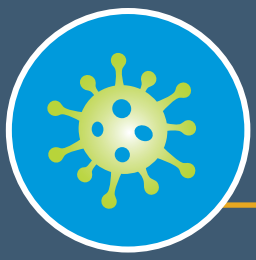
ANTIBIOTICS:

How the RISKs of USING may outweigh the RISKs of NOT-USING, particularly for infections commonly caused by viruses

Most antibiotics for common infections are considered safe, but this "reputation" may be overstated. For infections caused by viruses and those known to resolve on their own, the potential harms should be appreciated.

DON'T UNDERESTIMATE potential antibiotic harms!



High rates of antibiotic use leads to bacteria being RESISTANT to the drug's effects.

Antibiotics are responsible for almost 1 OUT OF 5 Emergency Room visits for adverse drug events.

It is common to have undesirable side effects.

RARE BUT SERIOUS adverse events can occur, e.g. tendon problems, severe skin reactions.

Allergic reactions can occur with any antibiotic.
The more serious reactions are rare but can be life-threatening.

There aren't really any harms with antibiotics are there?

Well – Yes
Actually there are!!!
Consider the following...

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Alex Crawley, BSP

Antibiotic Harms

Antibiotics are a valuable resource and judicious use is important. For many serious infections (e.g. pneumonia, bacterial meningitis, sexually transmitted infections) the benefits of antibiotics clearly outweigh potential harms. However, for conditions that are primarily viral (e.g. pharyngitis, acute sinusitis, acute bronchitis), the benefits are minimal and likely outweighed by harms.

Of note: antibiotic-related adverse drug events account for 1 out of every 5 visits to the Emergency Department.[1]

How common are overall harms with antibiotics?

- In a meta-analysis (10 trials, 2450 patients) comparing antibiotics to placebo for acute rhinosinusitis, common adverse events (such as **nausea**, **vomiting**, **diarrhea**, or **abdominal pain**) occurred in 27% of patients on antibiotics versus 15% on placebo (NNH = 8-12).[2,5] The antibiotics used in this meta-analysis included **penicillins**, **macrolides**, and **tetracyclines**. Trials examining other populations have found similar numbers of adverse events.[3,4,5]
- A recent meta-analysis comparing amoxicillin or amox/clav to placebo found risk of **yeast infection** (candidiasis) to be about 8x higher in those on antibiotics (NNH = 23).[6]

Overall harms:	**NNH = 8-12**
Yeast infection:	**NNH = 23**

How common are allergic reactions with antibiotics?

- Allergic reactions can occur with any antibiotic; **penicillin** is particularly well studied. About 5-10% of patients will self-report a penicillin allergy;[7,8] however the vast majority of these reactions are delayed reactions, occurring days to weeks after initiating therapy, and do not typically indicate a true allergy.[9] Anaphylaxis occurs in about 0.01% of patients taking penicillin; about 10% of these reactions are fatal (i.e. 0.001% of all patients prescribed penicillin).[10,11,12]

Rash, hives:	**NNH ≈ 20**
Anaphylaxis:	**NNH ≈ 10,000**

How common are serious harms with antibiotics?

Rare but serious adverse events are associated with all antibiotics. Large, long-term randomized controlled trials are uncommon, and so it is difficult to put a precise estimate on how prevalent these events are. However, some adverse events include:

Serious harms:	**NNH from 300 to 30,000**

- ***Clostridium difficile* infection**: associated most often with **clindamycin** (RR≈4), cephalosporins, and fluoroquinolones; risk varies depending on patient factors.[13,14,15]
- **Stevens Johnson Syndrome, Toxic Epidermal Necrolysis, & other severe skin reactions**: these events occur a few times per 100,000 antibiotic prescriptions.[16] Cotrimoxazole in particular has a higher association than most other antibiotics.[17]
- **QT prolongation**: associated most often with macrolides (esp. **clarithromycin** and **erythromycin**) and fluoroquinolones (esp. **levofloxacin** and **moxifloxacin**). Risk of QT prolongation is also dependent on other factors (e.g. cardiac, metabolic, other drugs, etc.). See RxFiles QT Prolongation.
- **Tendon rupture with fluoroquinolones**: one large cohort study found a risk of 3.5% for tendon rupture in adults over the age of 65.[18]
- **Hyperkalemia with cotrimoxazole**: in older adults taking medications which can raise potassium (such as **ACEIs**, **ARBs**, **spironolactone**, or **NSAIDs**), **cotrimoxazole** was associated with sudden death (NNH ≈ 300).[19,20]
- **Contraceptive failure/drug interaction?** Birth control failure is a well-documented event with rifampin. It is thought to be unlikely with other antibiotics, although a backup birth control method is still recommended.

What about antimicrobial resistance?

- Resistance to an antibacterial can develop quickly. For example, strains of *Streptococcus pneumoniae* resistant to **levofloxacin** were documented in the same year levofloxacin was introduced to the market.[21] Rare, but worrisome, reports of bacteria resistant to every available antimicrobial can be found in the literature.[22]

  The good news is that when prescribing patterns change, resistance rates decline.[23,24]

NNH as low as 1???

Every course of antibiotic is likely to result in some emerging resistance which could affect the next choice of antibiotic regimen for that individual, especially if within 3 months of the previous antibiotic. Of course, the NNH for catastrophic resistance would be much higher.

Final Thoughts:

- There are many more harms than can be covered here! For example: serum sickness like reactions, pulmonary fibrosis with nitrofurantoin, tooth discoloration with tetracyclines.
- A quote from the team: *Harms speak louder when there is little or no benefit to offset them!*

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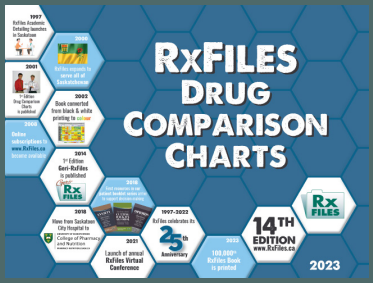

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