

Supplemental Content

Evaluating different strategies for outpatient antimicrobial surveillance

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Supplemental Table 1. Diagnostic categories applied to cohort 1

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Supplemental Table 1. Diagnostic categories applied to cohort 1

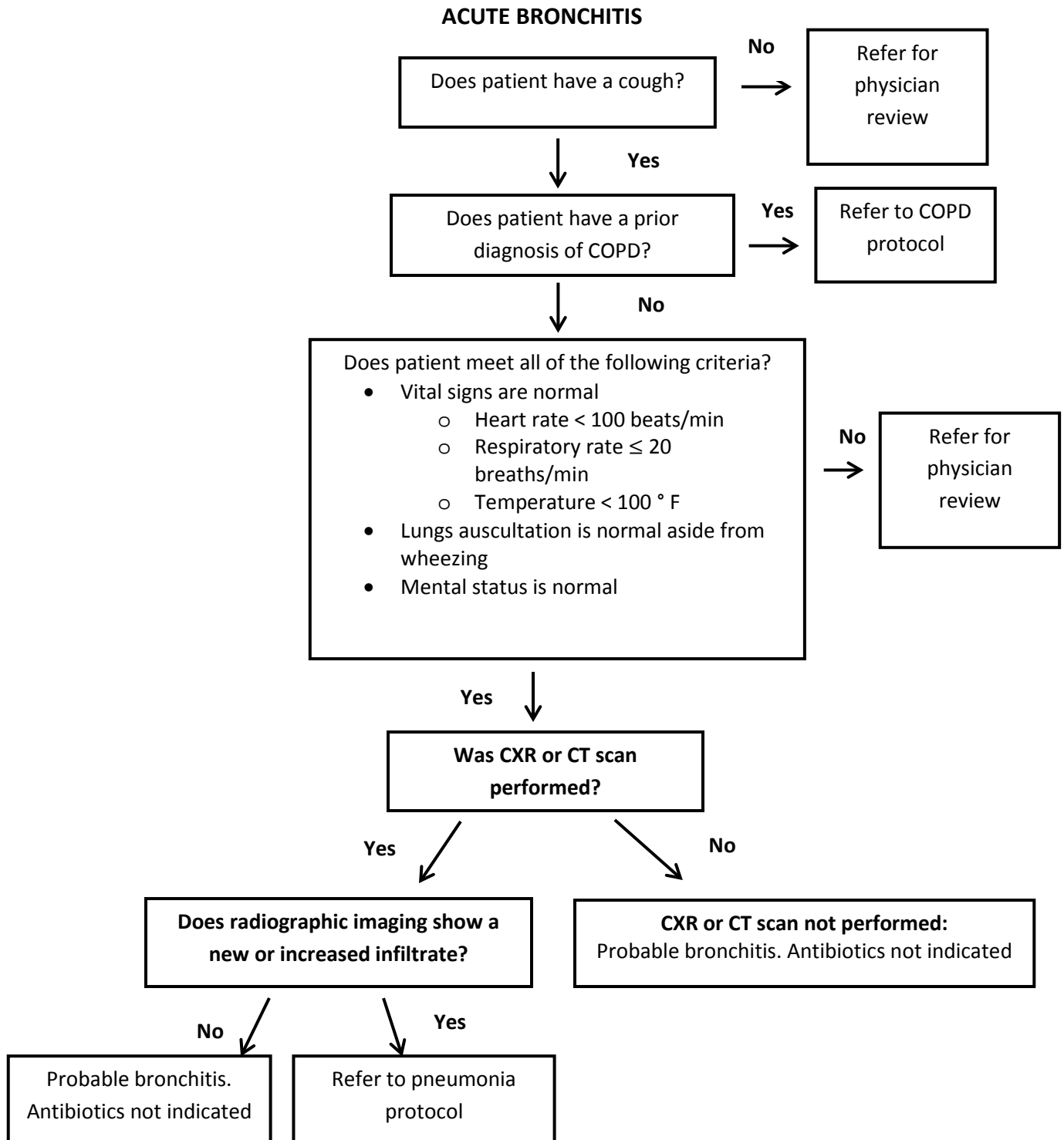
Broad category	Specific infectious syndromes
Acute respiratory tract infections (ARTIs)	Acute Bronchitis Influenza Pertussis Pneumonia Upper respiratory tract infection
Ear, nose, and throat (ENT) infections	Epiglottitis Laryngitis, acute Mastoiditis Otitis externa Otitis media Parotitis, acute bacterial Peri-tonsillar abscess Pharyngitis Tonsillitis Rhinosinusitis, acute or chronic
Exacerbations of COPD or asthma	Asthma with acute exacerbation COPD with acute exacerbation
Gastroenteritis	Gastroenteritis, infectious Clostridium difficile-associated diarrhea
Genitourinary (GU)	Female-specific infections <ul style="list-style-type: none"> • Bacterial vaginosis • Bartholin’s cyst, infected • Pelvic inflammatory disease • Trichomoniasis • Vulvovaginal candidiasis Male-specific infections <ul style="list-style-type: none"> • Balanitis • Epididymitis/orchitis • Prostatitis • Urethritis Sexually-transmitted diseases <ul style="list-style-type: none"> • Chlamydia • Gonorrhea • Syphilis Urinary tract infections (UTI) <ul style="list-style-type: none"> • Cystitis • Pyelonephritis
Intra-abdominal infection	Anorectal abscess Cholecystitis Diverticulitis
Miscellaneous	Fungal infections

	<ul style="list-style-type: none"> • Endemic mycoses • Candidal infections, non-vulvovaginal <i>Helicobacter pylori</i> Lyme disease Rickettsial diseases Non-infectious syndromes <ul style="list-style-type: none"> • Dermatologic: acne, rosacea, hidradenitis suppurativa • Small bowel bacterial overgrowth
Musculoskeletal (MSK)	Arthritis, infectious Bursitis, infectious Orthopedic device-related infection Osteomyelitis
Odontogenic infections	Dento-alveolar infections Periodontal infections
Skin and soft tissue infections (SSTI)	Abscess Carbuncle Cellulitis Erysipelas Furuncle Impetigo Lymphadenitis, suppurative Paronychia Soft tissue cyst, infected

Supplemental Table 2. ICD-10 codes used to identify cases for manual chart review in cohort 2

Infection syndrome	ICD-10 codes
Bronchitis	J20.0, J20.1, J20.2, J20.3, J20.4, J20.5, J20.6, J20.7, J20.8, J20.9, J40
COPD exacerbation	J44.0, J44.1
Cystitis	N30.90, N30.91, N30.80, N30.81, N30.01, N30.00, B37.41, N39.0, N41.0
Influenza	J09.X, J09.X1-X3, J09.X9, J10.0, J10.00, J10.08, J10.1, J10.2, J10.8, J10.81-10.83, J10.89, J11.0, J11.00, J11.08, J11.1, J11.2, J11.8, J11.81-J11.83, J11.89
Otitis media	A38.0, H65.00-H65.07, H65.111-H65.119, H65.191-H65.199, H65.90-H65.93, H66.001-H66.019, H66.40-H.66.43, H6690-H66.93, H67.1, H67.2, H67.3, H67.9
Pharyngitis	J02.0, J02.8, J02.9, J31.2
Pneumonia	J12.0-J12.3, J12.89, J12.9, J13, J14, J15.0, J15.1, J15.2, J15.211, J15.212, J15.29, J15.3-J15.9, J16.8, J17, J18.0, J18.1, J18.2, J18.8, J18.9
Sinusitis	J01.00, J01.01, J01.10, J01.11, J01.20, J01.21, J01.30, J01.31, J01.80, J01.81, J01.90, J01.91
Upper respiratory tract infection	J06.9, J00

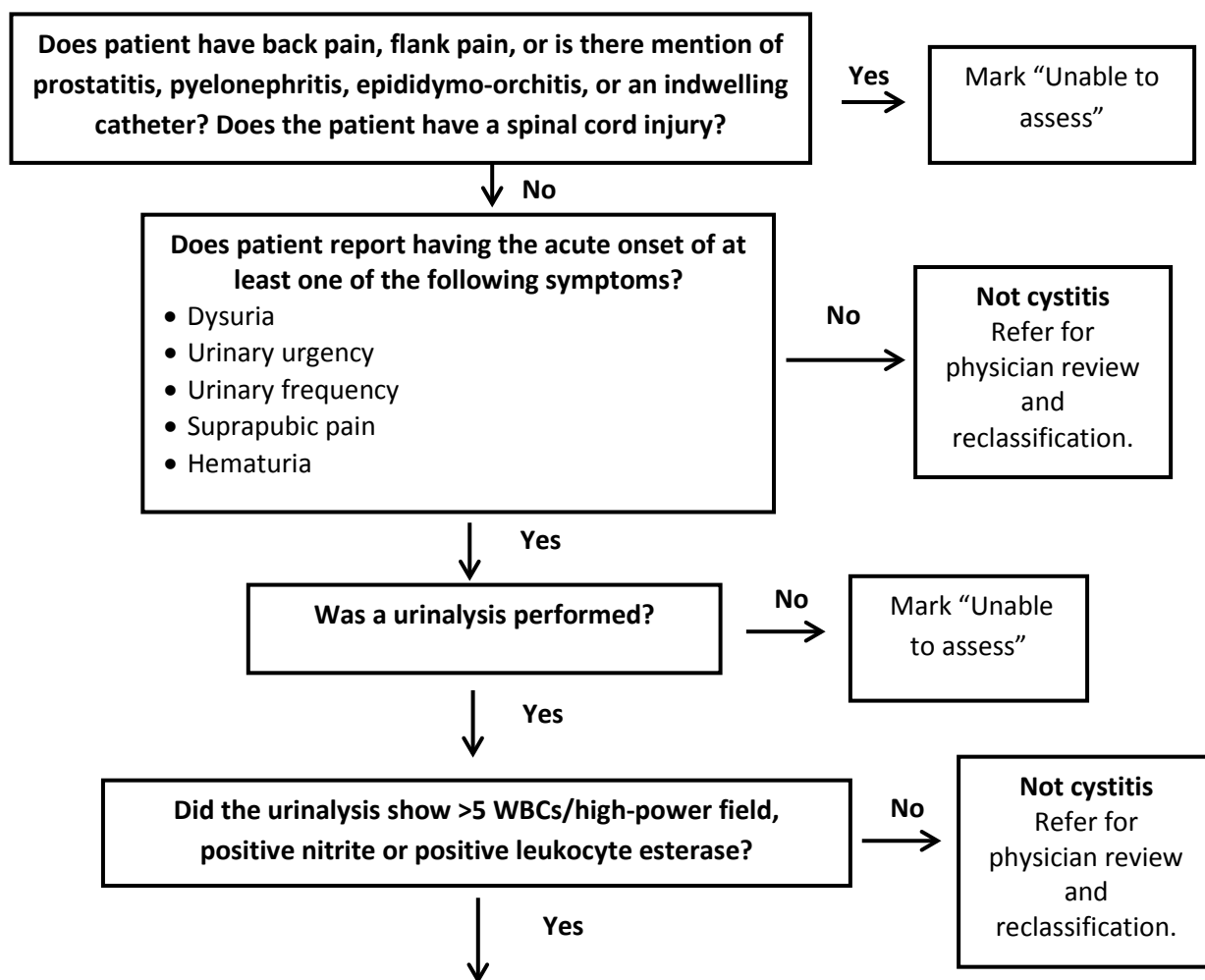
Supplementary Figures 1-9: Standardized protocols used to assess antimicrobial necessity



Irwin RS, Baumann MH, Bolser DC, et al. Diagnosis and management of cough: ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129(1 Suppl).

Harris AM, Hicks LA, Qaseem A, et al.. Appropriate Antibiotic Use for Acute Respiratory Tract Infection in Adults: Advice for High-Value Care From the American College of Physicians and the Centers for Disease Control and Prevention. *Ann Intern Med*. Mar 15 2016;164(6):425-434.

Cystitis

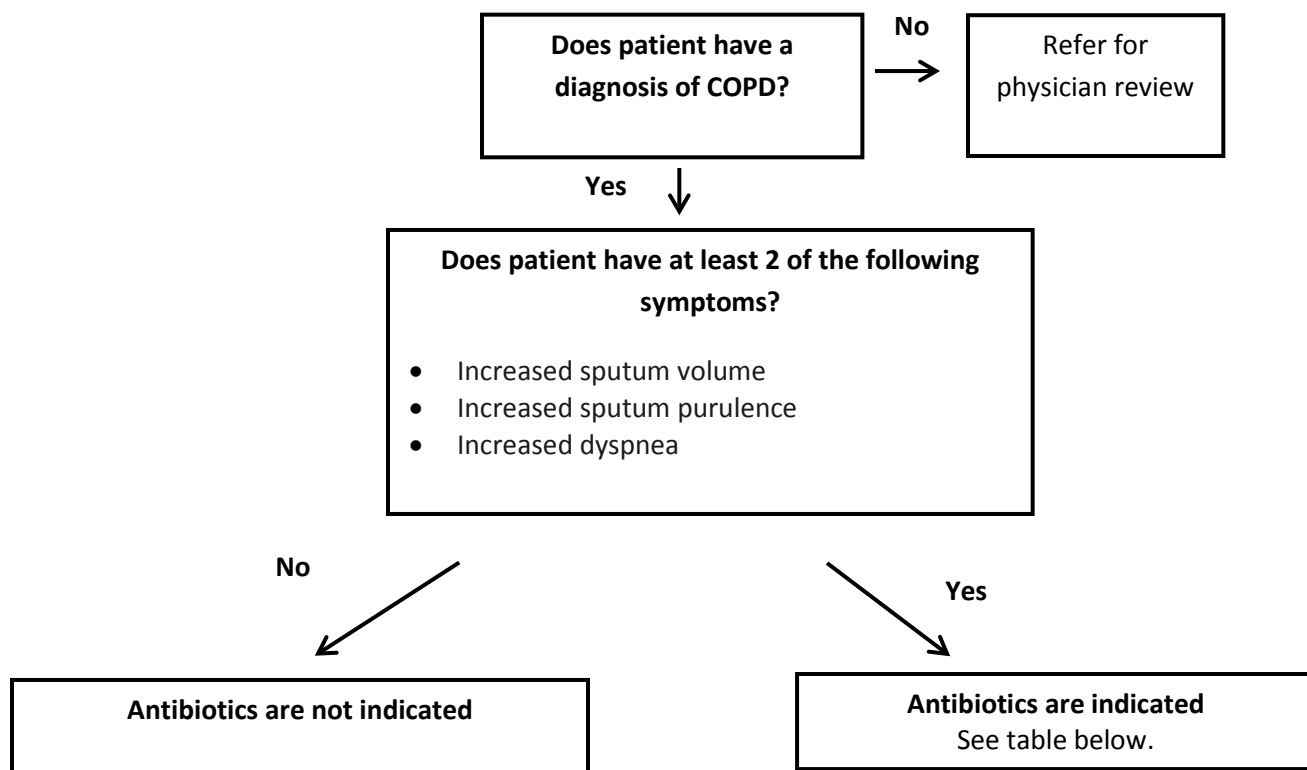


Drug	Dose	Male duration*	Female duration*
Nitrofurantoin	100 mg BID	7 days	5-7 days
Trimeth-sulfamethoxazole	DS BID	7 days	3 days
Fosfomycin	3 g once	3 doses	Once
Amoxicillin/clavulanate	500 - 875 mg/125 mg BID/TID	7 days	7 days
Cefpodoxime	100 mg BID	7 days	7 days
Ciprofloxacin	250 mg BID	7 days	3 days
Levofloxacin	250 mg daily	7 days	3 days

* A longer duration may be appropriate in more complicated cases, including patients with structural abnormalities of their urinary tract.

Meyer HE, Lund BC, Heintz BH, Alexander B, Egge JA, Livorsi DJ. Identifying Opportunities to Improve Guideline-Concordant Antibiotic Prescribing in Veterans with Acute Respiratory Infections or Cystitis. *Infect Control Hosp Epidemiol* 2017; 38:724-8.

COPD Exacerbation

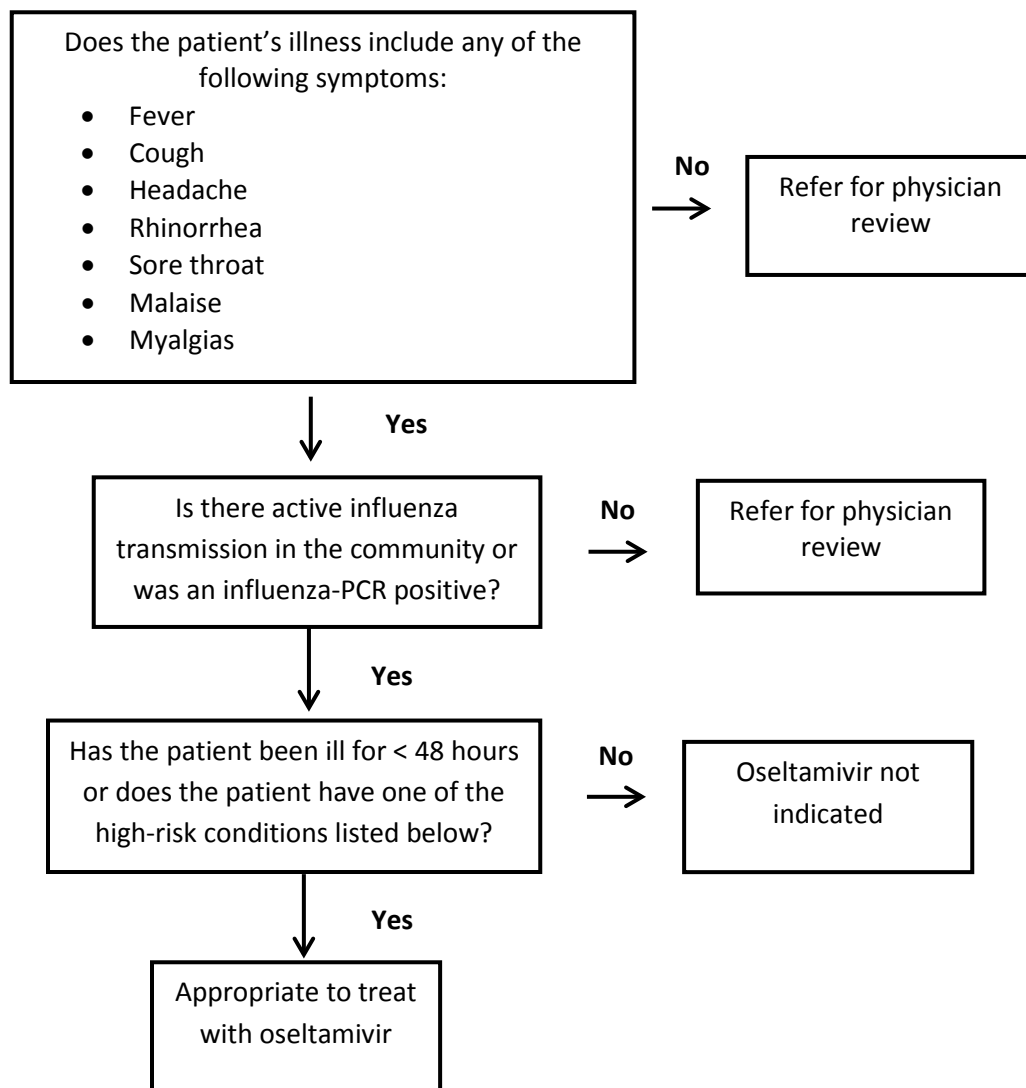


Uncomplicated COPD with no risk factors for antibiotic-resistance: <65 years of age, FEV1 ≥50% predicted, < 4 exacerbations per year, and no antibiotic use within the prior 90 days		
Drug	Dose	Duration
Amoxicillin/clavulanate	500 mg/125 mg TID or 875 mg/125 mg BID	5 days
Azithromycin	500 mg x1, 250 mg daily	5 days
Cefuroxime	250-500 mg BID	5 days
Cefdinir	300 mg BID or 600 mg daily	5 days
Cefpodoxime	200 mg BID	5 days
Doxycycline	100 mg BID	5 days
Complicated COPD with risk factors for antibiotic resistance: ≥65 years of age, FEV1 <50% predicted, ≥ 4 exacerbations per year, or antibiotic use within the prior 90 days		
Drug	Dose	Duration
Amoxicillin/clavulanate	500 mg/125 mg TID or 875 mg/125 mg BID	5 days
Cefuroxime	250-500 mg BID	5 days
Cefdinir	300 mg BID or 600 mg daily	5 days
Cefpodoxime	200 mg BID	5 days
Moxifloxacin	400 mg daily	5 days
Levofloxacin	500 mg – 750 mg daily	5 days

Martinez FJ, Anzueto A. Appropriate outpatient treatment of acute bacterial exacerbations of chronic bronchitis. Am J Med 2005; 118 Suppl 7A: 39S-44S.

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017. Available from: <http://goldcopd.org>.

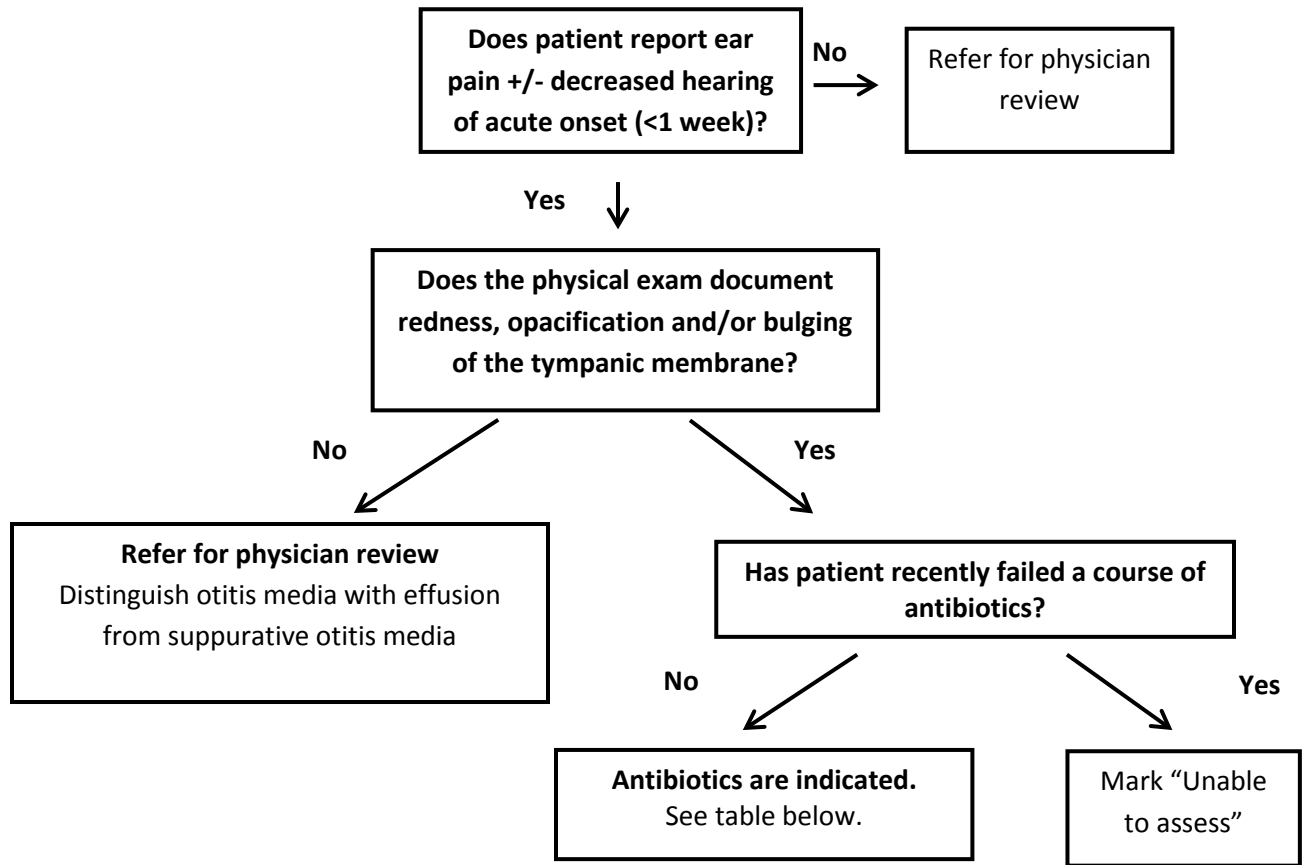
Influenza



Persons at higher risk for influenza complications recommended for antiviral treatment include:

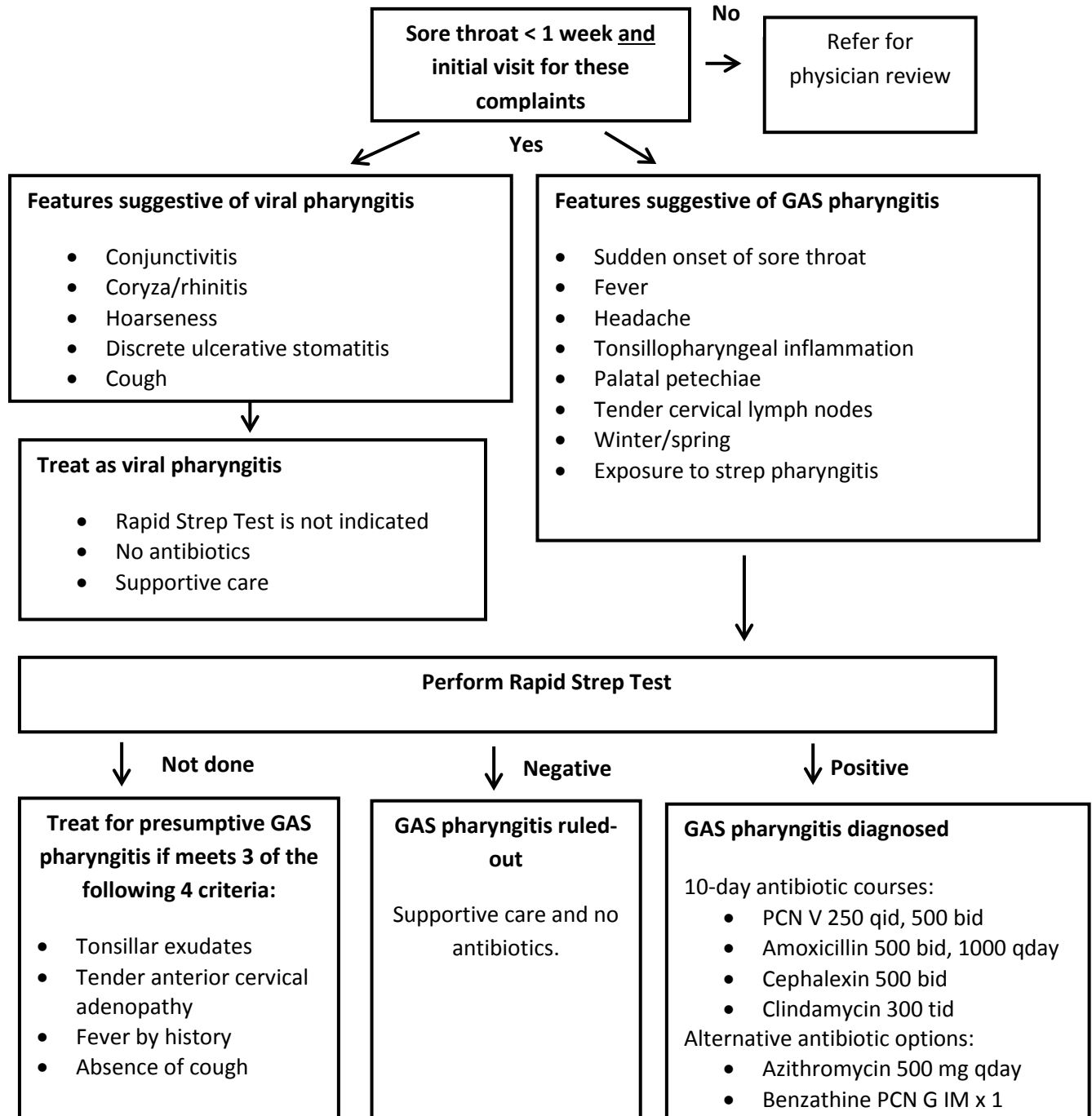
- 1) adults aged 65 years and older;
- 2) persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematologic (including sickle cell disease), and metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle, such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury);
- 3) persons with immunosuppression, including that caused by medications or by HIV infection;
- 4) women who are pregnant or postpartum (within 2 weeks after delivery);
- 5) persons aged younger than 19 years who are receiving long-term aspirin therapy;
- 6) American Indians/Alaska Natives;
- 7) persons who are morbidly obese (i.e., body mass index is equal to or greater than 40); and
- 8) residents of nursing homes and other chronic care facilities

Otitis media



Recommended antibiotic therapy for otitis media		
Drug	Dose	Duration
Amoxicillin	500 bid or TID, 250-875 bid	5-10 days
Amoxicillin/clavulanate	500 mg/125 mg TID or 875 mg/125 mg BID	5-10 days
Cefuroxime	500 mg BID	5-10 days
Cefdinir	300 mg BID or 600 mg daily	5-10 days
Cefpodoxime	200 mg BID	5-10 days
Ceftriaxone	2 grams IM or IV	1 dose

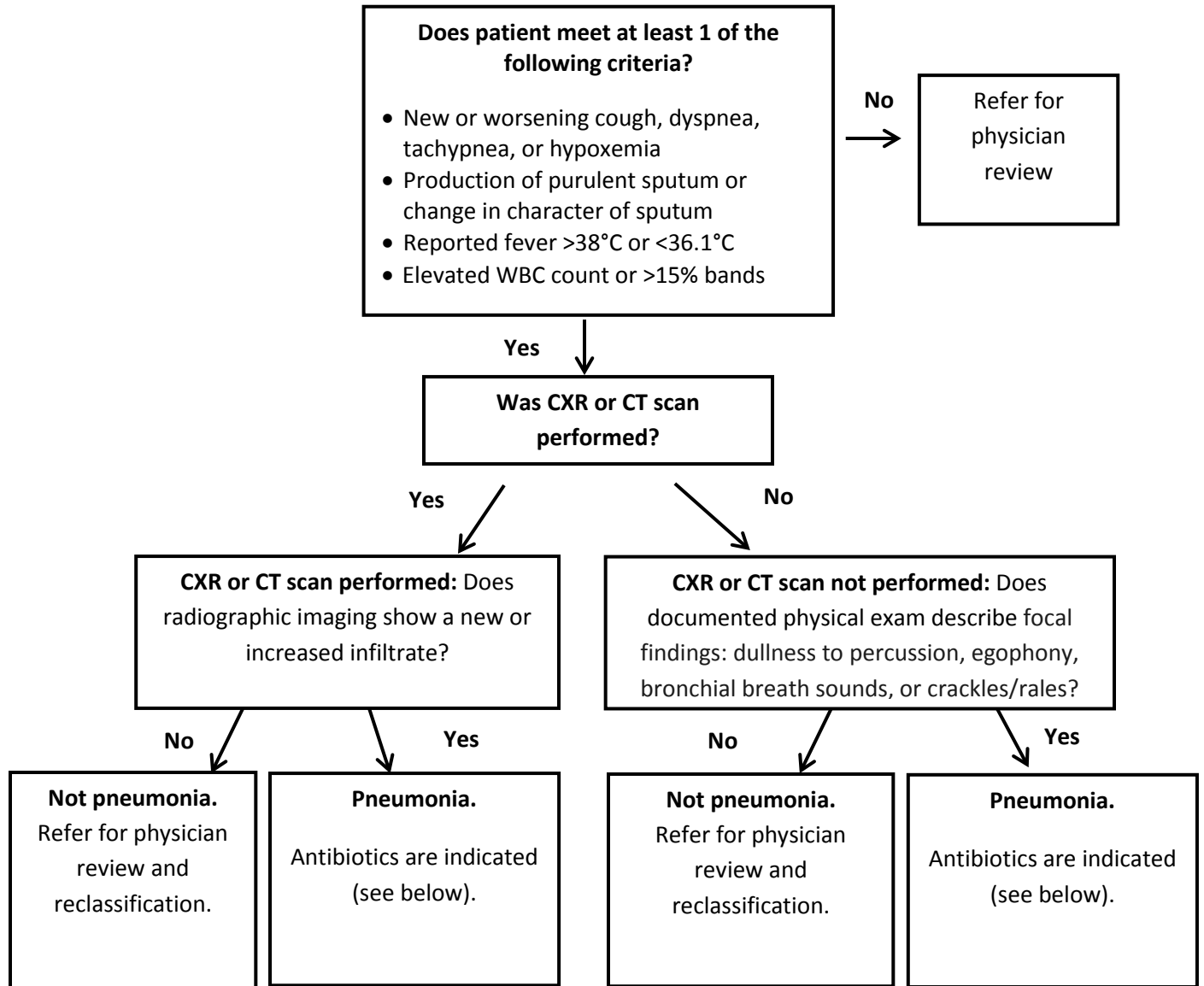
Pharyngitis



Harris AM, Hicks LA, Qaseem A, et al.. Appropriate Antibiotic Use for Acute Respiratory Tract Infection in Adults: Advice for High-Value Care From the American College of Physicians and the Centers for Disease Control and Prevention. *Ann Intern Med.* Mar 15 2016;164(6):425-434.

European Society for Clinical Microbiology and Infectious Diseases Sore Throat Guideline Group. Guideline for the management of acute sore throat. *Clin Microbiol Infect* 2012; 18 (Suppl. 1): 1-27.

Pneumonia

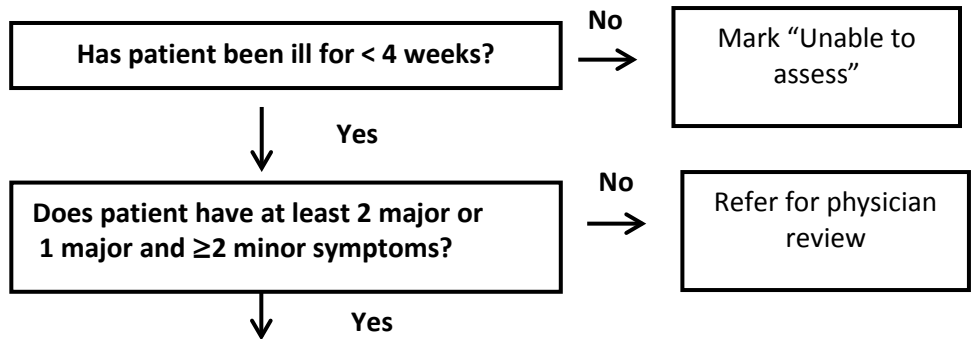


Uncomplicated: No comorbidities, no antibiotic use within the past 90 days		
Drug	Dose	Duration*
Azithromycin	500 mg x1, 250 mg daily	5 days
Doxycycline	100 mg BID	5 days
Complicated: presence of comorbidities (chronic heart, lung, liver, renal disease, diabetes, alcoholism, malignancies, asplenia, immunosuppression), use of antimicrobials within the past 90 days, > 65 years old		
Drug	Dose	Duration
Moxifloxacin	400 mg daily	5 days
Levofloxacin	500 mg – 750 mg daily	5 days
Beta-lactam PLUS azithromycin or doxycycline	Amoxicillin, Amoxicillin/clavulanate, Cefpodoxime or Cefuroxime PLUS azithromycin or doxycycline	5 days

A duration of at least 5 days is recommended and patient should be afebrile for 2-3 days and have no more than 1 sign associated with clinical instability before discontinuation of therapy duration. A longer course may be appropriate in certain situations

1. Postma DF, van Werkhoven CH, van Elden L, et al. Antibiotic Treatment Strategies for Community-Acquired Pneumonia in Adults. NEJM 2015; 372: 1312-23.
2. Mandell LA, Wunderink RG, Anzueto A et al. Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. Clinical Infectious Diseases 2007; 44:527–72

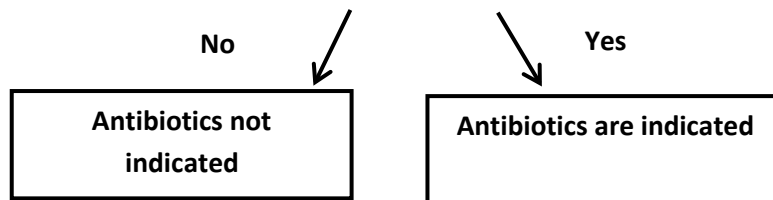
Rhinosinusitis



Major Criteria	Minor Criteria
Purulent anterior nasal discharge or purulent or discolored posterior nasal discharge	Headache
Nasal congestion or obstruction	Ear pain, pressure or fullness
Fever (acute sinusitis)	Halitosis
Facial congestion/fullness or facial pain/pressure	Dental pain
Hyposmia or anosmia	Cough

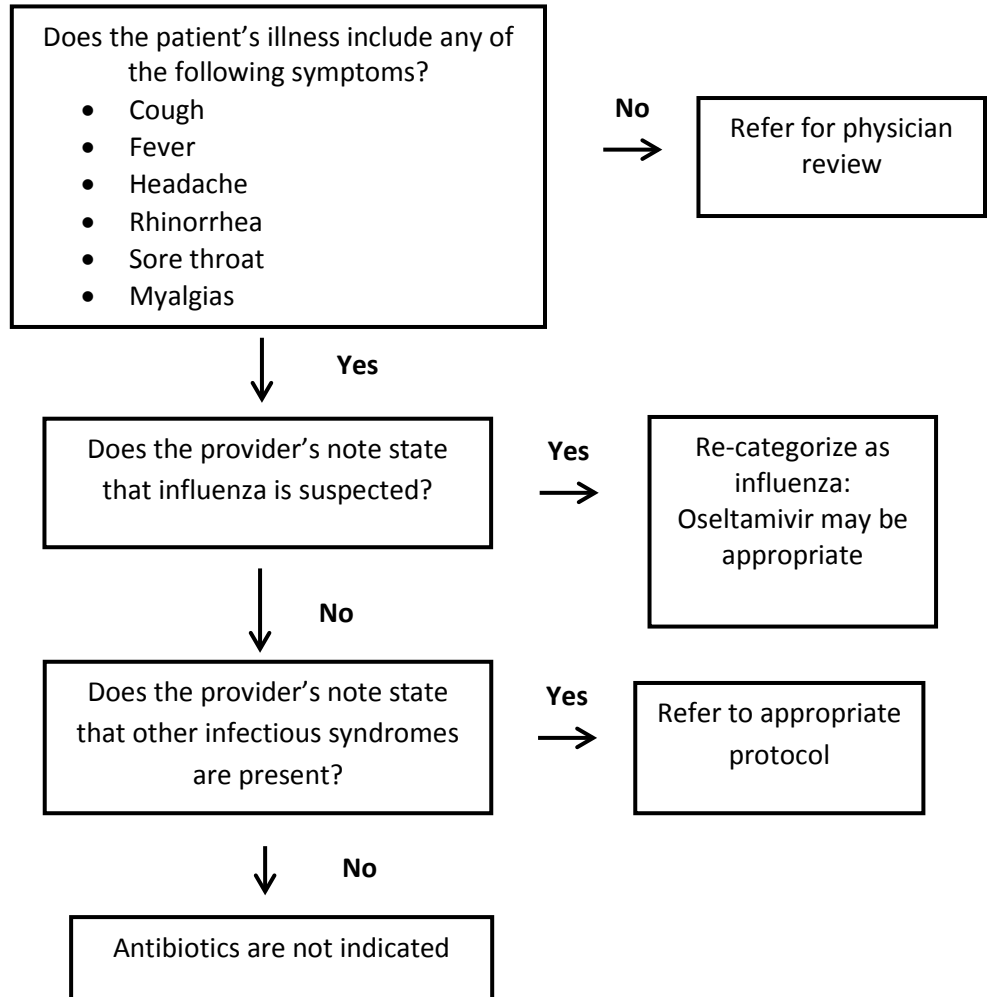
Does patient meet one of the following criteria?

1. Onset with persistent symptoms that last ≥ 10 days and are not improving
2. Onset with severe symptoms, characterized by high fever of at least 39°C (102°F) and purulent nasal discharge for at least 3 consecutive days at the beginning of illness
3. Onset with worsening symptoms (new onset fever, headache, nasal discharge), characterized by typical viral URI symptoms that appear to improve followed by the sudden onset of worsening symptoms after 5–6 days (“double-sickening”)

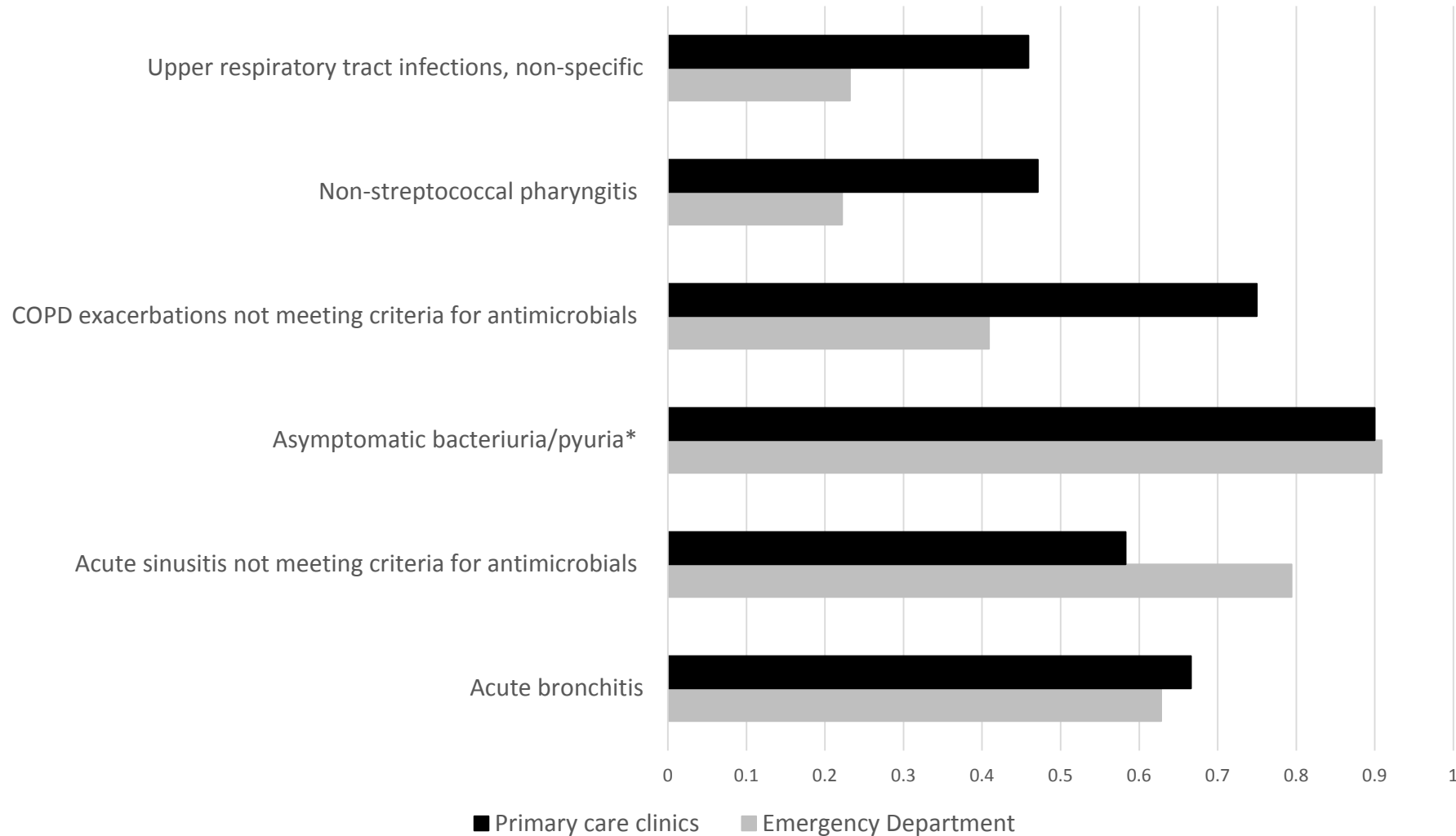


No penicillin allergy		
Drug	Dose	Duration
Amoxicillin-clavulanate	500 mg/125 mg TID or 875 mg/125 mg BID/TID	5-7 days
Cefdinir	300 mg BID	5-10 days
Doxycycline	100 mg BID or 200 mg daily	5-7 days
Penicillin allergy		
Drug	Dose	Duration
Doxycycline	100 mg BID or 200 mg daily	5-7 days
Levofloxacin	500 – 750 mg daily	5-7 days
Moxifloxacin	400 mg daily	5-7 days
Cefdinir	300 mg BID OR 600 mg daily	5-10 days

Upper respiratory tract infection, nonspecific



Supplemental Figure 10. Rates of antimicrobial overtreatment for 6 infectious syndromes in both the Emergency Department and primary care clinics at the Iowa City VA Medical Center



*Cases of asymptomatic bacteriuria/pyuria were identified by reviewing ICD-10 codes from patient-visits for cystitis. Since the denominator does not reflect all cases of asymptomatic bacteriuria/pyuria, the overtreatment rate is artificially high.

Sample sizes for each infectious syndrome are as follows (sample size for ED, sample size for primary care): acute bronchitis (113, 51); acute sinusitis not meeting criteria for antimicrobials (34, 24); asymptomatic bacteriuria/pyuria (22, 10); COPD exacerbations not meeting criteria for antimicrobials (22, 4); non-streptococcal pharyngitis (36, 17); upper respiratory tract infections, non-specific (99, 37). There were also 5 cases of suspected otitis media that did not have documented findings meeting diagnostic criteria for otitis media. There were no cases of influenza or confirmed pneumonia that qualified as antimicrobial overtreatment.