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Original Article

The devil's in the defaults: An interrupted time-series analysis of the impact of default duration elimination on exposure to fluoroquinolone therapy

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Abstract

Objective: To determine whether removal of default duration, embedded in electronic prescription (e-script), influenced antibiotic days of therapy.

Design: Interrupted time-series analysis.

Setting: The study was conducted across 2 community hospitals, 1 academic hospital, 3 emergency departments, and 86 ambulatory clinics.

Patients: Adults prescribed a fluoroquinolone with a duration <31 days.

Interventions: Removal of standard 10-day fluoroquinolone default duration and addition of literature-based duration guidance in the order entry on December 19, 2017. The study period included data for 12 months before and after the intervention.

Results: The study included 35,609 fluoroquinolone e-scripts from the preintervention period and 31,303 fluoroquinolone e-scripts from the postintervention period, accounting for 520,388 cumulative fluoroquinolone DOT. Mean durations before and after the intervention were 7.8 (SD, 4.3) and 7.7 (SD, 4.5), a nonsignificant change. E-scripts with a 10-day duration decreased prior to and after the default removal. The inpatient setting showed a significant 8% drop in 10-day e-scripts after default removal and a reduced median duration by 1 day; 10-day scripts declined nonsignificantly in ED and ambulatory settings. In the ambulatory settings, both 7- and 14-day e-script durations increased after default removal.

Conclusion: Removal of default 10-day antibiotic durations did not affect overall mean duration but did shift patterns in prescribing, depending on practice setting. Stewardship interventions must be studied in the context of practice setting. Ambulatory stewardship efforts separate from inpatient programs are needed because interventions cannot be assumed to have similar effects.

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Excess days of antimicrobial therapy can lead to unintended patient safety risks, antimicrobial resistance, and cost.[1–3] New literature supports shorter durations than used historically. A single day of excess antibiotics has significant associated harm, including a 7% absolute risk increase of antibiotic resistance as well as increased odds of acute kidney injury and *Clostridioides difficile* infection.[4–13] Thus, antibiotic duration is an important component of antimicrobial exposure that should be assessed and optimized by antimicrobial stewardship programs (ASPs) to reduce patient harm.[3,14,15] The majority of antibiotic exposure occurs in the ambulatory setting, where there are few ASPs to influence appropriate prescribing, including decisions on therapy durations.[16,17] ASPs are often well established in the inpatient setting and can assist in optimizing durations through audit and feedback during hospitalization.[1,18] Antimicrobial courses, however, are often completed after discharge, and inpatient stewards are not often well positioned to influence discharge duration decisions.[9,10,19,20] These postdischarge days of therapy (DOT) account for 35%–48% of the overall treatment duration attributed to a hospital encounter.[16,20]

Novel strategies are needed to improve prescribing and to avoid patient safety concerns at discharge or in the ambulatory care setting.[17,21–25] Given resource limitations, development of strategies that are minimally resource intensive is critical. In a prior evaluation of our health system's data on discharge antibiotic prescriptions, the most common agents used were fluoroquinolones. Also, >75% of total antibiotic durations exceeded 7 days when counting both inpatient plus electronic prescription (e-script) DOT.[16] Furthermore, during audit and feedback, our

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ASP team noted that e-script durations often differed in length from institutional guidance and what was documented by the primary team in progress notes. While evaluating this discordance, we discovered that e-scripts for antibiotics had preset durations that were not consistent with current literature and that were applied to all e-scripts whether originating in the ambulatory setting or during the transition from inpatient to outpatient.

Duration decisions differ by practice setting. For example, ambulatory clinicians prescribe for a specified duration after a single encounter, whereas inpatient clinicians prescribe a duration to complete an antibiotic course that started in the hospital. We sought to determine the impact of removing default durations for fluoroquinolone e-scripts to reduce excess days of therapy administered after discharge from the hospital as well as in the ambulatory setting. We hypothesized that 10-day default durations built into the electronic health record (EHR), which exceeds literature-based durations for many indications, increased antibiotic durations in the outpatient and postdischarge settings.

Methods

We performed a multicenter, interrupted time-series analysis to assess change in prescribing practice after default duration removal within Duke University Health System (DUHS). DUHS includes a 950-bed academic hospital, 2 community hospitals with >570 beds combined, 3 emergency departments, and 86 outpatient clinics. All DUHS sites used Epic EHR software (Epic Systems, Verona, WI) during the study. At baseline, the DUHS instance of Epic had prebuilt default durations in the e-script order-entry processes for oral fluoroquinolone antibiotics. The defaulted duration for oral fluoroquinolone e-scripts was 10 days, except for 7 days for ciprofloxacin 100 mg e-scripts. The duration could be adjusted by prescribers at order entry; however, there were no prompts to do so. On December 19, 2017, the fluoroquinolone default durations at DUHS were removed, leaving a blank duration field requiring prescribers to enter a duration in days or an end date (where the system calculated the days duration). Changes to the duration field of the order entry occurred in e-scripts across all practice settings. In addition, we added decision support through a link within the order entry to institutional evidence-based guidelines on duration of therapy for common diagnoses, which was housed on our internal website, CustomID (https://CustomID.org). Education regarding these changes was provided through systemwide presentations, memos from hospital leadership, and just-in-time education during audit and feedback activities. Aside from these interventions, there were no other stewardship changes during the study period targeted toward fluoroquinolone duration.

The analysis included 2 periods: 12 months (December 18, 2016–December 18, 2017) prior to removal of default duration on December 19, 2017, and 12 months following the intervention (December 20, 2017–December 20, 2018). All adult patients (≥18 years) with an encounter accompanied by a DUHS fluoroquinolone e-script order were included. Antibiotics prescribed for a duration ≥30 days were excluded to eliminate prophylactic use. Prescribing data, demographics, and diagnosis codes were extracted. Descriptive information on comorbidities, modified Charlson comorbidity index (mCCMI), and infectious syndrome diagnosis were defined using discharge diagnosis codes and previously described methods.[16,26]

We calculated multiple antibiotic use outcomes to assess the effects of the default removal on prescribing practice patterns. The primary outcome was mean duration of e-scripts. Second, we calculated the percent of e-scripts with 5-, 7-, 10-, and 14-day durations to better characterize duration decisions that may not be reflected in the mean estimates. Among patients who were cared for on the inpatient setting, we also calculated total fluoroquinolone length of therapy (LOT). We defined total LOT as the sum of inpatient days (calculated using electronic medication administration records and CDC methods) plus the days prescribed in the e-script upon discharge linked by the encounter identifier.[16,27] Postdischarge adherence could not be measured.

We evaluated the impact of default removal on antibiotic use outcomes using descriptive statistics and graphs of monthly estimates. Then, we used an interrupted time-series linear regression model to estimate the monthly linear trend prior to default removal, the level change at the time of default removal, and the change in trend after default removal as follows[28]:

$$Y_t = \beta_0 + \beta_1 * time + \beta_2 * intervention + \beta_3 * time\ after\ intervention + et_t$$

Because default removal occurred in the middle of the month, the estimates for December 2017 were set to missing to provide a clean break in model predictions between the monthly measures and the 2 study periods.

First, we evaluated all settings in aggregate for the health system. Then, we planned several a priori subgroup analyses because we anticipated that different practice settings may show differential baseline practice and responses to the intervention even though all shared a common EHR system. We separately assessed the 3 practice settings: ambulatory care, inpatient, and emergency department. Because our intent was descriptive for the practice settings subgroups, we did not adjust for multiple statistical comparisons. Thus, interpretations of subgroup model results should be viewed as descriptive rather than for hypothesis testing. Data were analyzed using SAS version 9.4 software (SAS Institute, Cary, NC). This study was reviewed by the DUHS Institutional Review Board and was determined to be an exempt quality improvement activity.

Results

The analysis included 35,609 encounters with fluoroquinolone e-scripts in the preintervention period and 31,303 in the postintervention period. There were 4,306 (14%) fewer encounters with a fluoroquinolone e-scripts in the postintervention period. Groups were largely similar in baseline characteristics, except patients in the postintervention period had slightly higher comorbidity scores (Table 1). Most encounters in our cohort (77%) occurred in the ambulatory care setting. Ciprofloxacin (70%) was the most commonly prescribed fluoroquinolone agent.

Overall, the mean duration did not significantly change in level or change in trend after the intervention (Fig. 1). There were no significant changes in mean duration for any of the 3 setting subgroups, with the exception of a 0.05% increase (95% CI, 0.0022–0.1013) in the postintervention trend for the ambulatory care setting (Supplementary Material online).

The percent 10-day e-script default duration was declining significantly in the preintervention period at ∼0.6% per month (Table 2; preintervention trend, −0.61; 95% CI: −0.87 to −0.34), largely driven by practice in the ambulatory care and inpatient settings (Supplementary Material online). At the time of the intervention, 30% of all fluoroquinolone e-scripts were written for 10 days (Fig. 1B). This continued to decrease to 25% after the

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Table 1. Characterization of Patient Encounters With a Fluoroquinolone Electronic Prescription Before and After Duration Default Removal

Characteristic	Baseline 12/2016–12/2017 (N=35,609), No. (%)[a]	Post-Intervention 12/2017–12/2018 (N=31,303), No. (%)[a]	Total (N=66,912), No. (%)[a]
Age, median y (IQR)	59.7 (44.8–70.9)	61.0 (46.5–71.5)	60.3 (45.6–71.2)
Sex, female	21,590 (60.6)	18,622 (59.5)	40,212 (60.1)
Race			
Caucasian/White	24,929 (70.0)	22,022 (70.4)	46,951 (70.2)
Black or African American	7,981 (22.4)	6,862 (21.9)	14,843 (22.2)
Other or unknown	2,697 (7.6)	2,417 (7.7)	5,114 (7.6)
Hispanic ethnicity	1,040 (2.9)	966 (3.1)	2,006 (3.0)
Comorbidities[b]			
Diabetes	7,283 (21.3)	6,875 (22.7)	14,158 (21.2)
Chronic kidney disease	3,164 (9.3)	3,142 (10.4)	6,306 (9.8)
Pulmonary disease	660 (1.9)	538 (1.8)	1,198 (1.9)
Congestive heart failure	297 (0.9)	349 (1.2)	646 (1.0)
Liver disease	232 (0.7)	238 (0.8)	470 (0.7)
Metastatic cancer	39 (0.1)	70 (0.2)	109 (0.2)
mCCMI, median (IQR)	1.29 (0–2.8)	1.57 (0–3)	1.43 (0–2.8)
Infectious syndrome[b]			
Urinary tract	7,158 (49.7)	5,627 (46.4)	12,785 (48.2)
Pneumonia	1,636 (11.4)	1,384 (11.4)	3,020 (11.4)
Intra-abdominal	1,565 (10.9)	1,497 (12.3)	3,062 (11.5)
Skin and soft tissue	499 (3.5)	444 (3.7)	943 (3.6)
Prescribed agent			
Ciprofloxacin	25,089 (70)	22,060 (70)	47,149 (70)
Levofloxacin	8,988 (25)	7,903 (25)	16,891 (25)
Moxifloxacin	1,530 (4)	1,340 (4)	2,870 (4)
Prescribing practice setting			
Ambulatory care	27,710 (78)	24,063 (77)	51,773 (77)
Inpatient, at discharge	4,902 (14)	4,625 (15)	9,527 (14)
Emergency department	2,997 (8)	2,615 (8)	5,612 (8)

Note. IQR, interquartile range; mCCMI, age-modified Charlson comorbidity index.
[a]Units unless otherwise specified.
[b]Comorbidity and infectious syndrome data were measured using discharge diagnosis codes. 3.5% of encounters had missing diagnosis data.

intervention and stabilized at this level. An immediate, significant 8% decrease in 10-day e-scripts occurred in the inpatient setting (Supplementary Material online). Summary statistics demonstrated 1-day shorter median duration for both median e-scripts and median total antibiotic LOT for inpatients (Table 3). At the time of the intervention, a significant 1.9% increase in level occurred for 7-day durations among all sites, and a significant 0.8% increase in 14-day prescriptions occurred in ambulatory care settings (Supplementary Material online).

Discussion

Removal of the default antibiotic duration had different impacts on antibiotic durations by practice setting. When looking at the overall mean DOT in all settings, we observed no significant shift from the preintervention to postintervention periods. However, when reviewing subgroups, we did observe a change in e-script duration selections for inpatient to outpatient transitions, in which median antibiotic LOT was reduced by 1 day. A statistically significant increasing change in trend was observed in the ambulatory setting (Supplementary eTable 1 online). The selection of days duration shifted in both the inpatient and ambulatory settings away from 10 days, with corresponding increases in 7- and 14-day durations in the ambulatory setting (Fig. 1B). No notable shifts in duration selection were seen in the ED. To our knowledge, this is the first analysis of an EHR duration intervention in 3 different setting types. Although this study was focused on antimicrobial stewardship, default orders for other therapeutics

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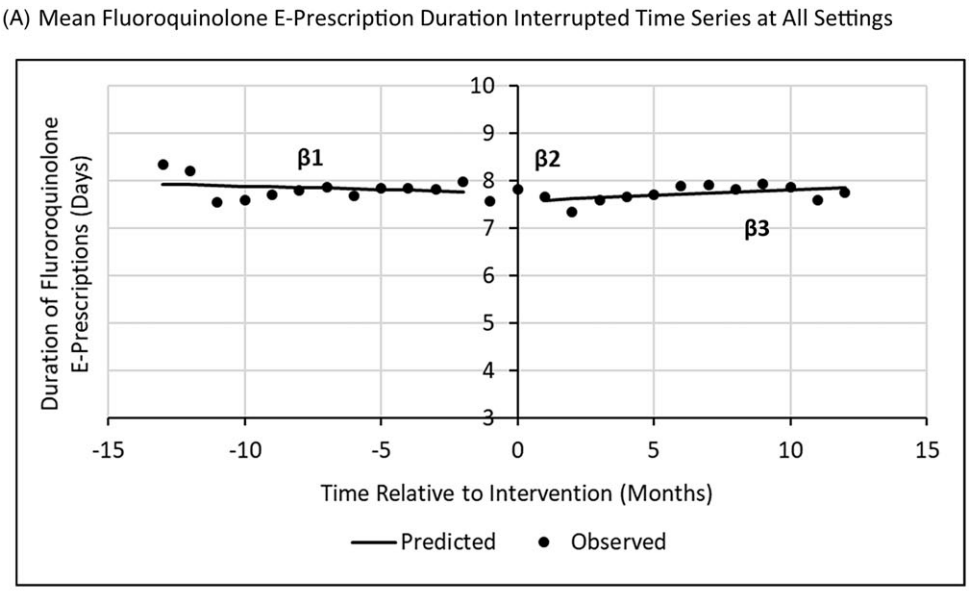

Parameter	Estimate (95% Confidence Interval)	Standard Error	P-value
Baseline trend β1	-0.0141 (-0.044, 0.0158)	0.0153	0.3552
Level change after intervention β2	-0.1784 (-0.5092, 0.1523)	0.1688	0.2904
Trend change after intervention β3	0.0388 (-0.0035, 0.0811)	0.0216	0.0721

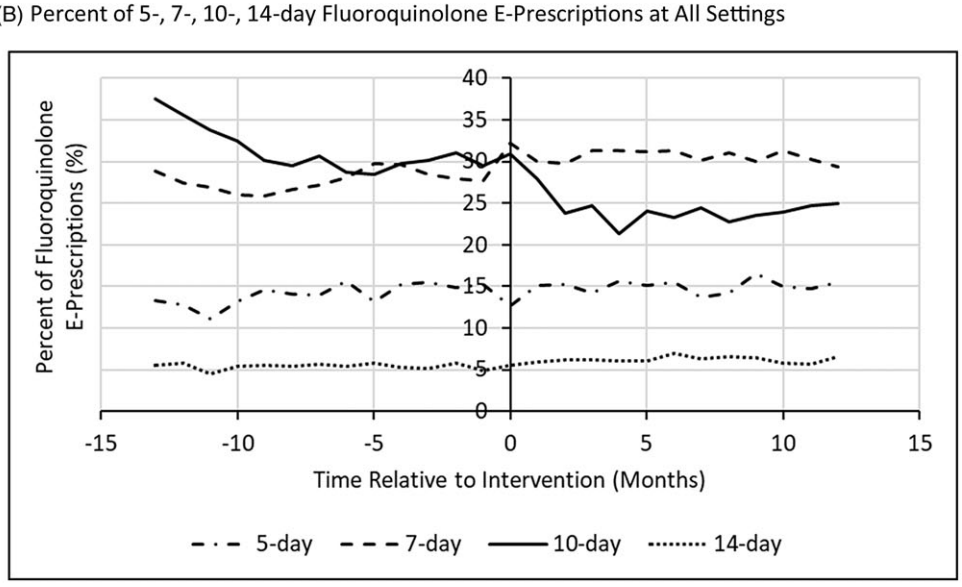

Figure 1. (A) Mean fluoroquinolone electronic prescription duration and (B) percent of fluoroquinolone electronic prescriptions with selected durations at all settings

can have a substantial impact on length of therapy in other therapeutic classes, such as opioids.[29–32]

Default removal favorably affected inpatient transition of care patients, which was the original target of our inpatient ASP team, whose observations of inadvertent lengthening of therapy on hospital discharge was the rationale for the system change. In the preintervention period, order-entry processes had no clear indicator of what was added intentionally to guide the prescriber versus what was prebuilt in the EHR without a clear clinical rationale. Default duration may have been perceived as decision support. The default durations in our EHR did not encourage prescribers to account for hospital-administered antibiotic days, effectively restarting the clock on the antimicrobial course of therapy at time of discharge. Removal of prepopulated durations in fluoroquinolone e-scripts may have prompted more thoughtful selection of antibiotic durations for inpatient providers. Due to the

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Table 2. Effects of Default Duration Removal on Proportion of 10-day Electronic Prescriptions, Stratified by Practice Setting

Practice Setting	Parameter	Estimate (95% CI)	*P* Value
All settings	Pre-trend	**−0.6087** (−0.8727 to −0.3447)	<.0001
	Post-level change	−2.3421 (−5.2618 to 0.5776)	.12
	Post-trend change	**0.5375** (0.1642 to 0.9108)	.004
Ambulatory care	Pre-trend	**−0.7207** (−1.0363 to −0.4050)	<.0001
	Post-level change	−0.9972 (−4.4882 to 2.4937)	.58
	Post-trend change	**0.5906** (0.1442 to 1.0369)	.01
Inpatient, at discharge	Pre-trend	**−0.2909** (−0.555 to −0.0268)	.03
	Post-level change	**−8.4312** (−11.3521 to −5.5103)	<.0001
	Post-trend change	0.36 (−0.0135 to 0.7335)	.06
Emergency department	Pre-trend	0.2087 (−0.2869 to 0.7043)	.41
	Post-level change	−4.9884 (−10.4704 to 0.4936)	.07
	Post-trend change	0.0588 (−0.6422 to 0.7597)	.87

Note. Bold indicates a statistically significant change in proportion of 10-day prescriptions.

Table 3. Fluoroquinolone Electronic Prescription Duration in the Baseline and After Default Duration Removal

	Baseline			Postintervention Period		
Variable	N	Mean d (SD)	Median d (IQR)	N	Mean d (SD)	Median d (IQR)
All sites	35,609	7.8 (4.3)	7 (5–10)	31,303	7.7 (4.5)	7 (5–10)
Inpatient, discharge DOT	4,902	7.3 (5.3)	6 (4–10)	4,625	7.1 (6.2)	5 (3–10)
Inpatient, total LOT	4,902	12.4 (8.9)	11 (7–15)	4,625	12.6 (9.6)	10 (7–15)
Ambulatory care	27,710	7.9 (4.3)	7 (5–10)	24,063	7.9 (4.3)	7 (5–10)
Emergency department	2,997	7.7 (2.6)	7 (7–10)	2,615	7.6 (2.4)	7 (7–10)

Note. DDR, default duration removal; SD, standard deviation; IQR, interquartile range; DOT, days of therapy; LOT, length of therapy. N represents the number of encounters with a fluoroquinolone electronic prescription for each setting and study period.

inability to modify e-scripts for different locations (eg, inpatient, ambulatory, ED) our EHR change was applied in all settings. In the ambulatory setting, we observed a reversion back to traditional 7- and 14-day conventions, which likely exceeded necessary durations for most ambulatory patients. Notably, half of the fluoroquinolone e-scripts were for urinary tract infection, for which randomized control trial data indicate that 14 days is not necessary for most patients.[33–36] The ED subgroup showed no overall change in duration or shifts in e-script duration selection, which suggested that ED providers were not relying on defaults, even in the preintervention period. Based on these findings, we believe that different approaches to improve antimicrobial prescribing and system-level decision support are needed for different locations. Specifically, EHRs should allow for differentiated durations or decision support, depending on the location of e-script origination to allow more nuanced support that best fits the practice setting.

Fluoroquinolones were chosen for this pilot intervention due to their high associations with collateral damage including multiple black-box warnings and *C. difficile* infection.[37,38] Data from the United Kingdom demonstrated 80% reduction in the rates of *C. difficile* after reducing fluoroquinolone utilization both in and outpatient, further supporting the desire for targeted exposure reduction.[39] Our postintervention population was smaller than the preintervention period (14% reduction). This change was likely not due to the intervention but rather due to shifts away from fluoroquinolone prescribing after the 2016 US Food and Drug Administration (FDA) black-box warning in which fluoroquinolone prescribing for common, uncomplicated infections was discouraged.[37,38] Additionally, we noted the postintervention population had a higher mCCMI. Thus, our observations may also reflect a shift in fluoroquinolone prescribing toward more complex populations and away from common, uncomplicated diagnoses. These populations might tend to be selected for longer durations, which could have influenced assessment of the default removal intervention toward a null effect. Though our initial intent was to optimize duration in patients being discharged, durations in all settings need dedicated system improvement and stewardship efforts.

The different impacts in the inpatient and ambulatory setting signal a need for further stewardship interventions in ambulatory settings. Ambulatory stewardship, while required by the The Joint Commission MM.09.01.03 as of 2020, is far from established as demonstrated by a recent survey of 129 institutions.[40] Among the respondents, 88% of the inpatient institutions had fully functional ASPs compared to 7% of the ambulatory cohort, and only 13 sites reported meeting the 4 CDC core elements of outpatient stewardship.[40] The majority of human antibiotic consumption occurs in the ambulatory setting, with up to 50% being unnecessary. More active interventions are needed in this area; however, adequate personnel resources and research are also needed.[23,41]

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Defaults influence behavior. This has been confirmed both outside of healthcare with financial choices, food selection, and energy choices as well as those within healthcare, with increased vaccination, screening, and decreased unneeded imaging.[42,43] Change is more difficult when a decision appears to be made with a defaulted choice. The challenge with defaults is making "the right choice" in setting the duration that is appropriate for the patient and location. In the ambulatory setting, a duration is typically set for the entire course with that single agent. In the inpatient setting, multiple antibiotics may be prescribed over time as more information is gained to completed the full course. This ultimately led us to remove the default because selecting a perfect duration for both settings and all clinical scenarios was not feasible. However, given the limited overall impact, a more optimal intervention for ambulatory settings may be to lower the default rather than having a blank field. Additionally, while the intervention intended to shorten all durations, it had variable effects in reduced durations in some and lengthening in others, an important negative finding. Further studies are needed to determine the impact of duration defaults on anti-infectives to better guide both inpatient and ambulatory stewardship programs.

Our study had several limitations. First, due to the interrupted time-series design, we were unable to control for unmeasured, temporally associated confounding variables. Inclusion of an historic control for the fluoroquinolone group attempted to capture preceding trends, and we described some mild shifts in comorbidity using descriptive pooled data. As mentioned, with the FDA black-box warning, other factors may have influenced duration decisions. We also had a robust inpatient ASP team providing interventions and education for inpatient providers, which could have influenced decisions on duration in that group in addition to effects from system defaults. We did not have robust resources for stewardship focused on outpatient areas. Additionally, there was no assessment of adverse effects or patient-level outcomes related to the intervention. Although our analysis included different settings, these are all within the same healthcare system, which may limit external validity but also emphasizes the variety existing within a single system. The e-script data did not capture written prescriptions and prescriptions for patients discharged to skilled nursing facilities because e-scripts were not utilized for those patients. Finally, we did not use modeling to account for clustering by site in our aggregate model; instead, we used subgroup analyses to better describe setting-specific variation.

Antibiotic durations remain a critical target to reduce antibiotic resistance and unintended consequences of antibiotic use. Defaulted durations in the EHR affect duration selection. This EHR modification reduced fluoroquinolone LOT associated with inpatient to outpatient transitions of care. However, it did not significantly impact fluoroquinolone durations in other settings despite shifts away from the 10-day default duration. More research is needed to determine the best interventions in the ambulatory setting to improve antibiotic prescribing.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2024.16

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