

The Frequency Of Antibiotic De-Escalation Over Six US Hospitals: Results from a Multicenter Cross-Sectional Study

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ABSTRACT (revised)

Background:

Use of patient-specific culture data to optimize empiric therapy is a cornerstone of rational hospital antibiotic use. The frequency with which cultures are obtained and therapy tailored to results is unknown.

Methods:

We performed a cross-sectional study using retrospective chart review of 1,200 adult inpatients, hospitalized >24hrs, with >=1 active antibiotic order. Patients were enrolled for 4 index dates at quarterly intervals during a 1-year study period (9/2009-10/2010). Infectious disease (ID) specialists recorded demographics, comorbidities, antibiotic therapy, imaging studies and culture results in a 17d window, and categorized changes to therapy. No change was defined as the continuation of the course as initially ordered; de-escalation was a change resulting in narrower coverage; escalation was a switch to/addition of an antibiotic resulting in broader coverage. A Cox proportional hazard model stratified by infection site was used to model time to de-escalation. Patients receiving <=1 antibiotic prescription and/or exclusively prophylactic courses were excluded from the analysis.

Results:

Of 1,200 charts that were reviewed, 631 patients(52.6%) were included in the analysis. Of these, 288 (45.7%) were not changed, 192 (30.4%) were de-escalated and 151 (24%) were escalated. De-escalated prescriptions included 18 fully discontinued courses (2.85%), 61 de-escalations without culture results (9.7%), and 113 de-escalations based on cultures (17.9%). The **no-change** category included 250 continued as initially ordered (39.6%) and 38 switches to equivalent antibiotics (6%). De-escalation was most common for urinary infections (46%). Patients that received fewer prescriptions, were started on broad-spectrum antibiotics, had elevated WBC at start of course, shorter pre-therapy LOS had higher probability of de-escalation. However, positive culture and imaging study had no significant effect.

Conclusion:

Although patients with suspected infections were frequently cultured, clinicians changed antibiotics in less than half of patients receiving multiple therapies. Availability of positive culture and/or imaging study suggestive of infection did not have a significant impact on de-escalation probability.

OBJECTIVES

- Describe patterns of changing antibiotic therapy for different infection sites
- Determine the effect of culture and imaging studies on the likelihood of de-escalation, controlling for patient history, comorbidities and parameters of infection at the time of starting and stopping antibiotics.

METHODS

Population: inpatients at 6 hospitals: Veterans Affairs (n=1), teaching (n=2) and non-teaching (n=3)

Study period: 4 index dates chosen at equal intervals 9/2009 - 10/2010 (11/20, 2009; 2/10, 2010; 10/20, 2010, 8/10, 2010)

Inclusion: patients with active order for antibiotic prescription on index date

Exclusion: ambulatory (LOS <24 hrs), pediatric (age <18yrs) and psychiatric admissions

1,200 patients (50 per date per facility)

Infectious Disease Physician Chart Review:

Patient history and allergies
Indications for antibiotics, start/stop dates for <9 ABX
<6 admission ICD9 codes (Charlson comorbidity score)
Microbiology reports (14d window)
Radiology reports (3d window)
Infection parameters (fever and WBC)

For all patients on >1 non-prophylactic ABX and LOS>=3d

NO CHANGE:
continued as initially ordered or switch to equivalent

ESCALATION:
addition of Rx and/or switch-> increase in spectrum

DE-ESCALATION:
switch to targeted therapy and/or change in number and/or spectrum ->decrease in spectrum

Included de-escalated w culture, de-escalated w/o culture, discontinuation of all antibiotics

Table 1: Grouping of antibiotics by spectrum of activity, used to define de-escalation

Class	Rank
1G cephalosporins, anti-staph pens, metronidazole (CDI)	1
Fluoroquinolones, ESP macrolides, amoxi-clav, 3G cephalosporins, oral vancomycin (CDI)	2
Antipseudomonal penicillins, cefepime, vancomycin	3
Carbapenems, colistin, tigecycline, linezolid, daptomycin	4

RESULTS

Table 2: Changes to antibiotic therapy for patients receiving >1 antibiotic prescription (N= 631)

Change	N	%	Time of change (mean)	LOS (mean)	Abx count (mean)	Age (mean)	Had culture collected (N)	Relevant culture (% of cases)	Number of cultures collected (mean)	Had imaging study (N)	Number of imaging studies (mean)	Relevant imaging study (%)
De-escalation	192	30.43%	4.7	12.4	2.9	63.5	174	52%	4.08	174	2.53	42%
Escalation	151	23.93%	5.9	27.1	3.3	63.6	144	50%	6.21	146	2.64	53%
No change	288	45.64%	5.6	18.1	2.5	64.9	267	39%	4.30	265	2.23	50%
Total	631	100.00%	5.2	18.5	2.8	64.2	585	46%	4.69	585	2.42	48%

Exclusion:

- 440 patients (36.7%) were excluded because they received <2 antibiotics
- 129 patients (10.8%) on >=2 antibiotics, LOS<3 days or had received exclusively prophylactic courses

Table 3: De-escalation patterns by primary site of infection (N= 631)

Site	N	%	Day of change (mean)
Respiratory (RTI)	200	100.00%	4.9
De-escalation	55	27.50%	4.9
Escalation	46	23.00%	4.6
No change	99	49.50%	6.1
Skin and soft tissue (SSTI)	95	100.00%	6.0
De-escalation	22	23.16%	4.5
Escalation	26	27.37%	7.5
No change	47	49.47%	4.7
Gastrointestinal	90	100.00%	5.0
De-escalation	31	34.44%	4.4
Escalation	23	25.56%	5.7
No change	36	40.00%	5.6
Urinary (UTI)	74	100.00%	3.7
De-escalation	34	45.95%	4.1
Escalation	15	20.27%	3.3
No change	25	33.78%	2.8
Bloodstream (BSI)	70	100.00%	6.1
De-escalation	25	35.71%	5.4
Escalation	15	21.43%	7.8
No change	30	42.86%	4.3
Other	40	100.00%	5.5
De-escalation	9	22.50%	4.2
Escalation	12	30.00%	6.4
No change	19	47.50%	6.0
Prophylaxis	62	100.00%	6.7
De-escalation	16	25.81%	5.2
Escalation	14	22.58%	7.4
No change	32	51.61%	14.0

Note: Other infections incl. CNS, unspecified fevers and leukocytosis.
Time of change for no change group defined as hospital day of discharge or discontinuation of all therapy (whichever came first);

Specification of Cox proportional hazard model:

- Co-variates retained after univariate analysis of the association between de-escalation and patient history, antibiotic use and infection parameters if P<0.15.
- Site of infection and presence of relevant diagnostic information (i.e., positive culture or imaging study suggestive of infection as determined by chart reviewer) kept in all tested models

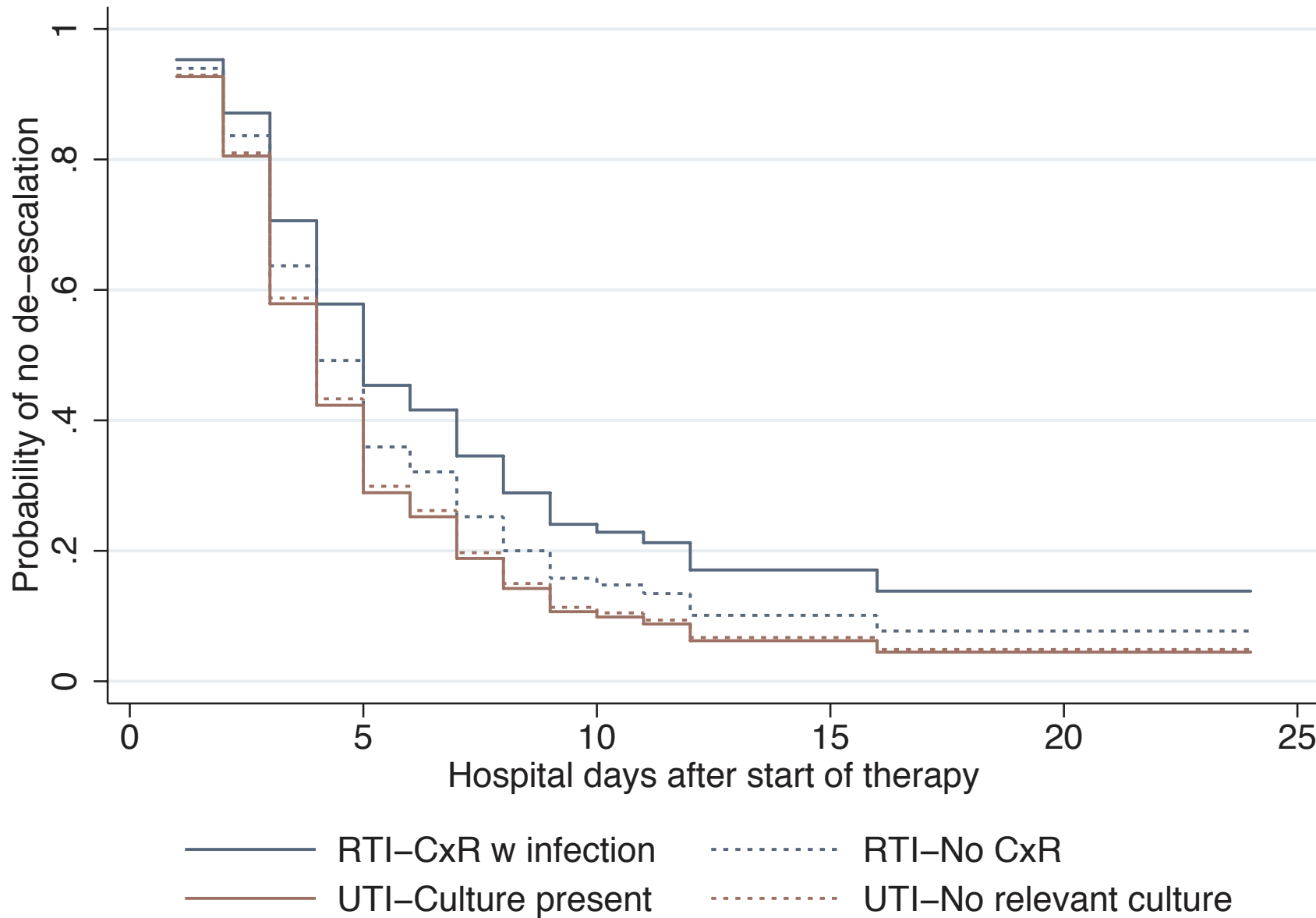
Table 4: Cox proportional hazard model for factors related to time to de-escalation compared to patients with no change in antibiotics (N= 367)

Variable	Hazard ratio (HR)	P-value	95% Confidence Interval (CI)
Number of antibiotics	0.83	0.026	[0.70-0.98]
Severe comorbidities (Charlson score >2)	0.82	0.273	[0.57-1.17]
Age (51-65 years) (Reference: all other age categories)	1.43	0.028	[1.04-1.97]
ICU	0.74	0.1	[0.51-1.1]
Start on vancomycin, pip/taz or levofloxacin	1.63	0.01	[1.13-2.37]
Elevated WBC at start	1.33	0.087	[0.96-1.85]
Elevated WBC at stop of first course	0.61	0.013	[0.41-0.90]
Fever present at start	0.77	0.122	[0.55-1.07]
LOS prior to first antibiotic	0.99	0.048	[0.98-1]
Relevant (positive) culture	1.03	0.868	[0.75-1.42]
Relevant imaging study	0.77	0.149	[0.54-1.10]
Infection site (Reference - Gastrointestinal)			
Bloodstream	0.77	0.403	[0.42-1.42]
Other	0.76	0.525	[0.32-1.78]
Prophylaxis	0.92	0.817	[0.47-1.83]
Respiratory	1.28	0.375	[0.74-2.21]
Skin and soft tiss	0.87	0.635	[0.50-1.54]
Urinary tract	1.73	0.069	[0.96-3.12]

Note: Time at risk was defined as the interval between start of earliest antibiotic and de-escalation (failure event) and discontinuation of therapy and/or discharge (whichever came first).

RESULTS (continued)

Figure 1: Cox proportional hazard model of UTI (red) and respiratory tract infection (blue) de-escalation probability, with and without diagnostic information (no differences p<0.10)



CONCLUSIONS

- Over 45% of patients in the hospital on antibiotics continue on their course without change. Of the 30% of patients who have their antibiotic de-escalated, this occurs on average after 4.7 days of antibiotics.**
- Patients more likely to have their antibiotics de-escalated were:**
 - Started on vancomycin, piperacillin/tazobactam or levofloxacin
 - Receiving fewer antibiotics
 - Aged 51-65
 - Had an elevated WBC at start of antibiotics that normalized
 - Being treated for a presumed urinary tract infection
- Presence of positive culture or imaging data suggestive of infection did not impact de-escalation**

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