Impact of Education and Data Feedback on Guideline Concordant Prescribing for Urinary Tract Infections in the Outpatient Setting

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Key points: Outpatient antimicrobial stewardship was effective at enhancing guideline-concordant antibiotic prescribing for urinary tract infections (UTIs). This quality improvement initiative was also associated with a reduction in the use of fluoroquinolones for outpatient UTIs.
ABSTRACT

**Background:** Urinary tract infections (UTIs) are the most common outpatient indication for antibiotics and an important target for antimicrobial stewardship (AS) activities. With The Joint Commission standards now requiring outpatient AS, data supporting effective strategies are needed.

**Methods:** We conducted a two-phase, prospective, quasi-experimental study to estimate the effect of an outpatient AS intervention on guideline-concordant antibiotic prescribing in a primary care (PC) and urgent care (UC) clinic between August 2017 and July 2019. Phase 1 of the intervention included the development of clinic-specific antibiograms and UTI diagnosis and treatment guidelines, presented during educational sessions with clinic providers. Phase 2, consisting of routine clinic- and provider-specific feedback, began approximately twelve months after the initial education. The primary outcome was percent of encounters with first- or second-line antibiotics prescribed according to clinic-specific guidelines, and was assessed using an interrupted time series approach.

**Results:** Data were collected on 4,724 distinct patients seen during 6,318 UTI encounters. The percent of guideline-concordant prescribing increased by 22% (95% CI: 12% to 32%) after Phase 1 education, but decreased by 0.5% every two weeks afterwards (95% CI: -0.9% to 0%). Following routine data feedback in Phase 2, guideline concordance stabilized and significant further decline was not seen (-0.6%, 95% CI: -1.6% to 0.4%). This shift in prescribing patterns resulted in a 52% decrease in fluoroquinolone use.

**Conclusions:** Clinicians increased guideline-concordant prescribing, reduced UTI diagnoses, and limited use of high-collateral damage agents following this outpatient AS intervention. Routine data feedback was effective to maintain the response to the initial education.

**Keywords:** antibiotics; fluoroquinolones; outpatient antimicrobial stewardship; urinary tract infections
INTRODUCTION

Approximately 10% of adult ambulatory care visits conclude with an antibiotic prescription, 30% of which are unnecessary [1-3]. Of those needed, nearly 50% are prescribed inappropriately [2, 3]. While outpatient antimicrobial stewardship (AS) improves prescribing without adversely affecting patient outcomes, lack of incentives and resources limit the implementation of formalized programs [4, 5]. The Joint Commission (TJC) recently recognized outpatient AS as a patient safety priority and outlined new requirements for accredited ambulatory health care organizations [6]. These new standards will drive development of outpatient AS programs. Several national organizations have published best practices for implementing outpatient AS [2, 5, 7, 8].

With over 8.6 million annual ambulatory care visits, urinary tract infections (UTIs) are the most commonly diagnosed outpatient bacterial infection and an important target for outpatient AS [5, 9]. Infectious Diseases Society of America (IDSA) guidelines emphasize fluoroquinolone-sparing treatment for uncomplicated UTIs due to increasing antibiotic resistance and known associated collateral damage [10]. Additionally, the Food and Drug Administration updated boxed warnings suggest avoiding fluoroquinolones for indications where there are safer alternatives, such as uncomplicated UTIs [11]. Despite this guidance, overall concordance with IDSA guidelines is poor in ambulatory practices and fluoroquinolones are still used in more than 40% of uncomplicated UTIs [12-15]. Our study aimed to estimate the impact of an AS intervention, including local guidelines, education, and clinic data feedback, on guideline-concordant prescribing rates and urinary tract infection diagnoses.
METHODS

We conducted a prospective, two-phase, quasi-experimental study to estimate the effect of a multi-faceted education and data feedback intervention on antibiotic prescribing for UTI at one primary care (PC) and one urgent care (UC) clinic in Durham, NC.

Study Outcomes

The primary outcome, rate of guideline concordance, was defined as percent of UTI encounters where first- or second-line antibiotics were prescribed according to clinic-specific, antiobigram-based guidelines. Secondary outcomes included: (1) UTI diagnosis rates, (2) return visits for UTI within 30 days, (3) new antibiotic prescriptions written for UTI within 30 days, (4) clinic encounters, emergency department (ED) visits, or inpatient admissions due to antibiotic adverse events within 30 days, (5) average duration of therapy prescribed for UTI, and (6) four-factor guideline concordance rates (i.e. antibiotic, dose, frequency, and duration all align with developed guidelines). Guideline concordance and UTI diagnosis rates were assessed on all patients while all other secondary outcomes were evaluated through chart review on a random 4% sample of the population. Recognizing that standardized guidelines are not applicable in all clinical scenarios, we pursued an additional aim to assess the percent of patients with UTI diagnoses eligible for application of the clinic-specific guideline and used this to establish a target for percent guideline-concordance at each clinic.

Interventions

Clinic-specific, urinary source antibiograms were created for the PC and UC clinic using urine cultures obtained from patients seen at either clinic between January 1, 2015 and December 31, 2016. UTI diagnosis and treatment guidelines were developed for each clinic based on these antibiograms and consensus guidelines (Supplementary Figures 1-4) [10, 16-19]. Clinic guidelines emphasized reducing fluoroquinolone use, avoiding asymptomatic bacteriuria (ASB) treatment, and using appropriate durations of therapy. PC guidelines promoted nitrofurantoin, sulfamethoxazole-trimethoprim, and oral beta-lactams for cystitis and fluoroquinolones for pyelonephritis. Due to
increased resistance, UC guidelines recommended nitrofurantoin and oral beta-lactams for cystitis and adjunctive intramuscular ceftriaxone in combination with fluoroquinolones or sulfamethoxazole-trimethoprim for pyelonephritis.

Phase 1 began with a one-hour educational session during mandatory quarterly provider meetings at PC on August 15, 2017 and UC on November 7 and November 14, 2017. Educators focused on the importance of antibiotic stewardship, reviewed the appropriate diagnosis, treatment, and duration of therapy for UTIs, and discussed clinic-specific guidelines. Digital copies of the guidelines and a link to CustomID®, an online Duke infectious diseases resource, were provided to all clinicians [20]. “Commitment to Patients” posters, adapted from those created by the CDC, were provided to clinics, though unforeseen restrictions limited the intended high-visibility [21]. Data were emailed to the clinic once during Phase 1 and included monthly trends in UTI diagnoses, percent of guideline concordance, percent of mixed growth urine cultures, antibiotic prescribing data, and a copy of the UTI guidelines to serve as reinforcement of the initial education session. The baseline period was twelve months prior to the education session and the Phase 1 intervention included encounters from education to September 2018 for PC and November 2018 for UC.

A second in-person educational session in September 2018 for PC and November 2018 for UC started Phase 2 and was delivered during mandatory provider meetings. Original content presented in 2017 was reviewed along with data from Phase 1. In total, 11 of 14 (79%) PC and 72 of 96 (75%) UC providers attended education sessions and 100% of providers were emailed education following sessions. There was low clinician turnover between the study periods. In Phase 2, four routine data feedback emails and one in-person feedback session were provided to clinicians at PC and three emails were sent to UC with the last sent in April 2019. Data included trends in UTI diagnoses, guideline concordance, antibiotics prescribed, and actionable recommendations to improve prescribing based on findings from chart review. Additionally, peer-comparison reports were emailed directly to PC providers in January and March 2019. In these reports, fluoroquinolone prescribing rates for each provider were compared to the clinic average and the “top performers” with the lowest rates of fluoroquinolone use, an approach used in other outpatient AS studies [22]. A detailed timeline
of study interventions is provided in Figure 1 and a sample of data feedback reports can be found in Supplementary Figures 5 and 6.

**Patient Selection and Eligibility**

Patients were identified using the Duke Enterprise Data Unified Content Explorer (DEDUCE), a web-based clinical research tool [23]. DEDUCE was queried monthly for adult patients with a diagnosis code of acute cystitis or acute pyelonephritis between August 1, 2016 and July 30, 2019. Chart review validated that non-specific codes such as “dysuria” and “UTI site not specified” were used for a diagnosis of cystitis. A list of included International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modification [ICD-9-CM] and [ICD-10-CM] diagnosis codes is located in Supplementary Table 1. Encounters without antibiotics prescribed within five days of the visit date were excluded from data analysis.

A random sample from at least 4% of all encounters were chart reviewed to evaluate all secondary outcomes except for UTI diagnosis rates. To determine goal guideline adherence rates, patients evaluated during chart review were defined as guideline eligible if they lacked the following features: recurrent UTI (two unique UTI episodes within the prior six months or three episodes within the prior twelve months), received antibiotics within the 30 days prior to UTI diagnosis, allergies or intolerances to all first- and second-line antibiotics, a second bacterial infection which warranted antibiotics, urine cultures within the last year which were resistant to all first- and second-line antibiotics, or indications that may support the treatment of ASB (pregnant, immunosuppressed, or patients undergoing genitourinary procedures associated with mucosal bleeding) [16].
Patient Consent Statement

This quality improvement study was deemed exempt by the Duke University Institutional Review Board and waivers of informed consent were granted.

Statistical Analysis

For the primary outcome, a segmented, linear regression with piecewise linear spline for time was used to model the level of change and trends in both the baseline and post-intervention periods, an approach similar in design to multiple prior evaluations [24-27]. Specifically, the model adjusted for intervention (Phase 0 vs. Phase 1 vs. Phase 2), clinic (PC vs. UC), and allowed time (measured in two-week intervals) to have different slopes at different phases. The secondary outcome, number of UTI encounters, was assessed similarly using a segmented Poisson regression model. Remaining secondary outcomes, collected and managed in REDCap electronic data capture tools hosted at Duke University, were assessed in the random sample of encounters described above [28]. For the primary outcome, significance of the test was assessed at alpha=0.05. For secondary outcomes, point estimates and their 95% confidence intervals (CIs) were reported. Data management and analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, North Carolina).

RESULTS

A total of 4,724 patients and 6,318 encounters met inclusion criteria of an acute UTI at PC or UC between August 1, 2016 and July 30, 2019. Twenty percent (N=1,296) of encounters were excluded from further analysis because either no antibiotics were prescribed within five days of the encounter or antibiotic data were invalid (Figure 2). Of the remaining 5,022 encounters which resulted in antibiotic prescriptions, 4,875 (97%) were associated with a diagnosis of cystitis, the majority (83%) of which were at UC. Encounter characteristics were similar throughout the study (Table 1).

The segmented, linear regression analysis results on concordance over time are summarized in Supplementary Tables 2 and 3. We observed no significant time-related effect on guideline concordance in the Phase 0 baseline period (-0.1%; 95% CI: -0.6% to 0.3%; P=0.578). Immediately after Phase 1 education, an overall significant 21.8% increase in percentage of prescriptions for
guideline-concordant antibiotics was observed (95% CI: 11.5% to 32%; P<0.001). This effect diminished by 0.5% (95% CI: -0.9% to 0%; P=0.049) for each two-week period after the intervention. We observed a non-significant increase in the percent of antibiotics that were guideline-concordant upon beginning Phase 2 when compared to the Phase 1 period (3.9%; 95% CI: -13.2% to 20.9%; P=0.656). There was no significant change over time in the rate of guideline-concordant antibiotic prescriptions throughout the Phase 2 period (-0.6%; 95% CI: -1.6% to 0.4%; P=0.232). The reversion back to baseline prescribing habits observed in the Phase 1 period halted with Phase 2 data feedback. Overall, the mean percent of guideline concordance increased at PC from 65.8% at baseline to 72.6% in Phase 1 and further to 75% with routine data feedback. At UC, concordance increased from 35.8% at baseline to 57.3% in Phase 1 and 61% in Phase 2 (Figure 3).

In the baseline period, the number of UTI diagnoses did not change over time (incidence rate ratio (IRR) =1 per two weeks, 95% CI: 0.99 to 1) (Supplementary Table 3). After Phase 1 education, UTI diagnoses decreased immediately by 21% (IRR = 0.79, 95% CI: 0.67 to 0.93). This immediate reduction was not seen again after education delivery in Phase 2 (IRR=1.04, 95% CI: 0.8 to 1.36) (Supplementary Figure 7). Overall, the mean number of UTI diagnoses per two-week period decreased at PC throughout the study period from 15 ± 3.5 at baseline, to 9.9 ± 4.1 during Phase 1, and 7.5 ± 3.9 encounters per two-week period during Phase 2. A similar trend was noted at UC with two-week UTI diagnosis counts of 70.3 ± 11.1 at baseline, 50 ± 9.8 during Phase 1, and 53.7 ± 7.6 during Phase 2. Overall clinic visit volumes were stable throughout the study period.

At baseline, fluoroquinolones were prescribed during 26.7% of UTI visits at PC and 25% of UTI visits at UC (Table 2). Fluoroquinolone prescriptions decreased to 17.3% and 15.3% during Phase 1 and further to 16% and 11.5% during Phase 2 at PC and UC, respectively. Overall there was a 52.1% relative reduction in fluoroquinolone use for UTI and a 65.4% increase in nitrofurantoin (Table 2).

Manual chart reviews to assess remaining secondary endpoints were performed on 71 (8.3%) and 166 (4%) encounters at PC and UC, respectively. Demographics of this sample were similar to
the overall population. 25 of 71 (35.2%) PC encounters and 39 of 166 (23.5%) UC encounters were identified as scenarios where the developed guidelines would not apply. Therefore, an estimated target goal for guideline-concordance was 65% for PC and 76% for UC. The most common reasons for exclusion from the developed guidelines were antibiotics prescribed within the last 30 days or patients with recurrent UTIs, which were the case for 20 (28.2%) PC encounters and 29 (17.5%) UC encounters. Secondary endpoints were assessed using the remaining 173 total encounters at PC and UC.

The number of encounters meeting the four-factor guideline-concordant criteria increased throughout the study from 15 of 79 (19%) at baseline to 16 of 69 (23.2%) during Phase 1 and 7 of 25 (28%) during Phase 2 (Supplementary Table 4). Inappropriate durations of therapy, defined as differing from guideline-recommendations, was the most common reason for divergence. Despite this, the mean duration of therapy decreased from 7.6 ± 2.4 days at baseline to 7.3 ± 2.1 days and 6.6 ± 1.6 days among all sampled encounters during Phase 1 and 2, respectively (Supplementary Table 5). Treatment failure and antibiotic adverse effects were infrequent and tests for statistical significance were not conducted due to the small sample size (Supplementary Table 6). Unnecessary treatment of asymptomatic bacteriuria was identified in 4 (5%), 4 (6%), and 4 (16%) patients during Phase 1, 2, and 3 respectively.

**DISCUSSION**

Inappropriate fluoroquinolone prescribing for UTI is a potential target for outpatient stewardship programs [10, 14]. In this study, we developed a multifaceted intervention with the aim of improving management of UTI in two outpatient clinics. The provision of education and guidelines during Phase 1 significantly increased rates of guideline-directed antibiotics and use of non-fluoroquinolone therapies for UTI. Despite the initial increase in guideline-concordant prescribing, prescribing patterns trended back towards baseline without continued reinforcement, a challenge reported by other investigators [29, 30]. In the second phase of this study, we added routine feedback with the aim of enhancing durability of guideline concordance. While this additional AS intervention
did not significantly change rates of guideline-concordant antibiotic prescriptions, as occurred in Phase 1, the significant decline in concordance rates seen during Phase 1 halted. This sustained response to the intervention is highlighted by the steady reduction in fluoroquinolone prescribing across all phases of this study.

Upon evaluation of secondary outcomes, we found that UTI diagnoses declined after the start of Phase 1. A focus of the education throughout both phases of the intervention was appropriate diagnosis of UTI, thus lower number of UTI diagnoses may indicate that more patients were identified as ASB and not treated. Despite an overall reduction in antibiotic durations and UTI diagnoses, chart review data suggest further opportunity to target durations of therapy and ASB. No evidence of harm following the initiative was detected. Management of UTIs after the intervention resulted in decreased exposure to broad-spectrum antibiotics and improved adherence with national guidelines.

Our findings are consistent with prior outpatient AS research for other infections, which suggests that displaying patient-centered AS posters, educating clinicians, and providing data feedback are effective strategies to promote stewardship [31, 32]. Data supporting the use of these interventions for UTI are limited. One French study assessed the impact of regional UTI guidelines in combination with provider education on antibiotic prescribing. While there were statistically significant reductions in norfloxacin prescribing, the study assessed antibiotic prescribing across all indications and did not directly analyze trends in other antibiotics commonly (but not specifically) prescribed for UTI, including beta-lactams and sulfamethoxazole-trimethoprim [27]. Our study adds to these findings and provides an analysis of antibiotics that are specifically prescribed during a UTI encounter.

Our study is not without limitations. Identification of our cohort relies on the accurate use of diagnosis codes by clinicians. Often, patients treated for UTI were coded with non-specific diagnoses such as “dysuria.” In our review of the random subset of patients, we confirmed intent to treat a UTI even among those coded with non-specific diagnoses. Diagnosis code shifting, a practice by which a
provider intentionally miscodes a visit to justify an antibiotic prescription, has been seen in outpatient AS studies [2]. We assessed diagnostic accuracy by performing chart reviews on a random subset of all clinic visits and verified the diagnosis code matched the clinical intent in almost all cases. Additionally, diagnosis rates for pyelonephritis, an allowable code for broader agents, were consistent throughout the study.

We excluded encounters without antibiotic prescriptions within 5 days from our analysis. Based on chart review, these visits were often found to be unrelated to UTI (e.g. dysuria resulting from vulvovaginal candidiasis). While we hypothesize that a reduced number of UTI encounters treated with antibiotics is partially a result of decreased treatment of asymptomatic patients, we are unable to confirm this.

Lastly, we may not have seen the maximal effects of our intervention due to inherent implementation challenges. While we intended for Commitment Posters to be posted in high-visibility areas, restrictions set by our health system required they be placed in alternative areas and likely limited their impact. There was limited provider turnover thus our findings may not be reproducible in settings with more frequent staff changes, such as clinics staffed by medical residents. Our data feedback intervention was emailed at routine intervals and there is no guarantee that all clinicians reviewed the data feedback. Secondary outcomes such as antibiotic duration of therapy, treatment failure, or adverse effects were only evaluated on a random subset chart review. Future studies that leverage the electronic health record to evaluate these outcomes on a larger scale would be beneficial.

The present study suggests that the provision of clinic-specific urinary antibiograms along with treatment guidelines, clinician education, and data feedback to clinicians was successful at increasing guideline concordance, including a robust shift away from fluoroquinolones towards other agents with narrower spectrum and lower collateral damage, and reducing UTI diagnoses. While routine data feedback helped to maintain the initial improvement in guideline-concordant antibiotic
selection, significant additional benefit was not realized. The provision of routine data feedback and peer-comparison reports was time-intensive to implement and may be impractical for institutions to maintain. Future studies are warranted to further understand the sustainability and scalability of AS interventions to optimize outpatient antibiotic use, given the new TJC standards. The success of these stewardship strategies could be employed in other infectious syndromes, or other non-infectious disease states, where outpatient prescribing diverges from national guideline recommendations.
POTENTIAL CONFLICTS OF INTEREST

All authors report no potential conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Table 1. Patient demographics for UTI encounters at PC and UC where antibiotics were prescribed

| Demographics | Primary Care | Urgent Care |
|--------------|--------------|-------------|
|              | Phase 0 (N=404) | Phase 1 (N=288) | Phase 2 (N=165) | Phase 0 (N=1,897) | Phase 1 (N=1,301) | Phase 2 (N=967) |
| Age, mean (SD) | 56.3 (18.1) | 57.9 (18.5) | 58.1 (18.1) | 48.8 (20.4) | 48.4 (20.8) | 48.6 (20.1) |
| Female sex, N (%) | 373 (92.3) | 268 (93.1) | 146 (88.5) | 1643 (86.6) | 1127 (86.6) | 835 (86.1) |
| Race, N (%) | | | | | |
| Caucasian/White | 226 (55.9) | 172 (59.7) | 90 (54.5) | 1179 (62.2) | 764 (58.7) | 535 (55.3) |
| Black or African | 146 (36.1) | 97 (33.7) | 58 (35.2) | 489 (25.8) | 339 (26.1) | 298 (30.8) |
| American | | | | | |
| Other or Unknown | 32 (7.9) | 19 (6.6) | 17 (10.3) | 229 (12.1) | 198 (15.2) | 134 (13.9) |
| Hispanic Ethnicity, N (%) | 16 (4.0) | 9 (3.1) | 8 (4.8) | 147 (7.7) | 109 (8.4) | 71 (7.3) |
| Payer Group, N (%) | | | | | |
| Private | 230 (56.9) | 138 (47.9) | 83 (50.3) | 1236 (65.2) | 845 (65.0) | 619 (64.0) |
| Medicare | 157 (38.9) | 131 (45.5) | 71 (43.0) | 517 (27.3) | 353 (27.1) | 258 (26.7) |
| Medicaid | 15 (3.7) | 18 (6.3) | 11 (6.7) | 132 (7.0) | 97 (7.5) | 84 (8.7) |
| Other or Unknown | 2 (0.5) | 1 (0.3) | 0 | 12 (0.6) | 6 (0.5) | 6 (0.6) |
| Encounter Diagnosis, N (%) | | | | | |
| Cystitis | 394 (97.5) | 283 (98.3) | 159 (96.4) | 1832 (96.6) | 1259 (96.8) | 948 (98.0) |
| Pyelonephritis | 10 (2.5) | 5 (1.7) | 6 (3.6) | 65 (3.4) | 42 (3.2) | 19 (2.0) |

Demographics based on the number of unique UTI encounters, not the number of unique patients.
Table 2. Antibiotics prescribed for UTIs at PC and UC before and after the education

| Category                        | Primary Care (PC) | Urgent Care (UC) | Combined PC and UC |
|---------------------------------|-------------------|------------------|--------------------|
|                                 | Phase 0 (N=416)   | Phase 1 (N=306)  | Phase 2 (N=516)   | Percent Change |
|                                 | N (%)             | N (%)            | N (%)             |               |
| Nitrofurantoin                  | 122 (29.3)        | 125 (41.5)       | 64 (36.6)         | + 24.7        |
| Fluoroquinolone                | 111 (26.7)        | 52 (17.3)        | 28 (16.0)         | - 40.0        |
| TMP-SMX                         | 116 (27.9)        | 53 (17.6)        | 33 (18.9)         | - 32.4        |
| PO Cephalosporin               | 42 (10.1)         | 45 (15.0)        | 28 (16.0)         | + 58.5        |
| IM Ceftriaxone                 | (1.0)             | (3.0)            | (4.0)             | + 316         |
| Otherb                          | 21 (5.0)          | 17 (5.6)         | 15 (8.6)          | + 69.8        |
|                                 | 573 (27.7)        | 586 (40.7)       | 501 (47.8)        | + 72.9        |
|                                 | 518 (25.0)        | 220 (15.3)       | 120 (11.5)        | - 54.2        |
|                                 | 460 (22.2)        | 155 (10.8)       | 125 (11.9)        | - 46.3        |
|                                 | 185 (8.9)         | 237 (16.5)       | 157 (15.0)        | + 67.8        |
|                                 | 202 (9.7)         | 173 (12.0)       | 100 (9.5)         | - 2.1         |
|                                 | 134 (6.5)         | 69 (4.8)         | 45 (4.3)          | - 33.6        |

*Defined as the relative change in antibiotic use throughout the entire study period, from Phase 0 to Phase 2.

Uncommonly prescribed antibiotics and those which may have been chosen for an alternative diagnosis.

Fosfomycin prescribed in < 1% of all encounters.

**Category includes amoxicillin, clarithromycin, clindamycin, doxycycline, fosfomycin, and moxifloxacin.**

**TMP-SMX = trimethoprim-sulfamethoxazole; PO = oral; IM = intramuscular.**
FIGURE LEGENDS

Figure 1. Study timeline. Timeline for primary care and urgent care are separate; timelines at either clinic have been either truncated or expanded to align the beginning of each phase of the intervention.

Figure 2. Flow diagram describing the patient encounters included in the analysis.

Figure 3. Time-series analysis comparing rates of UTI visits with prescriptions for guideline (GL) concordant-antibiotics at the Primary Care (PC) and Urgent Care (UC) clinics. Predicted concordance lines are plotted using predicted values for each clinic, obtained from the segmented regression analysis results.
Figure 3

Baseline (Phase 0)  One-Time Education (Phase 1)  Data Feedback (Phase 2)

Percent Guideline Concordance

Time (in 2-week blocks relative to initial education at t=0)