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RhAPP
RHEUMATOLOGY ADVANCED
PRACTICE PROVIDERS





Bugs & Drugs

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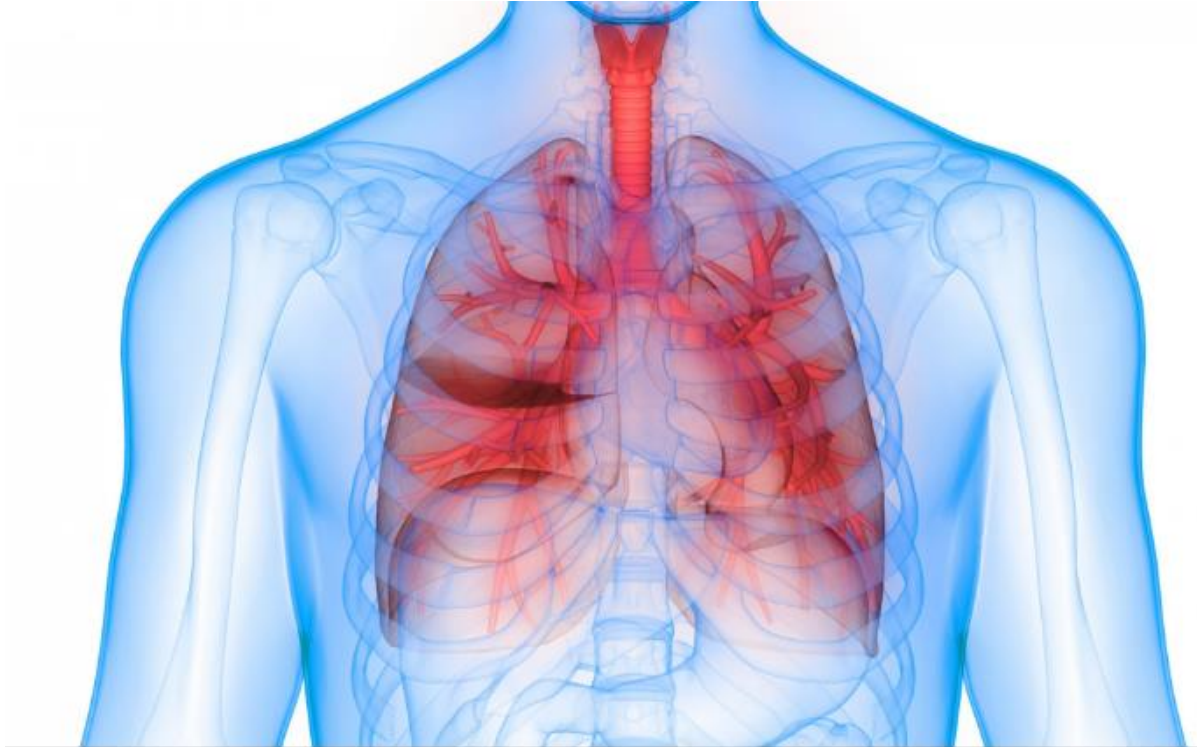
Disclosures

- No actual or potential conflicts of interest to disclose regarding this presentation

Learning Objectives

- Recognize potential short falls of antibiotics discussed
- Identify potential alternative antibiotic choices for the infectious processes discussed
- Select potential candidates for nirmatrelvir/ritonavir & molnupiravir

Azithromycin for Community Acquired Pneumonia (CAP)



Azithromycin for CAP

Common pathogens in community acquired pneumonia (CAP)

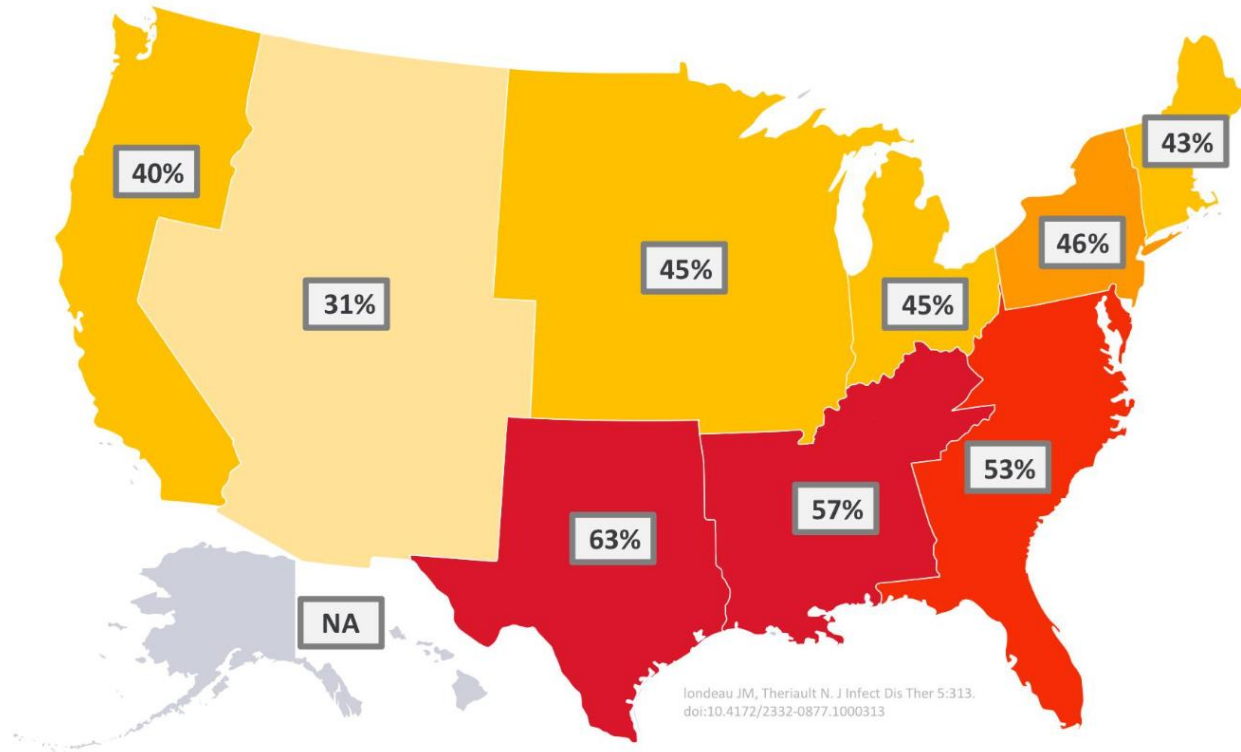
Typicals

- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Moraxella catarrhalis*

Atypicals

- *Mycoplasma pneumoniae*
- *Chlamydia pneumoniae*
- *Legionella spp.*

S. pneumoniae Resistance to Azithromycin



Azithromycin: Alternative for CAP

- Doxycycline
 - Less resistance
 - Same duration
 - Generally well tolerated
 - Avoid taking with foods or medications containing Ca^{2+} , NaHCO_3 , Zn^{2+} , Fe , Mg^{2+} (2 hours before or 6 hours after) to avoid chelation
 - Causes sensitivity to the sun

Sulfamethoxazole/Trimethoprim for Urinary Tract Infection (UTI)



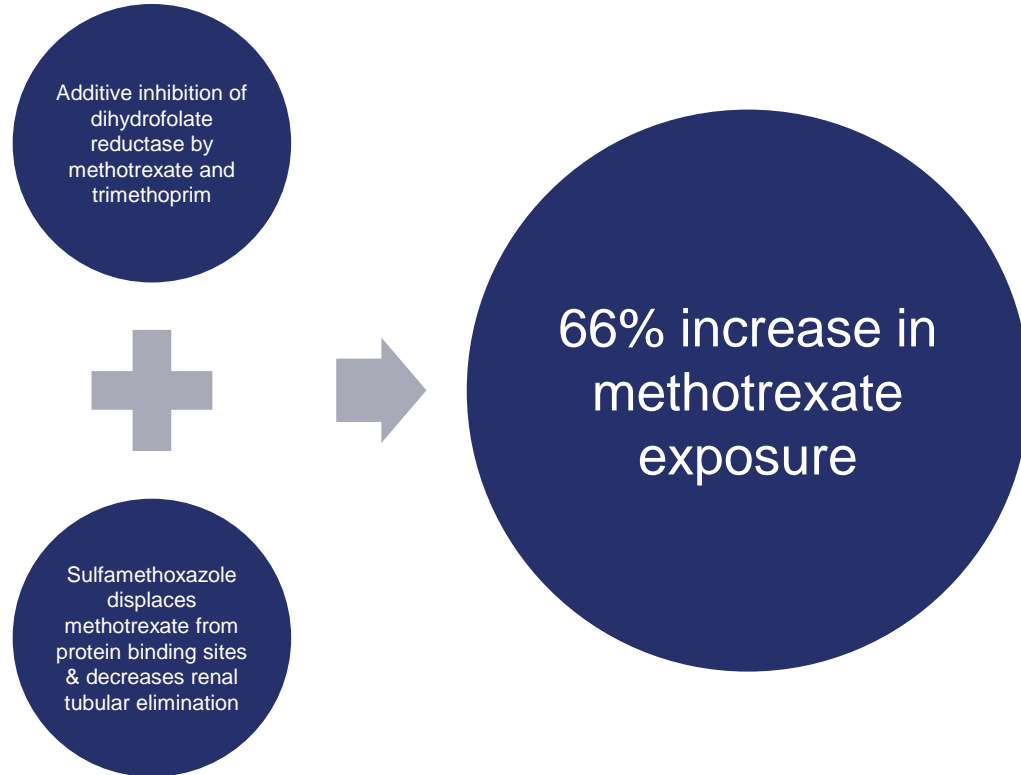
Bactrim for UTI

Review > Clin Infect Dis 2011 Mar 1;52(5):e103-20. doi: 10.1093/cid/ciq257.

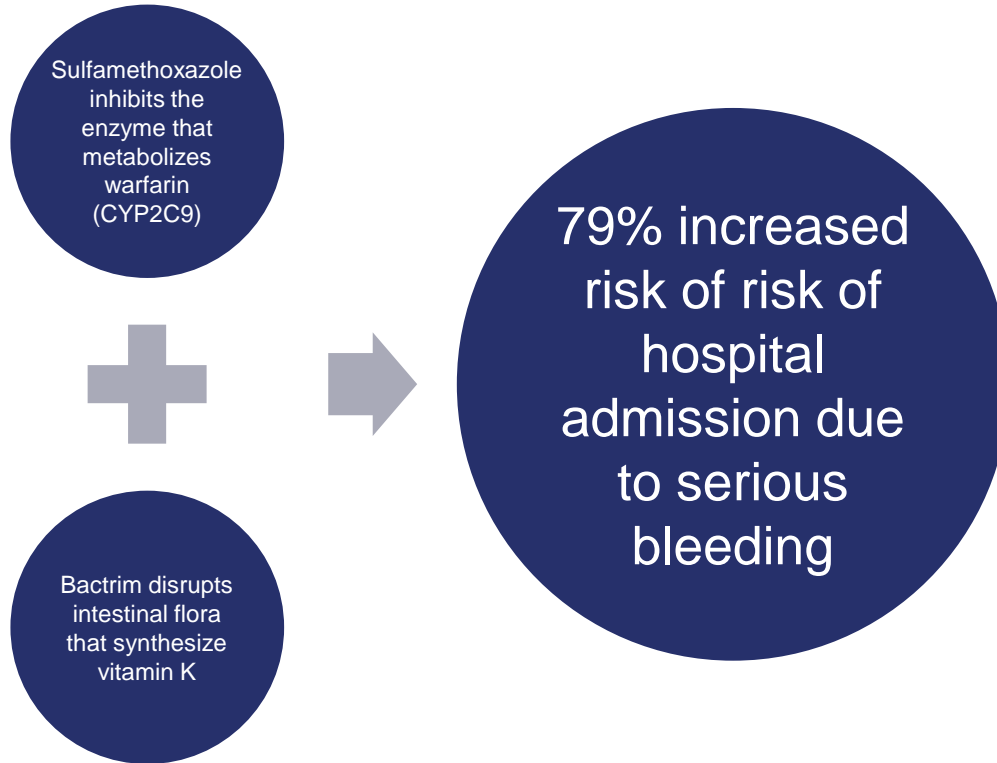
International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases

- IDSA recommends against empiric use when *E.coli* resistance is >10%
- Adverse affects
- Drug-drug interactions

Bactrim Drug-Drug Interactions of Note: Methotrexate



Bactrim Drug-Drug Interactions of Note: Warfarin



Bactrim Drug-Drug Interactions of Note: ACE Inhibitors, ARBs, Spironolactone

Trimethoprim
impairs renal
potassium
excretion

Additive
potassium
sparing effects
w/ ACEi,
ARBS, &
spironolactone

12 times higher risk
of hyperkalemia
then with other
antibiotics

Bactrim: Alternatives for Lower UTI

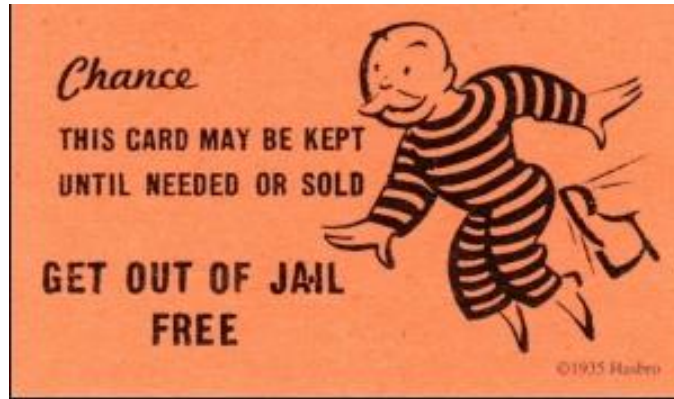
- Nitrofurantoin
 - Extremely low resistance to common urinary pathogens
 - Well tolerated
 - Data for use in patients with creatinine clearance as low as 30 ml/min

Bactrim: Alternatives for Lower UTI

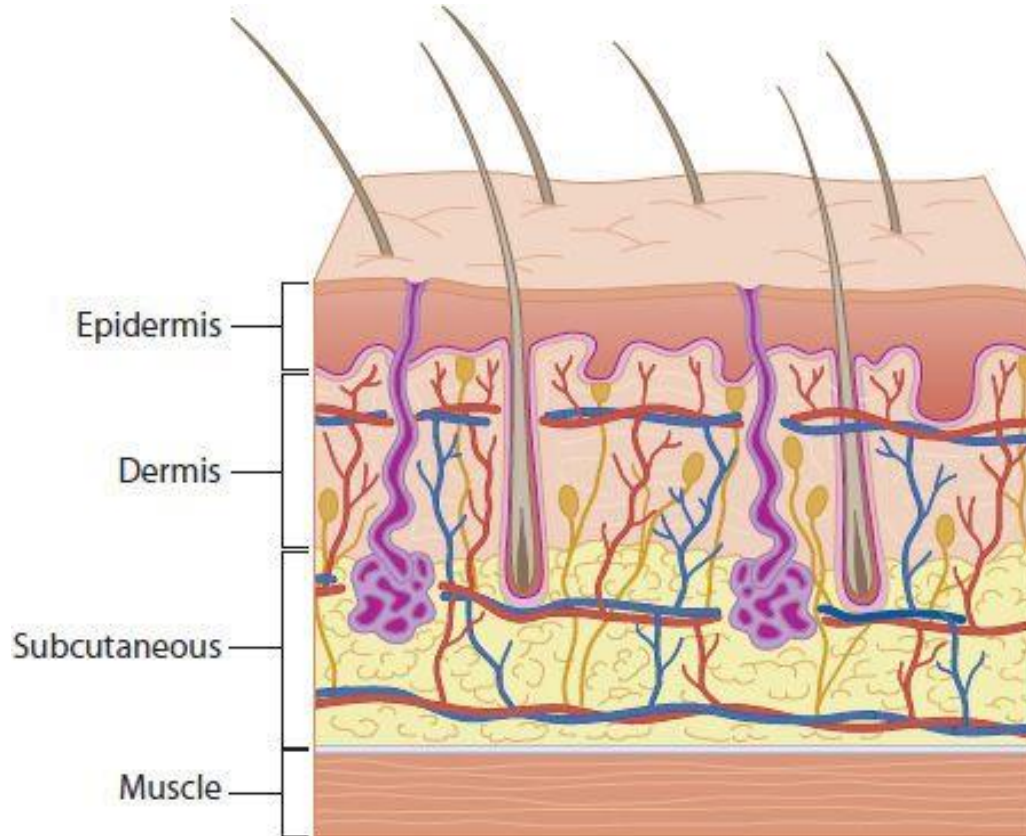
- Cephalexin
 - Generally well tolerated
 - Less resistance for lower cystitis
 - Clinical & Laboratory Standards Institute (CLSI) has higher breakpoints for systemic infections such as pyelonephritis
 - Use caution in this population

Alternatives for Lower UTI

- Fosfomycin
 - Uncomplicated: 3g PO x1
 - Complicated: 3g PO q48h x 3 doses



Clindamycin for Skin and Soft Tissue Infection (SSTI)



Clindamycin for SSTI

- *Staphylococcus aureus* resistance
 - Inducible resistance
- Adverse affects
 - Diarrhea
 - *Clostridioides difficile* infection
 - Odds ration 15-20 x placebo

Clindamycin: Alternatives for SSTI

Purulent SSTI

- Trimethoprim/sulfamethoxazole
- Doxycycline

Non-purulent

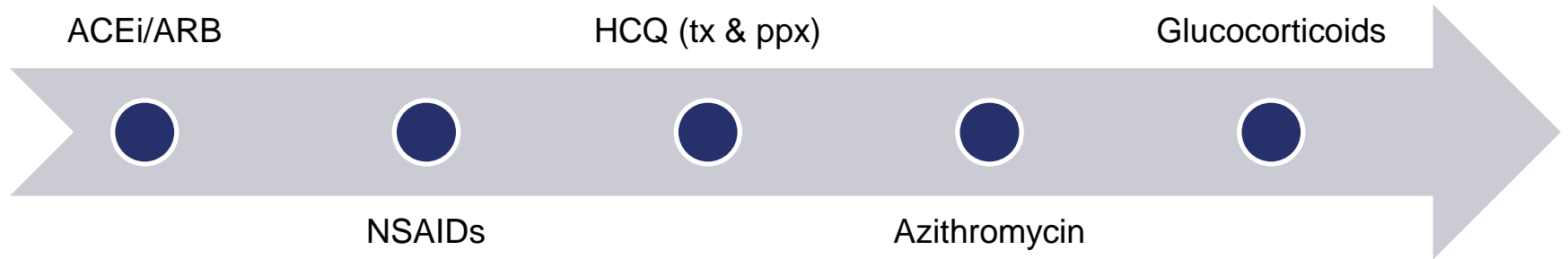
- Dicloxacillin
- Cephalexin

Alternatives for SSTI

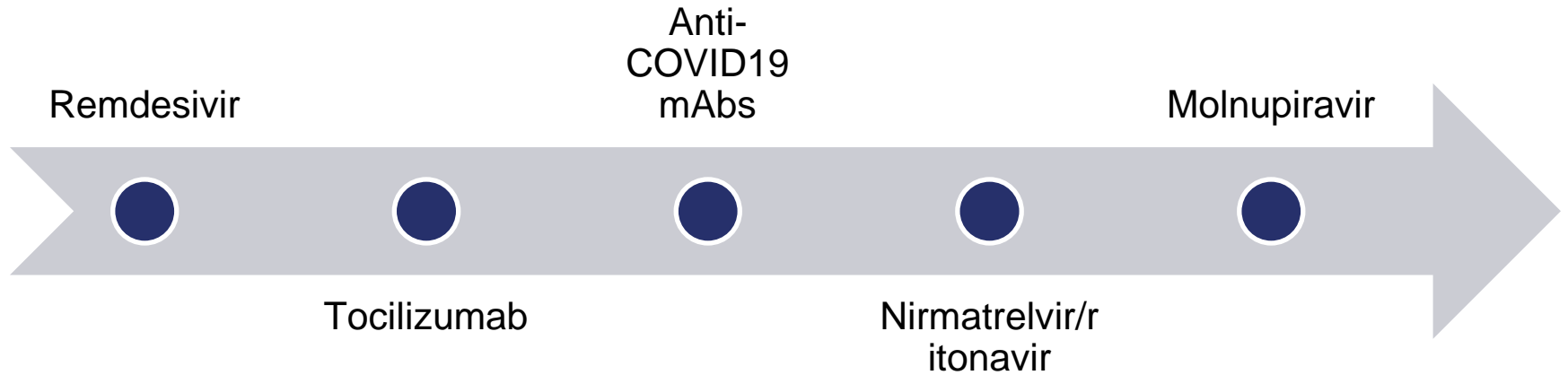
- Linezolid
 - Available as a generic which has greatly reduced its price
 - Caution
 - Serotonin syndrome when combined with other pro-serotonergic medications
 - Myelosuppression
 - Associated with therapy ≥ 14 days



COVID-19 Therapy Timeline



COVID-19 Therapy Timeline



Nirmatrelvir/ritonavir (Paxlovid™) Molnupiravir (Lagevrio™)

Eligibility

- COVID-19+
- Ambulatory
- Symptom onset \leq 5 days
- eGFR \geq 30 mL/min
- \geq 12 y/o AND \geq 40 kg:
- No, or mild-moderate liver dysfunction (Child-Pugh Class A or B):
- High risk criteria

High Risk Criteria

- Age \geq 65
- DM
- BMI $>$ 25
- Chronic lung disease
- CKD
- Current smoker
- Immunosuppressive disease/treatment
- CV disease
- HTN
- Sickle cell
- Active cancer
- Medically-related technological dependence

Nirmatrelvir/ritonavir (Paxlovid™)

- Drug-drug interactions

- Resources

- Liverpool COVID Drug Interactions



- IDSA Recommendations



- Micromedex/Lexicomp

Contraindicated

- | | | |
|---------------------|------------------------|---|
| o alfuzosin | o ivabradine | o quinidine |
| o amiodarone | o lomitapide | o ranolazine |
| o apalutamide | o lovastatin | o rifampin |
| o carbamazepine | o lumacaftor/ivacaftor | o St. John's Wort (<i>hypericum perforatum</i>) |
| o clozapine | o lurasidone | o sildenafil (Revatio®) for pulmonary arterial hypertension |
| o colchicine | o methylergonovine | o silodosin |
| o dihydroergotamine | o midazolam (oral) | o simvastatin |
| o dronedarone | o naloxegol | o tolvaptan |
| o eletriptan | o pethidine | o triazolam |
| o eplerenone | o phenobarbital | o ubrogepant |
| o ergotamine | o phenytoin | o voclosporin |
| o finerenone | o pimozide | |
| o flecainide | o primidone | |
| o flibanserin | o propafenone | |

<https://www.covid19-druginteractions.org/about>

<https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/management-of-drug-interactions-with-nirmatrelvirritonavir-paxlovid/>

Molnupiravir (Lagevrio™)

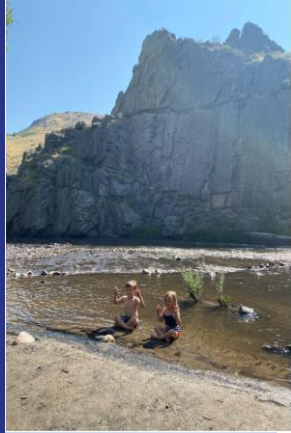
- Reproductive issues
 - Avoid in pregnancy
 - Contraception
 - Female: during course & for 4 days after last dose
 - Male: during course and for 3 months after last dose
- Bone and cartilage toxicity
 - Avoid <18 y/o

Oral Anti-COVID Therapy Comparison

	Nirmatrelvir/ritonavir	Molnupiravir
Data	57-88% RRR hospitalization/death	30% RRR hospitalization/death
Eligibility	Mild-moderate COVID-19 High risk for progression to severe disease	
Caution	Drug-drug interactions	Reproductive issues

Conclusion

- Azithromycin monotherapy for CAP is unlikely to be the optimal empiric therapy
- Sulfamethoxazole/trimethoprim is not ideal empiric therapy for the treatment of UTI
- Clindamycin for SSTI is unlikely to be the optimal empiric therapy
- Nirmatrelvir/ritonavir and Molnupiravir are still active against current COVID-19 strains and may be appropriate in patients with rheumatologic disorders



Thank you!

