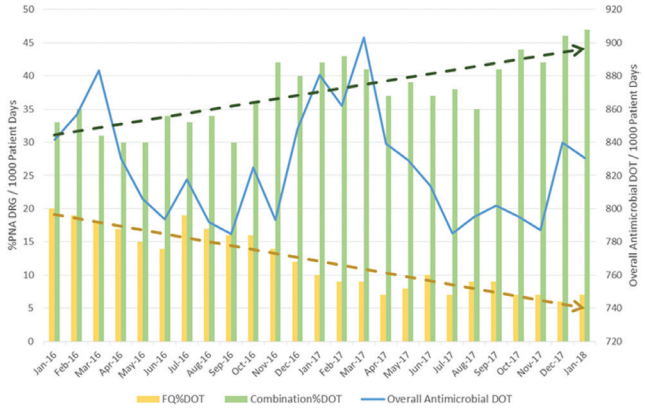
Figure 2: Novant Health Antimicrobial Utilization in PNA DRGs versus Overall Use



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216. Step-down Therapy With Oral Fluoroquinolones vs. Oral β-Lactams for Hospitalized Adult Patients with Community-Acquired Pneumonia: A Multi-Hospital Cohort Study

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Background. Community-acquired pneumonia (CAP) guidelines recommend transition to an oral (PO) β-lactam (BL) regimen or fluoroquinolone (FQ) when patients are clinically stable. Due to collateral damage associated with FQs, stewardship efforts often focus on reducing initial FQ use for CAP therapy. We hypothesized that FQ use remains prevalent in CAP treatment despite initial intravenous (IV) BL therapy, and examined factors associated with switching to a PO BL vs. an FQ and the impact on outcomes.

Methods. In this retrospective cohort study, data were collected from January 2016 through February 2018 on non-ICU medical patients admitted with CAP at 46 Michigan hospitals. Patients were included if they received IV BL (ceftriaxone or ampicillin-sulbactam) plus macrolide/doxycycline by hospital day 2 and switched to a PO respiratory FQ or BL by therapy day 4. Exclusions included positive culture, concomitant infection, HCAP, unstable on day 4, or severe immune deficiency. Data were analyzed using logistic generalized estimating equation models, accounting for hospital-level clustering; outcomes were adjusted using the inverse probability of treatment weighting by propensity scores.

Results. Of 555 included patients, 54.4% were switched to a PO BL vs. 45.6% to an FQ by day 4 of therapy. The groups had similar durations of therapy (8 days), time to clinical stability, prior antibiotics, and COPD, but the BL group was older, with a higher Pneumonia Severity Index, CURB-65, and more cardiovascular (CV) disease (Figure 1). In multivariable analysis, CV disease and higher CURB-65 were more common and diabetes (DM) less common in the PO BL group (Figure 2). Sharing antibiotic use data with providers were associated with less FQ use (83.1% vs. 70.8%, OR 0.51, 95% CI 0.27, 0.97, $P = 0.04$). On adjusted analysis there were no differences in patient outcomes (Figure 3).

Conclusion. Among CAP patients started on an IV BL regimen, nearly half were switched to a PO FQ by therapy day 4, including more patients with DM. Although there were sicker patients in the BL group, there were no differences in outcomes between cohorts. To reduce FQ use, stewardship programs should share antibiotic use data and provide guidance for step-down therapy in clinically stable CAP patients.

Figure 1. Comparison of Clinical and Treatment Characteristics of Oral Fluoroquinolone and Oral Beta-lactam Groups (n=555)

Variable	FQ (n=253)	BL[1] +/- atypical[2] (n=302)	P value*
Baseline Characteristics			
Age (Median (IQR))	65.20 (52.20-74.60)	72.05 (58.70-80.70)	0.015
Gender (male)	125 (49.6%)	150 (49.7%)	0.72
Charlson comorbidity index (Median (IQR))	2.00 (0.00-4.00)	2.00 (1.00-4.00)	0.10
Diabetes	72 (28.5%)	69 (22.8%)	0.21
COPD or asthma	107 (42.3%)	153 (50.7%)	0.08
Cardiovascular disease	67 (26.5%)	151 (50.0%)	<0.001
Malignancy	5 (2.0%)	11 (3.6%)	0.58
Moderate or severe chronic kidney disease	55 (21.7%)	73 (24.2%)	0.47
Liver disease	6 (2.4%)	12 (4.0%)	0.50
Current/former alcohol abuse	32 (12.6%)	33 (10.9%)	0.86
Received immunosuppressive therapy[3]	110 (43.5%)	141 (46.7%)	0.95
Antibiotics before admission	39 (15.4%)	43 (14.2%)	0.75
Concomitant proton pump inhibitor use	92 (36.4%)	130 (43.0%)	0.06
Non-Ambulatory	4 (1.6%)	9 (3.0%)	0.32
Home oxygen	18 (7.1%)	28 (9.3%)	0.59
Severity of Illness			
CURB-65[4] (>=2)	122 (48.2%)	190 (62.9%)	0.017
CURB-65[4] (Median (IQR))	1.00 (1.00-2.00)	2.00 (1.00-3.00)	0.005
≥2 SIRS criteria	219 (86.6%)	258 (85.4%)	0.21
PSI[5] (Median (IQR))	81.75 (59.10-99.35)	91.90 (70.60-115.40)	0.0157
Day clinical stability[6] reached (Mean (SD))	2.5 (0.9)	2.8 (0.7)	0.08
Treatment-related Characteristics			
Antibiotic duration (Median (IQR))	8.00 (7.00-9.00)	8.00 (7.00-9.00)	0.12
Days on IV therapy (Mean (SD))	2.4 (0.7)	2.5 (0.6)	0.016

CAP, Community-acquired pneumonia; BL, Beta-lactam; FQ, Fluoroquinolone; COPD, chronic obstructive pulmonary disease; SIRS, Systemic Inflammatory Response Syndrome; IQR, Interquartile range; PSI, pneumonia severity index; IV intravenous
*P value <0.05 considered significant
[1]BL includes: amoxicillin, amoxicillin/clavulanate, cefuroxime, 3rd generation cephalosporins
[2]Atypical coverage includes: azithromycin, clarithromycin, or doxycycline
[3]Immunosuppressive therapy defined as corticosteroids or immunosuppressive medications on admission or in 30 days prior
[4]CURB-65: clinical prediction rule for predicting mortality in CAP patients
[5]Pneumonia Severity Index: Clinical prediction rule to identify low vs high risk CAP patients
[6]Clinical stability: afebrile with less than or equal to one vital sign abnormality by day 5 (HR >100, RR>24, SBP <90, altered mental status, oxygen saturation <90% or new oxygen requirement)

Figure 2. Multivariable Model for Clinical Characteristics Associated with Oral Fluoroquinolone vs. Oral Beta-lactam +/- Atypical coverage

Variable	OR* (95% CI)	P-value**
Cardiovascular disease	0.69 (0.54, 0.87)	0.002
CURB-65 (per unit increase)	0.82 (0.71, 0.95)	0.009
Diabetes	1.39 (1.00, 1.93)	0.048

BL, Beta-lactam; FQ, Fluoroquinolone; OR, Odds ratio

*Odds ratios > 1 indicates factors associated with treatment with a fluoroquinolone; **P value <0.05 considered significant

Figure 3. Distributions of Outcomes in Oral Fluoroquinolone vs Oral Beta-lactam Cohorts (n=555)

Variable	FQ (n=253)	BL +/- atypical (n=302)	Unadjusted OR* or RR	Unadjusted P-value**	Adjusted OR or RR	Adjusted P-value
30-day all-cause mortality[a]	4 (1.6%)	2 (0.7%)	2.28 (0.40, 12.80)	0.3508	3.44 (0.61, 19.45)	0.1615
30-day pneumonia-related mortality[a]	0 (0.0%)	0 (0.0%)				
30-day all-cause re-admission[a]	15 (5.9%)	29 (9.6%)	0.62 (0.40, 0.96)	0.0335	0.76 (0.46, 1.26)	0.2867
Clostridium difficile infection[b]	3 (1.2%)	1 (0.3%)	4.34 (0.44, 43.36)	0.2108	3.46 (0.34, 34.96)	0.2927
Adverse drug event[c]***	12 (4.7%)	18 (6.0%)	0.64 (0.32, 1.28)	0.2078	0.65 (0.30, 1.41)	0.2790
Urgent care/ED[a]	19 (7.5%)	29 (9.6%)	0.77 (0.40, 1.46)	0.4208	0.73 (0.36, 1.47)	0.3733
Length of stay (median (IQR))	3.00 (3.00-4.00)	3.00 (3.00-4.00)	0.93 (0.88, 0.99)	0.0207	0.98 (0.92, 1.04)	0.4988

BL, Beta-lactam; FQ, Fluoroquinolone; CAP, Community-acquired pneumonia; OR, Odds ratio; RR, Risk reduction; ED; emergency department; LOS, length of stay; COPD, chronic obstructive pulmonary disease; PSI, pneumonia severity index; IV intravenous

*P value <0.05 considered significant; **Odds ratios > 1 indicates outcomes associated with treatment with a fluoroquinolone

***Adverse drug events defined as rash, diarrhea, acute kidney injury, neutropenia, thrombocytopenia, allergic reaction

[a]Mortality, readmissions, and ED visits are adjusted for age, LOS, Charlson, discharge to nursing home, insurance, cardiovascular disease, CURB-65, days to clinical stability, PSI, days on IV therapy, COPD

[b]*Clostridium difficile* rates are adjusted for age, history of antibiotic use (and number of antibiotics), transfer from skilled nursing facility, prior hospitalization, length of hospital stay, proton-pump inhibitor use, Charlson comorbidity index, cardiovascular disease, CURB-65, days to clinical stability, PSI, days on IV therapy, COPD

[c]*Adverse drug events and LOS* are adjusted for age, Charlson comorbidity index, gender, cardiovascular disease, CURB-65, days to clinical stability, PSI, days on IV therapy, COPD

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217. Bang for the Buck: Lessons Learned From an Ambulatory Stewardship Pilot to Reduce Excess Antibiotic Prescribing for Adult Upper Respiratory Infections

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