Remote Antimicrobial Stewardship in Community Hospitals

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Abstract: Antimicrobial stewardship has become standard practice at university medical centers, but the practice is more difficult to implement in remote community hospitals that lack infectious diseases trained practitioners. Starting in 2011, six community hospitals within the Vidant Health system began an antimicrobial stewardship program utilizing pharmacists who reviewed charts remotely from Vidant Medical Center. Pharmacists made recommendations within the electronic medical record (EMR) to streamline, discontinue, or switch antimicrobial agents. Totals of charts reviewed, recommendations made, recommendations accepted, and categories of intervention were recorded. Linear regression was utilized to measure changes in antimicrobial use over time. For the four larger hospitals, recommendations for changes were made in an average of 45 charts per month per hospital and physician acceptance of the pharmacists’ recommendations varied between 83% and 88%. There was no significant decrease in total antimicrobial use, but much of the use was outside of the stewardship program’s review. Quinolone use decreased by more than 50% in two of the four larger hospitals. Remote antimicrobial stewardship utilizing an EMR is feasible in community hospitals and is generally received favorably by physicians. As more community hospitals adopt EMRs, there is an opportunity to expand antimicrobial stewardship beyond the academic medical center.

Keywords: antibiotics; antimicrobials; electronic medical record; stewardship; community hospitals
1. Introduction

The overuse and misuse of antimicrobial agents is a global problem that has led to the development of antimicrobial resistance in both the hospital and community setting. One of the primary strategies for combating resistance is through the use of antimicrobial stewardship programs (ASPs) [1,2]. The ASP’s primary goal includes optimizing antimicrobial use through reduction of unnecessary antimicrobial use and confirmation of proper antimicrobial use (including drug, dose, route, and duration), in order to achieve the best clinical outcomes. While ASPs have been proven effective in both academic hospitals [3] and smaller community hospitals [4], small community hospitals tend to have more difficulty establishing these programs. These difficulties include staffing constraints, lack of funding, and lack of administrative and medical staff support [5].

Vidant Medical Center (VMC) has had a successful ASP in place since 2001. The ASP uses a primary strategy of prospective audit with feedback. Given the success of the ASP at the tertiary care center, we expanded the ASP to six of the seven community hospitals within the Vidant Health (VH) system. In December 2011 the ASP was implemented at Vidant Roanoke-Chowan Hospital (VROA), in March 2012 at Vidant Bertie Hospital (VBER), Vidant Chowan Hospital (VCHO), and The Outer Banks Hospital (OBH), in October 2013 at Vidant Duplin Hospital (VDUP), and in December 2013 at Vidant Beaufort Hospital (VBEA). We were able to accomplish this process through use of the electronic medical record (EMR) Epic (Madison, WI, USA), which is shared across the VH system [6]. To date, we are unable to locate any previous attempt at managing an ASP via EMR and central monitoring. We currently collect data on intervention outcomes, cost savings, physician acceptance rates, number of charts reviewed, number of recommendations made, anti-methicillin-resistant Staphylococcus aureus (MRSA) drug use, anti-pseudomonal drug use, broad spectrum drug use, and total antimicrobial drug use.

2. Methods

2.1. Central ASP at VMC

VMC is a 909-bed, tertiary-care academic medical center affiliated with the Brody School of Medicine at East Carolina University (Greenville, NC, USA). VMC’s ASP was established in 2001 and has been reviewed in previous publications [7,8]. This ASP was formed by the Antimicrobial Utilization & Stewardship Subcommittee (AUSS) and was approved by the Pharmacy and Therapeutics Committee and the medical staff executive committee. When the ASP first started it had an infectious diseases physician director and one pharmacist (1 full time equivalent [FTE]), with an additional pharmacist added in 2004 (0.5 FTE) and two additional pharmacists added when the program expanded to the community hospitals (1.5 FTE). All members of the ASP are physically located at VMC. The VH ASP fully operates five days per week with on-call and follow-up services provided on the weekend. Patient chart review for VMC is completed by one of the pharmacists for all adult patients that have been on a restricted or controlled antibiotic for ≥72 h.
2.2. Expansion of the ASP to Vidant Community Hospitals

VMC is the flagship hospital of the VH system. Including VMC, VH currently has eight hospital locations across eastern North Carolina with six of seven community hospitals being a part of this ASP. These six community hospitals are described in Table 1. None of the community hospitals within this ASP have infectious diseases consult services. While some of these hospitals do have a few order sets that were in place prior to the ASP, there are no formal infection related guidelines at any of these hospitals. To initiate implementation of an ASP at each community hospital, the physician director and pharmacist representative(s) visited each hospital to describe the program, discuss specifics, and begin to build relationships with the local physicians, pharmacists, infection control practitioners, and microbiology staff.

| Hospital Name                                      | Beds | ASP Start Date | Services                                      |
|----------------------------------------------------|------|----------------|-----------------------------------------------|
| Vidant Beaufort Hospital, Washington, NC (Hospital A) | 142  | December 2013  | medical, surgical, intensive care, emergency,  |
|                                                    |      |                | and orthopedics                               |
| Vidant Chowan Hospital, Edenton, NC (Hospital B)     | 49   | March 2012     | medical, surgical, intensive care, emergency,  |
|                                                    |      |                | and orthopedics                               |
| Vidant Duplin Hospital, Kenansville, NC (Hospital C) | 81   | October 2013   | medical, surgical, intensive care, emergency,  |
|                                                    |      |                | and orthopedics                               |
| Vidant Roanoke-Chowan Hospital, Ahoskie, NC (Hospital D) | 114  | December 2011  | medical, surgical, intensive care, emergency,  |
|                                                    |      |                | orthopedics, and wound care                    |
| Vidant Bertie Hospital, Windsor, NC (Hospital E)     | 6    | March 2012     | medical and emergency                          |
| The Outer Banks Hospital, Nags Head, NC (Hospital F)  | 21   | March 2012     | medical, surgical, emergency, and orthopedics  |

At these hospitals, any adult patient that receives a controlled antimicrobial for ≥24 h triggers a chart review by the ASP pharmacist and is listed on the EMR-generated report that is run daily Monday through Friday. A full list of all controlled antimicrobials can be found in Table 2. The formulary restriction program in place at VMC is not currently in place at the community hospitals. The time window for antibiotic use that triggered a chart review was shortened from 72 h to 24 h at the community hospitals after it was noticed that the length of stay at the community hospitals was generally shorter than it is at VMC. Based on microbiology culture results, radiology reports, and the working diagnosis, the pharmacist, with input from the physician director, makes recommendations to change or stop the controlled antimicrobial agent(s) by leaving a note in the EMR. These recommendations are generally based off of the guidelines published by the Infectious Diseases Society of America (IDSA). After a note is left, the physician can make the recommended change(s) on his/her own or reply in a progress note or as an addendum to the ASP note with the reason why current therapy will continue. After 24 h, if the recommendation is not acknowledged by the primary provider then the ASP pharmacist implements the recommendation per protocol as a telephone order from the ASP physician director.
Table 2. Antimicrobials classified as controlled by the antimicrobial stewardship program for community hospitals.

| Controlled Antimicrobials |
|---------------------------|
| Acyclovir                 |
| Amikacin                  |
| Amphotericin B lipid complex |
| Ampicillin/sulbactam      |
| Azithromycin              |
| Aztreonam                 |
| Cefepime                  |
| Cefotaxime                |
| Ceftaroline               |
| Ceftaroline (or colistin) |
| Colistimethate (or colistin) |
| Dalbavancin               |
| Daptomycin                |
| Ertapenem                 |
| Fidaxomicin               |
| Fluconazole               |
| Flucytosine               |
| Ganciclovir               |
| Linezolid                 |
| Meropenem                 |
| Micafungin                |
| Moxifloxacin              |
| Piperacillin/tazobactam   |
| Posaconazole              |
| Tedizolid                 |
| Tigecycline               |
| Tobramycin                |
| Vancomycin                |
| Voriconazole              |
| Non-formulary antibiotics |
|                          |

2.3. ASP Data Collection

Antimicrobial drug use was measured for each hospital for all antimicrobials used in defined daily dose per 1000 patient-days (DDD/1000 PD) according to World Health Organization (WHO) standards (http://www.whocc.no/atcddd/). This drug usage included anti-fungals, anti-virals, and anti-bacterial agents, including drugs that are not considered controlled and that are not evaluated by the ASP. Certain antimicrobials are also divided into additional categories. Anti-pseudomonal agents included ceftazidime (not on formulary), cefepime, piperacillin/tazobactam, meropenem, doripenem (not on formulary), imipenem (not on formulary), ciprofloxacin, levofloxacin (not on formulary), aminoglycosides, and aztreonam. Anti-MRSA agents included ceftaroline, clindamycin, daptomycin, dalbavancin, doxycycline, linezolid, tedizolid, tigecycline, trimethoprim/sulfamethoxazole, and vancomycin. This data was collected by the ASP on a quarterly basis and was used to trend usage over time.

Each recommendation left by the ASP and accepted by the primary provider was then classified under one of nine different types of intervention. The intervention types included: additional test required to make diagnosis, adverse event avoided, antibiotic-pathogen matched, dose adjusted, empiric antibiotic recommendation, drug discontinued, intravenous (IV) to oral (PO) switch, de-escalation of therapy, and indwelling urinary catheter discontinued or changed. Each quarter we determined how many of the accepted interventions fell into each of these categories. For all of the interventions that resulted in a drug being discontinued, we estimated a cost-avoidance for the hospital determined by the institutional acquisition cost of the drug and the number of days of therapy spared (assuming the initial order continued through completion of a seven day course). Seven days was used as the default duration because all antimicrobial orders are automatically given a duration of seven days in the EMR. Patients who had drugs discontinued but were then discharged are documented...
separately. The number of charts reviewed, number of recommendations made (percent intervention), and number of recommendations accepted by the primary provider (physician acceptance rate) were also collected for each hospital on a monthly basis.

2.4. Surveillance Definitions

Nosocomial Gram-negative and Gram-positive data sets were created by querying MedMined® (CareFusion, Birmingham, AL, USA). These definitions are the same as those currently used at VMC [6]. All clinical care unit specimens (blood, sterile fluid, sputum, urine, wounds and anaerobic specimens) taken between 1 July 2010 and 30 June 2015 from hospitals A–F were included. Percent susceptible was defined as the percentage of total isolates that were susceptible to the selected antimicrobial. Intermediately susceptible isolates were classified as resistant. Susceptibility profiles were compared on a year-by-year basis.

2.5. Epic

Currently every hospital in the VH system uses Epic. Each hospital’s remote ASP uses the same process and reporting as VMC [6]. First, an electronic progress note with the ASP recommendation was entered into the EMR. The ASP pharmacist then entered a unique order into the system entitled “antimicrobial management”. This order functioned as a best practice alert. Whenever a physician or other provider logged into a patient’s chart, the EMR automatically opened a new window with a message from the ASP to the provider. This communication window alerted the provider that the ASP had left a recommendation in the EMR. The provider then had 24 h to respond to (i.e., accept or reject) the recommendation per medical staff guidelines. At this time, the “antimicrobial management” order was discontinued. Internally written reports from the Epic reporting manual were used to identify patients and collect usage, outcome, and workload data.

2.6. Statistics

Statistical analysis was performed using IBM SPSS Statistics versions 22 and 23 (IBM Corp., Armonk, NY, USA). Linear regression was used to examine antimicrobial use and antimicrobial susceptibility from ASP implementation date through June 2015. A p-value of ≤0.05 was considered significant.

3. Results

3.1. Workload and Physician Acceptance

Total number of charts reviewed, recommendations made, and recommendations accepted are in Table 3. The first month for each hospital was omitted due to the beginning of the ASP being in the middle of the month. The average number of charts reviewed per month ranged from 17 to 148. The percent of recommendations made per charts reviewed per month ranged from 40% to 63%. The percent of recommendations accepted per month by the physician ranged from 81% to 95%.
Table 3. Monthly antimicrobial stewardship program (ASP) activity (first full month of ASP through June 2015).

| Hospital | A | B | C | D | E | F |
|----------|---|---|---|---|---|---|
| First full month of ASP | January 2014 | April 2012 | November 2013 | January 2012 | April 2012 | April 2012 |
| Adult inpatient days | 14,840 | 17,134 | 11,379 | 41,169 | 5017 | 9531 |
| Total number of charts reviewed | 1563 | 1753 | 1179 | 6797 | 669 | 943 |
| Average number of charts reviewed/month | 87 | 45 | 59 | 148 | 17 | 24 |
| Average number of recommendations/month | 39 | 25 | 24 | 93 | 9 | 12 |
| Average number of recommendations accepted/month | 33 | 20 | 21 | 78 | 8 | 9 |
| Recommendations/charts reviewed (%) * | 45% | 57% | 40% | 63% | 54% | 47% |
| Recommendations accepted (%) * | 83% | 85% | 88% | 87% | 95% | 81% |

* Based on actual numbers not averages.

3.2. Intervention Outcomes and Cost Savings

Classification of outcomes for accepted interventions between January 2014 and June 2015 are in Table 4. The recommendations by the ASP most often resulted in antimicrobial drug discontinuation. Hospital drug cost savings were also calculated for each drug discontinued using the days of antibiotic therapy avoided and multiplying by the institutional acquisition cost of antibiotic therapy per day. As mentioned above, seven days was used as the default assumed duration because all antimicrobial orders are automatically given a duration of seven days in the EMR. The total cost savings associated with the drugs discontinued between January 2014 and June 2015 were as follows: hospital A, $16,928; hospital B, $7008; hospital C, $5887; hospital D, $53,618; hospital E, $4309; hospital F, $1616. These cost savings reflect only drug cost and do not account for other costs savings which include but are not limited to IV supplies, nursing time, pharmacy time, or avoidance of opportunistic infections. Patients who were discharged without antimicrobial therapy are documented separately, since there is no cost avoidance for the hospital. The number of patients who were discharged without antimicrobial therapy between January 2014 and June 2015 were as follows: hospital A, 57 patients; hospital B, 35 patients; hospital C, 30 patients; hospital D, 154 patients; hospital E, 14 patients; hospital F, 14 patients.

Table 4. Accepted interventions from January 2014 through June 2015 by hospital.

| Intervention (Number over Past 18 Months) | A | B | C | D | E | F |
|------------------------------------------|---|---|---|---|---|---|
| Additional Test Required to Make Diagnosis | 9 | 2 | 2 | 24 | 4 | 2 |
| Adverse Event Avoided | 34 | 10 | 21 | 45 | 7 | 9 |
| Antibiotic-Pathogen Matched | 31 | 20 | 27 | 68 | 5 | 3 |
| Dose Adjusted | 76 | 33 | 51 | 106 | 7 | 10 |
| Empiric Antibiotic Recommendations | 50 | 48 | 40 | 128 | 15 | 11 |
| Drug Discontinued | 279 | 168 | 132 | 747 | 78 | 50 |
| IV to PO | 100 | 84 | 63 | 345 | 43 | 32 |
| Foley Discontinued or Changed | 2 | 1 | 2 | 2 | 1 | 0 |
| De-escalation of therapy | 38 | 17 | 23 | 105 | 7 | 12 |
Table 5. Changes in the use of various categories of antimicrobial agents for hospitals A–F measured in DDD/1000 PD.

| Class              | Jan–Mar 2011 | Apr–Jun 2011 | Jul–Sep 2011 | Oct–Dec 2011 | Jan–Mar 2012 | Apr–Jun 2012 | Jul–Sep 2012 | Oct–Dec 2012 | Jan–Mar 2013 | Apr–Jun 2013 | Jul–Sep 2013 | Oct–Dec 2013 | Jan–Mar 2014 | Apr–Jun 2014 | Jul–Sep 2014 | Oct–Dec 2014 | Jan–Mar 2015 | Apr–Jun 2015 | p-Value  |
|--------------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|----------|
| **Hospital A**     |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |          |
| Quinolones         | -            | -            | -            | -            | -            | -            | -            | -            | -            | 176          | 157          | 156          | 161          | 155          | 157         | 112          | 178          | 159         | 128       | N/S      |
| Cephalosporins     | -            | -            | -            | -            | -            | -            | -            | -            | -            | -            | 205          | 188          | 206          | 204          | 185          | 209         | 238          | 250          | 237         | 291       | * 0.003  |
| Macrolides         | -            | -            | -            | -            | -            | -            | -            | -            | -            | -            | 125          | 229          | 194          | 150          | 270          | -           | 100          | 115          | 124         | 99        | 143      |
| Anti-Pseudomonal   | -            | -            | -            | -            | -            | -            | -            | -            | -            | -            | 248          | 231          | 267          | 210          | 228          | 239         | 259          | 254          | 201         | 226       | N/S      |
| Anti-MRSA          | -            | -            | -            | -            | -            | -            | -            | -            | -            | -            | 265          | 271          | 249          | 244          | 276          | 342         | 247          | 301          | 233         | 334       | N/S      |
| **Total**          | -            | -            | -            | -            | -            | -            | -            | -            | -            | -            | 1043         | 1199         | 1230         | 1141         | 1275         | 1329        | 1219         | 1243         | 1108        | 1245      | N/S      |
| **Hospital B**     |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |          |          |
| Quinolones         | -            | -            | 378          | 420          | 370          | 354          | 250          | 220          | 114          | 110          | 108          | 161          | 155          | 156          | 141          | 195          | 177          | 161        | <0.001   |
| Cephalosporins     | -            | -            | 338          | 410          | 387          | 360          | 384          | 333          | 322          | 372          | 319          | 291          | 399          | 355          | 348          | 374          | 334         | 428       | N/S      |
| Macrolides         | -            | -            | 226          | 295          | 265          | 310          | 226          | 275          | 334          | 228          | 236          | 228          | 271          | 208          | 186          | 334          | 301         | 297       | N/S      |
| Anti-Pseudomonal   | -            | -            | 630          | 554          | 470          | 513          | 369          | 361          | 170          | 184          | 166          | 175          | 226          | 199          | 236          | 265          | 205         | 309       | * 0.001  |
| Anti-MRSA          | -            | -            | 294          | 267          | 224          | 361          | 276          | 221          | 229          | 307          | 246          | 264          | 296          | 338          | 322          | 252          | 256         | 324       | N/S      |
| **Total**          | -            | -            | 1750         | 1772         | 1623         | 1918         | 1492         | 1378         | 1334         | 1405         | 1259         | 1281         | 1526         | 1465         | 1436         | 1640         | 1513        | 1671      | N/S      |
| **Hospital C**     |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |          |          |
| Quinolones         | -            | -            | -            | -            | -            | -            | -            | -            | -            | -            | 137          | 131          | 141          | 122          | 182          | 147         | 129          | 133         | 150        | 141       | 128      |
| Cephalosporins     | -            | -            | -            | -            | -            | -            | -            | -            | -            | -            | 330          | 318          | 275          | 270          | 323          | 305         | 372          | 426         | 342        | 294       | 331      |
| Macrolides         | -            | -            | -            | -            | -            | -            | -            | -            | -            | -            | 372          | 324          | 305          | 273          | 259          | 280         | 227          | 205         | 259        | 206       | * <0.001 |
| Anti-Pseudomonal   | -            | -            | -            | -            | -            | -            | -            | -            | -            | -            | 174          | 134          | 213          | 176          | 161          | 175         | 167          | 183         | 183        | 202       | 200      |
| Anti-MRSA          | -            | -            | -            | -            | -            | -            | -            | -            | -            | -            | 306          | 434          | 371          | 366          | 511          | 336         | 399          | 389         | 360        | 282       | 258      |
| **Total**          | -            | -            | -            | -            | -            | -            | -            | -            | -            | -            | 1438         | 1448         | 1476         | 1352         | 1573         | 1484        | 1507         | 1498        | 1494       | 1292      | 1352     |
| **Hospital D**     |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |              |          |          |
| Quinolones         | 296          | 262          | 287          | 222          | 230          | 188          | 190          | 169          | 138          | 122          | 133          | 179          | 154          | 135          | 119          | 119          | 132          | 101        | * <0.001 |
| Cephalosporins     | 235          | 183          | 217          | 226          | 209          | 291          | 197          | 194          | 214          | 241          | 247          | 290          | 252          | 316          | 330          | 280          | 331         | 393       | * <0.001 |
| Macrolides         | 163          | 100          | 102          | 120          | 159          | 102          | 106          | 135          | 135          | 113          | 104          | 144          | 199          | 140          | 143          | 166          | 171         | 163       | * 0.029  |
| Anti-Pseudomonal   | 482          | 470          | 448          | 385          | 317          | 311          | 280          | 280          | 208          | 217          | 212          | 233          | 211          | 256          | 226          | 215          | 244         | 280       | * <0.001 |

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Table 5. Cont.

| Class            | Jan–Mar 2011 | Apr–Jun 2011 | Jul–Sept 2011 | Oct–Dec 2011 | Jan–Mar 2012 | Apr–Jun 2012 | Jul–Sept 2012 | Oct–Dec 2012 | Jan–Mar 2013 | Apr–Jun 2013 | Jul–Sept 2013 | Oct–Dec 2013 | Jan–Mar 2014 | Apr–Jun 2014 | Jul–Sept 2014 | Oct–Dec 2014 | Jan–Mar 2015 | Apr–Jun 2015 | p-Value |
|------------------|---------------|---------------|---------------|--------------|---------------|---------------|---------------|--------------|---------------|---------------|---------------|--------------|---------------|---------------|---------------|--------------|---------------|------------|
| **Hospital D**   |               |               |               |              |               |               |               |              |               |               |               |              |               |               |              |               |               |           |
| Anti-MRSA        | 275           | 300           | 296           | 275          | 300           | 296           | 275           | 300          | 296           | 275           | 300           | 296           | 275           | 300           | 296           | 275           | 300           | 296           | N/S       |
| Total            | 1282          | 1164          | 1136          | 1214         | 1090          | 1005          | 1038          | 1062         | 1373          | 1195          | 1277          | 1355         | 1159          | 1277          | 1353          | 1349        | 1353        | N/S       |
| **Hospital E**   |               |               |               |              |               |               |               |              |               |               |               |              |               |               |               |              |               |               |           |
| Quinolones       | -             | 624           | 580           | 537          | 584           | 406           | 372           | 250          | 226           | 168           | 152           | 281          | 237          | 195           | 218          | 251          | 204       | *<0.001    |
| Cephalosporins   | -             | 428           | 410           | 405          | 412           | 443           | 435           | 128          | 467           | 480           | 362           | 391          | 427          | 492           | 640          | 478          | 790          | 632          | 575       | *0.008    |
| Macrolides       | -             | 286           | 210           | 393          | 351           | 215           | 577           | 744          | 302           | 264           | 299          | 492          | 640          | 478           | 790          | 632          | 575          | 790          | 632       | N/S       |
| Anti-Pseudomonal | -             | 697           | 674           | 609          | 656           | 483           | 428           | 409          | 82            | 220           | 303          | 181          | 199          | 276           | 197          | 255          | 143          | 388          | *<0.001  |
| Anti-MRSA        | -             | 119           | 268           | 256          | 236           | 416           | 243           | 286          | 385           | 257           | 269          | 357          | 231          | 337           | 296          | 339          | 352          | 279          | N/S       |
| **Hospital F**   |               |               |               |              |               |               |               |              |               |               |               |              |               |               |               |              |               |               |           |
| Quinolones       | -             | -             | -             | -            | 328           | 419           | #             | 350          | 329           | 362           | 359           | 366           | 375          | 424           | 375          | 375          | 424          | 375          | 375       | N/S       |
| Cephalosporins   | -             | -             | -             | -            | 518           | 379           | #             | 760          | 460           | 520           | 523           | 516           | 494           | 619           | 572          | 533           | 423          | 487       | N/S       |
| Macrolides       | -             | -             | -             | -            | 215           | 179           | #             | 394          | 283           | 297           | 430           | 233           | 241           | 362           | 322          | 182           | 260          | 270       | N/S       |
| Anti-Pseudomonal | -             | -             | -             | -            | 305           | 431           | #             | 446          | 242           | 316           | 418           | 273           | 325           | 423           | 516           | 352           | 344          | 402       | N/S       |
| Anti-MRSA        | -             | -             | -             | -            | 288           | 347           | #             | 383          | 332           | 394           | 417           | 399           | 481           | 730           | 784          | 618           | 178          | 547       | N/S       |
| **Total**        | -             | -             | -             | -            | 1764          | 2006          | #             | 2161         | 1695          | 2130          | 2456          | 1975          | 2153          | 2934          | 2933          | 2171         | 1783        | 2253    | N/S       |

DDD/1000 PD, defined daily dose per 1000 patient-days; N/S, not significant; MRSA, methicillin-resistant Staphylococcus aureus; * Linear Regression: \( p \leq 0.05 \); Arrows indicate ASP start date for individual hospitals; # We were unable to calculate usage data for this quarter.
3.3. Antimicrobial Use

No hospital had a statistically significant change in total antimicrobial usage between their ASP start date and June 2015 (Table 5). Quinolone use decreased 57.4% in hospital B ($p = 0.001$), 65.9% in hospital D ($p < 0.001$), and 67.3% in hospital E ($p < 0.001$). Hospitals B, D, and E also had statistically significant decreases in anti-pseudomononal prescribing. No hospital had a statistically significant change in anti-MRSA prescribing rates. There were significant increases in cephalosporin use in hospitals A, D and E. Macrolide use decreased in hospitals C and D and increased in hospital E.

3.4. Antibiotic Susceptibility Profile

Only hospital D had enough isolates for statistical analysis. *P. aeruginosa* susceptibility was examined because this organism is a common nosocomial pathogen. Between 2011 and 2015, susceptibility of *P. aeruginosa* improved to ciprofloxacin (38% to 76%, $p = 0.13$), piperacillin-tazobactam (66% to 100%, $p = 0.05$), and meropenem (60% to 95%, $p = 0.06$) at hospital D (Table 6). In the same time period, *E. coli* susceptibility to ciprofloxacin improved from 38% in 2011 to 54% by 2015 ($p = 0.19$) (Table 6). There were no significant changes in rates of MRSA or *Clostridium difficile* infections at any of the facilities over the study period (data not shown).

### Table 6. Susceptibility rates for selected antimicrobials and organisms at hospital D by year.

| Antimicrobial       | 2011       | 2012       | 2013       | 2014       | 2015       | $p$-Value |
|---------------------|------------|------------|------------|------------|------------|-----------|
| *E. coli*           |            |            |            |            |            |           |
| Ciprofloxacin       | 16/51 (38%)| 28/56 (50%)| 19/55 (34%)| 26/44 (59%)| 23/42 (54%)| 0.19      |
| *P. aeruginosa*     |            |            |            |            |            |           |
| Ciprofloxacin       | 12/31 (38%)| 8/14 (57%) | 23/28 (82%)| 20/30 (66%)| 20/26 (76%)| 0.13      |
| Piperacillin/tazobactam | 20/30 (66%)| 21/24 (84%)| 20/27 (74%)| 27/30 (90%)| 23/23 (100%)| 0.05      |
| Meropenem           | 18/30 (60%)| 21/24 (84%)| 26/28 (92%)| 28/30 (93%)| 20/21 (95%)| 0.06      |

The numerator represents the number of organisms that were susceptible to the given antibiotic and the denominator is the total number of organisms tested. The number in parentheses is the percentage of the total number that were susceptible to the given antibiotic.

4. Discussion

In 2007, the IDSA and the Society for Healthcare Epidemiology of America (SHEA) released guidelines for developing institutional programs to better antimicrobial stewardship through use of the EMR [9]. VH has demonstrated long-term beneficial effects of an ASP and has used the EMR as a means of optimizing antimicrobial use [6,8]. This study is unique in that we can find no record of any hospital system using their EMR to remotely practice antimicrobial stewardship at community hospitals.

Following expansion of the ASP to the community hospitals, 40%–63% of charts reviewed resulted in a recommendation being made with an 81%–95% physician acceptance rate. None of these recommendations occurred before the ASP was extended remotely to the community hospitals. This method provides an option for antimicrobial stewardship for smaller community hospitals and shows that physicians are willing to accept ASPs remotely.
The most commonly accepted intervention noted is drug discontinuation. This was associated with an average antimicrobial drug cost savings of $20,860.25 per hospital for the 4 largest hospitals over an 18 month period from January 2014 through June 2015. Again, this does not take into account additional cost savings that occur when adverse events are avoided, drugs are changed IV to PO, patient outcomes are optimized, and antimicrobial resistance is avoided.

One of the main targets with each remote ASP was the reduction of quinolone use due to its increased risk for both Clostridium difficile infections (CDI) and MRSA infections [10,11]. Overall, we saw statistically significant decreases in quinolone use at hospitals B, D and E but did not see significant changes at hospitals A, C or F. This decrease in quinolone use may be a driving factor for the decrease in anti-pseudomonal drug usage as well. Two possible reasons why hospitals A and C did not experience decreases in quinolone use could be due to the fact that their quinolone use was considerably lower at the beginning of ASP implementation and because the ASP is newer at both of these hospitals.

Some hospitals did see an increase in cephalosporin use. This may be a result of implementation of a dose optimization protocol that attempted to maximize pharmacokinetic and pharmacodynamic properties for certain pathogens and patient populations. For example, all surgical cefazolin dosing was increased from 1 g to 2 g, empiric cefepime dosing for hospital acquired infections was increased from 1 g to 2 g every 12 h to 2 g every 8 h given by extended infusion, and ceftriaxone dosing was increased from 1 g to 2 g based on type of infection and patient specific parameters. While macrolide usage varied based on hospital, periodic analysis showed that most use of azithromycin is driven by the emergency department in the form of empiric sexually transmitted disease treatment or first dose for those not admitted to the hospital.

One important note to make is related to total antimicrobial use at each hospital. Overall, there was not a statistically significant decrease in total antimicrobial use at any of the community hospitals. The ASP does not review patients in the emergency department, those who come to the hospital daily for infusions, or those who are on antibiotics for less than the 24 h period it takes to flag on the report. However, all of this antimicrobial usage is included within the total usage reported. In addition, total usage includes antimicrobials that are not on the controlled list and that would never flag for ASP review.

The goal of ASPs is not only to reduce unnecessary use of antimicrobials, but also to improve resistance profiles. Because isolate numbers at each hospital were small, only hospital D’s isolate pool was large enough to analyze. There were improvements in antibiotic susceptibilities of P. aeruginosa to ciprofloxacin, piperacillin/tazobactam, and carbapenems over the four year time period.

Establishing a remote ASP is not without challenges. There can be variation in local resources including diagnostics and formulary. While the VH formulary is now standardized, there is still variation in what drugs are stocked by each pharmacy and there are currently no formulary restrictions at the community hospitals. Determining how to identify patients can also be a challenge and may have to be modified over time. Distinguishing cases that need stewardship assistance vs. a formal infectious diseases consult can also be a challenge.

Being a successful remote ASP does not stop with patient chart review. Continuing to develop relationships with the local staff (physicians, pharmacists, microbiology staff, and infection control practitioners) at the community hospitals is critical to improving patient care, as we view this as a team effort towards antimicrobial stewardship. The ASP pharmacists attempt to visit each community
hospital on a yearly basis in order to provide some face-to-face interaction, conduct educational opportunities desired by the pharmacy or physician staff, share results of the program, and gather feedback. This process also allows formal ASP introduction to any new or temporary staff. It is common for acceptance rates of new physicians to be low until they become comfortable with the advantages of the program. In addition to daily chart review, the ASP has been responsible for tasks including, but not limited to, helping manage antimicrobial shortages and formulary, creating order sets, answering questions for the local wound care centers, and distributing a guide book that is updated yearly and includes key information about managing infectious diseases.

There are several limitations to this study. First, this study is based on aggregate data; the impact of the duration of antimicrobial use for an individual patient cannot be determined. Second, this dataset cannot correct for seasonal variation. Each ASP was implemented at a different time, with the oldest program running for four years and the youngest running for only one year. Because of these limitations, there were currently not enough data points to properly analyze antimicrobial patterns over the course of a year. Third, because of the small hospital sizes and small number of bacterial isolates, there was limited data regarding improvements in hospital antibiograms.

5. Conclusions

Remote ASPs utilizing the EMR provide an excellent alternative to the creation of new ASPs at small community hospitals with limited resources. Our data show that antimicrobial recommendations can be made and accepted at community hospitals at high percentages. Our data also show that we can potentially alter prescribing habits, save money, and change susceptibility patterns at community hospitals remotely as well. Overall, we have demonstrated successful implementation of a remote ASP through use of the EMR at small community hospitals.

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Author Contributions

Z.H.W. performed the statistical analysis. N.A., N.C.N. and P.P.C. contributed extensively to the writing and editing of the manuscript, reviewed patient charts, and made stewardship recommendations.

Conflicts of Interest

Z.H.W., N.C.N. and N.A. have no disclosures or conflicts of interest.

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