

Inappropriate Antibiotic Prescribing

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My objective for today...



Mind Blowing Idea #1

- Overuse of antibiotics doesn't cause resistance



Mind Blowing Idea #1

- Overuse of antibiotics doesn't cause resistance
- Use of antibiotics causes resistance



Mind Blowing Idea #1

- Overuse of antibiotics doesn't cause resistance
- Use of antibiotics causes resistance
- And side effects, and allergic reactions



↑

- Over the top
- Under the top
- Use of the hands
- Arm position



Case 1

- 21 y/o man with anoxic brain injury due to drowning, chronically ventilated via tracheostomy, many comorbidities including renal failure
- Admitted every few weeks/months with a diagnosis of ventilator-associated pneumonia
- *Pseudomonas* was frequently isolated
- Over the course of several months, the *Pseudomonas* was first resistant to cefepime, then later cefepime and piperacillin-tazobactam and meropenem

- He was given a course of ceftolazane-tazobactam, a new last-resort antibiotic used in the most resistant cases of gram negative infection
- Unfortunately, his next infection was with *Pseudomonas* resistant to all FDA-approved antibiotics and doctors were able to offer no further therapy so patient was transitioned to comfort measures



ANTIBIOTIC RESISTANCE THREATS
in the United States, 2013



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

NATIONAL SUMMARY DATA

Estimated minimum number of illnesses and deaths caused by antibiotic resistance*:

At least  **2,049,442** illnesses,
 **23,000** deaths

**bacteria and fungus included in this report*




Estimated minimum number of illnesses and death due to *Clostridium difficile* (*C. difficile*), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:

At least  **250,000** illnesses,
 **14,000** deaths

WHERE DO INFECTIONS HAPPEN?

Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in health care settings, such as hospitals and nursing homes.



“If current trends continue unabated, the future is easy to predict. Some experts say we are moving back to the pre-antibiotic era. No. This will be a post-antibiotic era. In terms of new replacement antibiotics, the pipeline is virtually dry, especially for gram-negative bacteria. The cupboard is nearly bare. A post-antibiotic era means, in effect, an end to modern medicine as we know it. Things as common as strep throat or a child’s scratched knee could once again kill.

Some sophisticated interventions, like hip replacements, organ transplants, cancer chemotherapy, and care of preterm infants, would become far more difficult or even too dangerous to undertake.

Antimicrobial resistance is a global crisis – a slow motion tsunami. The situation is bad, and getting worse.”

- Margaret Chan, Director General of WHO

Mind Blowing Idea #2

- Instead of giving antibiotics “just to be on the safe side”, consider whether the safer option might actually be to NOT give them



Mind Blowing Idea #2

- Instead of giving antibiotics “just to be on the safe side”, consider whether the safer option might actually be to NOT give them
- That might mean some extra work (follow-up)



Case 2

- 48 y/o woman with a recent history of hospitalization for surgery to remove a rectal mass goes to see her primary care doctor for cough with green sputum and sinus pressure
- She asks for an antibiotic
- The doctor tells her she likely has a virus, possibly with a bacterial superinfection (“bronchitis”), and that it will probably get better on its own without antibiotics
- The patient says that she is leaving in 6 days on a two-week trip to Asia and that it would be awful to be sick on vacation
- The doctor agrees that he should give her an antibiotic “to be on the safe side” and prescribes 10 days of amoxicillin-clavulanate for sinusitis

Phone calls

- The patient goes on her trip. Her respiratory symptoms largely resolve in 3 days but she completes the entire 10 day course as prescribed.
- Seven days into her trip, she develops a fever, profuse diarrhea, and a local hospital is contacted. She is transported home. **Follow-up** of her findings are and then being
- She is diagnosed with *Clostridioides* (formerly *Clostridium*) *difficile* infection (*C. diff*) and suffers two recurrences after treatment

Tele-health



And Beatrice was never invited to a Halloween party ever again.

Beatrice the Biologist

Mind Blowing Idea #3

- “Finish the course” is a message that should be dropped from the discussion about antibiotic resistance





ANALYSIS

The antibiotic course has had its day

With little evidence that failing to complete a prescribed antibiotic course contributes to antibiotic resistance, it's time for policy makers, educators, and doctors to drop this message, argue **Martin Llewelyn and colleagues**

Martin J Llewelyn *professor of infectious diseases*^{1 2}, Jennifer M Fitzpatrick *specialist registrar in infection*², Elizabeth Darwin *project manager*³, SarahTonkin-Crine *health psychologist*⁴, Cliff Gorton *retired building surveyor*⁵, John Paul *consultant in microbiology*⁶, Tim E A Peto *professor of infectious diseases*⁷, Lucy Yardley *professor of health psychology*⁸, Susan Hopkins *consultant in infectious diseases and microbiology*⁹, Ann Sarah Walker *professor of medical statistics and epidemiology*³

“Complete the course”: a barrier to antibiotic conservation

The fallacious belief that antibiotic courses should always be completed to minimise resistance is likely to be an important barrier to reducing unnecessary antibiotic use in clinical practice and to developing evidence to guide optimal antibiotic use. The idea is deeply embedded, and both doctors and patients currently regard failure to complete a course of antibiotics as irresponsible behaviour.^{31 32}

Target Selection vs. Collateral Selection

Box 1: Selection of antibiotic resistance

Target selection—For certain “professional” pathogens, such as *Mycobacterium tuberculosis*, spontaneous resistance conferring mutants may be selected during treatment, can be transmitted before cure is achieved, or can re-emerge after treatment failure. Other professional pathogens where this may apply include HIV, malaria, gonorrhoea, and *Salmonella typhi*

Collateral selection—Many bacterial species that live harmlessly in the gut, on our skin and mucus membranes, or in the environment can also cause disease as opportunist pathogens. For such organisms, resistance selection occurs predominantly during antibiotic treatment of other infections. Resistance in opportunists may be passed easily to other strains of the same species of bacteria or to different species. Key examples include methicillin resistance in *Staphylococcus aureus*, extended spectrum β -lactamase producing *Enterobacteriaceae* and carbapenem resistance in *Klebsiella pneumoniae*

40 RCTs Over 25 Years Agree: “Shorter is Better”

Table

Infections for Which Short-Course Therapy Has Been Shown to Be Equivalent in Efficacy to Longer Therapy

Disease	Treatment, Days	
	Short	Long
Community-acquired pneumonia ¹⁻³	3-5	7-10
Nosocomial pneumonia ^{6,7}	≤8	10-15
Pyelonephritis ¹⁰	5-7	10-14
Intraabdominal infection ¹¹	4	10
Acute exacerbation of chronic bronchitis and COPD ¹²	≤5	≥7
Acute bacterial sinusitis ¹³	5	10
Cellulitis ¹⁴	5-6	10
Chronic osteomyelitis ¹⁵	42	84

Abbreviation: COPD, chronic obstructive pulmonary disease.

So how do I decide how long to treat a bacterial infection?

To figure out how long antibiotics need to be given, use the following rules:

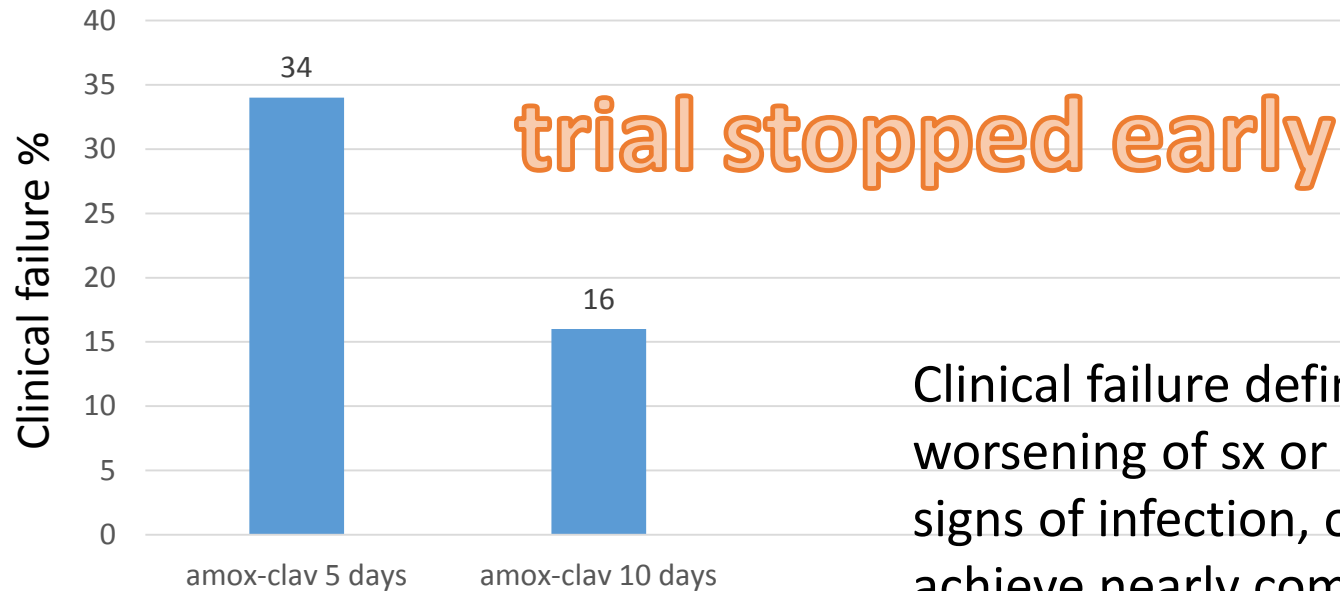
1. Choose a multiple of 5 (fingers of the hand) or 7 (days of the week).
2. Is it an outpatient problem that is relatively mild? If so, choose something less than 10 days. After application of our multiples rule, this should be 5 or 7 days.
3. Is it *really* mild, so much so that antibiotics probably aren't needed at all but clinician or patient are insistent? Break the 5/7 rule and go with 3 days. Ditto uncomplicated cystitis in young women.
4. Is it a serious problem that occurs in the hospital or could end up leading to hospitalization? With the exception of community-acquired pneumonia (5 or 7 days), 10 days is the minimum.
5. Patient not doing better at the end of some course of therapy? Extend treatment, again using a multiple of 5 or 7 days.
6. Does the infection involve a bone or a heart valve? Four weeks (28 days) at least, often 6 weeks (42 days). Note that 5 weeks (35 days) is not an option — here the 5's and 7's cancel each other out, and chaos ensues.
7. The following lengths of therapy are inherently weird, and should generally be avoided: 2, 4, 6, 8, 9, 11, 12, 13 days. Also, 3.14159265 days.

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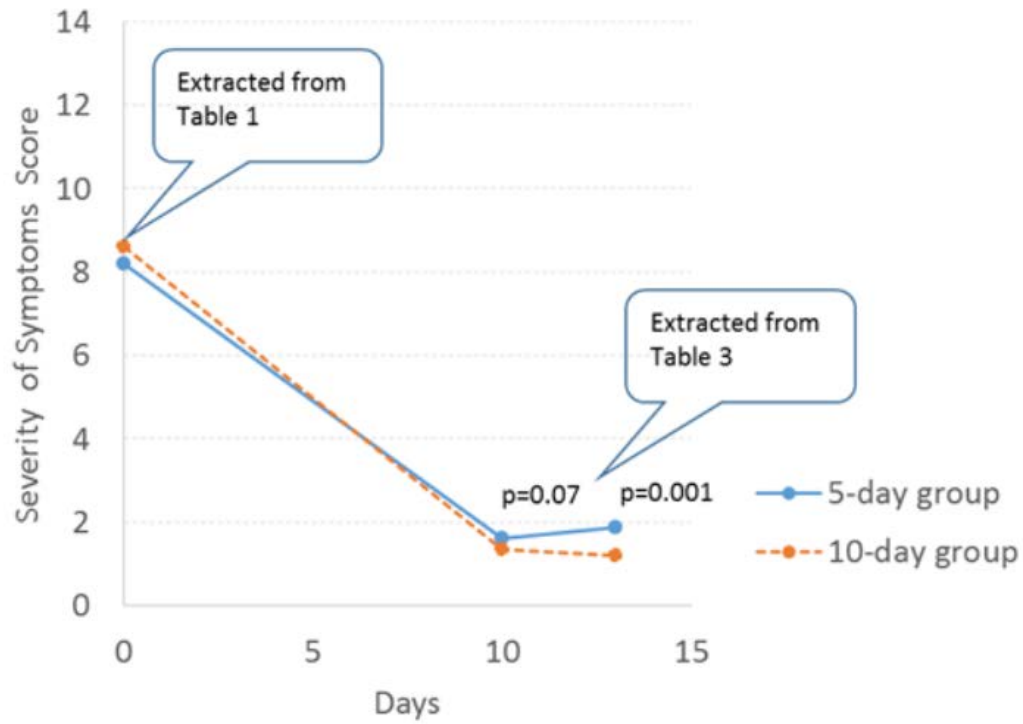
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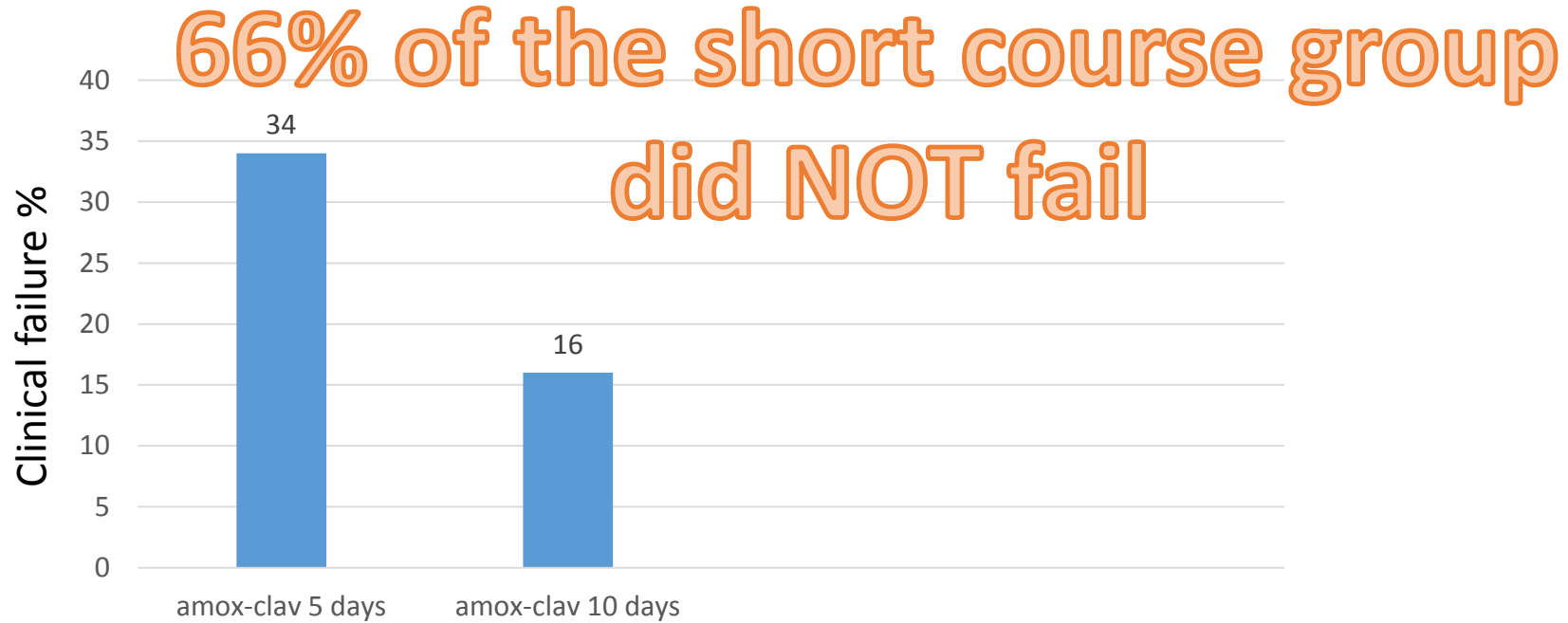
Clinical Failure (%)



Clinical failure defined as worsening of sx or otoscopic signs of infection, or failure to achieve nearly complete resolution of signs and sx of otitis by end of treatment



Clinical Failure (%)



Mind Blowing Idea #4

- As a medical society, we may have to accept some “failures” (patients that go on to have persistent symptoms) when we choose to observe rather than treat with antibiotics



Mind Blowing Idea #3

- As a medical society, we may have to accept some “failures” (patients that go on to have persistent symptoms) when we choose to observe rather than treat with antibiotics
- The more we allow ourselves to accept that, the more patients will benefit from avoidance of antibiotics



Case

- 89 yo woman with dementia who is otherwise physically well and active lives in a nursing home
- She has “good days” and “bad days”
- On her bad days she is more agitated, combative and confused than she is on her good days
- On particularly bad days, often encouraged by visiting family members, a urine culture is sent to see if a UTI might be contributing to her behavior
- More often than not, her urinalysis shows a high number of white blood cells and her urine culture is positive
- When this happens, she receives antibiotics, and within a few days her behavior improves

- On one such day, after urinalysis and culture are found to be positive, she is given cipro to treat a presumed UTI
- The physician in the nursing home knows about the importance of not treating asymptomatic bacteriuria, but the last time he tried not treating her when she had a positive culture, she started complaining of burning with urination a couple of weeks later
- One day after completing the course of cipro, she complains of severe leg pain
- Achilles tendon rupture, a known complication of cipro, is diagnosed
- Recovery is long and painful, and her physical and psychological health deteriorate rapidly as a result of this setback

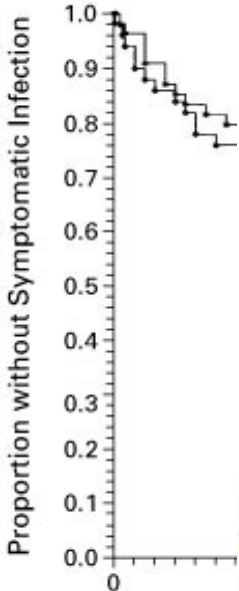
The Only Useful Urine Culture is a Negative One

Table 2. Prevalence of asymptomatic bacteriuria in selected populations.

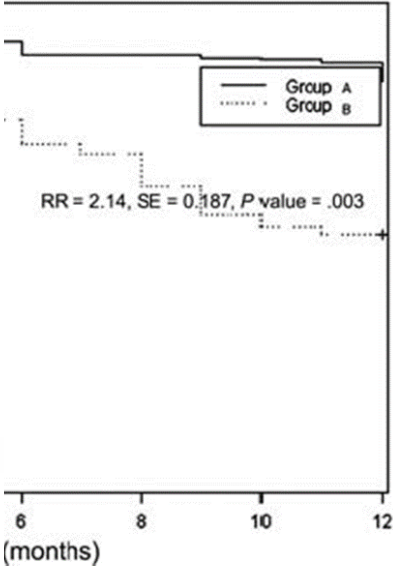
Population	Prevalence, %	Reference
Healthy, premenopausal women	1.0–5.0	[31]
Pregnant women	1.9–9.5	[31]
Postmenopausal women aged 50–70 years	2.8–8.6	[31]
Diabetic patients		
Women	9.0–27	[32]
Men	0.7–11	[32]
Elderly persons in the community ^a		
Women	10.8–16	[31]
Men	3.6–19	[31]
Elderly persons in a long-term care facility		
Women	25–50	[27]
Men	15–40	[27]
Patients with spinal cord injuries		
Intermittent catheter use	23–89	[33]
Sphincterotomy and condom catheter in place	57	[34]
Patients undergoing hemodialysis	28	[28]
Patients with indwelling catheter use		
Short-term	9–23	[35]
Long-term	100	[22]

^a Age, >70 years.

Proportion of Women with Diabetes Who Remained Free of Symptomatic Urinary Tract Infection, According to Whether They Received Antimicrobial Therapy or Placebo



Proportion of Women Who Remained Free of Symptomatic Urinary Tract Infection, to Whether They Received Antimicrobial Therapy or Placebo at Enrollment.



Harding GK et al. N Engl J Med 2002;347:1576-1583.

Cai et al. CID 2012;55(6):771-7

Summary

- Antibiotics are important but dangerous weapons in our arsenal
- Give yourself permission to observe patients off antibiotics...and to use shorter courses...some might progress and that's OK, because others will benefit from antibiotic avoidance
- Bacterial colonization should not be feared
- When it comes to resistance, think globally and act locally

