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Assessments of Opportunities to Improve Antibiotic Prescribing in an Emergency Department: A Period Prevalence Survey

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3

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24 **Abstract**

25 **Introduction** Approximately 30% of all outpatient antimicrobials are inappropriately prescribed.
26 Currently, antimicrobial prescribing patterns in ED are not well described. Determining
27 inappropriate antimicrobial prescribing patterns and opportunity for interventions by antimicrobial
28 stewardship programs (ASP) are needed.

29 **Methods** A retrospective chart review was performed among a random sample of non-admitted,
30 adult patients that received an antimicrobial prescription in the ED from January 1, 2015 to
31 December 31, 2015. Appropriateness was measured using the Medication Appropriateness Index
32 (MAI), and was based on provider adherence to local guidelines. Additional information collected
33 included patient characteristics, initial diagnoses, and other chronic medication use.

34 **Results** Of 1,579 ED antibiotic prescriptions in 2015, we reviewed a total of 159 (10.1%)
35 prescription records. The most frequently prescribed antimicrobial classes included penicillins
36 (22.6%), macrolides (20.8%), cephalosporins (17.6%), and fluoroquinolones (17.0%). The most
37 common indications for antibiotics were bronchitis or upper respiratory tract infection (URTI)
38 (35.1%), followed by skin and soft tissue infection (SSTI) (25.0%), both of which were the most
39 common reason for unnecessary prescribing (28.9% of bronchitis/URTIs, 25.6% of SSTIs). Of
40 the antimicrobial prescriptions reviewed, 39% met criteria for inappropriateness. Among 78
41 prescriptions with a consensus on appropriate indications, 13.8% had inappropriate dosing,
42 duration, or expense.

43 **Conclusion** Consistent with national outpatient prescribing, inappropriate antibiotic prescribing
44 in the ED occurred in 39% of cases with the highest rates observed among patients with bronchitis,
45 URTI, and SSTI. Antimicrobial stewardship programs may benefit by focusing on initiatives for
46 these conditions among ED patients. Moreover, creation of local guideline pocketbooks for these

47 and other conditions may serve to improve prescribing practices and meet the Core Elements of
48 Outpatient Stewardship recommended by the Centers for Disease Control and Prevention.

49

50 **Keywords:** Antimicrobial, antimicrobial stewardship, emergency department

51

52

53 **Background**

54 Overuse of antimicrobials is a major driver of antimicrobial resistance which threatens the health
55 of people all over the world [1, 2]. On May 20th, 2017, antimicrobial resistance was recognized
56 and discussed at the Group of Twenty (G20) Summit by leaders from around the world. Together
57 with the World Health Organization, World Organization for Animal Health, and Food and
58 Agriculture Organization of the United Nations, the G20 is preparing a global report with three
59 recommendations: promote conservation of antimicrobials, optimize utilization as underuse, like
60 overuse, can contribute to antimicrobial resistance, and invest in innovations that can help bring
61 new antimicrobials, vaccines, and diagnostics to market [3]. Consistent with the first two
62 recommendations, antimicrobial stewardship programs (ASPs) have improved antimicrobial use
63 in hospitals through those interventions [4]. However, nearly two-thirds of antibiotic expenditures
64 occur in the outpatient setting, indicating an important area of need for antimicrobial stewardship
65 (AMS) [5, 6].

66

67 To improve antimicrobial use in outpatient settings, the Centers for Disease Control and
68 Prevention (CDC) recently released the Core Elements of Outpatient Stewardship [6]. These
69 recommendations include four elements: commitment to improving antibiotic prescribing and
70 patient safety, implementation of at least one policy or practice, tracking and reporting
71 antimicrobial prescribing practices, and providing education and expertise to clinicians and
72 patients on antimicrobial prescribing. These core elements are timely as calls to action for AMS
73 targeting emergency departments (ED) as part of the outpatient setting have gained interest [7, 8].
74 Prior to addressing the Core Elements of Outpatient Stewardship individually, the CDC
75 recommends identifying high priority indications (e.g. respiratory infections) for targeted

76 intervention. Overall, 1/3 of antibiotics in the outpatient setting, including EDs and outpatient
77 clinics, are inappropriately prescribed with respiratory tract infections attributing to the majority
78 of inappropriate prescriptions, yielding a significant area of opportunity for AMS [9, 10].
79 However, overall rates of inappropriate prescribing specific to ED settings are lacking in the US.
80 Therefore, the objective of this study was to determine rates of inappropriate antimicrobial use and
81 define specific areas of opportunity for AMS interventions in the ED.

82

83 **Methods**

84 *Setting and Patients*

85 The Providence Veterans Affairs Medical Center (PVAMC) is a 119-bed teaching hospital located
86 in Providence, Rhode Island. Patients included in this period prevalence study were a randomly
87 selected 10% sample of non-admitted patients 18 years of age or older, who were prescribed an
88 antimicrobial medication in the PVAMC ED and filled at the PVAMC pharmacy from January 1,
89 2015 to December 31, 2015. In 2012, the PVAMC implemented an ASP, in which the infectious
90 diseases pharmacy fellows provide prospective audit and feedback for admitted patients [11].
91 However, ED patients were not routinely monitored by the ASP during this study period.
92 Moreover, the ASP distributed an antimicrobial guidebook, but no specific interventions or
93 education had been provided to the emergency department on the use of the local guidelines before
94 or during this period.

95

96 *Data Collection and Assessment*

97 Data collection was performed by a clinical pharmacist and an internal medicine physician. Both
98 clinicians had complete access to the electronic medical records of the included patients. Specific

99 data collected included: patient demographics, encounter infectious diagnosis, temperature, white
100 blood cell count, antimicrobial prescribed (dose, route, duration), concomitant chronic
101 medications, and appropriateness of antibiotic prescribing based on chart assessment. Both the
102 clinical pharmacist and physician retrospectively assessed the appropriateness of antibiotic therapy
103 prescribed based on the documented diagnosis received in the ED for each patient.

104

105 Appropriateness was measured using the Medication Appropriateness Index (MAI) [12]. The MAI
106 is a validated tool that assesses the appropriateness of 10 different areas of medication prescribing:
107 indication, effectiveness, dosage (based on indication and renal function), directions, practicality,
108 drug-drug interactions, drug-disease interactions, duplication, duration, and expensiveness [13,
109 14]. For every prescribed medication, the reviewers answered each of the 10 questions in the MAI
110 with either A (appropriate), B (not clearly appropriate), or C (inappropriate). Assessments on the
111 appropriateness of therapy were made according to local antibiotic use guidelines summarized in
112 a guidebook tool (<http://web.uri.edu/antimicrobial-stewardship/>) which was derived from national
113 practice guidelines endorsed by the Infectious Diseases Society of America (IDSA) and/or CDC.
114 Study data were collected and managed using REDCap electronic data capture tools hosted within
115 the VA [15].

116

117 *Compliance with ethics guidelines*

118 This study was reviewed and approved by the Institutional Review Board and Research and
119 Development Committee of the Providence Veterans Affairs Medical Center. This article does not
120 contain any new studies with human or animal subjects performed by any of the authors.

121

122 *Data Analysis*

123 Descriptive statistics were used for patient characteristics, clinical presentation including
124 infectious diagnosis, characteristics of prescribed antibiotic (dose, duration, etc.), and MAI results.
125 MAI responses were categorized as appropriate (appropriate) and inappropriate (inappropriate or
126 not clearly appropriate) [16]. In calculating inappropriate prescribing rates, for a prescription to be
127 defined as inappropriate, it had to be categorized as such by consensus between the clinical
128 pharmacist and internal medicine physician. Kappa statistics for interrater reliability were
129 calculated for the overall MAI, each MAI category, and by infection type [17, 18].

130

131 **Results**

132 Of 1,579 ED-associated antibiotic prescriptions in 2015, we reviewed a total of 159 (10.1%)
133 prescription records for 148 patients, excluding 2 patients who were subsequently admitted during
134 the same visit. Patient characteristics and prescribing indications can be found in Table 1. The
135 median age was 60 and most patients were male (91.2%). Concomitant chronic medication use
136 was common (median 8, interquartile range 3-13). The most common indications for antibiotics
137 were bronchitis or upper respiratory tract infection (URTI, 35.1%), followed by skin and soft tissue
138 infection (SSTI, 25.0%). As reflected in Table 2, frequently prescribed antibiotics included
139 penicillins (22.6%), macrolides (20.8%), cephalosporins (17.6%), and fluoroquinolones (17.0%).

140

141 A summary of inappropriate prescribing based on MAI criteria is shown in Table 3. Thirty-nine
142 percent of antimicrobial prescriptions were classified as inappropriate. Inappropriate prescribing
143 varied by indication: bronchitis/URTI (15/52, 28.9%), SSTI (10/39, 25.6%), intra-abdominal
144 infections (15.0%; 3/20), community-acquired pneumonia (CAP, 3/9, 33.3%), urinary tract

145 infection (UTI, 2/8, 25.0%), and other conditions (4/14, 28.6%). Of the 79 (49.7.8%) prescriptions
146 with a consensus on appropriate indication, inappropriate prescribing was noted among 13.8% of
147 prescriptions with regards to dose, duration, or expense while the other MAI categories reflected
148 no inappropriate prescribing based on reviewer consensus. CAP and UTI dosing were found to be
149 inappropriate in 11.1% and 12.5% of cases, respectively. Inappropriate durations were found in
150 6.0% of bronchitis/URTI, 7.7% of SSTI, and 5.0% of intra-abdominal infections. Excessive
151 expense was noted in 11.1% of CAP, and only 2% of bronchitis/URTI.

152

153 Overall, interrater reliability of the MAI was high ($k=0.90$). The kappa statistics for indication,
154 dose, and duration were 0.46, 0.47, and 0.26, respectively. Though other MAI categories had high
155 positive agreement for appropriateness (median 85, IQR 79-98), kappa statistics could not be
156 calculated for these MAI categories due to the lack of negative agreement (determined as
157 inappropriate by both reviewers). Kappa scores by indication were also high, with a median of
158 0.82 (IQR 0.58 to 0.91).

159

160 **Discussion**

161 The present study reflects the first ED inappropriate prescribing assessment reported in the US,
162 with 39% of prescribing found to be inappropriate as defined by the Medication Appropriateness
163 Index and local guidelines. The two most common indications, SSTI and bronchitis/URTI also had
164 the highest rates of inappropriate prescribing (25.6% and 28.9%) aside from CAP where ~1/3 of
165 antibiotics were not indicated based on diagnostic criteria from a chart review. These results are
166 consistent CDC data which found ~1/3 of antibiotic prescriptions in the outpatient setting,
167 including outpatient clinics and EDs, as being inappropriate [9].

168

169 Similar to studies from outpatient clinic settings, we found an opportunity for AMS among patients
170 with a diagnosis of bronchitis or URTI patients with 28.9% of prescribing being inappropriate
171 based on indication [9, 10]. In our older population of Veterans, the prevalence of chronic
172 obstructive pulmonary disease (COPD) is more than double that of the general US population [19,
173 20]. Therefore, many of these patients may have had a history of COPD, and thus component of
174 COPD exacerbation requiring antibiotics. Our local guidance, concordant with national guidelines
175 for bronchitis and URTIs, infrequently recommends antibiotics since >90% of patients presenting
176 with a new onset cough for outpatient treatment have a virus [21].

177

178 To assist in diagnostic uncertainty for respiratory indications, rapid diagnostic testing, both
179 procalcitonin and respiratory viral panels, have been shown to help in decreasing inappropriate
180 antibiotic use among patients presenting with respiratory illnesses with possible infectious
181 etiologies [22, 23]. However, these technologies may be suboptimal in decreasing inappropriate
182 antibiotic use unless there is education and AMS guidance along with audit and feedback [24].
183 Future efforts should focus on how to optimize implementation of diagnostic testing within the ED
184 to increase appropriate use of antibiotics in patients with respiratory tract infections. Clinician
185 education has also been shown to be an effective intervention modality for decreasing
186 antimicrobial use in adults with acute respiratory infections treated in EDs [25].

187

188 Another important area of opportunity identified for improved prescribing was with SSTIs. We
189 found 25.6% of prescribing for SSTIs was inappropriate based on indication. Current national
190 guidelines recommend against the use of antibiotics for uncomplicated skin abscesses which have

191 undergone incision and drainage, yet this practice remains common [26, 27]. A study of the
192 National Hospital Ambulatory Medical Care Survey (NHAMCS) from 2007-2010 found that 87%
193 of visits for abscesses which had incision and drainage were still prescribed antibiotics [27].
194 Adaptation of and education on ED-specific national guidelines may encourage ED providers to
195 execute more judicious use [28].

196
197 While comprehensive assessments of inappropriate antibiotic prescriptions in the ED have not
198 been previously reported in the US, a recent study in France found that 59.9% (455/760) of
199 prescriptions in the ED were inappropriate [29]. This was higher than our observed 39% which
200 may be due to differences in patient populations, as well as national and local treatment guidelines.
201 Similar to our study however, they found high rates of inappropriate prescribing for respiratory
202 tract infections (46.5%), SSTIs (71.2%), and UTIs (38.4%). We also observed high inappropriate
203 prescribing for UTIs (37.5%). Education on optimal empiric treatments given high resistance to
204 therapies like fluoroquinolones has been shown to improve empiric prescribing [30, 31].

205
206 To date, there has been a single study reporting on a comprehensive AMS initiative in the ED [32].
207 This was a single center study at a 497-bed tertiary university hospital in France with about 35,000
208 ED visits per year. An intervention bundle was employed consisting of a 0.2 infectious diseases
209 (ID) physician full-time equivalent for advising during business hours, educating staff every 6
210 months on stewardship principles, creating a treatment guideline pocketbook, appointing an ED
211 antimicrobial champion to attend daily staff meetings and promote optimal antimicrobial use, and
212 reviewing ED antibiotic prescribing and culture results twice weekly by the ID physician.
213 Antimicrobials were prescribed in 769 visits during the pre-implementation period and 580 visits

214 in the post-implementation period. Prescriptions were not compliant with guidelines in 62.9% of
215 the pre- and 46.7% of the post-implementation visits ($p < 0.001$). Non-indicated prescriptions
216 decreased by 8.2% (< 0.001), while prescriptions with excessive duration decreased by 2.2% (non-
217 significant). The bundled intervention in this study consisted of various stewardship activities
218 which would be useful to address inappropriate antimicrobial prescribing in an ED. These
219 activities are also supported by a systematic review of AMS in outpatient settings [33].

220

221 Measuring inappropriate rates of antimicrobial prescribing is important, yet challenging [34]. A
222 recent study evaluating antimicrobial appropriateness with computerized case vignettes, as
223 reviewed by two infectious diseases physicians, demonstrated a kappa of 0.01 after initial
224 independent review, 0.34 after discussion of case disagreements, and 0.72 after uniform
225 application of institutional guideline criteria. In our initial pilot study, 50 randomly selected
226 patients were evaluated using national guidelines without a summary tool or local guidelines and
227 resulted in a lower overall interrater reliability ($k = 0.30$), hence the use of local guidelines
228 substantially improved our interrater reliability ($k = 0.90$). The importance of assessing antibiotic
229 appropriateness using local guidelines to decrease subjectivity and increase reproducibility of
230 assessments has been suggested elsewhere [35]. In fact, this is part of the CDC core elements for
231 outpatient stewardship's initial steps: establishing standards for antibiotic prescribing [6]. They
232 recommend to consider adapting national guidelines to establish clear expectations for appropriate
233 antibiotic prescribing.

234

235 There are several limitations to this study. Our study was a single center in a VA ED. Moreover,
236 given our sample size, outcomes of inappropriate prescribing were not assessed. Future

237 comprehensive assessments of inappropriate antibiotic prescribing in the ED should be evaluated
238 in community hospital settings to assess differences among non-Veteran populations and should
239 attempt to evaluate outcomes of inappropriate prescribing. Due to data collection limitations, this
240 study did not capture patients who did not fill their prescriptions at the PVAMC pharmacy.
241 Additionally, we only evaluated patients that were prescribed an antibiotic, indicating a potential
242 selection bias. The use of the kappa statistic limited our ability to calculate interrater reliability
243 for some MAI categories due to a lack of negative agreement (determined as inappropriate by
244 both reviewers), especially when there were high rates of appropriateness. We evaluated only
245 empiric prescribing and did not evaluate culture results, therefore our inappropriate rates of
246 antibiotic use are likely conservative. However, extensive literature on the value of AMS in
247 culture result follow-up reflects both the need and benefit of AMS in optimizing definitive
248 therapy and discontinuation of therapy in the absence of organism growth [36-40]. While our
249 local guidelines provided objective assessment criteria for many indications, they were not
250 exhaustive, and therefore, decisions on certain indications relied more heavily on clinical
251 judgement.

252

253 **Conclusion**

254 Consistent with national outpatient prescribing, inappropriate prescribing was identified in 39% of
255 antibiotic prescriptions in the ED with the highest rates among patients with bronchitis, URTI, and
256 SSTI. ASPs may benefit by focusing on initiatives for these conditions in the ED setting.
257 Moreover, creation of local guideline pocketbooks may improve prescribing practices, with these
258 activities together meeting the CDC recommended Core Elements of Outpatient Stewardship.

259

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280 ***Compliance with ethics guidelines***

281 This study was reviewed and approved by the institutional review board at our institution. This
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283 authors.

284 ***Data Availability***

285 The datasets generated and analyzed during the current study are available from the corresponding
286 author on reasonable request.

287 ***Open Access***

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405 **Table 1.** Patient characteristics

Characteristics	N = 148
Age (years), median (IQR)	60 (44-69)
Male	135 (91.2%)
White	125 (84.5%)
Temperature (C), median (IQR)	36.7 (36.5-37.0)
White blood cells (measurement), median (IQR) (n=64)	8.4 (6.5-11.2)
Concomitant medications, median (IQR)	8 (3-13)
Indication	
Bronchitis or URTI	52 (35.1%)
CAP	8 (5.4%)
COPD	5 (3.4%)
Flu	1 (0.7%)
Intra-abdominal	12 (8.1%)
Other	14 (9.5%)
Prophylaxis	7 (4.7%)
SSTI	37 (25.0%)
UTI	8 (5.4%)

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407 **Table 2.** Antimicrobials prescribed

Drug class	N=159
Antiviral	8 (5.0%)
Clindamycin	4 (2.5%)
Cephalosporin	28 (17.6%)
Fluoroquinolone	27 (17.0%)
Macrolide	33 (20.8%)
Metronidazole	8 (5.0%)
Penicillins	36 (22.6%)
Sulfonamide	4 (2.5%)
Other	11 (6.9%)

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410 **Table 3:** Inappropriate prescriptions by MAI category

MAI category	no. (%)
Indication	40 (25.2)
Effectiveness	0 (0)
Dosage	2 (1.3)
Correct directions	0 (0)
Drug-drug interaction	0 (0)
Drug-disease interaction	0 (0)
Practical directions	0 (0)
Expense	12 (7.5)
Duplication	0 (0)
Duration	8 (5.0)
Total	62 (39.0)

411 MAI, medication appropriateness index

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