Effects of Broad-spectrum Antibiotics on Healthcare-Associated Pneumonia (HCAP)

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Background

In 2005, the American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) identified ***HCAP*** as any patient who:

- Was hospitalised in an acute care hospital for ≥2 days within 90 days of the infection
- Resided in a nursing home or long-term care facility
- Received recent intravenous antibiotic therapy within the past 30 days
- Received wound care within the past 30 days
- Received haemodialysis within the past 30 days

Figure 1: A patient with signs of pneumonia in the left lower lobe of her lung. (Eccles, 2015)

A ***broad-spectrum antibiotic*** is effective against both Gram-positive and Gram-negative bacteria, in contrast to a ***narrow-spectrum antibiotic***, which is effective against specific families of bacteria.

Currently, the guidelines for HCAP recommend the use of broad-spectrum antibiotics.

Aims & Significance

Our project aims to investigate the validity of the hypothesis that broad-spectrum antibiotics are more effective in improving the clinical outcome (30-day mortality) of HCAP.

- Pneumonia is the second leading cause of death in Singapore in 2015. (19.4%)
- Inappropriate use of antibiotics increases the mortality risk. Over 30% to 50% of cases experience a wrong choice of antibiotics (Ventola, 2015). Therefore, it is of paramount importance that a suitable spectrum of antibiotics be used.
- There has been controversy surrounding which type of antibiotics should be used to treat HCAP patients.

Figure 2: Antibiotics used for each type of pneumonia

Method: (a) Systematic Review – Qualitative Analysis

1. Search Criteria
("healthcare associated pneumonia" OR "nursing home acquired pneumonia") AND ("broad spectrum antibiotics" OR "narrow spectrum antibiotics")

- **Inclusion criteria:**
  - HCAP patients
  - Use of broad-spectrum antibiotics
- **Exclusion criteria:**
  - Non-English articles
  - Only CAP / HAP included only

2. Data Extraction:

- 17 articles were reviewed by 3 investigators
- Extraction and assessment of the quality of the articles were performed in a blinded fashion
- Any disagreements between the investigators was resolved independently by a fourth investigator

3. Classification

- Analyse the conclusions of the individual articles
- Group the articles with similar conclusions
- Formulate points based on the content of the grouped articles

Method: (b) Meta-analysis – Quantitative Analysis

The effect size and total sample size of each article was extracted (Figure 3) and analysed using SPSS software,

- **Effect size:** Magnitude of the result as it occurs in a population
- **Total Sample size:** Population of study

	Effect_Size	Total_Sample_Size	Source	Random
1	.9300	85097	Michael B. Rothberg et al. (2015)	0
2	.9600	108	Matsuda S. et al. (2016)	1
3	.2200	217	Falcone M. et al. (2012)	0
4	.9890	321	Takaya Maruyama et al. (2013)	0
5	1.6700	3593	Attridge RT et al. (2016)	0
6	.5600	173	Whitney R. Bukel et al. (2016)	0
7	1.1400	228	Chen JI et al. (2013)	0
8	.9000	167	Brandon J. Webb et al. (2012)	0

Figure 3 Data Entry

Random-effects model

- Used when there is concern about (statistical) heterogeneity among studies
- Accounts for variability between studies

$$\chi^2 = \sum_{t=1}^{k} \frac{(n_i - 1)(r_i - \bar{r})^2}{(1 - \bar{r})^2}$$

$$I^2 = \left(\frac{\chi^2 - df}{\chi^2}\right) \times 100\%$$

Results

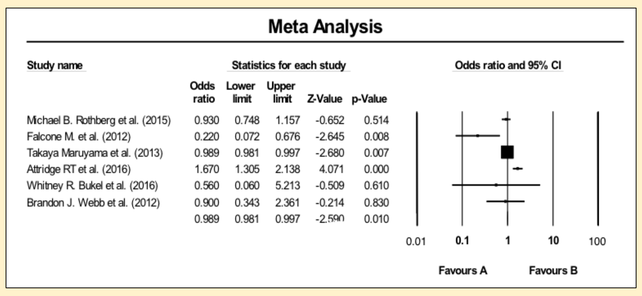

Figure 4 Analysis of individual studies

- **Forest Plot for Measures of Association and Differences**
  - Input: odds ratio, confidence interval, lower & upper limits
  - Generated: forest plot, Z-value, p-value

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*****  Inverse Variance Weighted Regression  *****

*****  Random Intercept, Fixed Slopes Model  *****

------- Descriptives -------
      Mean ES      R-Square            k
       .9241         .0011        8.0000

------- Homogeneity Analysis -------
                Q            df           p
Model          .0090       1.0000       .9244
Residual      7.9261       6.0000       .2436
Total         7.9351       7.0000       .3383

------- Regression Coefficients -------
                B        SE   -95% CI   +95% CI        Z        P     Beta
Constant     .9192     .1496     .6260    1.2124   6.1452    .0000    .0000
Random       .0408     .4299    -.8018     .8835    .0949    .9244    .0337

------- Maximum Likelihood Random Effects Variance Component -------
v     =    .15320
se(v) =    .07865

------ END MATRIX -----
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Figure 5 Analysis using SPSS

- **Homogeneity Analysis**
  - Chi-squared test: $\chi^2 = 7.9351$
  - I^2 test: $I^2 = 11.78\%$
  - Studies are heterogeneous.
- **Random Effects Model**
  - Estimated via iterative maximum likelihood
  - Confidence Interval (CI) range: -0.8018 ~ 0.8835
  - Difference is insignificant, hypothesis is not proven.

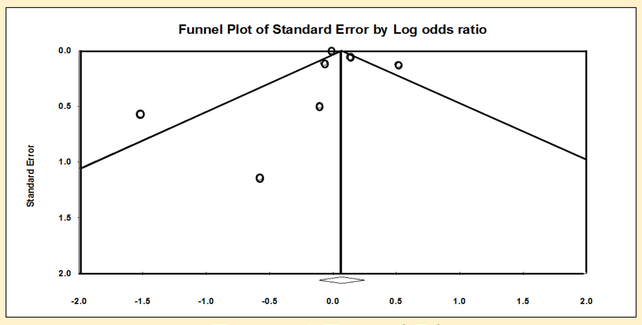

Figure 6 Funnel Plot

- **Funnel Plot for Publication Bias Analysis**
  - Asymmetrical shape indicates presence of publication bias

Conclusion

The results from our meta-analysis does not support our hypothesis that treatment using broad-spectrum antibiotics shows lower mortality rate. Hence, there is insufficient evidence to support the use of broad-spectrum antibiotics among HCAP patients.

Discussion

Risk Factors of HCAP:

1. Immunosuppression
2. Residence in a nursing home
3. Recent receipt of antibiotics in the preceding 30 days
4. Previous hospitalisation in the preceding 90 days
5. Haemodialysis in the preceding 30 days
6. Presence of Methicillin-resistant Staphylococcus aureus (MRSA) in the past 90 days

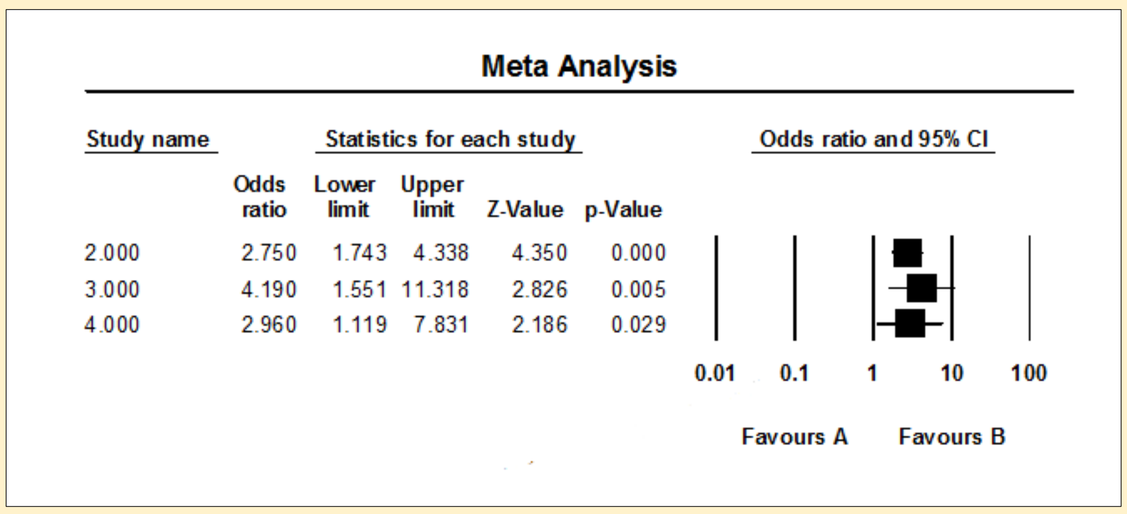

Figure 7: Residence in a nursing home, were investigated for any independent association with MDROs

There are other risk factors involved that results in Multi-Drug Resistant Organisms (MDRO). Hence, the HCAP model might not accurately predict MDRO risks.

Acknowledgement

We would like to thank Dr Hanley Ho from Institute of Infectious Diseases and Epidemiology and Tan Tock Seng Hospital and our senior, Ms Nguyen Phi Yen, who is currently studying in NUS, for their expertise and guidance.