COVID-19 Mortality from Secondary Acquired Infections

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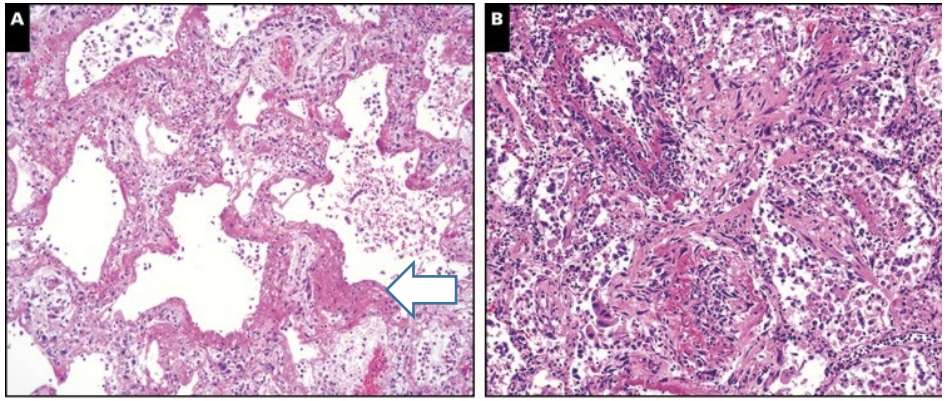
How life has changed: COVID-19 and AMR
Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria
9 September 2020

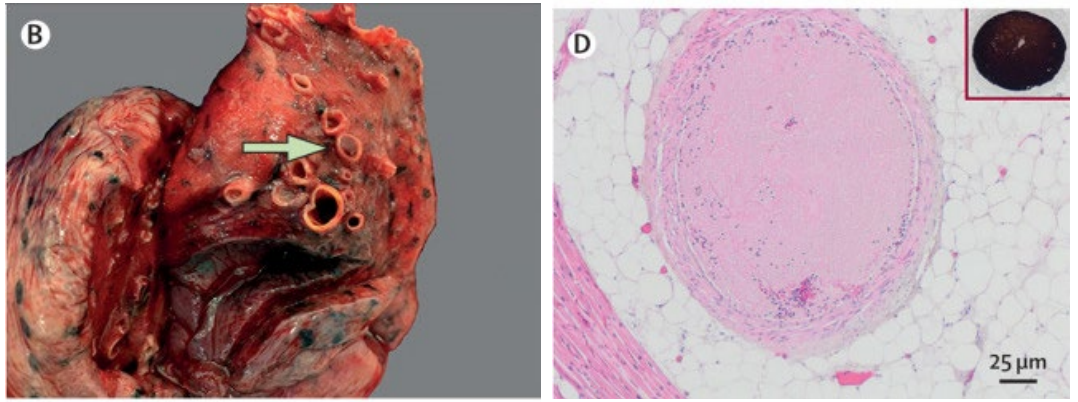
Pitt

VAPHS
VA Pittsburgh Healthcare System

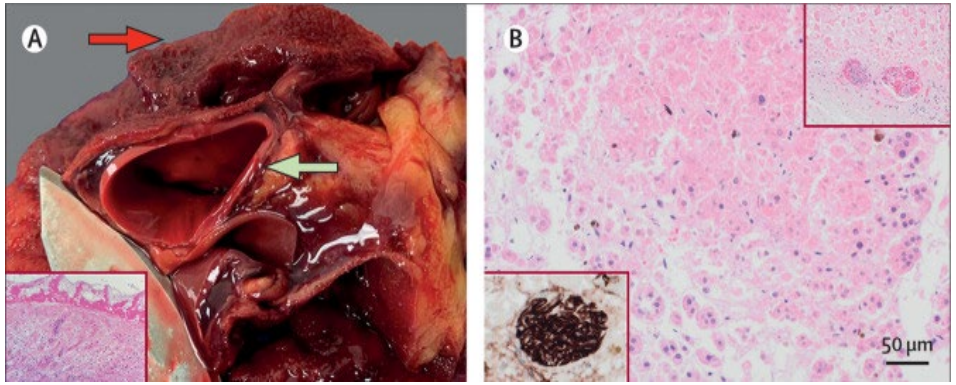
Why do COVID-19 patients die?



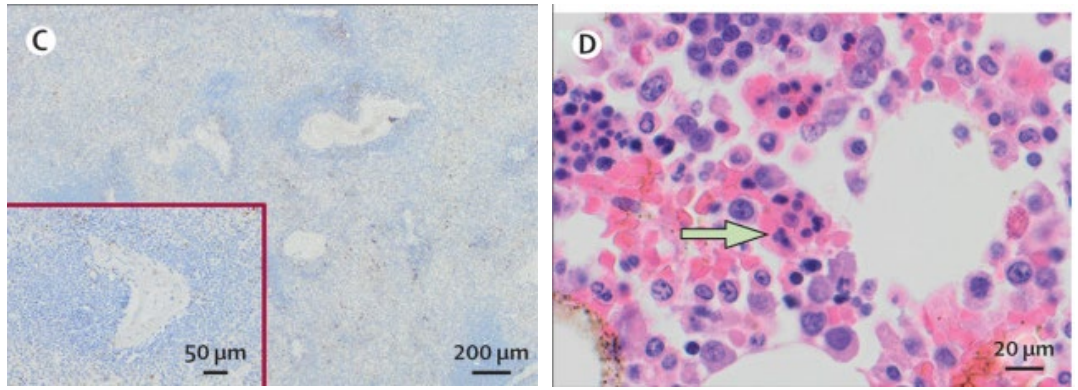
Diffuse alveolar damage causing acute respiratory distress syndrome (ARDS)



Thromboembolic disease



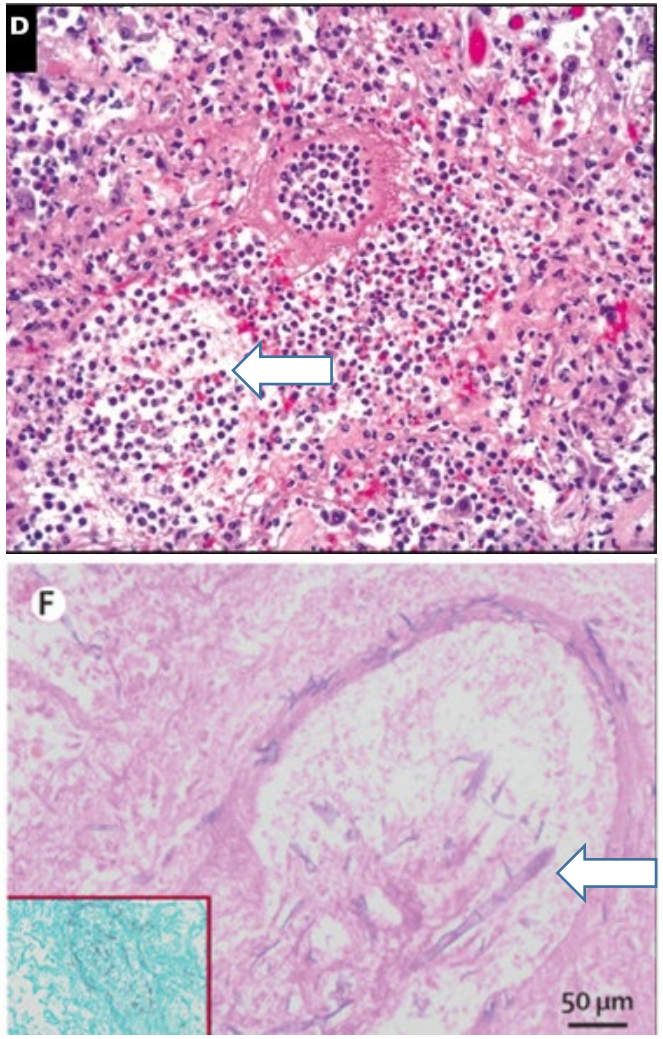
Multisystem organ failure



Immune depletion and dysregulation

Postmortem histopathology images from Sekulic et al. Am J Clin Path 2020; Hanley et al. Lancet Microbe 2020.

Do patients die of secondary infections?



37% of COVI-19 autopsies have histopathologic findings in lungs that are consistent with superimposed bronchopneumonia or pulmonary infection[1]

- Findings due to superimposed infection or COVID-19?
- Very limited microbiology and AMR data
- More often focal process rather than diffuse disease
- Often not recognized or treated with antimicrobials ante-mortem

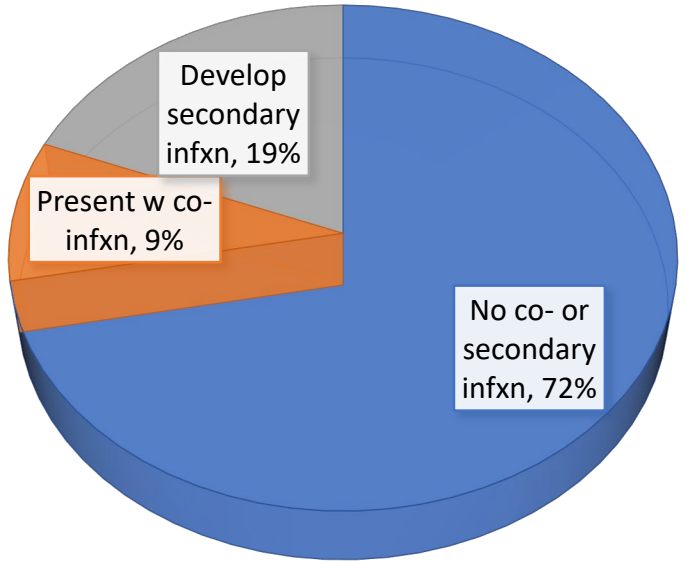
Sizeable minority of COVID-19 decedents die <u>with</u>, but not necessarily <u>from</u>, superimposed bacterial or (less often) fungal infections

Images from Sekulic et al. Am J Clin Path 2020; Hanley et al. Lancet Microbe 2020. 1. Histopathologic findings: Intra-alveolar PMN infiltrates or abscess/empyema, in absence of classic viral pneumonia histopathology. N=106/289, from review of data from 51 peer-reviewed publications through 28 August 2020, includes hospital- and community-based deaths

Types of COVID-19 secondary infections

VAPHS experience, through 7/31/20

Buehrle et al. Antimicrob Agents Chemother 2020



Bloodstream infections
- Endocarditis, septic emboli, abscesses

Urinary tract infections

Skin and soft tissue infections

Clostridiodes difficile infections

Co-infections
- Community acquired pneumonia, urinary tract infection, skin/soft tissue infection, *C difficile* infection, febrile neutropenia

Secondary infections
- Hospital/ventilator pneumonia, bloodstream infection, urinary tract infection, *C. difficile* infection

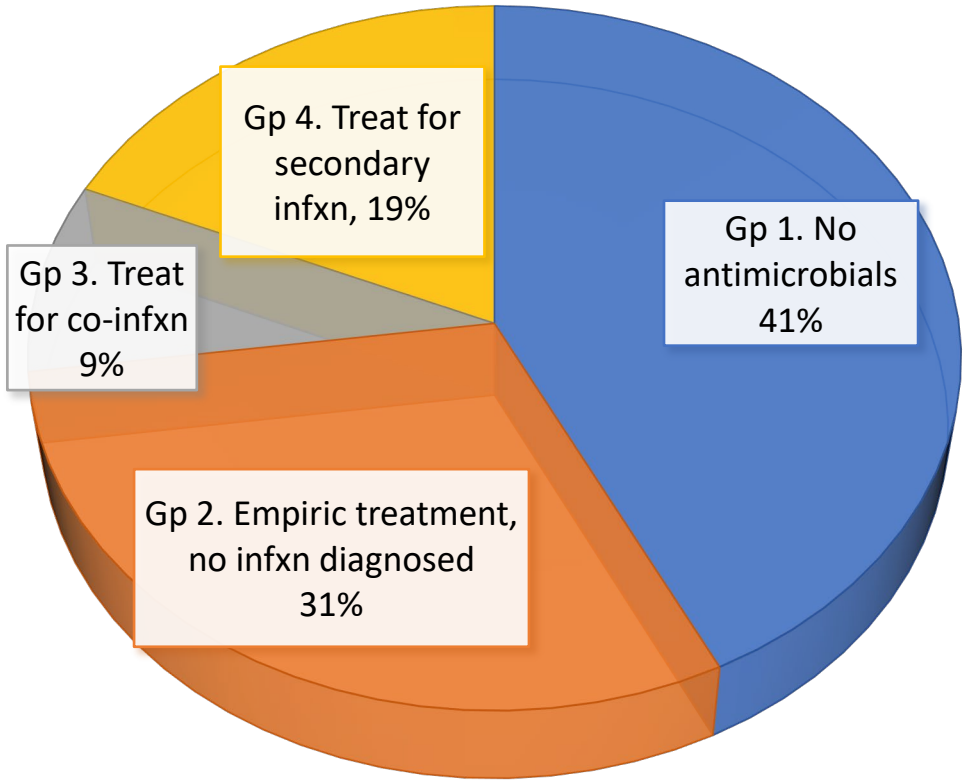
Microbiology and AMR will reflect local epidemiology and host risk factors

Lung: *P. aeruginosa, K. pneumoniae, C. koseri, S. maltophilia*

Urine: *E. Coli*, *Proteus, K. pneumoniae*
- MDR, ESBL, CRE infections diagnosed

Blood: *S. aureus*, coag negative *Staph*, *Strep* spp., *Candida*

COVID-19: Antimicrobial stewardship strategies

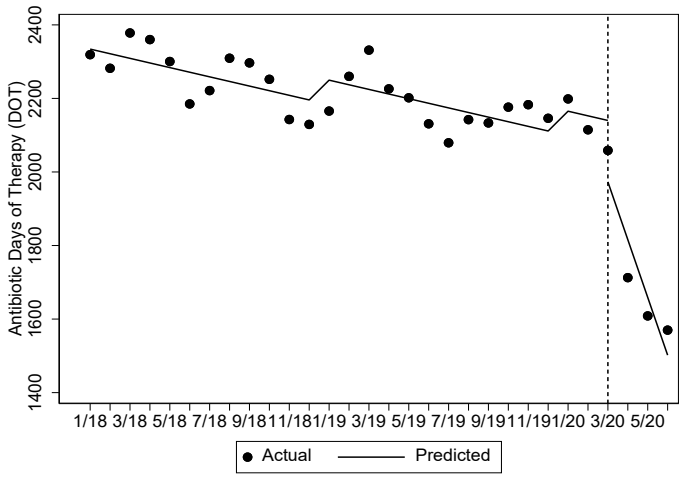


Stewardship group	Stewardship objectives
1. No treatment	Limit unnecessary use, include rapid diagnostics (negative predictive values)
2. Empiric treatment	Target most likely pathogens, rapid de-escalation, limit duration, aggressive diagnostic testing (NPVs)
3. Treat co-infection	Promote narrow spectrum, short course, oral
4. Treat secondary infection	Target nosocomial pathogens, promote narrow spectrum, short course

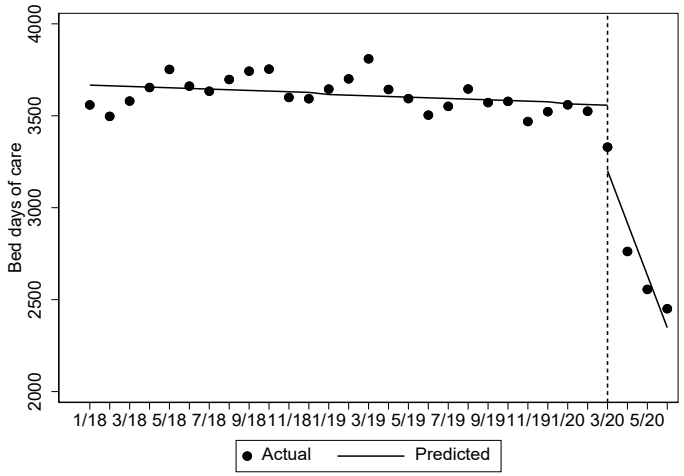
Buehrle et al. Antimicrob Agents Chemother 2020

Impact of COVID-19 on hospital antibiotic use

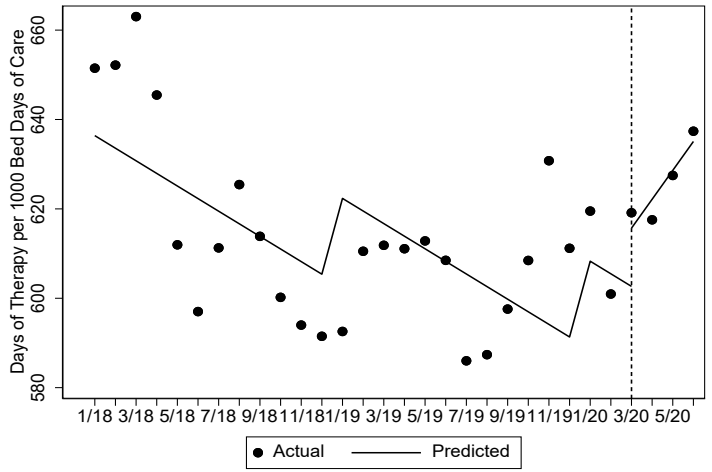
VAPHS Days of therapy (DOT)



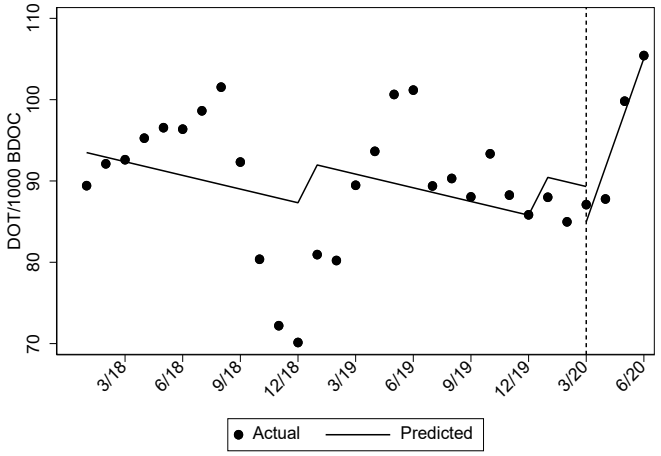
VAPHS bed days of care (BDOC)



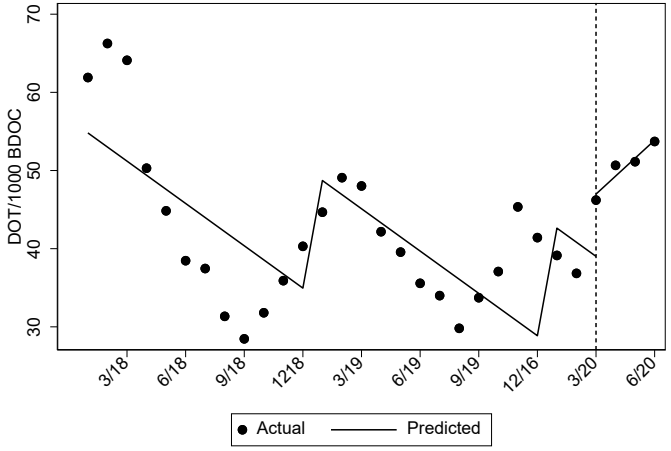
VAPHS DOT/1,000 BDOC



Non-antipseudomonal PNCs DOT/1,000 BDOC



Macrolides DOT/1,000 BDOC

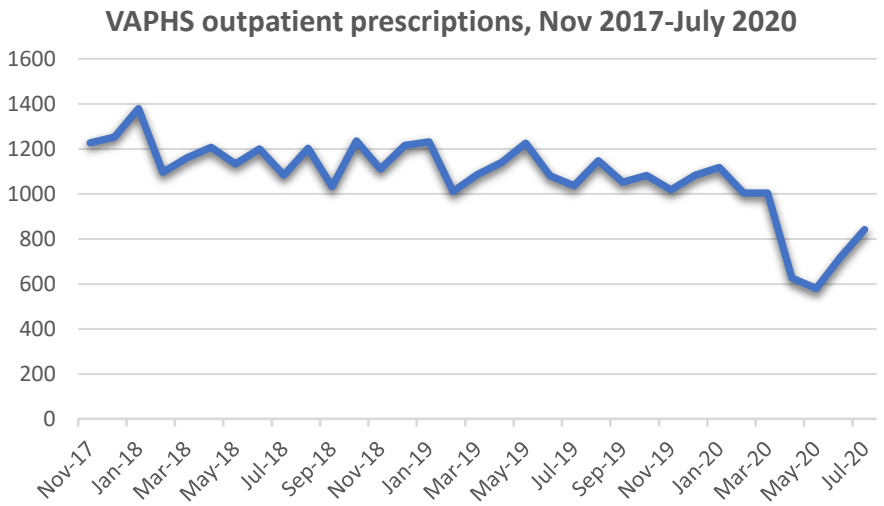


Significantly increased DOT/1000 BDOC of agents vs. CAP

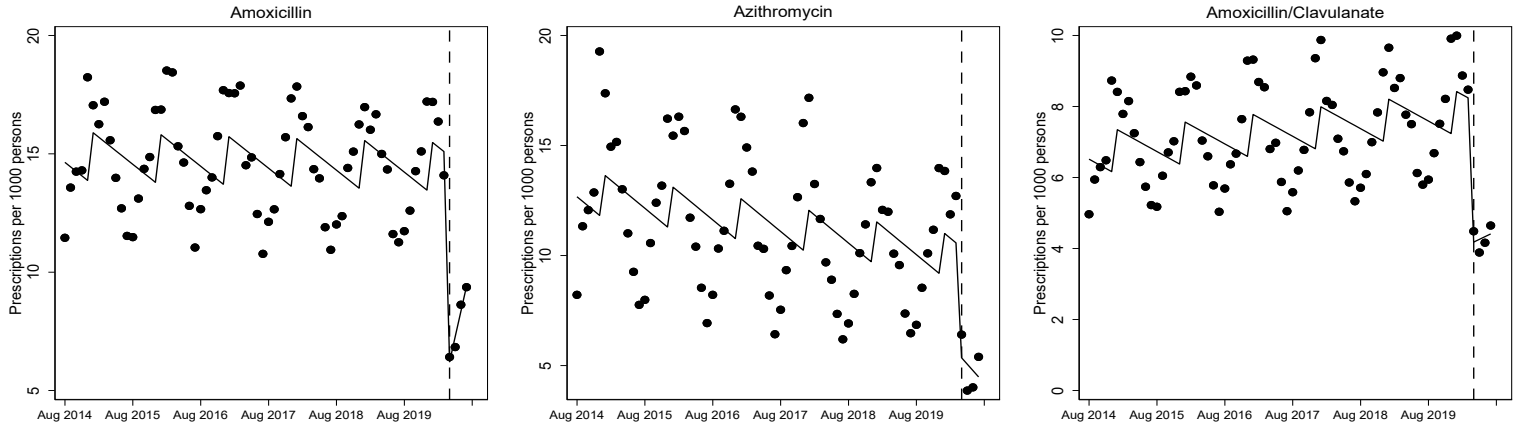
- Patients with CAP/suspected CAP disproportionately presenting to hospital?
- Over-treatment of suspected CAP?

Buehrle et al. Antimicrob Agents Chemother 2020

Outpatient antibiotic use



US prescription fills, 2014-July 2020 (IQVIA NPA data)



Significant reductions in prescription fills in April 2020 for the ten most commonly prescribed outpatient antibiotics

- No significant rebound, April-July 2020: Azithromycin, amoxicillin-clavulanate, levofloxacin
- Rebound April-July 2020, but still below baseline: Amoxicillin, doxycycline

Prescription fills for outpatient antibiotics recommended against CAP or commonly used against respiratory tract infections remain significantly below baseline

- Patients not seeking care? Clinicians less likely to prescribe (unnecessary) agents?

Will COVID-19 result in increased AMR?

Pro

- Antibiotic prescribing in excess of secondary infections, suggesting inappropriate use
- Many COVID-19 epicentres also AMR epicentres
- Burden of antibiotic use in hospitalized patients increased, even outside of epicentres
- Reports of HAI outbreaks associated with breakdowns in infection prevention
- Effects of COVID-19 on public health infrastructure, sanitation, healthcare delivery, governance may indirectly impact AMR and transmission
- Secondary infections may increase as COVID-19 treatment evolves (e.g., dexamethasone)
- Co-circulation of SARS-CoV-2 and influenza may fuel inappropriate antibiotic prescribing

Con

- Overall antibiotic use in humans has decreased in many places
- Major determinant of AMR rates is spread, which may be decreased with COVID-19 travel restrictions, enhanced attention to infection prevention, etc.
- Better COVID-19 outcomes may decrease pools of high risk critically ill patients, including those on ventilators, receiving hemodialysis, etc.
- Increased emphasis on diagnosing respiratory viral infections may decrease inappropriate antibiotic treatment
- Data from southern hemisphere suggest that impact of influenza may be lessened by COVID-19 precautions

COVID-19 and AMR story will be dynamic, and likely to differ from region to region, hospital to hospital, and unit to unit within hospitals

- AMR was a major problem before COVID-19, and it will remain a problem

Clancy, Buehrle and Nguyen. J Antimicrob Chemother-AMR 2020; Collignon and Beggs. J Antimicrob Chemother-AMR 2020

COVID-19 and AMR: Needs moving forward

- Report our experiences and data
- More rigorous microbiology and definitions of superimposed infections in clinical and postmortem studies
- Surveillance data on antimicrobial use and AMR
- Education
  - It’s OK not to get/give an antibiotic
  - AMR has not gone away