Is HCAP a Useful Concept?

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With the Advent of HCAP, We Have 3 or 4 Types of Pneumonia: CAP, HCAP, HAP/VAP

• “Healthcare-associated pneumonia is a relatively new clinical entity that includes a spectrum of adult patients who have a close association with acute care hospitals or reside in chronic care settings that increase their risk for pneumonia caused by multidrug-resistant pathogens.”

Definitions and Frequency of Different Types of Pneumonia Among Inpatients

- Retrospective data base (59 U.S. hospitals) evaluation of 4543 culture positive hospitalized pneumonia patients
  - CAP (48.9%), HAP (18.4%), VAP (11%), and HCAP (21.7%)

Outcomes of Different Types of Pneumonia

- **Demographics**: HCAP sig older than CAP (77 vs. 73, p<0.01), similar to HAP, VAP
  - 49.6% HCAP from nursing home
  - Less vent support on admit with CAP than HCAP (16.9% vs. 24.1%, p<0.01)
  - More comorbidities with HCAP than CAP (p<0.01)

**Bacteriology of Different Types of Pneumonia**

**Bacteriology:**

- More *S. aureus*, MRSA and *P. aeruginosa* in HCAP than CAP ($p<0.01$).
- HCAP: 46.7% SA (56.8% of these MRSA), 25.3% *P. aeruginosa*

- MRSA as percentage of all *S. aureas* HCAP>HAP>CAP >VAP

How Do We Define Therapy For Pneumonia?

• By Site of Origin?
  – There are populations of patients with CAP, HCAP, HAP and VAP that are at risk for MDR gram negatives and gram positives
    • Risk factors for MDR pathogens are common in all forms of pneumonia

• By Severity of Illness alone?
  – Patients in our out of ICU can have MDR pathogens, depending on risk factors present

• By Mortality Risk?
  – Different populations of pneumonia patients have a high mortality risk. This relates more to host factors, than to pathogens, unless those pathogens are treated inappropriately

• By Risk Factors For MDR Pathogens?
  – More logical and a unifying concept
  – An indirect relationship to severity of illness
For All Pneumonia Patients, Can We Identify Those At Risk and Not At Risk For MDR Pathogens?

- Risks for MDR Gram-negatives in CAP, HCAP, HAP and VAP
  - Prior antibiotic therapy
  - Prolonged (>4 days) hospital stay
  - From nursing home with MDR pathogens
  - Poor functional status (feeding tube, poor ADL, aspiration)
  - Immune suppression
- MDR’s more common with severe illness
PNEUMONIA 2012: Risk for MDR Pathogens Crosses All Types and Severities

ICU Treated Patients

Expanded Spectrum of HCAP

At Risk For MDR Pathogens

Not At Risk For MDR Pathogens
HCAP vs. CAP: A Single Center Study Showing MDR Pathogens are Common

- 683 culture positive pneumonia patients: 67.4% were HCAP, 32.6% CAP
  - 93% hospitalized in last 6 months, 69% in last 3 months
  - 28% from nursing home
- Bacteriology of HCAP: 31% MRSA, 10% pneumococcus, 26% P. aeruginosa, 29% other enteric gram negatives
- Higher mortality for HCAP (24.6% vs. 9.1%, p < 0.001)
- More inappropriate therapy (in first 24 hours) for HCAP and this was an independent risk for mortality
Are MDR Pathogens Really Common in HCAP?

- Observational, prospectively evaluated cohort of 727 non-severe admitted pneumonia patients
- 601 CAP, 126 HCAP patients
- **Definition of HCAP**: Home IV therapy, home wound care or nursing care w/i 30 days; hospital clinic or dialysis center w/i 30 days; hospitalized for ≥ 2 days in last 90 days, from nursing home
  - Prior antibiotics= within 3 months
- HCAP older (69.5 vs. 63.7 years, p< 0.001), more comorbidity, higher PSI
- **HCAP bacteriology**: S. pneumoniae (more drug resistant than CAP), less Legionella, more aspiration (20.6% vs. 3%, p< 0.01), more H. influenzae, S. aureus (2.4% vs. 0%, p=0.005), gram negatives (4% vs 1%, p=0.03)
- More inappropriate therapy (5.6% vs 2%, p=0.03), higher mortality (10.3% vs 4.3%, p=0.007)
HCAP Studies Include a Heterogeneous Population: Therefore Different Findings

Table 2 Initial antibiotic therapy and clinical outcomes of healthcare-associated pneumonia as compared with community-acquired pneumonia in three studies

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td></td>
<td>HCAP (n=988)</td>
<td>CAP (n=2221)</td>
<td>P</td>
</tr>
<tr>
<td>Inappropriate antibiotic therapy (%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Bacteraemia (%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>ICU admission (%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Need for mechanical ventilation (%)</td>
<td>24.1</td>
<td>16.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>8.8(^a)</td>
<td>7.5(^a)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Early case fatality rate ((&lt;48\ h); %)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Overall case fatality rate (%)</td>
<td>19.8</td>
<td>10.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

|                                          | HCAP \(n=126\) | CAP \(n=601\) | P            |
| Inappropriate antibiotic therapy (%)     | 5.6          | 2.0             | 0.03         |
| Bacteraemia (%)                          | 8.7          | 10.6            | NS           |
| ICU admission (%)                        | 6.3          | 8.7             | NS           |
| Need for mechanical ventilation (%)      | 3.2          | 4.7             | NS           |
| Length of hospital stay (days)           | 9\(^b\)      | 8\(^b\)         | 0.003        |
| Early case fatality rate (\(<48\ h\); %)| 3.2          | 0.8             | 0.053        |
| Overall case fatality rate (%)           | 10.3         | 4.3             | 0.007        |

|                                          | HCAP \(n=431\) | CAP \(n=208\) | P            |
| Inappropriate antibiotic therapy (%)     | 26.3         | 13.0           | <0.001       |
| Bacteraemia (%)                          | 30.9         | 37.5           | NS           |
| ICU admission (%)                        | 48.7         | 37.0           | 0.005        |
| Need for mechanical ventilation (%)      | 44.5         | 31.3           | 0.001        |
| Length of hospital stay (days)           | –            | –               | –            |
| Early case fatality rate (\(<48\ h\); %)| –            | –               | –            |
| Overall case fatality rate (%)           | 24.6         | 9.1            | <0.001       |

HCAP in Korea: Risk of MDR Pathogens

- Retrospective study of hospitalized CAP and HCAP – 182 HCAP (66% recent hospitalization), 163 CAP
- HCAP with more comorbidity, higher PSI
- S. pneumoniae most common in BOTH groups, BUT potentially drug resistant organisms more in HCAP (29.3% vs. 13%, p=0.04) and more inappropriate rx. (24.6% vs. 8.7%, p=0.03), higher mortality (19.2% vs. 7.4%)
- In multiple logistic regression, severity of illness, NOT HCAP predicted mortality
  – Park et al. Resp Med 2010; 104: 1729-1735
Suggest therapy for NHAP:
Avoid broad-spectrum rx and use 1 drug if functionally active, no recent antibiotics.
Triple therapy (incl. MRSA) if poor ADL, prior antibiotics. MDR= Multi-Drug resistant pathogen
HCAP in Japan: Differentiation from CAP, Risk Factors for MDR Pathogens

• Retrospective, observational study of HCAP and CAP (141 HCAP, 230 CAP)
  • HCAP: 61% from NH, 39% with recent admit, 7% dialysis
  - HCAP vs. CAP: more with severe illness (46% vs 23%), higher mortality for moderate severity (11.1 vs. 1.9%), more MDR pathogens, more with recent antibiotics (63% vs. 21%), probable aspiration (58% vs. 18%), poor functional status (57% vs. 11%), more inappropriate rx. (21 vs 10%)
  - 55% HCAP with etiologic diagnosis. HCAP bacteriology:
    • 24% GNB (5.7% Pseudomonas, 2.1% Acinetobacter, 0.7% ESBL)
    • 31% Gram positive (3.5% MRSA)
    • MDR risks: prior antibiotics (OR=3.1) tube feed (OR=2.5)
  - 22% (vs. 6% CAP) with MDR pathogens, and these often with inappr rx and treatment failure (71% failure rate)
Which HCAP Patients Are At Risk For MDR Pathogens?

- Data set from Micek 2007. 639 patients admitted with pneumonia (approx 2/3 had HCAP)
- 289 with resistant pathogens (157 were MRSA), and 87% had at least one HCAP risk factor.
- 350 without resistance and 51.4% had at least one HCAP risk.
- Scoring system for MDR risk:
  - recent admit (4 pts)
  - NH residence (3 pts)
  - hemodialysis (2 pts)
  - ICU admit (1 pt).

### Table 2. Independent Variables Associated With Resistant Infection

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent hospitalization</td>
<td>4.21 (2.89-6.15)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Nursing home resident</td>
<td>2.75 (1.74-4.33)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Long-term hemodialysis</td>
<td>2.11 (1.03-4.31)</td>
<td>.04</td>
</tr>
<tr>
<td>ICU admission</td>
<td>1.62 (1.14-2.28)</td>
<td>.007</td>
</tr>
</tbody>
</table>

**Figure.** Point score and risk stratification for pneumonia due to a resistant pathogen. P<.001 for trend.
How Useful is This Predictive Rule?

- 977 Pneumonia patients in ED: almost ¾ with HCAP
- 46.7% with resistant organisms: MRSA (22.7%), PA (19.1%), K. pneumoniae (5.6%), Acinetobacter (4.8%). Had higher risk score
  - 91% with RO had HCAP
  - 65% with non-RO had HCAP
- Shorr et al. CID 2012; 54:193-198

| Table 2. Screening Characteristics of Healthcare-Associated Pneumonia Versus Risk Score |
|---------------------------------|-----------------|-----------------|--------|--------|-----------------|
|                                 | Sensitivity     | Specificity     | PPV    | NPV    | Accuracy        |
| HCAP definition                 | 91.0%           | 34.3%           | 54.8%  | 81.3%  | 60.7%           |
| Risk score >0                   | 88.6%           | 54.5%           | 63.0%  | 84.5%  | 70.4%           |

Abbreviations: HCAP, healthcare-associated pneumonia; NPV, negative predictive value; PPV, positive predictive value.
Is Hemodialysis Associated Pneumonia (HDAP) a Form of HCAP?

- Retrospective, 69 patients with HDAP (27 severe disease)
- Bacteriology (sputum cultures): S. aureus (37.7%; of which almost ¾ were MRSA), S. pneumoniae (10.1%), K. pneumoniae (8.7%), H. influenzae (7.2%), M. catarrhalis (5.8%), P. aeruginosa (2.9%)
- Similar bacteriology, regardless of severity, but worse outcome if more severe illness.
- MDR with higher mortality (18.2% vs. 8.5%, p= 0.24)
- Both severity and risk for MDR pathogens determines mortality risk
  - Kawasaki et al. J. Infect Chemother ; on line March 2011
Mortality Risk In HCAP and CAP Relates To Functional Status

- Prospective observational study of 273 patients admitted with a diagnosis of pneumonia (radiographic and clinical), who provided consent for observation.
- Patients were identified as having CAP (n=200) or HCAP (n=73).
- In-hospital death: 12.3% in pts with HCAP and 7% in pts with CAP (p=0.22).
- Calculation of Barthel index, a functional status score based on activities of daily living.
  - Min: 0
  - Max: 100.
  - Lower score reflects worse functional status.
  - Variables: self feed, transfer from bed and chair, get on the toilet, self bathe, get dressed, walk, climb stairs and control of bowels and bladder, grooming abilities.
Death Rate By Barthel’s Index: Useful in Both CAP and HCAP

- Mortality in HCAP was not well predicted by PSI and CURB-65
- Mortality in CAP was predicted better by CURB-65 than by PSI
The Controversy About HCAP Therapy

• Europeans seem bothered by the HCAP concept
  – Prefer to classify HCAP patients as CAP if from nursing home or home care; HAP if prior hospital stay; immune suppressed if appropriate risks
  • Ewig, Welte, Chastre, Torres. Lancet ID 2010; 4: 279-97
  – Heterogeneous definitions, questionable microbiologic data (esp retrospective), not enough emphasis on aspiration.
  – Concern about promoting overtreatment

• Still a useful concept in the United States
  – Some (maybe not all) HCAP patients are at risk for pneumonia with MDR pathogens
  • If not recognized, may lead to undertreatment
  – Makes HCAP patients EXEMPT from compliance with CAP core measures for antibiotic choice
Therapy of HCAP: A Gap in Care vs. Knowledge

- Survey of 855 doctors comparing treatment of CAP and HCAP in patient scenarios vs. knowledge of guidelines
- Select guideline compliant rx for CAP, 78% of the time vs. 9% of the time for HCAP scenarios. Often no MRSA coverage (72% of incorrect answers)
- 71% were aware of HCAP guidelines, 79% said they agree with guidelines and that they follow them.
What Therapy for NHAP?

- Retrospective evaluation of 334 NHAP patients
  - 77% rx per CAP guidelines, the rest per HCAP recommendations
  - Similar comorbidities and PSI class in both groups
- Time to clinical stability and mortality same in both groups
- Longer LOS and time to oral therapy with HCAP regimen
- More anti-Pseudomonal and MRSA empiric therapy in NHAP with higher PSI class (>30% if PSI V)
Is It Necessary To Follow HCAP Guidelines?

- 2732 CAP, 563 HCAP patients (106 in ICU) in Canada. HCAP with few MDR pathogens (ex. *P. aeruginosa* in 8%)
  - HCAP with higher mortality, esp with inappropriate rx.
  - 19% compliance with HCAP guidelines, yet 89% got effective rx. Mortality not affected by guideline concordance.

- HCAP and CAP in the UK. HCAP older; more comorbidity, limitation of care, and severe illness; worse functional status; higher mortality; few MDR pathogens.
  - 93% of HCAP patients got CAP therapy
  - Conclude that increased mortality related to pt. factors, not therapy, and therefore no need to follow HCAP guidelines

- 15,071 Veterans with HCAP definition (pneumonia + 1 risk ), none in ICU. 8% HCAP therapy, 76% CAP therapy, 16% non-concordant therapy
  - HCAP therapy with increased mortality after propensity model adjustment
• Functional status determines mortality risk and is related to need for MDR pathogen therapy
• In multivariate analysis, Barthel Index predicts mortality, and CAP compliance is not in model
Proposed Algorithm for HCAP Therapy

HCAP Is Present
(from a nursing home, home infusion therapy, home wound care, dialysis center, hospitalized in past 90 days)

Assess Severity of Illness (ICU or mechanical ventilation) and MDR Risks (recent antibiotic therapy, poor functional status, recent hospitalization, immune supression)

Severe Illness

NO

0–1 MDR Risks:
Treat for common CAP pathogens (consider oral Rx)
Quinolone, β-lactam/Macrolide

YES

2 MDR Risks:
Consider hospital admit
Treat for MDR pathogens with HAP recommendations

0 MDR Risks:
Consider IV therapy with β-lactam
PLUS Macrolide or Quinolone

≥ 1 MDR Risks:
Treat for MDR pathogens with HAP recommendations
Need 3 drugs

Classification of pneumonia using the algorithm

Patients with radiographic pneumonia (n=469)

Criteria for HCAP
- Resident of nursing-home or extended-care facility
- Hospitalization for more than 2 days within last 90 days
- Attendance at hospital or hemodialysis clinic within last 30 days
- Intravenous antibiotic therapy or chemotherapy within last 30 days
- Home wound care
- Exposure to a family member infected with MDR pathogens

Excluded (n=24)
- Did not consent (n=3)
- Hospital acquired pneumonia (n=13)
- Pulmonary tuberculosis (n=3)
- Patients with interstitial pneumonia (n=3)
- Acute lung injury with witnessed aspiration (n=1)
- Obstructive pneumonia with small cell lung cancer (n=1)

CAP (n=124)

Yes
HCAP (n=321)

Assess severity of illness
Need for mechanical ventilation or ICU admittance
AND
Presence of risk factors for drug-resistant pathogens
Antibiotic therapy in the past 180 days,
Poor functional status (Barthel Index <50)
Hospitalization for more than 2 days in the past 90 days
Immunosuppression

Severe pneumonia

No
n=202

Group 1 (0-1 Risks) n=110

Yes
n=119

Group 2 (≥ 2 Risks) n=92

Group 3 (0 Risks) n=41

Group 4 (≥ 1 Risks) n=78

## Table 3. Causative Microorganisms

<table>
<thead>
<tr>
<th>All patients</th>
<th>CAP</th>
<th>All HCAP</th>
<th>Group 1 in HCAP</th>
<th>Group 2 in HCAP</th>
<th>Group 3 in HCAP</th>
<th>Group 4 in HCAP</th>
<th>*P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=445</td>
<td>n=124 (%)</td>
<td>n=321 (%)</td>
<td>n=110 (%)</td>
<td>n=92 (%)</td>
<td>n=41 (%)</td>
<td>n=78 (%)</td>
<td></td>
</tr>
<tr>
<td><strong>Streptococcus pneumoniae</strong></td>
<td>31(25)</td>
<td>106(33)</td>
<td>42(38.2)</td>
<td>24(26.1)</td>
<td>17(41.5)</td>
<td>23(29.5)</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>Staphylococcus aureus</strong></td>
<td>1(0.8)</td>
<td>37(11.5)</td>
<td>4(3.6)</td>
<td>14(15.2)</td>
<td>3(7.3)</td>
<td>16(20.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Enterobacteriaceae</strong></td>
<td>3(2.4)</td>
<td>25(7.8)</td>
<td>4(3.6)</td>
<td>10(10.9)</td>
<td>0</td>
<td>11(14.1)</td>
<td>0.037</td>
</tr>
<tr>
<td><strong>Pseudomonas aeruginosa</strong></td>
<td>1(0.8)</td>
<td>22(6.9)</td>
<td>2(1.8)</td>
<td>7(7.6)</td>
<td>1(2.4)</td>
<td>12(15.4)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Haemophilus influenzae</strong></td>
<td>8(6.5)</td>
<td>11(3.4)</td>
<td>3(2.7)</td>
<td>5(5.4)</td>
<td>3(7.3)</td>
<td>1(1.3)</td>
<td>0.157</td>
</tr>
<tr>
<td><strong>Moraxella catarrhalis</strong></td>
<td>0</td>
<td>4(1.2)</td>
<td>2(1.8)</td>
<td>0</td>
<td>2(4.9)</td>
<td>0</td>
<td>0.269</td>
</tr>
<tr>
<td><strong>Streptococcus milleri group</strong></td>
<td>1(0.8)</td>
<td>4(1.2)</td>
<td>3(2.7)</td>
<td>1(1.1)</td>
<td>0</td>
<td>0</td>
<td>0.572</td>
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<tr>
<td><strong>Sphingobacterium variabile</strong></td>
<td>1(0.8)</td>
<td>11(3.4)</td>
<td>3(2.7)</td>
<td>4(4.3)</td>
<td>1(2.4)</td>
<td>3(3.8)</td>
<td>0.109</td>
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<tr>
<td><strong>Acinetobacter baumannii</strong></td>
<td>0</td>
<td>2(0.6)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2(2.6)</td>
<td>0.52</td>
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<tr>
<td><strong>Anaerobes</strong></td>
<td>2(1.6)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.077</td>
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<tr>
<td><strong>Streptococcus epidermidis</strong></td>
<td>0</td>
<td>1(0.3)</td>
<td>1(0.9)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.721</td>
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<tr>
<td><strong>Drug-resistant pathogens</strong></td>
<td>17(13.7)</td>
<td>79(24.6)</td>
<td>18(16.4)</td>
<td>28(30.4)</td>
<td>5(12.2)</td>
<td>28(35.9)</td>
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<tr>
<td><strong>Chlamydophila pneumoniae</strong></td>
<td>5(4.1)</td>
<td>16(5)</td>
<td>4(3.6)</td>
<td>8(8.7)</td>
<td>0</td>
<td>4(5.1)</td>
<td>0.671</td>
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<td><strong>Chlamydia psittaci</strong></td>
<td>0</td>
<td>3(0.9)</td>
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<td>3(3.3)</td>
<td>0</td>
<td>0</td>
<td>0.374</td>
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<td><strong>Mycoplasma pneumoniae</strong></td>
<td>12(9.7)</td>
<td>13(4.0)</td>
<td>6(5.5)</td>
<td>2(2.2)</td>
<td>2(4.9)</td>
<td>3(3.8)</td>
<td>0.021</td>
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<tr>
<td><strong>Legionella pneumophila</strong></td>
<td>1(0.8)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.279</td>
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<tr>
<td><strong>Influenza virus</strong></td>
<td>6(4.8)</td>
<td>9(2.8)</td>
<td>6(5.5)</td>
<td>0</td>
<td>2(4.9)</td>
<td>1(1.3)</td>
<td>0.215</td>
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<tr>
<td><strong>Respiratory syncytial virus</strong></td>
<td>2(1.6)</td>
<td>4(1.2)</td>
<td>0</td>
<td>3(3.3)</td>
<td>0</td>
<td>1(1.3)</td>
<td>0.534</td>
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<tr>
<td><strong>Parainfluenza virus 3</strong></td>
<td>3(2.4)</td>
<td>4(1.2)</td>
<td>1(0.9)</td>
<td>1(1.1)</td>
<td>0</td>
<td>2(2.6)</td>
<td>0.304</td>
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<tr>
<td><strong>Unknown</strong></td>
<td>60(48.4)</td>
<td>109(34)</td>
<td>44(40)</td>
<td>29(31.5)</td>
<td>14(34.1)</td>
<td>22(28.2)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

All data are presented as n (%) unless otherwise stated. CAP: community-acquired pneumonia; HCAP: healthcare-associated pneumonia. Numbers include mixed population of pathogens: 17 in CAP and 63 in HCAP. Enterobacteriaceae included *Klebsiella pneumoniae* 2, *Escherichia coli* 1 in CAP and *Klebsiella pneumoniae* 12, *Escherichia coli* 7, *Serratia marcescens* 1, *Morganella morganii* 3 and *Proteus mirabilis* 2 in HCAP. Drug-resistant pathogens included *Streptococcus pneumoniae* 11 (resistance to penicillin 5, erythromycin 8, levofloxacin 2, imipenem 1), *Haemophilus influenzae* 5 (beta-lactamase-producing ampicillin-resistant 2 and beta-lactamase-nonproducing ampicillin-resistant 3) and macrolide-resistant *Mycoplasma pneumoniae* 1 in CAP and *Streptococcus pneumoniae* 45 (resistance to penicillin 14, erythromycin 30, levofloxacin 5 and imipenem 4), *Haemophilus influenzae* 2 (beta-lactamase-producing ampicillin-resistant 2), *Staphylococcus aureus* 22 (resistance to methicillin 22). Enterobacteriaceae produced extended spectrum beta-lactamases 7 (*Escherichia coli* 4, *Klebsiella pneumoniae* 2 and *Proteus mirabilis* 1) and *Pseudomonas aeruginosa* 8 (resistance to levofloxacin 7, imipenem 5, piperacillin 2 and amikacin 1) in HCAP. Influenza virus included *Influenza A* 3 and *Influenza B* 3 in CAP and *Influenza A* 9 in HCAP. *Compared with CAP and All HCAP.
Table 4. Causative Microorganisms in Each HCAP Group Classified by MDR Risk

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>HCAP with 0-1 MDR risks (Groups 1-3)</th>
<th>HCAP with ≥ 2 MDR risks (Groups 2-4)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumoniae</td>
<td>59(39.1)</td>
<td>47(27.6)</td>
<td>0.03</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>7(4.6)</td>
<td>30(17.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>4(2.6)</td>
<td>21(12.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>3(2)</td>
<td>19(11.2)</td>
<td>0.001</td>
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<tr>
<td>Haemophilus influenzae</td>
<td>6(4.0)</td>
<td>6(3.5)</td>
<td>0.834</td>
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<tr>
<td>Moraxella catarrhalis</td>
<td>4(2.6)</td>
<td>0</td>
<td>0.048</td>
</tr>
<tr>
<td>Streptococcus milleri group</td>
<td>3(2.0)</td>
<td>1(0.6)</td>
<td>0.268</td>
</tr>
<tr>
<td>Streptococcus sp</td>
<td>4(2.6)</td>
<td>7(4.1)</td>
<td>0.47</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>0</td>
<td>2(1.2)</td>
<td>0.28</td>
</tr>
<tr>
<td>Streptococcus epidermidis</td>
<td>1(0.7)</td>
<td>0</td>
<td>0.47</td>
</tr>
<tr>
<td>Drug-resistant pathogens</td>
<td>23(15.2)</td>
<td>56(32.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>4(2.0)</td>
<td>12(7.1)</td>
<td>0.072</td>
</tr>
<tr>
<td>Chlamydia psittaci</td>
<td>0</td>
<td>2(1.2)</td>
<td>0.5</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>8(5.3)</td>
<td>5(2.9)</td>
<td>0.285</td>
</tr>
<tr>
<td>Legionella pneumophila</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Influenza virus</td>
<td>8(5.3)</td>
<td>1(0.6)</td>
<td>0.012</td>
</tr>
<tr>
<td>Respiratory syncytial virus</td>
<td>0</td>
<td>4(2.4)</td>
<td>0.077</td>
</tr>
<tr>
<td>Parainfluenza virus 3</td>
<td>1(0.7)</td>
<td>3(1.8)</td>
<td>0.357</td>
</tr>
<tr>
<td>Unknown</td>
<td>58(38.4)</td>
<td>51(30)</td>
<td>0.112</td>
</tr>
</tbody>
</table>

All data are presented as n (%) unless otherwise stated. HCAP: healthcare-associated pneumonia. MDR: multidrug-resistant. Numbers include mixed population of pathogens: 21 in HCAP with 0-1 Risks and 42 in HCAP with ≥ 2 Risks. Enterobacteriaceae included Klebsiella pneumoniae 4 in HCAP with 0-1 Risks and Klebsiella pneumoniae 8, Escherichia coli 7, Serratia marcescens 1, Morganella morganii 3 and Proteus mirabilis 2 in HCAP with ≥ 2 Risks. Drug-resistant pathogens included Streptococcus pneumoniae 21 (resistance to penicillin 7, erythromycin 15, levofloxacin 3, imipenem 2), Haemophilus influenzae 1 (beta-lactamase-producing ampicillin-resistant 1) and Pseudomonas aeruginosa 2 (resistance to levofloxacin 2 and imipenem 1) in HCAP with 0-1 Risks and Streptococcus pneumoniae 34 (resistance to penicillin 7, erythromycin 15, levofloxacin 2 and imipenem 2), Haemophilus influenzae 3 (beta-lactamase-producing ampicillin-resistant 3), Staphylococcus aureus 22 (resistance to methicillin 22), Enterobacteriaceae produced extended spectrum beta-lactamases 7 (Escherichia coli 4, Klebsiella pneumoniae 2 and Proteus mirabilis 1) and Pseudomonas aeruginosa 6 (resistance to levofloxacin 5, imipenem 4 and amikacin 1) in HCAP with ≥ 2 Risks. Influenza virus included Influenza A 8 in HCAP with 0-1 Risks and Influenza A 1 in HCAP with ≥ 2 Risks.