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EST. 1881

Risks of Screening and Treating Asymptomatic Bacteriuria in a Post Antibiotic Era

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Objective

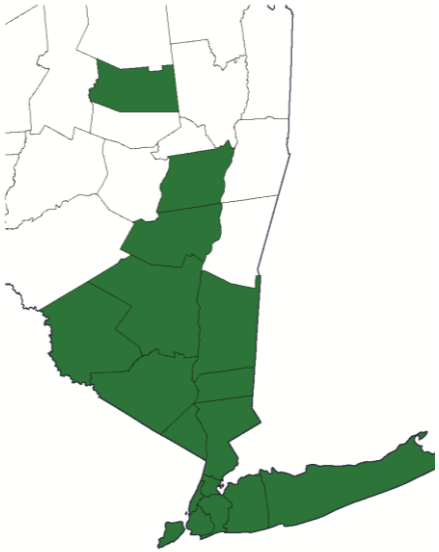
- Describe the patient groups that may and may not benefit from for screening and treatment of asymptomatic bacteriuria

CDC Threat Report 2019

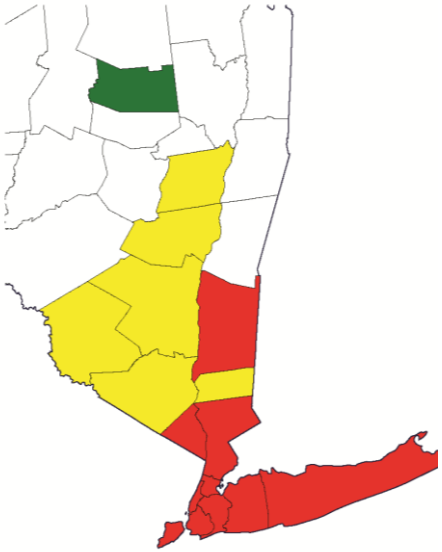
"To stop antibiotic resistance, our nation must:

Stop referring to a coming post-antibiotic era—it's already here. You and I are living in a time when some miracle drugs no longer perform miracles and families are being ripped apart by a microscopic enemy. The time for action is now and we can be part of the solution."

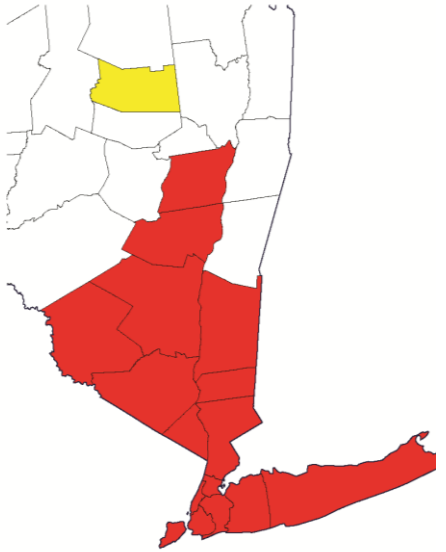
– Robert R. Redfield, M.D. Director, U.S. Center for Disease Control and Prevention



Nitrofurantoin



Trimethoprim-Sulfamethoxazole



Ciprofloxacin

Legend: Red: > 20%; Yellow: 10-20%; Green: < 10%

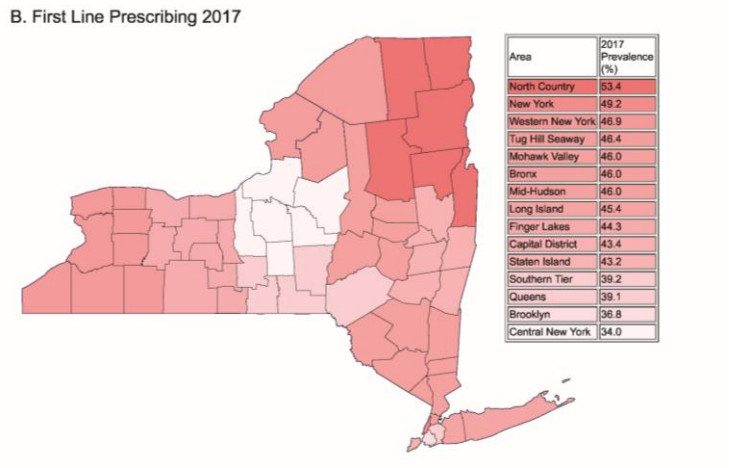
New York State is not immune!

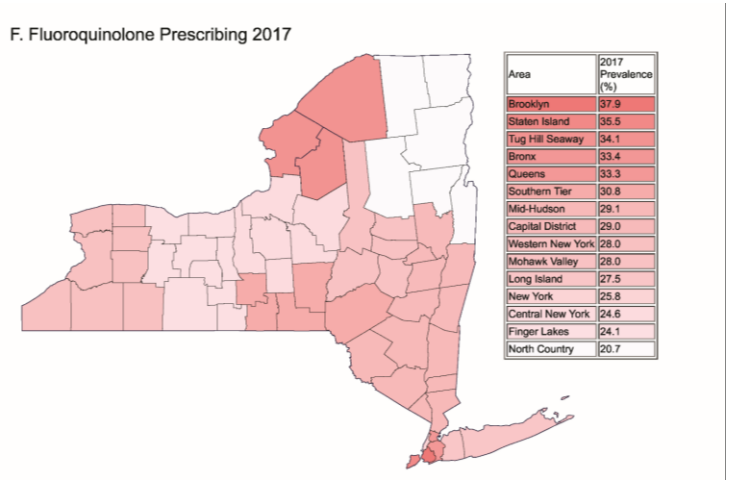
- A recent survey of 50,900 *Escherichia coli* urinary isolates from New York State demonstrated that high prevalence of resistance two out of three major to agents used to treat UTIs:
  - Nitrofurantoin: 3%
  - Trimethoprim-Sulfamethoxazole: 27%
  - Ciprofloxacin: 22%

Rank EL, Lodise T, Avery L, et al. Open Forum Infect Dis. 2018 Nov 16;5(11):ofy297.

In NYS, these agents are frequently prescribed in the elderly

- A retrospective evaluation of 50,658 New York State Medicare Part D prescription claims for Medicare Part B Beneficiaries with diagnosis codes for cystitis between 2016-2017.
- Approximately, 93.4% of patients received nitrofurantoin, trimethoprim-sulfamethoxazole or a fluoroquinolone
  - 64.3% first line agent
  - 29.1% received a fluoroquinolone
- Take away point: It is likely that we are suboptimally treating our elderly patients when it comes to UTI in NYS.





Yu J, McKenna VA, Dumyati GK, Lubowski T, Carreno JJ. IDWEEK 2019.

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How can health-systems pharmacists and technicians help?

5 WAYS HOSPITAL PHARMACISTS CAN *BE ANTIBIOTICS AWARE*

1. Verify Penicillin Allergy

- Although 10% of the population in the United States reports a penicillin allergy, less than 1% of the population is truly penicillin allergic.[1]

4. Avoid Treatment of Asymptomatic Bacteriuria

- Patients with asymptomatic bacteriuria should not be treated with antibiotics in most cases.[4]
- Consider the importance of signs and symptoms consistent with urinary tract infection (UTI) when reviewing positive urine cultures and/or making treatment recommendations.

relevant cultures).[3]

- Prompt the provider to consider **stopping** or **tailoring** antibiotic therapy as appropriate.

4. Avoid Treatment of Asymptomatic Bacteriuria

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- Consider the importance of signs and symptoms consistent with urinary tract infection (UTI) when reviewing positive urine cultures and/or making treatment recommendations.

5. Use the Shortest Effective Antibiotic Duration

- Guidelines for treatment duration are available for common infectious diseases such as pneumonia, UTI, and skin and soft tissue infection.[5,6,7]
- Alert the provider if the total days of inpatient and post-discharge antibiotic therapy exceeds the recommended duration.

IDSA defined groups

Patient Group	Screen and Treat?
Pediatric Patients	No
Pregnant Women	Yes
Older Adults	No
Diabetes	No
Kidney Transplant	No
Non-Renal Solid Organ Transplant	No
Neutropenia	No Recommendation
Spinal Cord Injury	No
Urinary Catheter	No
Nonurological Surgery	No
Endourological Surgery	Yes

Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Pediatric Patients

- Recommend AGAINST screening and treating
- Theoretical Benefits:
  - Prevent symptomatic UTI (no evidence) including pyelonephritis (low quality)
  - Prevent renal scarring (no evidence)
  - Prevent renal insufficiency (no evidence)
- Risks:
  - A theoretical analysis of 100,000 pediatric patients would produce:
    - 20,000 false positives
    - 143 false negatives
    - $2 million dollars (1992) or 3.72 million dollars (2019)
  - Antimicrobial resistance (high quality)
  - Antimicrobial related adverse effects (high quality)

Kemper KJ, Avner ED. Am J Dis Child. 1992;146(3):343–346.
Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Healthy Nonpregnant Women

- Recommend AGAINST screening and treating
- Theoretical Benefits:
  - Prevention of symptomatic UTI (no evidence) and pyelonephritis (moderate evidence AGAINST)
- Risks:
  - Increased risk of subsequent UTI (moderate quality)
  - Antimicrobial resistance (high quality)
  - Antimicrobial related adverse events (high quality)

Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Pregnant Women

- Recommend screening and treatment

- Benefits:
  - Reduce risk of pyelonephritis (moderate quality)
  - Reduce risk of pre-term birth (low quality)
  - Reduce risk of very low birth weight (moderate quality)

- Risks:
  - Antimicrobial resistance (high quality)
  - Antimicrobial related adverse events (high quality)

Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Netherlands' Study

- Prospective observational cohort (n = 5132) with nested Randomized Controlled Trial (n = 248)
- Randomized pregnant patients with ASB to nitrofurantoin, placebo or no treatment
- Main Endpoint: Pyelonephritis
  - Untreated: 6/208 (2.9%)
  - Treated: 77/4035 (1.9%)
  - Adjusted odds ratio (aOR) 1.5, 95% CI 0.6-3.5
- Limitation: Underpowered to detect this difference

Kazemier BM et al. Lancet Infect Dis. 2015 Nov;15(11):1324-33..

Older Adults

- Recommend AGAINST screening and treating

- Potential Benefits:
  - Survival benefit (low-quality evidence against)
  - Prevention of sepsis (very low-quality evidence against)

- Risks:
  - Antimicrobial resistance (high quality)
  - Antimicrobial related adverse events (high quality)

Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

ASB with Mental Status Changes

- Patients with ASB and Mental Status Changes (delirium, confusion) are more likely to be treated with antimicrobials than patients with ASB alone

- Treatment outcomes:
  - No difference in behavioral rating scale at 1 and 3 months
  - No difference in in-hospital mortality (0% vs. 4.2%, P = 0.32)
  - Numerically higher incidence of C. difficile infection (aOR, 2.45 [95% CI: 0.86 – 6.96]).

Potts L, Cross S, MacLennan WJ, Watt B. Arch Gerontol Geriatr. 1996;23(2):153–161.
Silver SA, Baillie L, Simor AE. Can J Infect Dis Med Microbiol. 2009;20(4):107–111.
Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

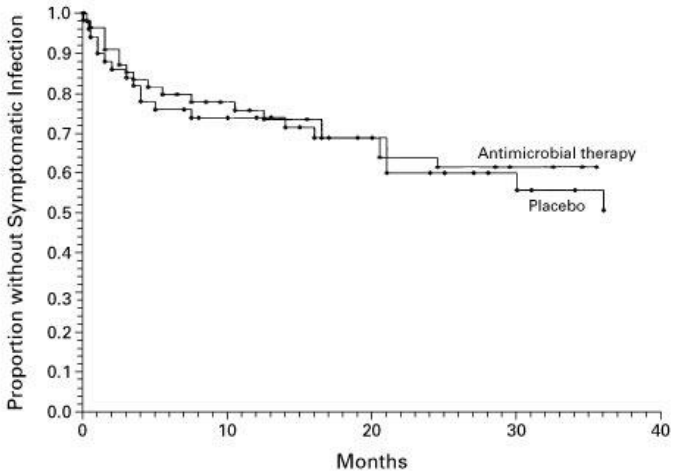
ASB with Falls

- Up to 80% of older adults who fall do not have ASB
- Therefore falls should not automatically trigger an investigation of UTI
- However, if other signs of systemic inflammatory response syndrome are present, additional investigation may be warranted

Rhoads J, Clayman A, Nelson S. Director 2007; 15:22–6.
Rowe T, Towle V, Van Ness PH, Juthani-Mehta M. J Am Geriatr Soc 2013; 61:653–4.
Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Diabetes

- Recommend AGAINST screening or treating
- Potential benefits:
  - Reduce risk of symptomatic UTI (moderate quality against) pyelonephritis (moderate quality against)
  - One randomized controlled trial (n = 105) demonstrated that treatment did not reduce symptomatic UTI (40% vs. 42%, P = 0.67) or pyelonephritis (RR: 2.13, [95% CI: 0.81 – 5.62]).
- Risks:
  - Antimicrobial resistance (high quality)
  - Antimicrobial related adverse events (high quality)



Harding GK, Zhanel GG, Nicolle LE, Cheang M; N Engl J Med 2002; 347:1576–83.
Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Kidney Transplant (> 1 month)

- Recommend AGAINST screening and treating
- Potential benefits:
  - Prevent pyelonephritis (high-quality evidence against)
  - Prevent graft rejection (high-quality evidence against)
  - Improve graft function (moderate-quality evidence against)
- Risks:
  - Promotes reinfection with increasingly resistant organisms
  - Antimicrobial related adverse events (high quality)

Gołębiewska JE, Dębska-Ślizień A, Rutkowski B. Transpl Infect Dis 2014; 16:605–15.
Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

University Hospital in Geneva

- Retrospective study of 334 episodes of asymptomatic bacteriuria in patients with renal allografts
- One hundred and one episodes (30%) were treated
- Outcomes:
  - No cases of pyelonephritis in either group
  - No cases of acute rejection in either group

El Amari EB, Hadaya K, Bühler L, et al. Nephrol Dial Transplant 2011; 26:4109–14.
Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Rabin Medical Center

- Retrospective cohort study of 112 cases of asymptomatic bacteriuria in patients with renal transplant

- Most patients (90) were untreated

- Outcomes (treated vs. untreated):
  - Pyelonephritis or sepsis: 9.1% vs. 4.4% ($P \geq 0.05$)
  - Graft loss: 0% vs. 2.2% ($P \geq 0.05$)

Green H, Rahamimov R, Goldberg E, et al. Eur J Clin Microbiol Infect Dis 2013; 32:127–31.
Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Kermanshah University of Medical Sciences

- Prospective randomized controlled trial of 88 patients with renal transplants and ASB
- Randomized in 1 to 1 to receive treatment or no treatment
- Outcomes assessed at 9 – 12 months:
  - No difference in incidence of symptomatic UTI (P > 0.05)
  - No difference in serum creatinine changes between groups (P > 0.05)

Moradi M, Abbasi M, Moradi A, Boskabadi A, Jalali A. Urol J 2005; 2:32–5.
Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

University of Madrid

- Randomized controlled trial of 112 patients with renal transplants and ASB
- Randomized 1 to 1 to treatment or no antimicrobial treatment
- Outcomes (treatment vs. control)
  - Pyelonephritis: 7.5% vs. 8.4% (P > 0.99)
  - Acute graft rejection: 18.9% vs. 20.3% (P = 0.84)
  - Graft loss: 1.9% vs. 1.7% (P > 0.99)

Origüen J, López-Medrano F, Fernández-Ruiz M, et al. Am J Transplant 2016; 16:2943–53.
Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Non-Renal Solid Organ Transplant

- Recommend AGAINST screening and treating

- Potential benefits:
  - No studies identified

- Risks:
  - Antimicrobial resistance (high quality)
  - Antimicrobial related adverse events (high quality)

Vidal E, Torre-Cisneros J, Blanes M, et al. Transpl Infect Dis 2012; 14:595–603.
Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Neutropenia

- No recommendation
- High-risk neutropenic patients should be monitored closely per current standards of care considering:
  - Urinary tract infections may be infrequent in neutropenic patients (2.8%)
  - Urinary tract is an infrequent source for bacteremia in neutropenic patients (0.9%)
- Further research needed in this area

Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Spinal Cord Injury (SCI)

- Recommend AGAINST screening and treating
- Potential Benefits:
  - Unclear
- Risks:
  - ASB may be *protective* in certain individuals with SCI
  - Antimicrobial resistance (high quality)
  - Antimicrobial related adverse events (high quality)
- Caveats:
  - Use of standardized assessment tool can help distinguish ASB from symptomatic bacteruria in patient with SCI

Goetz LL, Cardenas DD, Kennelly M, et al. Spinal Cord 2013; 51:700–4.
Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

International Spinal Cord Injury Basic Data Set

- Fever
- Malaise
- Lethargy or sense of unease
- New or worsening urinary incontinence or leaking around the catheter
- Spasticity
- Cloudy urine
- Malodorous urine
- Back pain
- Bladder pain
- Dysuria
- Autonomic dysreflexia

Goetz LL, Cardenas DD, Kennelly M, et al. Spinal Cord 2013; 51:700–4.

Indwelling Catheter

- Recommend AGAINST screening and treating in patients with short-term and long-term catheters

- Potential benefits:
  - Prevent symptomatic UTI, sepsis and death
  - Unclear if treatment prevents these outcomes

- Risks:
  - Antimicrobial resistance (high quality)
  - Antimicrobial related adverse events (high quality)

Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Nonurologic Surgical Procedures

- Recommend AGAINST screening and treating

- Potential benefits:
  - Prevention of prosthetic infection developing in orthopedic patients (low-quality evidence against)
  - Prevention of symptomatic UTI (low-quality evidence against)

- Potential Risks:
  - Antimicrobial resistance (high quality)
  - Antimicrobial related adverse events (high quality)

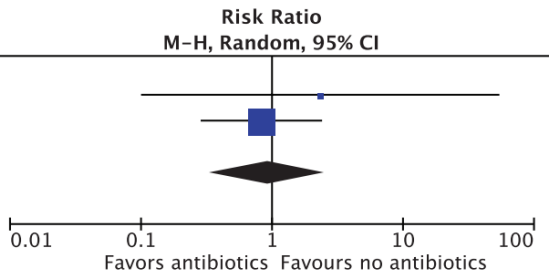
Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Treatment of ASB in Nonurologic Surgical Procedures

A. Risk of Prosthetic Joint Infection

Study or Subgroup	Antibiotics Events	Antibiotics Total	No antibiotics Events	No antibiotics Total	Weight	Risk Ratio M-H, Random, 95% CI
Cordero-Ampuero 2013	0	1	0	1		Not estimable
Drekonja 2013	1	26	0	20	10.3%	2.33 [0.10, 54.42]
Sousa 2014	6	154	7	149	89.7%	0.83 [0.29, 2.41]
Total (95% CI)		**181**		**170**	**100.0%**	**0.92 [0.34, 2.53]**
Total events	7		7			

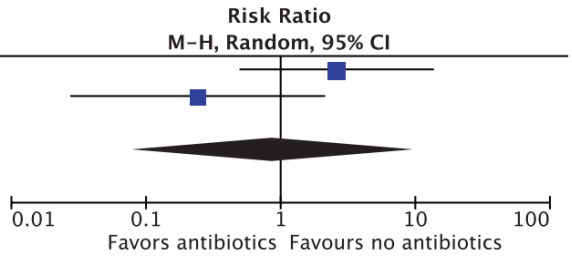
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.37$, df = 1 (P = 0.54); $I^2 = 0\%$
Test for overall effect: Z = 0.16 (P = 0.88)



B. Risk of Symptomatic UTI

Study or Subgroup	Antibiotics Events	Antibiotics Total	No antibiotics Events	No antibiotics Total	Weight	Risk Ratio M-H, Random, 95% CI
Drekonja 2013	2	11	3	43	54.2%	2.61 [0.49, 13.74]
Sousa 2014	1	154	4	149	45.8%	0.24 [0.03, 2.14]
Total (95% CI)		**165**		**192**	**100.0%**	**0.88 [0.08, 9.79]**
Total events	3		7			

Heterogeneity: $Tau^2 = 2.07$; $Chi^2 = 3.12$, df = 1 (P = 0.08); $I^2 = 68\%$
Test for overall effect: Z = 0.11 (P = 0.92)



Sousa R, Muñoz-Mahamud E, Quayle J, et al. Clin Infect Dis 2014; 59:41–7.
Drekonja DM, Zarmbinski B, Johnson JR. JAMA Intern Med 2013; 173:71–2.
Cordero-Ampuero J, González-Fernández E, Martínez-Vélez D, Esteban J. Clin Orthop Relat Res 2013; 471:3822–9.
Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Urological Surgical Procedures

- Recommend screening and treating

- Benefits:
  - Prevention of symptomatic UTI (moderate-quality evidence)
  - Prevention of sepsis (moderate-quality evidence)

- Risks:
  - Antimicrobial resistance (high quality)
  - Antimicrobial related adverse events (high quality)

Nicolle LE, Gupta K, Bradley SF, et al. Clin Infect Dis. 2019;68(10):e83–e110.

Summary

Patient Group	Screen and Treat?
Pediatric Patients	No
Pregnant Women	Yes
Older Adults	No
Diabetes	No
Kidney Transplant	No
Non-Renal Solid Organ Transplant	No
Neutropenia	No Recommendation
Spinal Cord Injury	No
Urinary Catheter	No
Nonurological Surgery	No
Endourological Surgery	Yes

Assessment Questions

- Which of the following most accurately describes the benefits of treating asymptomatic bacteriuria in the described populations?

A. Prevention of acute renal transplant rejection in patients more than 30 days post-transplant
B. Prevention of pyelonephritis in patients who are pregnant
C. Prevention of sepsis in elderly patients who have non-localizing symptoms
D. Prevention of *Clostridioides difficile* in patients with diabetes

Assessment Question

- Which of the following most accurately describes the risks of antimicrobial prescribing in patients with asymptomatic bacteriuria?

A. Colonization with multidrug resistant organisms
B. *Clostridioides difficile* infection
C. Increased healthcare costs
D. All of the above

Assessment Question

- In which of the following patients do the benefits of screening and treating asymptomatic bacteriuria outweigh the risks of treating asymptomatic bacteriuria?
  - A. 47-year-old female with no comorbid conditions presenting with 5-day history of cough
  - B. 68-year-old female with hypertension and diabetes presenting with acute delirium after starting several prescriptions
  - C. 55-year-old male with prostate cancer undergoing transurethral resection of the prostate
  - D. 36-year-old male with kidney transplant for systemic lupus erythematosus, presenting with a chief complaint of diarrhea