibromyalgia | 9.6% | 11.6% | 0.2975 |
| CHF | 2.5% | 5.9% | 0.0115 |
| COPD | 13.6% | 13.9% | 0.8853 |
| Depression | 18.1% | 12.6% | 0.0082 |
| Diabetes  | 16.9% | 20.7% | 0.1171 |
| Dyslipidemia | 29.9% | 26.1% | 0.1541 |
| Hypertension | 36.4% | 40.0% | 0.2252 |
| Liver/GB/pancreatic disease | 6.8% | 6.9% | 0.9628 |
| MI/CAD | 10.2% | 8.8% | 0.4349 |
| Osteoarthritis | 14.7% | 13.7% | 0.6347 |
| Renal failure/dialysis | 2.8% | 5.6% | 0.0345 |
| Sleep disorders | 11.9% | 13.9% | 0.3127 |
| Smoking | 16.1% | 14.0% | 0.3239 |
| Thyroid disease | 13.6% | 10.3% | 0.0848 |
| **Pre-index medications (≥5%)** |   |   |   |
| Chemotherapy | 5.4% | 7.1% | 0.2529 |
| Inhalers for lung disease | 30.8% | 30.2% | 0.8409 |
| CAP-related antimicrobials | 57.1% | 52.6% | 0.1364 |
| Antifungals | 5.4% | 5.1% | 0.8515 |
| Beta-lactams | 27.7% | 28.6% | 0.7401 |
| Fluoroquinolones | 22.0% | 18.1% | 0.0959 |
| Folate pathway inhibitors | 8.5% | 6.9% | 0.3219 |
| Macrolides | 23.7% | 20.0% | 0.1265 |
| Tetracyclines | 7.6% | 6.8% | 0.5759 |
| **Mean (SD) total all-cause pre-index healthcare costs**  | 17,075 (49,044) | 15,090 (34,241) | 0.3844 |

\*Parametric t-test for continuous variables and the Chi-square test for categorical variables.

Abbreviations. CAP, community-acquired pneumonia; CCI, Charlson Comorbidity Index; CAD, coronary artery disease; CHF, congestive heart failure, CHF; COPD, chronic obstructive pulmonary disease; EC, empiric combination therapy; EM, empiric monotherapy; GB, gallbladder; MI, myocardial infarction.

**Table S3. Characteristics of the Index Hospitalization, EM vs. EC**

| ***Index Treatment Type*** | **EM** | **EC** | **P-value** |
| --- | --- | --- | --- |
| **Characteristic**  | **N=354** | **N=1,270** |
| **Number of hospital beds (%)** |  |  | 0.3629 |
| 1-99 beds | 8.8% | 8.8% |  |
| 100-199 beds | 22.9% | 21.3% |  |
| 200-299 beds | 13.6% | 14.2% |  |
| 300-499 beds | 28.5% | 33.6% |  |
| 500+ beds | 26.0% | 22.0% |  |
| Unknown | 0.3% | 0.2% |  |
| **Hospital location (%)** |  |  | 0.097 |
| Urban | 92.7% | 95.3% |  |
| Rural | 7.1% | 4.6% |  |
| Unknown | 0.3% | 0.2% |  |
| **Teaching status (%)** |  |  |  |
| Teaching | 25.7% | 32.4% | 0.0297 |
| Non-Teaching | 74.0% | 67.4% |  |
| Unknown | 0.3% | 0.2% |  |
| **Index therapy class (≥5%; not mutually exclusive)** |  |  |  |
| Beta-lactams | 13.3% | 93.0% | <.0001 |
| Fluoroquinolones | 79.4% | 46.4% | <.0001 |
| Glycopeptide | 0.8% | 29.8% | <.0001 |
| Macrolides | 5.1% | 62.4% | <.0001 |
| **Index therapy class (≥5%; mutually exclusive)** |  |  |  |
| **Monotherapy** | 100.0% | 0.0% | <.0001 |
| Beta-lactams | 13.3% |  |  |
| Fluoroquinolones | 79.4% |  |  |
| Macrolides | 5.1% |  |  |
| **Combination therapy** | 0.0% | 100.0% |  |
| Beta-lactams + Macrolides  |  | 38.9% |  |
| Beta-lactams + Fluoroquinolones  |  | 12.6% |  |
|  Beta-lactams + Fluoroquinolones + Macrolides  |  | 10.9% |  |
|  Beta-lactams + Fluoroquinolones + Glycopeptide  |  | 10.1% |  |
| Beta-lactams + Glycopeptide + Macrolides  |  | 5.0% |  |
| **Index CAP type** |  |  |  |
| HCAP (≥5%) | 56.2% | 56.3% | 0.9774 |
| 90-day pre-index hospitalization  | 33.6% | 36.1% |  |
|  Pre-index corticosteroid use | 42.1% | 39.3% |  |
| COP | 43.8% | 43.7% |  |
| **Admitting source (%)** |  |  |  |
| ER | 80.8% | 82.2% | 0.0055 |
| Referral and transfer | 9.3% | 4.7% |  |
| Routine admission  | 9.9% | 12.6% |  |
| Other | 0.0% | 0.5% |  |
| **Discharge disposition (%)** |  |  | 0.1339 |
| Alive - home | 94.1% | 89.8% |  |
| Expired | 0.0% | 0.0% |  |
| LAMA or discontinued care | 0.3% | 0.6% |  |
| Transferred - long term care | 0.6% | 0.8% |  |
| Transferred - other institution  | 2.5% | 2.8% |  |
| Transferred - short-term hospital | 0.8% | 1.4% |  |
| Unknown/other  | 1.7% | 4.6% |  |
| **ICU transfer**  |  |  |  |
| Any ICU transfer (%) | 13.3% | 25.3% | <0.0001 |
| Mean (SD) ICU days | 4.6 (5.7) | 5.1 (6.4) | 0.5751 |
|  Mean (SD) ICU days, all patients | 0.6 (2.6) | 1.3 (3.9) | 0.0018 |
| **Mechanical ventilation (%)** | 6.5% | 12.4% | 0.0019 |
| **Vasopressors (%)** | 4.8% | 6.0% | 0.3973 |
| **Mean (SD) LOS** | 4.8 (2.8) | 6.0 (4.7) | <0.0001 |
| **Mean (SD) total hospitalization cost** | $13,813 ($11,430) | $18,830($27,569) | 0.0008 |

Abbreviations. CAP, community-acquired pneumonia; COP, community-onset pneumonia; EC, empiric combination therapy; EM, empiric monotherapy; HCAP, healthcare-associated pneumonia; ICU, intensive care unit; LAMA, left against medical advice; LOS, length of stay.

**Table S4. HCRU over the 1-Year Follow-Up, EM vs. EC**

|  |  |  |
| --- | --- | --- |
|  | **All-Cause** | **CAP-Related** |
| ***Index Treatment Type*** | **EM** | **EC** | **P-value\*** | **EM** | **EC** | **P-value\*** |
|  | **N=354** |  **N=1,270** | **N=354** |  **N=1,270** |
| **Proportion (%) with utilization** |  |  |  |  |  |  |
| ER visit | 58.5% | 57.9% | 0.8396 | 18.6% | 21.7% | 0.2189 |
| Physician office visit | 99.7% | 97.9% | 0.0185 | 61.9% | 60.5% | 0.6353 |
| Lab/pathology test | 91.2% | 90.2% | 0.5686 | 21.8% | 24.6% | 0.2596 |
| Radiology exam | 86.7% | 84.3% | 0.2669 | 41.0% | 39.1% | 0.5342 |
| All other outpatient  | 95.8% | 94.5% | 0.3410 | 41.5% | 45.0% | 0.2498 |
| **Mean number of services** |  |  |  |  |  |  |
| Prescription fills | 45.3 | 44.5 | 0.7592 | 3.2 | 3.1 | 0.5833 |
| Physician office visits | 18.5 | 19.1 | 0.7238 | 1.3 | 1.5 | 0.1694 |
| Lab/pathology tests | 28.5 | 31.7 | 0.3552 | 1.1 | 1.6 | 0.1108 |
| Radiology exams | 6.1 | 5.4 | 0.2679 | 0.6 | 0.7 | 0.5758 |
| All other outpatient | 38.4 | 43.0 | 0.2911 | 2.9 | 3.0 | 0.8673 |

\*Parametric t-test for continuous variables and the Chi-square test for categorical variables.

All other outpatient = outpatient ancillary and HCPCS drugs.

Abbreviations. CAP, community-acquired pneumonia; EC, empiric combination therapy; EM, empiric monotherapy; HCPCS, Healthcare Common Procedure Coding System; HCRU, healthcare resource utilization.

**Table S5. Healthcare Cost over the 1-Year Follow-Up, EM vs. EC**

|  |  |  |  |
| --- | --- | --- | --- |
|   | **EM** | **EC** | **P-Value** |
|   | **(N=354)** | **(N=1,270)** |
| **Cost (2017 USD) per patient** | **Mean** | **SD** | **Median** | **Mean** | **SD** | **Median** |
|  | **All-Cause** |
| **TOTAL** | $55,296 | $99,062 | $26,789 | $63,777 | $125,164 | $30,009 | 0.2396 |
| Outpatient Pharmacy  | $5,363 | $10,391 | $1,819 | $5,668 | $13,781 | $1,635 | 0.6994 |
| Inpatient Hospitalizations | $25,999 | $36,382 | $12,812 | $37,106 | $99,743 | $16,093 | 0.0399 |
| Outpatient Medical | $23,934 | $83,010 | $6,257 | $21,004 | $57,996 | $6,088 | 0.4484 |
| ER | $1,466 | $5,108 | $190 | $1,168 | $4,120 | $155 | 0.2544 |
| Physician office visits | $6,121 | $49,385 | $1,220 | $3,948 | $20,776 | $1,264 | 0.2199 |
| Outpatient surgery | $1,702 | $6,660 | $0 | $1,712 | $5,431 | $0 | 0.9761 |
| Lab/pathology | $1,396 | $4,023 | $350 | $1,272 | $4,141 | $328 | 0.6144 |
| Radiology | $2,993 | $11,835 | $564 | $2,159 | $9,946 | $402 | 0.1819 |
| All other outpatient | $10,255 | $34,489 | $1,451 | $10,745 | $41,528 | $1,582 | 0.8388 |
|  | **CAP-Related** |
| **TOTAL** | $16,399 | $18,916 | $11,315 | $22,224 | $37,052 | $13,922 | 0.0044 |
| Outpatient Pharmacy  | $110 | $569 | $28 | $174 | $747 | $32 | 0.1320 |
| Inpatient Hospitalizations | $15,384 | $18,327 | $10,883 | $20,988 | $36,089 | $13,004 | 0.0048 |
| Outpatient Medical | $905 | $3,277 | $204 | $1,061 | $4,957 | $238 | 0.5760 |
| ER | $272 | $2,269 | $0 | $228 | $1,182 | $0 | 0.6211 |
| Physician office visits | $155 | $230 | $98 | $181 | $328 | $96 | 0.1636 |
| Outpatient surgery | $4 | $41 | $0 | $11 | $133 | $0 | 0.3591 |
| Lab/pathology | $36 | $207 | $0 | $51 | $234 | $0 | 0.2761 |
| Radiology | $92 | $259 | $0 | $115 | $417 | $0 | 0.3261 |
| All other outpatient | $345 | $2,184 | $0 | $475 | $4,662 | $0 | 0.6108 |

\*Parametric t-test for continuous variables.

All other outpatient = outpatient ancillary and HCPCS drugs.

Abbreviations. CAP, community-acquired pneumonia; EC, empiric combination therapy; EM, empiric monotherapy; HCPCS, Healthcare Common Procedure Coding System; HCRU, healthcare resource utilization.

**Figure S1. All-Cause and CAP-Related Readmission**



Abbreviations. CAP, community-acquired pneumonia, EC, empiric combination therapy; EM, empiric monotherapy.