

Expected Practice as a Novel Antibiotic Stewardship Intervention

Kabir Yadav,^{1,2} Eriko Masuda,^{3,4} Emi Minejima,^{3,5} and Brad Spellberg^{3,4}

¹Department of Emergency Medicine, Harbor-University of California Los Angeles (UCLA) Medical Center, Los Angeles, CA; ²Los Angeles Biomedical Research Institute, Los Angeles, CA; ³Los Angeles County + University of Southern California (USC) Medical Center, Los Angeles, CA; ⁴Department of Medicine, Keck School of Medicine at USC, Los Angeles, CA; ⁵University of Southern California School of Pharmacy, Los Angeles, CA

“Expected practice” is a recently described method to alter clinical behavior. We implemented an expected practice around short-course antibiotic therapy, which was associated with decreased antibiotic utilization for multiple bacterial infections. Thus, we describe this expected practice as a novel, simple, and inexpensive tool to enhance antibiotic stewardship.

Keywords. antibiotic stewardship; expected practice; quality improvement.

Society faces an ongoing crisis of antibiotic resistance, fueled by overuse of antibiotics. Nevertheless, recent studies have found that antibiotics are increasingly prescribed [1–3]. New strategies, particularly psychological tools to alter provider behavior, are needed to enhance the effectiveness of antibiotic stewardship efforts [4, 5].

One way to improve antibiotic utilization is to prescribe courses for only as long as necessary to optimize cure rates [6, 7]. Multiple randomized controlled trials have found that shorter courses of antibiotic therapy result in similar cure rates as traditional courses for many types of infections, including urinary tract infections (UTIs), skin and soft tissue infections (SSTIs), and pneumonia (PNA) [7]. Unfortunately, familiarity with short-course therapy as a stewardship tool is limited. A recent study found that only one-third of infectious diseases practitioners from 58 countries recommended short-course therapies [8]. Furthermore, primary providers may be concerned that they, and not the stewardship team, face the consequence of adverse outcomes of treatment decisions. Thus, fear of being blamed for the consequences of shortening durations

of therapy, combined with lack of familiarity of evidentiary basis, may inhibit uptake of this stewardship tool.

One mechanism that can simultaneously educate providers regarding evidenced-based practice while also establishing an institutional requirement for standard practice is “expected practice” (EP) [9]. Expected practices set an institution’s expectation for how its providers practice medicine, and hence set stronger standards of care compared with clinical guidelines, which are typically viewed more as literature-based suggestions or expert consensus. Expected practices are developed and implemented by coalitions of primary and specialty care experts and approved by system-wide leadership committees, so they take on official expectations of the medical staff and hospital leadership. We developed and implemented a novel expected practice for shorter-term antibiotic courses for standard infections. We sought to determine the impact of this expected practice on antibiotic prescribing behavior at our large, tertiary care, public hospital.

METHODS

Development and Implementation of the Expected Practice

Our expected practice on antibiotic durations ([Supplementary Figure 1](#)) was developed with input from primary care and infectious diseases committees, with final approval by the hospital’s Pharmacy and Therapeutics Committee and Medical Executive Committee. The expected practice was then posted electronically on the hospital’s intranet and disseminated via memo from the hospital’s Chief Medical Officer to all credentialed providers. Hospital-wide implementation began in October 2016, and the only form of subsequent reinforcement was through the existing daily stewardship rounds.

Existing Antibiotic Stewardship Activities

Our institutional antimicrobial stewardship program (ASP) includes prospective audit and feedback, antimicrobial restriction, and de-escalation rounds. There were no changes to this program during the baseline and interventional study periods. The only other new antibiotic stewardship initiative that started contemporaneously at the hospital was procalcitonin testing, which was implemented December 2016, after the expected practice was implemented.

Study Design and Setting

We conducted this quasi-experimental, pre/post quality improvement study at the Los Angeles County + University of Southern California (LAC+USC) Medical Center, a 676-bed public teaching hospital in downtown Los Angeles. The study was determined to be not human subjects research by the University of Southern California Health Sciences Campus Institutional Review Board.

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Correspondence: B. Spellberg, MD, LAC+USC Medical Center, 2051 Marengo Street, Los Angeles, CA 90033 (bspellberg@dhs.lacounty.gov).

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We established baseline outcomes by collecting all adult (age > 18 years) inpatient visits for a 12-month period before expected practice implementation in October 2016 (patient visits with a discharge date between October 1, 2015, and September 30, 2016). We treated the month of October as a burn-in period for the newly implemented expected practice and collected inpatient visits for the following 12 months (patient visits with a discharge date between November 1, 2016, and October 31, 2017). Any patients whose inpatient visit spanned both the baseline and the postimplementation period were excluded.

We selected patients for inclusion if any of the first 20 discharge diagnoses included ICD-10 codes for the 4 infectious diseases of interest: UTIs (cystitis N30.0*/N30.9*; UTI N39.0; pyelonephritis N10), SSTIs (cutaneous abscess L02; cellulitis L03), PNA (J13-J18), and ventilator-associated pneumonia (VAP; J95.851).

Main Outcome and Measures

Our primary outcome measure was antibiotic days of therapy (DOT) [10]. We defined DOT as the sum total of days of each antibiotic administered as an inpatient plus the outpatient days prescribed upon hospital discharge (ie, 2 antibiotics given for 10 days = 20 DOT). Our secondary outcome was total antibiotic exposure, defined as the sum total of milligrams of antibiotics administered as an inpatient plus the milligrams prescribed as an outpatient upon discharge from the hospital.

Statistical Analysis

We reported patient characteristics using summary statistics without inferential measures [11]. To adjust for covariates, we used a 0-truncated negative binomial multivariable regression to deal with overdispersion in the data. For each infection type, we modeled average duration of antibiotic therapy as a function of the presence of the expected practice in a pre/post fashion. For the primary analysis, we censored the small number of patients who had DOTs >90 days as being reflective of unusually complex hospital courses not relevant to the expected practice; we also ran a sensitivity analysis censoring >30 days of DOTs, and this did not meaningfully change the results. We adjusted for covariates (age, gender, insurance status, in-hospital mortality, and use of procalcitonin testing) and for severity of illness using a number of risk adjustment measures (Medicare Severity Diagnosis Related Group Relative Weights, intensive care unit days, in-hospital mortality, and expected mortality according to the 2017 Mortality Expected Risk Model from the Vizient Consortium, Irving, TX). We assessed in-hospital mortality as a balancing/safety measure, to determine if shortening antibiotic therapy resulted in patient harm, by logistic regression.

RESULTS

The patients in the pre- and post-EP periods were similar demographically and with respect to disease severity (Table 1). When adjusting for all covariates of interest, average antibiotic

Table 1. Characteristics of the Patients at Baseline and Postintervention

Variable	Baseline	Postintervention
Patient visits, No.		
UTI	1562	1512
SSTI	1378	1292
PNA	1184	1250
VAP	55	73
Age, median (IQR), y		
UTI	57 (45 to 68)	57 (43 to 68)
SSTI	50 (39 to 58)	49.5 (38 to 58)
PNA	57 (46 to 68)	57 (47 to 67)
VAP	54 (37 to 64)	56 (40 to 64)
Female gender, No. (%)		
UTI	913 (58)	880 (58)
SSTI	367 (27)	359 (28)
PNA	432 (36)	463 (37)
VAP	15 (27)	20 (27)
Medicaid/Medicare, %/%		
UTI	72/20	73/21
SSTI	82/8	79/12
PNA	69/21	70/21
VAP	64/22	71/18
DRG relative weight, median (IQR)		
UTI	1.16 (0.98 to 1.79)	1.17 (0.93 to 1.77)
SSTI	1.11 (0.84 to 1.75)	1.27 (0.84 to 1.77)
PNA	1.79 (1.43 to 2.63)	1.77 (1.32 to 2.45)
VAP	5.13 (2.30 to 10.94)	5.11 (3.25 to 10.92)
Expected mortality, median (IQR), %		
UTI	0.75 (0.18 to 2.2)	0.75 (0.18 to 2.4)
SSTI	0.18 (0.05 to 0.88)	0.19 (0.05 to 1.05)
PNA	1.4 (0.55 to 5.7)	1.5 (0.50 to 5.6)
VAP	10.3 (1.3 to 24.3)	10.4 (2.1 to 30.5)
Procalcitonin ordered, No. (%)		
UTI	N/A	276 (18)
SSTI	N/A	157 (12)
PNA	N/A	587 (47)
VAP	N/A	47 (64)

Abbreviations: DRG, diagnostic-related group; IQR, interquartile range; PNA, pneumonia; SSTI, skin and skin structure infection; UTI, urinary tract infection; VAP, ventilator-associated pneumonia.

DOT and antibiotic dose exposures significantly decreased for each of the studied diseases after introduction of the expected practice (Table 2). The point estimate of the decrease in average antibiotic DOT was 10%, 11%, 11%, and 27% for UTIs, SSTIs, pneumonia, and VAP, respectively (Table 1). Decreases in antibiotic exposure (mg) were larger, at 17%, 13%, 29%, and 35% for UTIs, SSTIs, pneumonia, and VAP, respectively.

We ran a sensitivity analysis to determine if the intervention's impact waned over time (change in duration of therapy in the second half of intervention vs baseline year compared with first half of intervention vs baseline year). For UTIs and PNAs, we found no significant difference in the shortening of therapy in the second half of the intervention year. For SSTIs and VAPs, the shortening of therapy was not statistically significant in the second half of the intervention vs baseline year compared with

Table 2. Change in Antibiotic Utilization in Patients Pre-EP vs Post-EP

Variable	Baseline	Postintervention	Difference, P Value
Mean EP antibiotic DOT (IQR), d			
UTI	14.3 (13.7 to 15.0)	12.9 (12.4 to 13.5)	-1.4 (-2.3 to -0.6); <i>P</i> = .001
SSTI	20.0 (19.2 to 20.9)	17.9 (17.1 to 18.7)	-2.2 (-3.3 to -1.0); <i>P</i> < .001
PNA	18.0 (17.2 to 18.8)	16.0 (15.3 to 16.7)	-2.0 (-3.2 to -0.9); <i>P</i> = .001
VAP	36.1 (31.5 to 40.8)	26.5 (23.6 to 29.4)	-9.6 (-16.0 to -3.3); <i>P</i> = .003
Mean EP antibiotic exposure (IQR), mg			
UTI	22 328 (21 247 to 23 408)	18 609 (17 693 to 19 526)	-3718 (-5185 to -2252); <i>P</i> < .001
SSTI	41 024 (38 974 to 43 073)	35 619 (33 778 to 37 460)	-5404 (-8227 to -2582); <i>P</i> < .001
PNA	33 078 (31 108 to 35 048)	23 647 (22 283 to 25 011)	-9430 (-12 028 to -6833); <i>P</i> < .001
VAP	97 185 (79 041 to 115 329)	62 938 (53 209 to 72 668)	-34 246 (-57 507 to -10 986); <i>P</i> = .004
Mean procalcitonin antibiotic DOT (IQR), d*			
UTI	13.3 (12.9 to 13.7)	17.4 (15.5 to 19.2)	+4.0 (2.2 to 5.9); <i>P</i> < .001
SSTI	18.9 (18.3 to 19.5)	20.3 (17.7 to 22.8)	+1.4 (-1.3 to 4.0); <i>P</i> = .3
PNA	16.5 (15.9 to 17.0)	18.4 (17.2 to 19.6)	+1.9 (0.5 to 3.3); <i>P</i> = .01
VAP	26.7 (24.0 to 29.4)	37.5 (32.2 to 42.8)	+10.8 (4.1 to 17.5); <i>P</i> = .002
Mean procalcitonin antibiotic exposure (IQR), mg*			
UTI	19 659 (18 967 to 20 350)	29 915 (26 297 to 33 532)	+10 256 (6537 to 13 975); <i>P</i> < .001
SSTI	38 515 (37 120 to 39 910)	35 223 (29 861 to 40 585)	-3292 (-8868 to 2285); <i>P</i> = .2
PNA	26 347 (25 158 to 27 537)	33 115 (30 197 to 36 032)	+6768 (3447 to 10 088); <i>P</i> < .001
VAP	64 947 (55 653 to 74 242)	99 129 (78 793 to 119 464)	+34 181 (9265 to 59 097); <i>P</i> = .007
In-hospital mortality, No. (%)			
UTI	62 (4)	74 (5)	OR, 1.1 (IQR, 0.7 to 1.6); <i>P</i> = .6
SSTI	17 (1)	18 (1)	OR, 0.9 (IQR, 0.4 to 1.9); <i>P</i> = .7
PNA	131 (11)	151 (12)	OR, 1.1 (IQR, 0.8 to 1.5); <i>P</i> = .4
VAP	13 (24)	17 (23)	OR, 0.9 (IQR, 0.3 to 2.6); <i>P</i> = .9

Abbreviations: DOT, days of therapy; DRG, diagnostic-related group; EP, expected practice; IQR, interquartile range; OR, odds ratio; PNA, pneumonia; SSTI, skin and skin structure infection; UTI, urinary tract infection; VAP, ventilator-associated pneumonia.

*Procalcitonin data are not stratified as baseline vs post-EP time periods, but rather by use of procalcitonin testing (left column = no procalcitonin test sent, right column = with procalcitonin test).

the first half; however, the duration still trended shorter in the second half of the intervention vs baseline year, and the analysis was underpowered as it was based on only half a year of data.

Interestingly, use of procalcitonin testing was associated with increased antibiotic DOT and dose exposure, and this effect was statistically significant in all disease groups except SSTIs. Thus, initiation of procalcitonin testing did not confound the improvements in antibiotic utilization observed in the intervention period. Finally, mortality did not change postintervention (Table 1).

DISCUSSION

We describe a substantial reduction in duration of therapy for common, acute bacterial infections after introduction of an expected practice, with no change in mortality. We chose to use an expected practice around durations of therapy because providers expressed concern that they would be individually exposed to blame if they prescribed short-course antibiotic therapy and the clinical outcome was bad. The expected practice document lists the randomized controlled trials that underpin the expectation in practice. It also sets a standard of practice that the medical staff of the hospital and hospital leadership expect to be complied with unless specific contrary circumstances are documented in the

chart. As such, the expected practice has alleviated concerns by our providers regarding both what the evidentiary basis of the practice is and the knowledge that they are acting in compliance with practice standards our institution has set. The expected practice required no technology and cost no money to implement other than the time spent by the various committees to develop the document and time spent by the ASP team reinforcing it on daily rounds. As these activities were done as part of the normal functions of each committee and ASP member, there were no additional time costs above and beyond routine function.

We were surprised to note that patients for whom procalcitonin testing was ordered generally experienced longer durations of antimicrobial therapy. These results contrast with a recent meta-analysis, which found that incorporation of procalcitonin results and guidelines into clinical practice reduced antibiotic durations by approximately 25% [12]. The most likely explanation for this discrepancy is confounding by indication, as procalcitonin was ordered at the providers' clinical discretion rather than being randomized. Thus, patients for whom procalcitonin was ordered likely had more complex illness.

A limitation of this study design is the potential for the intervention to create a Hawthorne effect, wherein clinicians

improve their prescribing behavior because they know they are being monitored. However, such an effect would still be a positive impact of the intervention if it could be sustained. Our sensitivity analysis showed no evidence of waning effect for UTIs or PNAs; a possible waning effect was seen for SSTIs and VAP; however, the intervention still trended toward benefit vs the baseline period in the second half of the year, despite smaller sample sizes and an underpowered comparison (only half the year). Another limitation is lack of data on infection relapses or readmissions. Nevertheless, we found no change in mortality, and short-course antibiotic interventions have been found safe to implement in multiple randomized controlled trials [7].

In summary, we report that implementation of an expected practice for shorter-course antibiotic regimens, supported by our antibiotic stewardship team, was associated with a marked decrease in antibiotics prescribed for common, acute bacterial illnesses. Expected practice is a promising new psychological tool to promote effective antimicrobial stewardship.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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References

1. Baggs J, Fridkin SK, Pollack LA, et al. Estimating national trends in inpatient antibiotic use among US hospitals from 2006 to 2012. *JAMA Intern Med* **2016**; 176:1639–48.
2. Klein EY, Van Boeckel TP, Martinez EM, et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc Natl Acad Sci U S A* **2018**; 115:E3463–70.
3. Durkin MJ, Jafarzadeh SR, Hsueh K, et al. Outpatient antibiotic prescription trends in the United States: a national cohort study. *Infect Control Hosp Epidemiol* **2018**; 39:584–9.
4. Spellberg B, Srinivasan A, Chambers HF. New societal approaches to empowering antibiotic stewardship. *JAMA* **2016**; 315:1229–30.
5. Spellberg B, Bartlett JG, Gilbert DN. The future of antibiotics and resistance. *N Engl J Med* **2013**; 368:299–302.
6. Rice LB. The Maxwell Finland Lecture: for the duration-rational antibiotic administration in an era of antimicrobial resistance and *Clostridium difficile*. *Clin Infect Dis* **2008**; 46:491–6.
7. Spellberg B. The new antibiotic mantra—“shorter is better.” *JAMA Intern Med* **2016**; 176:1254–5.
8. Macheda G, Dyar OJ, Luc A, et al; ESGAP and SPILE. Are infection specialists recommending short antibiotic treatment durations? An ESCMID international cross-sectional survey. *J Antimicrob Chemother* **2018**; 73:1084–90.
9. Soni SM, Giboney P, Yee HF Jr. Development and implementation of expected practices to reduce inappropriate variations in clinical practice. *JAMA* **2016**; 315:2163–4.
10. Polk RE, Fox C, Mahoney A, et al. Measurement of adult antibacterial drug use in 130 US hospitals: comparison of defined daily dose and days of therapy. *Clin Infect Dis* **2007**; 44:664–70.
11. Vandembroucke JP, von Elm E, Altman DG, et al; STROBE Initiative. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *PLoS Med* **2007**; 4:e297.
12. Schuetz P, Briel M, Mueller B. Clinical outcomes associated with procalcitonin algorithms to guide antibiotic therapy in respiratory tract infections. *JAMA* **2013**; 309:717–8.