

# Relationship between antibiotic treatment failure and 30 day mortality in adult outpatients with community acquired pneumonia

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# Rationale

- Current US CAP treatment guidelines are well established.
- But outcomes must be monitored due to antimicrobial resistance.
- Treatment failure leads to increased health resource utilization including extra antibiotics, ER visits, hospitalization or even mortality.
- Large-scale, “real-world” data may help guide clinicians to optimize antibiotic choice.

# Truven Dataset – Background and Design

- Truven Health Marketscan Commercial Claims and Encounters Database and Medicare Supplemental and Coordination Benefits Database
- Includes data containing medical and drug claims for over 40 million individuals annually including 4.3 million Medicare enrollees
- Study Period 2011-2015
- CAP identified by ICD-9-CM

## Study population:

- Adult outpatients with CAP diagnosis and monotherapy antibiotic prescription claim within 3 days
- Antibiotics included amoxicillin, amoxicillin-clavulanate, ceftriaxone, azithromycin, clarithromycin, levofloxacin, moxifloxacin, ciprofloxacin, doxycycline

# Methods

## Primary Endpoint

### Treatment Failure by Antibiotic Class

- Antibiotic Refill
- Antibiotic switch
- ER visit
- Hospitalization

### Secondary Analyses

- Antibiotic treatment failure by age and region
- Baseline variables that predict antibiotic treatment failure
- **Mortality rates associated with CAP**




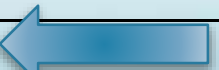
# Patient population ascertainment from Truven Claims Database

<b>Patient population</b>	
<b>Patients with CAP diagnosis with prescription claim within 3 days</b>	<b>890,784</b>
<b>Final sample size</b>	<b>413,801</b>
<b>Patients aged <math>\geq</math> 18 years old</b>	<b>251,947 (62.1%)</b>

# Basic demographics

- Mean age 52.2 years old
- 47.7% male
- 20.5% Medicare
- Almost 40% had multiple comorbidities
- 18% had COPD
- 14% had diabetes or related issues
- 9% had asthma

# Frequency of initial antibiotic prescribing for CAP in Adults in USA 2011-2015

COHORT	Age 18 and Older		
	Frequency	Percent of Total	Percent of Therapeutic Class
<b>TOTAL</b>	<b>257,165</b>	<b>100.0%</b>	
<b>Beta-lactam</b>	<b>16,749</b>	<b>6.5%</b>	
amoxicillin	2,622	1.0%	15.7%
amoxicillin-clavulanate	13,904	5.4%	83.0%
ceftriaxone	223	0.1%	1.3%
<b>Macrolide</b>	<b>112,054</b>	<b>43.6%</b>	
azithromycin	101,492	39.5%	90.6%
clarithromycin	10,562	4.1%	9.4%
<b>Fluoroquinolone</b>	<b>114,174</b>	<b>44.4%</b>	
levofloxacin	95,019	36.9%	83.2%
moxifloxacin	14,160	5.5%	12.4%
ciprofloxacin	4,995	1.9%	4.4%
<b>Tetracycline</b>	<b>14,188</b>	<b>5.5%</b>	
doxycycline	14,188	5.5%	100.0%

*Cipro and ceftriaxone were excluded from subsequent analysis due to small sample size.*

# Concomitant diseases by Drug Class (%)

	Overall %	B-lactam	Macrolide	Fluoroquinolone	Tetracycline
No comorbidities	59.7	55.1	65.7	54.6	56.0
COPD	18.1	20.8	15.3	20.3	20.1
Diabetes	11.5	13.0	9.4	13.2	12.6
Cardiovascular*	15.1	19.3	11.0	17.4	18.2
3+ CCI	11.1	14.3	8.1	13.6	12.9

# CCI= Charlson Comorbidity Index;

\* includes congestive heart failure, peripheral vascular and cerebrovascular disease

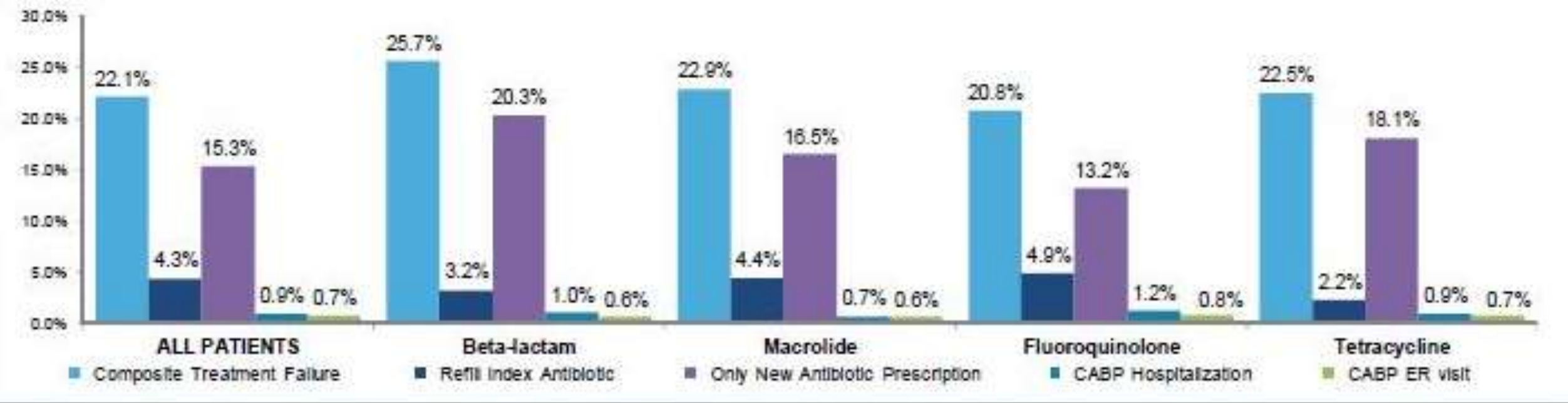


# Results-Antibiotic Treatment Failure by Drug Class

22.1% of all CAP patients reported Antibiotic Treatment Failure [ATF]

	$\beta$ -lactams [n=4,289]	Macrolides [n = 24,650]	Tetracycline [n = 3,240]	FQ [n = 23,562]	P-Value
<b>Total treatment failures</b>	<b>25.7%</b>	<b>22.9%</b>	<b>22.5%</b>	<b>20.8%</b>	<b>&lt;0.001</b>
<b>Reason for failure</b>					
Antibiotic refill	13.1%	19.9%	10.1%	24.2%	<0.001
Change to new antibiotic	78.9%	73.4%	80.8%	63.6%	<0.001
Emergency room visit	2.6%	2.8%	3.5%	3.9%	<0.001
Hospitalization	5.2%	3.3%	5.1%	7.7%	<0.001

# Antibiotic Treatment Failure by Drug Class



KEY: CABP – community-acquired bacterial pneumonia; ER – emergency room.

Note: The denominator for the calculation of treatment failure rates is the total sample of the study aged 18 years and older.

Adjusted treatment failure was estimated using logistic regression models, while controlling for demographics, clinical characteristics, and CABP diagnosis.

# Mortality Rates associated with CAP Treatment Failure

Death	MORTALITY STRATIFIED BY						P-value
	Overall		No Treatment Failure		With Treatment Failure		
	251,947	100.0%	196,206	100.0%	55,741	100.0%	<.0001
NO	232,864	92.4%	187,210	95.4%	45,654	81.9%	
YES	19,083	7.6%	<b>8,996</b>	<b>4.6%</b>	<b>10,087</b>	<b>18.1%</b>	

# Mortality Rates associated with CAP Treatment Failure

Death	TREATMENT FAILURE STRATIFIED BY						P-value
	Overall		No Treatment Failure		With Treatment Failure		
<b>Age 18 and Above</b>	251,947	100.0%	196,206	100.0%	55,741	100.0%	<.0001
NO	232,864	92.4%	187,210	95.4%	45,654	81.9%	
YES	19,083	7.6%	8,996	4.6%	10,087	18.1%	
<b>Age 65 and Above</b>	52,757	100.0%	39,185	100.0%	13,572	100.0%	<.0001
NO	46,613	88.4%	36,340	92.7%	10,273	75.7%	
YES	6,144	11.6%	2,845	7.3%	3,299	24.3%	

- Among adults 18+ who fail treatment for CAP, **18.1% die** within the next 30 days compared to 4.6% of non-treatment failures (p<0.0001)
- Among the elderly (i.e. 65+ years old) **24.3%** of patients with CAP who fail treatment die within the subsequent 30 days compared to 7.3% of non-treatment failures (p<0.0001)

# Summary

- Initial antibiotic failures rates were:
  - $\beta$ -lactams (25.7%)
  - macrolides (22.9%)
  - tetracyclines (22.5%)
  - fluoroquinolones (20.8%)

# Conclusions

- Approximately *one in four* adult outpatients aged 65yo prescribed antibiotic monotherapy for CAP *fail initial treatment*.
- We found a strong relationship between ATF and 30 day mortality
- Age and comorbidities influence antibiotic prescribing
- Prescribers should be aware of those CAP patients most at risk for poor outcomes and consider these factors to guide a comprehensive plan to optimize antibiotic treatment.