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Original Article

Evaluation of uncomplicated acute respiratory tract infection management in veterans: A national utilization review

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Abstract

Background: Antibiotics are overprescribed for acute respiratory tract infections (ARIs). Guidelines provide criteria to determine which patients should receive antibiotics. We assessed congruence between documentation of ARI diagnostic and treatment practices with guideline recommendations, treatment appropriateness, and outcomes.

Methods: A multicenter quality improvement evaluation was conducted in 28 Veterans Affairs facilities. We included visits for pharyngitis, rhinosinusitis, bronchitis, and upper respiratory tract infections (URI-NOS) that occurred during the 2015–2016 winter season. A manual record review identified complicated cases, which were excluded. Data were extracted for visits meeting criteria, followed by analysis of practice patterns, guideline congruence, and outcomes.

Results: Of 5,740 visits, 4,305 met our inclusion criteria: pharyngitis (n = 558), rhinosinusitis (n = 715), bronchitis (n = 1,155), URI-NOS (n = 1,475), or mixed diagnoses (>1 ARI diagnosis) (n = 402). Antibiotics were prescribed in 68% of visits: pharyngitis (69%), rhinosinusitis (89%), bronchitis (86%), URI-NOS (37%), and mixed diagnosis (86%). Streptococcal diagnostic testing was performed in 33% of pharyngitis visits; group A *Streptococcus* was identified in 3% of visits. Streptococcal tests were ordered less frequently for patients who received antibiotics (28%) than those who did not receive antibiotics 44%; $P < .01$). Although 68% of visits for rhinosinusitis had documentation of symptoms, only 32% met diagnostic criteria for antibiotics. Overall, 39% of patients with uncomplicated ARIs received appropriate antibiotic management. The proportion of 30-day return visits for ARI care was similar for appropriate (11%) or inappropriate (10%) antibiotic management ($P = .22$).

Conclusions: Antibiotics were prescribed in most uncomplicated ARI visits, indicating substantial overuse. Practice was frequently discordant with guideline diagnostic and treatment recommendations.

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Acute respiratory tract infections (ARIs), including rhinosinusitis, pharyngitis, bronchitis, and common cold (URI-NOS), account for 30% of antibiotics prescribed in outpatient settings, yet viruses cause most ARIs.[1] Antibiotics are indicated for rhinosinusitis and pharyngitis if specific criteria are met.[1,2] Infectious Diseases Society of America (IDSA) guidelines for management of streptococcal pharyngitis recommend identifying suitable candidates for group A *Streptococcus* testing and only prescribing antibiotics for patients with positive results.[3] IDSA guidelines recommend antibiotic treatment for bacterial rhinosinusitis based on identifying constellations of signs and symptoms to determine probability of bacterial infection: prolonged symptom duration, worsening after initial improvement, or severe presentation.[4,5] When antibiotics are indicated, guidelines recommend penicillin or penicillin derivatives except for patients with a β-lactam allergy. Numerous sources recommend against routine antibiotic prescribing for acute bronchitis (unless pertussis is suspected) or URI-NOS.[2,6–7]

The Veterans Healthcare Administration (VHA) provides care to 7 million veterans nationwide through >150 VA medical centers (VAMCs). In 2014, the VHA required each VAMC to implement an antimicrobial stewardship program (ASP). Many VAMCs developed robust inpatient ASPs[8]; however, most antibiotics are prescribed in the outpatient setting.[9] Antibiotic prescriptions for uncomplicated ARIs increased within the VHA between 2005 and 2012, and azithromycin was the leading antibiotic prescribed.[10]

The VA Center for Medication Safety (VAMedSAFE) is tasked with evaluating and promoting safe and effective drug therapy within VHA by performing medication utilization evaluations (MUEs). An MUE is a systematic, criteria-based quality improvement analysis of medication or disease(s) designed to improve patient outcomes.[11] VAMedSAFE previously partnered with the VA Antimicrobial Stewardship Task Force to conduct MUEs to monitor and improve antibiotic therapy for pneumonia and urinary tract infections.[8,12,13]

The purpose of the present MUE was to evaluate ARI diagnostic and treatment appropriateness and to inform development of a VHA-wide campaign to improve ARI management. Our objectives were (1) to determine frequency of appropriate antibiotic management (ie, appropriately withholding or initiating antibiotic therapy based on documentation of clinical and diagnostic criteria) congruent with published guidelines, and (2) to compare relevant outcomes between those who did and did not receive appropriate antibiotic management.

Methods

VAMedSAFE created a retrospective cohort of patient visits from veterans with an outpatient ARI diagnosis from 28 VAMCs that volunteered to participate in the MUE. The first eligible visit for each patient during the evaluation period was included. Diagnoses were identified by *International Classification of Diseases Tenth Edition, Clinical Modification* (ICD-10 CM) codes for acute rhinosinusitis, pharyngitis, bronchitis, or URI-NOS for visits occurring between October 1, 2015, and March 30, 2016 (see Supplementary Appendix A online).[14] Visits were excluded for the following reasons: complete lack of ARI symptom or treatment documentation, resolved ARI on visit date, hospitalization within 1 day after visit, antecedent ARI within 30 days, chronic sinusitis or pharyngitis, concurrent non-ARI infection requiring antibiotics, antibiotic self-treatment or chronic antibiotic use. Furthermore, we excluded patients with certain comorbidities: chronic lung disease (COPD), end-stage renal disease, active neoplasm, marrow or organ transplantation, HIV, and other immunocompromising conditions. Prescription for an oral antibiotic dispensed from the VHA <2 days before or <3 days after the encounter was attributed to the visit.[10]

Potential cases were extracted from electronic data using inclusion criteria by VAMedSAFE from the VHA Corporate Data Warehouse (CDW) in collaboration with the Informatics Decision Enhancement and Analytic Sciences Center (IDEAS 2.0).[15] Exclusions based on ICD-10 codes and prescription data, select patient demographics, comorbidities, and 30-day all-cause hospitalization were extracted as well. Local reviewers, blinded to specific ARI diagnoses, were provided lists of ≤250 visits per facility. These reviewers (antibiotic stewards and trainees) performed a manual review of electronic health records to confirm and/or extract inclusion and exclusion criteria, signs and symptoms, provider indicated diagnoses, laboratory test results, antibiotics(s) prescribed, and outcomes. Data abstraction protocol, case report form, and monthly teleconferences facilitated standardized data collection (Supplementary Appendix B online). Completed cases were uploaded to a VAMedSAFE database for integration and analysis.

Indications for antibiotic initiation and definitions of appropriate therapy were adapted from guideline recommendations.[2–7] For pharyngitis, penicillin, and amoxicillin were appropriate first-line therapies for patients with a positive rapid antigen detection test (RADT) or a throat culture positive for group A, C, or G *Streptococcus*.[3] First-generation cephalosporins, clindamycin, or macrolides were appropriate second-line therapies for patients with penicillin allergy. For rhinosinusitis, amoxicillin/clavulanate or amoxicillin were considered appropriate first-line therapies in patients with purulent nasal discharge and/or facial pain/pressure/fullness plus one of the following: prolonged (≥7 days), severe (temperature ≥38.9°C [102°F] for >2 days), or worsening symptoms after ≥4 days.[4,5] Tetracyclines, moxifloxacin, or levofloxacin were appropriate second-line therapies for patients with penicillin allergy. For acute bronchitis, azithromycin or trimethoprim/sulfamethoxazole therapy (in case of macrolide allergy) was considered appropriate if the provider documented suspicion of pertussis exposure or performed pertussis testing.[6,7] For URI-NOS, antibiotic therapy was considered inappropriate.[2] Based upon ARI diagnosis, documentation of diagnostic criteria, antibiotic initiation, and antibiotic selection, antibiotic management for each case was classified as appropriate or inappropriate. Visits with mixed ARIs (>1 simultaneous ARI diagnosis) or those with a "delayed prescription" filled outside the 3-day postvisit window were excluded from the appropriate management and outcomes assessments.

Demographics, signs, symptoms, diagnostics, antibiotics prescribed, and outcomes were compared with descriptive statistics, parametric tests, or nonparametric tests as indicated. A 2-tailed *P* value <.05 was considered significant. We used SAS^R version 9.4 software (SAS Institute, Cary NC) for these analyses.Outcomes were reported based upon appropriate and inappropriate antibiotic management classifications.

Based on the *VA Policy Handbook* guideline1058.05, which defines operations activities that constitute research, the Hines VA Institutional Review Board deemed this evaluation to be a quality improvement project and to be exempt from VA Human Subjects Research requirements.[16] Data use agreements were signed by all participating sites.

Results

Of the visits reviewed, 4,305 of 5,740 (75%) met criteria for assessment of diagnosis, and 3,884 of 5,740 (68%) met our criteria for assessment of antibiotic management appropriateness and

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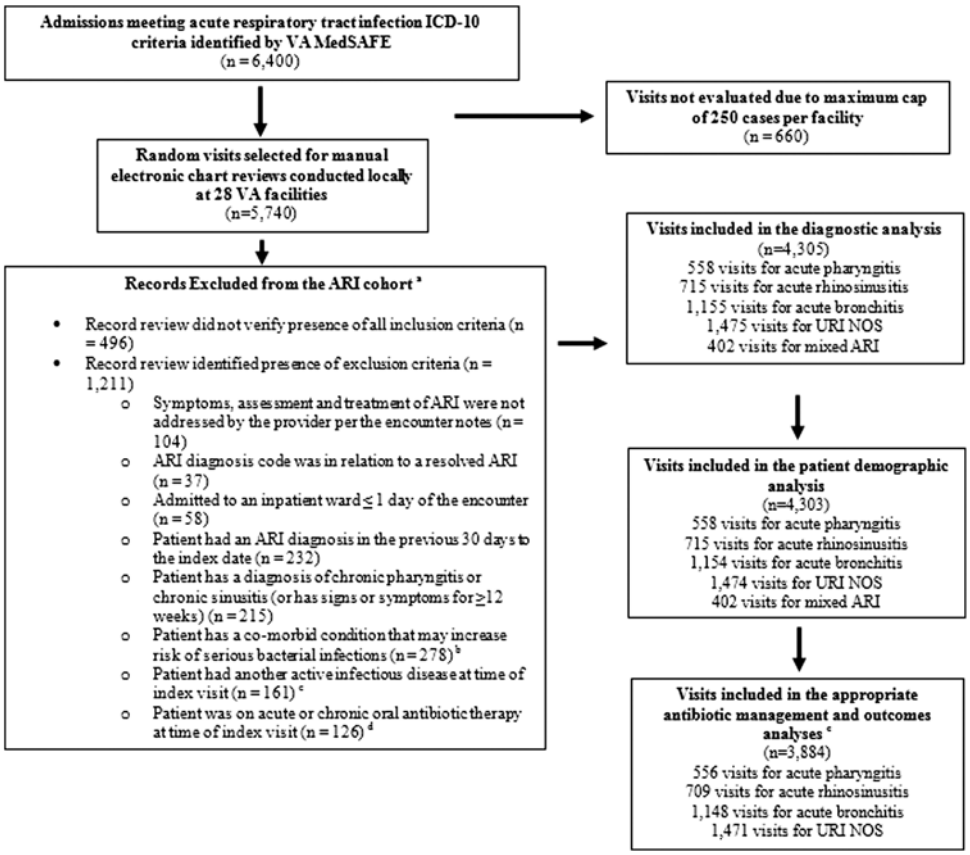

Fig. 1. Application of inclusion and exclusion criteria for acute respiratory tract infection (ARI) management evaluation. [a]Visits may have met >1 criteria resulting in exclusion or preventing inclusion. [b]Comorbid conditions include neoplasia, chronic lung disease (eg, COPD, asthma), end-stage renal disease, solid organ transplantation, or other immunocompromised state (Supplementary Appendix A online). [c]Other infectious diseases not excluded: concurrent hepatitis, genital herpes, or superficial (cutaneous) fungal infections. [d]Visits were not excluded if antibiotic agent was prescribed by a provider ≤2 days prior to the encounter if the antibiotic was for ARI signs or symptoms. [e]Patients with mixed ARI diagnoses, delayed antibiotic prescriptions, or with missing antibiotic prescription data were excluded from the appropriate antibiotic management and outcomes analyses.

outcomes (Fig. 1). Most patients were male and middle-aged, with limited comorbidity (Table 1). Few patients exhibited abnormal vital signs. Overall, 2,897 of 4,285 patients with uncomplicated ARIs (68%) received antibiotics. Recipients were more likely male, smokers, and to have been seen in the emergency department than antibiotic nonrecipients. Mid-level providers prescribed antibiotics more often than staff physicians, and medical trainees prescribed antibiotics less often than staff physicians or mid-level providers.

Of 715 patients diagnosed with rhinosinusitis, 567 (79%) had documentation of purulent nasal discharge and/or facial pain, pressure, or fullness upon presentation (Table 2). Of those 567 patients, 216 (38%) had documentation of additional criteria for antibiotic therapy, predominantly prolonged symptoms (≥7 days). Antibiotics were prescribed in 633 of 709 rhinosinusitis visits eligible for evaluation (89%); of these 633, 203 (32%) met complete diagnostic criteria for antibiotic therapy. When antibiotics were prescribed, 389 of these 633 patients (61%) received first-line antibiotics and 66 (10%) received second-line antibiotics. The remaining 178 patients (28%) received nonrecommended antibiotics. Based on chart documentation of rhinosinusitis symptoms, antibiotic selection, and appropriately withheld antibiotics, 226 of 709 patients (32%) received appropriate antibiotic management.

Of 558 patients with a pharyngitis diagnosis, 432 (77%) lacked Centor score component documentation or had Centor scores <2, indicating that few patients met streptococcal testing recommendations (Table 2).[17] Furthermore, β-hemolytic *Streptococcus* testing was performed in 185 of 558 visits (33%) and was more likely to be performed for patients with ≥2 Centor criteria (ie, 53 of 126 patients, 42%) than those with <2 criteria (ie, 13 of 432 patients, 31%; $P \leq .02$). Overall, 17 of 558 patients diagnosed with pharyngitis (3%) had a positive test for group A *Streptococcus*. Antibiotic therapy was prescribed to 384 of 556 patients with pharyngitis eligible for evaluation (69%); of these 384, 102 (27%) had ≥2 Centor criteria documented, indicating a likelihood of streptococcal pharyngitis high enough to warrant testing. Of the 384 patients with pharyngitis prescribed antibiotics, 147 (38%) received first-line therapy, 123 (32%) received second-line therapy, and 34 (9%) that received antibiotics had a documented penicillin allergy. Streptococcal tests were ordered less frequently for patients who received antibiotics (ie, 108 of 185, 28%) than those who did not receive antibiotics (ie, 77 of 185, 44%; $P < .01$). Based on evidence of β-hemolytic streptococcal infection, antibiotic selection, and appropriately withheld antibiotics, of 556 patients with pharyngitis eligible for evaluation, 194 (35%) received appropriate antibiotic management of pharyngitis.

Of 1,154 patients with an acute bronchitis diagnosis, 7 (<1%) had documentation of concern for pertussis exposure, confirmed exposure, or infection. These patients underwent diagnostic testing, but none tested positive for pertussis. Antibiotics were prescribed in 990 of 1,148 acute bronchitis visits eligible for evaluation (86%); among them, azithromycin was prescribed to 614 patients (62%). Based on chart documentation of pertussis concerns and appropriately withheld antibiotics, 159 of these 1,148 patients (14%) received appropriate antibiotic management for acute bronchitis. Antibiotics were prescribed to 550 of 1,471 patients (37%) eligible for evaluation and diagnosed with URI-NOS; among these 550, 330 (60%) received primarily azithromycin. Based on the proportion of patients who received antibiotics, 924 of 1,471 patients diagnosed with URI-NOS (63%) received

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Table 1. Patient Demographic, Provider, and Treatment Setting Characteristics

Characteristic	All Patients[a] (n = 4,303), No. (%)	Antibiotics Prescribed (n = 2,907), No. (%)	No Antibiotics Prescribed (n = 1,396), No. (%)	*P* Value[b] or Significance
Age, mean y (±SD)	50 (16)	50 (16)	49 (16)	.08
Male	3,564 (83)	2,449 (84)	1,114 (80)	**<.01**
Current smoker	1,117 (26)	839 (29)	278 (20)	**<.01**
β-lactam allergy	517 (12)	364 (13)	153 (11)	.15
Vital signs				
Temp. >38.3°C (101°F)	29 (<1)	21 (<1)	8 (<1)	.69
HR > 90 beats/min	1,129 (26)	758 (26)	371 (27)	.74
RR > 20 breaths/min	97 (2)	73 (3)	24 (2)	.12
Comorbidity[c]				
No comorbidities	3,979 (92)	2,673 (92)	1,304 (93)	Ref
1 comorbidity	270 (6)	191 (7)	79 (6)	1.2 (0.9,1.5)
≥2 comorbidity	56 (1)	43 (2)	13 (<1)	1.6 (0.9,3)
Treating provider[d]				
Staff physician provider	2,999 (70)	2,101 (70)	898 (30)	Ref
Mid-level provider	857 (20)	632 (74)	225 (26)	1.2 (1.0,1.4)
Medical trainees	351 (8)	117 (33)	234 (67)	0.2 (0.2,0.3)
Other provider	94 (2)	55 (59)	39 (42)	0.6 (0.4,0.9)
Treatment setting[e]				
Emergency department	2,218 (52)	1,570 (71)	648 (29)	Ref
Urgent care clinic	640 (15)	417 (65)	223 (35)	0.8 (0.6,0.9)
Primary care clinic	1,356 (32)	880 (65)	476 (35)	0.8 (0.7,0.9)
Other outpatient clinic	89 (2.0)	40 (45)	49 (55)	0.3 (0.2,0.5)

Note. HR, heart rate; RR, respiratory rate; OR, odds ratio; CI, confidence interval.
[a]Not all observations for each variable were recorded resulting in missing data for select characteristics. Two patients lacked antibiotic prescribing information documented (n = 4,303). Due to rounding, all percentages may not add up to 100%.
[b]Reported *P* values compare patients with antibiotics prescribed and patients with no antibiotics prescribed. Bold indicates significance.
[c]Comorbidities evaluated renal disease, diabetes, liver disease, chronic heart failure, and history of cerebrovascular accident/transient ischemic attack. Two patients in the "no comorbidities" category did not have documentation indicating whether antibiotics were prescribed recorded (n = 3,977). Significance is reported as the odds ratio (OR ± 95% CI) of receiving an antibiotic with "no comorbidities" as the reference group.
[d]Mid-level providers included physician assistants and nurse practitioners. Other providers included nonphysician trainees, nurses, pharmacists, or providers who were unidentifiable. Four patients did not have a type of provider recorded (n = 4,301). Significance is reported as the odds ratio (OR ±95% CI) of receiving an antibiotic with staff physician provider as the reference group.
[e]Other outpatient clinic included Women's clinic and select community-based outreach clinics (CBOC). Two patients did not have a treatment setting recorded (n = 4,303). Significance is reported as the odds ratio (OR ± 95% CI) of receiving an antibiotic with "emergency department" as the reference group.

appropriate antibiotic management. In total, 1,497 of 3,884 patients diagnosed with uncomplicated ARIs (39%) received appropriate antibiotic management.

After removal of visits with mixed diagnoses and delayed prescriptions, for 704 of 3,884 visits (18%), follow-up encounters (in person or by phone) related to the initial ARI visit had been recorded. Patient outcomes were assessed among 2 axes: patients who did or did not initially receive antibiotics (Table 3) and patients who did or did not receive appropriate antibiotic management (Table 4). Among patients who did (457 of 2,552, 18%) or did not (247 of 1,332, 19%) initially receive antibiotics, there was no difference in the frequency of additional encounters ($P = .65$). However, patients with rhinosinusitis who did not receive antibiotics (22 of 79, 28%) more commonly had a subsequent ARI-related encounter than patients who did receive antibiotics (106 of 630, 17%; $P = .02$). Patients who did not receive antibiotics in the initial encounter were more likely to receive an antibiotic during a subsequent encounter (84 of 1,332 [6%] vs 105 of 2,552 [4%]; $P < .01$), especially for patients with an initial diagnosis of acute bronchitis (12 of 158 [8%] vs 39 of 990 [4%]; $P = .04$) or URI-NOS (58 of 921 [6%] vs 19 of 550 [4%]; $P = .02$). Also, 30-day *Clostridium difficile* infection (2 of 3,884, <1%) and 30-day hospitalization (33 of 3,884, 1%) were uncommon and did not differ based on receipt of an antibiotic during the initial ARI visit.

Appropriate and inappropriate antibiotic management assessment revealed few differences in patient outcomes (Table 4). ARI-related return encounters were similar for patients who received appropriate (288 of 1,497, 19%) versus inappropriate initial antibiotic management (416 of 2,387, 17%; $P = .15$). However, patients who received initial appropriate management were more likely to receive an antibiotic during a return encounter (93 of 1,497, 6%) than those who received inappropriate initial management (96 of 2,387, 4%; $P < .01$). Patients who had antibiotics appropriately withheld were less likely to have a return encounter or patient initiated phone call than patients with antibiotics inappropriately withheld: 239 of 1,314 (18%) versus 8 of 18 (44%; $P < .01$) and 35 of 1,314 (3%) versus 2 of 18 (11%; $P = .03$), respectively. Conversely, patients who had antibiotics appropriately initiated were more likely to have a return encounter or to initiate a follow-up phone call than patients who had antibiotics inappropriately initiated:

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Table 2. Documentation of Diagnostic Criteria for Antibiotic Therapy in Patients With a Diagnosis of Rhinosinusitis or Pharyngitis[a]

Acute rhinosinusitis symptoms				
Characteristic	All Patients, No. (%)	Received Antibiotics, No. (%)	Did not Receive Antibiotics, No. (%)	*P* Value[b]
All patients	715 (100)	633 (89)	82 (12)	. . .
Patients with ≥1 of the following rhinosinusitis symptoms or treatment criteria	567 (79)	507 (80)	60 (73)	.15
Purulent nasal discharge	144 (20)	134 (21)	10 (12)	.06
Facial pain, pressure, or fullness	443 (62)	396 (63)	47 (57)	.36
Prolonged >7 d[c]	284 (40)	262 (41)	22 (27)	**.01**
Worsening after >4 d[c]	41 (6)	38 (6)	3 (4)	.39
Severe, fever >38.9°C (102°F)[c]	2 (<1)	2 (<1)	0 (<1)	.61
Antibiotic prescribing symptoms criteria met[d]	216 (30)	203 (32)	13 (16)	**<.01**
Acute pharyngitis symptoms				
Characteristic	All Patients, No. (%)	Received Antibiotics, No. (%)[b]	Did Not Receive Antibiotics, No. (%)[b]	*P* Value[c]
All patients	558 (100)	384 (69)	174 (31)	. . .
Centor criteria score[e]				
0 or not documented	213 (38)	134 (35)	79 (49)	**.02**
1	219 (39)	148 (31)	71 (41)	.61
2	96 (17)	76 (20)	20 (12)	**.02**
3	30 (6)	26 (7)	4 (2)	**.03**
4	0 (0)	0 (0)	0 (0)	. . .
0–1 Centor criteria documented	432 (77)	282 (73)	150 (86)	**<.01**
≥2 Centor criteria documented	126 (23)	102 (27)	24 (14)	**<.01**
No RADT or throat culture	373 (67)	276 (72)	97 (56)	**<.01**
RADT or throat culture obtained	185 (33)	108 (28)	77 (44)	**<.01**
≥2 Centor criteria documented and RADT or throat culture	53 (10)	38 (10)	15 (9)	.63
Total RADT and throat cultures positive[f]	33 (6)	28 (7)	5 (3)	**.04**
Group A *Streptococcus*	17 (3)	14 (4)	3 (2)	.22
Group C or G *Streptococcus*	8 (1)	7 (2)	1 (1)	.25

Note. RADT, rapid antigen detection test.
[a]Due to rounding, all percentages may not add up to 100%.
[b]Reported *P* values compared patients with antibiotics prescribed and patients with no antibiotics prescribed. Bold indicates significance.
[c]Symptoms categorized as prolonged, worsening, or severe could have been rhinosinusitis symptoms or nonrhinosinusitis symptoms.
[d]Antibiotic prescribing symptoms criteria met based on documentation of purulent nasal discharge and/or facial pain or pressure AND any combination of prolonged symptoms, severe criteria, or worsening criteria was used to define antibiotic prescribing criteria.
[e]The Centor criteria is a 4-point scale. Patients get a point for each of the following criteria they meet: temperature ≥38.3°C (101°F), enlarged cervical nodes, tonsillar exudate, and absence of cough.[17]
[f]Throat cultures were considered positive if there was growth of group A, C, or G *Streptococcus* reported.

54 of 230 (24%) versus 403 of 2,322 (17%; $P = .02$) and 12 of 230 (5%) versus 69 of 2,322 (3%; $P = .06$), respectively. No difference in outcomes based on appropriate or inappropriate antibiotic selection was observed. Finally, no difference in rates of *C. difficile* infection or hospitalization between antibiotic recipients and nonrecipients, or differences related to the appropriateness of antibiotic management, was observed.

Discussion

This cross-sectional MUE generated a number of noteworthy observations. First, an excessive proportion of patients with uncomplicated ARIs were treated with antibiotics. Antibiotics were given to ~67% of patients, whereas we found full justification for antibiotic therapy in ~10% of visits. Also, a chart-level review of rhinosinusitis and pharyngitis diagnostic documentation identified limited congruence with guideline recommended criteria for antibiotic treatment. Whereas 89% of patients diagnosed with rhinosinusitis received antibiotics, <33% had documented diagnostic criteria for treatment, suggesting that many patients may have received unnecessary antibiotics. In addition, <25% of pharyngitis cases had documentation of ≥2 Centor criteria, the recommended threshold for performing streptococcal diagnostic testing. Testing was performed in ~33% of cases, and providers were more likely to test patients meeting the recommended testing threshold. Antibiotics were prescribed less frequently in patients who underwent testing for β-hemolytic *Streptococcus* than those not tested, suggesting that improvements in testing could lower antibiotic

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Table 3. Follow-Up Outcomes for Patients with Uncomplicated Acute Respiratory Tract Infections (ARIs)[a]

	All Patients			Acute Pharyngitis			Acute Rhinosinusitis			Acute Bronchitis			URI-NOS		
Outcome	Antibiotic Prescribed, No. (%)	Antibiotic Withheld, No. (%)	*P* Value	Antibiotic Prescribed, No. (%)	Antibiotic Withheld, No. (%)	*P* Value	Antibiotic Prescribed, No. (%)	Antibiotic Withheld, No. (%)	*P* Value	Antibiotic Prescribe, No. (%)	Antibiotic Withheld, No. (%)	*P* Value	Antibiotic Prescribed, No. (%)	Antibiotic Withheld, No. (%)	*P* Value
Total	2552 (100)	1332 (100)		382 (100)	174 (100)		630 (100)	79 (100)		990 (100)	158 (100)		550 (100)	921 (100)	
Unique ARI-related return encounter	457 (18)	247 (19)	.63	71 (19)	34 (20)	.79	106 (17)	22 (28)	**.02**	198 (20)	35 (22)	.53	82 (15)	156 (17)	.31
30-d ARI-related return visit	248 (10)	146 (11)	.22	37 (10)	18 (10)	.81	57 (9)	9 (11)	.50	108 (11)	20 (13)	.52	46 (8)	99 (11)	.14
Unresolved/worsening symptoms	185 (7)	116 (9)	.10	31 (8)	13 (8)	.79	40 (6)	9 (11)	.10	80 (8)	17 (11)	.26	34 (6)	77 (8)	.13
Infectious complication	7 (<1)	3 (<1)	.77	1 (<1)	1 (1)	.57	1 (<1)	0 (<1)	.72	3 (<1)	0 (<1)	.49	2 (<1)	2 (<1)	.60
Antibiotic prescribed	105 (4)	84 (6)	**<.01**	18 (5)	11 (6)	.43	29 (5)	3 (4)	.75	39 (4)	12 (8)	**.04**	19 (4)	58 (6)	**.02**
Telephone	260 (10)	122 (9)	.31	45 (12)	21 (12)	.92	56 (9)	15 (19)	**<.01**	115 (12)	21 (13)	.55	44 (8)	65 (7)	.50
Patient initiated	81 (3)	37 (3)	.49	15 (4)	4 (2)	.33	15 (2)	3 (4)	.45	37 (4)	6 (4)	.97	14 (3)	24 (3)	.94
30-d *C. difficile* infection	1 (<1)	1 (<1)	.64	0 (<1)	0 (<1)	. . .	0 (<1)	0 (<1)	. . .	0 (<1)	0 (<1)	. . .	1 (<1)	1 (<1)	.71
30-d hospitalization	25 (1)	8 (<1)	.22	8 (2)	0 (<1)	**.05**	4 (<1)	0 (<1)	.48	8 (1)	0 (<1)	.26	5 (1)	8 (1)	.94

[a]Due to rounding, all percentages may not add up to 100%.

Table 4. Outcomes Associated with Appropriate and Inappropriate Antibiotic Management of Uncomplicated Acute Respiratory Tract Infections (ARIs)[a]

	Overall Management[b]			Antibiotics Withheld			Antibiotics Initiated			Antibiotic Selection[c]		
Outcome	Appropriate, No. (%)	Inappropriate, No. (%)	*P* Value	Appropriate, No. (%)	Inappropriate, No. (%)	*P* Value	Appropriate, No. (%)	Inappropriate, No. (%)	*P* Value	Appropriate, No. (%)	Inappropriate, No. (%)	*P* Value
Total	1497 (100)	2387 (100)		1314 (100)	18 (100)		230 (100)	2322 (100)		165 (100)	65 (100)	
Unique ARI-related return encounter	288 (19)	416 (17)	.15	239 (18)	8 (44)	<**.01**	54 (24)	403 (17)	**.02**	41 (25)	13 (20)	.43
30-day ARI-related return visit[d]	163 (11)	231 (10)	.22	142 (11)	4 (22)	.12	24 (10)	224 (10)	.70	17 (10)	7 (12)	.92
Unresolved/Worsening symptoms	127 (9)	174 (7)	.18	113 (9)	3 (17)	.23	17 (7)	168 (7)	.93	11 (7)	6 (9)	.50
Infectious complication	3 (<1)	7 (<1)	.58	3 (<1)	0 (<1)	.84	0 (<1)	7 (<1)	.40	0 (<1)	0 (<1)	NA
Antibiotic prescribed	93 (6)	96 (4)	<**.01**	82 (6)	2 (11)	.40	12 (5)	93 (4)	.38	9 (6)	3 (5)	.80
Telephone	149 (10)	233 (10)	.84	116 (9)	6 (33)	<**.01**	35 (15)	225 (10)	**.01**	27 (16)	8 (12)	.44
Patient initiated	44 (3)	74 (3)	.78	35 (3)	2 (11)	**.03**	12 (5)	69 (3)	.06	7 (4)	5 (8)	.29
30-d *C. difficile* infection[e]	1 (<1)	1 (<1)	.74	1 (<1)	0 (<1)	.91	0 (<1)	1 (<1)	.75	0 (<1)	0 (<1)	NA
30-d hospitalization	9 (1)	24 (1)	.18	8 (1)	0 (<1)	.74	2 (1)	23 (1)	.86	1 (<1)	1 (2)	.49

[a]Due to rounding, all percentages may not add up to 100%.
[b]Overall management was deemed appropriate if antibiotics were appropriately withheld or if antibiotics were appropriately initiated and the appropriated antibiotic was selected.
[c]Selection of antibiotic was only evaluated as appropriate or inappropriate if the patient's antibiotic was appropriately initiated. Since initiation and thus, selection, of antimicrobials is never appropriate for URI-NOS, patients in the URI-NOS were only included in the appropriate overall management group.
[d]ARI-related return visits included urgent care, emergency department, and primary care return visit.
[e]30-d *C. difficile* infection defined as positive toxin assay 30 d after index visit. Patients with a positive toxin assay 30 d prior and after the index visit were excluded.

prescribing. Although antibiotics were prescribed in ~67% of patients with pharyngitis, only 5% of patients tested positive for β-hemolytic *Streptococcus*. Of the patients treated, <33% received penicillin or amoxicillin.

Furthermore, documentation of suspected pertussis exposure and testing was rare, and the proportion of acute bronchitis cases treated with antibiotics was high. Only 7 documented cases of suspected exposure to pertussis occurred with no confirmed cases. Nonetheless, 86% of patients with acute bronchitis received antibiotics. Similarly, >33% of patients with URI-NOS, a condition for which antibiotics are never indicated, were treated with antibiotics. In addition, detailed assessments of patient outcomes relative to initial receipt of antibiotics indicated similar proportions of ARI-related return visits and low frequency of complications, *Clostridium difficile* infections, and hospitalizations. Patients who did not receive antibiotics during their initial encounter were more likely to receive them during a subsequent encounter; however, the overall frequency of subsequent visits with antibiotics prescribed was low. Although there were few differences in outcomes for patients who received or did not receive appropriate antibiotic management, patients who had antibiotics inappropriately withheld were more likely to seek follow-up care. Finally, patients who had antibiotics appropriately initiated were more likely to receive follow-up care than patients for whom antibiotics were inappropriately initiated. We were unable to ascertain the reason for this because there were no differences in worsening symptoms or infectious complications between these groups.

A strength of this analysis includes the systematic removal of complicated ARI cases through extraction from the CDW, which was confirmed by manual chart review. The manual chart review identified small numbers (ie, 278 of 5,740, 5%) of additional patients with significant pulmonary and immunological comorbidity (Fig. 1), conditions where antibiotic use might be justified, verifying that the combination of diagnostic coding and recent prescription of select medications (Supplementary Appendix A online) applied to electronic records was effective at identifying patients with comorbidity. Even though not all exclusions were identified by the algorithm, manual records review identified the remaining cases not meeting uncomplicated ARI criteria. The manual records review also facilitated collection of information on documentation of clinical diagnostic criteria and verification of outcomes. These data, which were not retrievable through CDW databases, were used to conduct a detailed assessment of appropriate antibiotic management and clinical endpoints.

This analysis has several limitations. The VHA population is predominantly male, and not all veterans receive care exclusively through the VHA, with most visits occurring in the emergency department. Some excluded cases identified through manual chart review indicated prior encounters that occurred outside the VHA, and it is possible that not all comorbidities were documented within the VHA record, which could have impacted the accuracy of appropriate antibiotic management estimates. Furthermore, the analysis excluded clinics without VHA pharmacy services for dispensing acute medications (ie, community-based outreach clinics). Point-of-care rapid diagnostic testing availability within the VHA may be lower than in private settings. A 2015 VA-wide survey of antimicrobial stewardship resources indicated that ~50% of VAMCs had RADT testing, whereas throat culture testing was more widely available.[18] This study was a quality improvement evaluation with a consensus-based approach to MUE protocol development, and the diagnostic and treatment criteria for rhinosinusitis were not identical to IDSA recommendations. For example, ≥7 days instead of 10 days was used to define the prolonged symptoms diagnostic threshold for treatment of rhinosinusitis, and amoxicillin in addition to amoxicillin clavulanate was considered acceptable first-line therapy.[4,5] Because sites volunteered to participate, we cannot rule out bias in the characteristics of participating sites. These findings should not be generalized beyond uncomplicated ARI cases because not all ARI visits identified by diagnostic codes met this definition.

Our findings parallel a VHA-wide analysis that reported an antibiotic prescribing rate of 69% in 2012.[10] Respiratory tract infections, primarily ARIs, account for 45% of all outpatient prescriptions, with an overall estimated annual appropriate antibiotic prescribing rate ranging from 45% to 63% for adults.[1] Our finding of 39% for appropriate antibiotic management based on manual records review is slightly lower than the claims-based estimate. Reports from nation-wide, commercially insured populations suggest overall outpatient antibiotic use decreased 9% between 2010 and 2016, with a 16% reduction in pediatrics but only a 5% reduction in adults.[19] We recently reported a similar drop in outpatient antibiotic prescription for uncomplicated ARIs within the VHA system within a similar timeframe.[20] Data on provider documentation of diagnostic criteria and their relationship to antibiotic treatment decisions for uncomplicated ARIs were limited.[21–24] Similarly, a recent observational cohort study identified an 83% prescription rate for rhinosinusitis in adults and that 38% had symptoms for <3 days.[19] That study found a lower (48%) antibiotic prescribing rate for pharyngitis and a higher rate of RADT testing for pharyngitis (91%). Antibiotics were prescribed in 47% of patients who had negative RADTs or no RADT tests. In our analysis, that patients who did not initially receive antibiotics were slightly more likely to subsequently receive one on a follow-up visit, which has been previously reported.[25] Finally, similar rates of return visits and low rates of complications for patients with ARIs irrespective of antibiotic treatment have been reported.[26,27]

Although many approaches have been utilized to improve ARI management, few have demonstrated sustainability.[28] Our evaluation informed the development of a national VHA ARI campaign to reduce unnecessary antibiotic use. The campaign components include provider-directed interventions of academic detailing coupled with audit/feedback. Preliminary results suggest improvements in appropriate antibiotic management for uncomplicated ARIs, although longitudinal follow-up is needed.[20] Because scalability requires the ability to accurately identify, track, and report cases efficiently, further work is needed to assess diagnostic and treatment decisions without the need for chart review. Improvements in electronic medical record templates to capture ARI symptoms and natural language processing may aid in that approach.[29–31] Finally, future work should include tools to capture and aid assessment of untoward patient outcomes, including antibiotic adverse events, rare infectious complications, and ecological effects such as antibiotic resistance associated with inappropriate management decisions.

Overall, we observed high rates of antibiotic prescription for uncomplicated ARIs in VHA outpatient settings, suggesting that considerable overuse did not change substantially between 2012 and 2016. Practice patterns were frequently discordant with guideline diagnosis and treatment recommendations. Most patient-related outcomes were similar irrespective of treatment approach suggesting that interventions to reduce use inappropriate antibiotic management are needed.

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