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A Pandemic Within a Pandemic
Antibiotic Use and Resistance and COVID-19

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2023 Nebraska Antimicrobial Stewardship Summit

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Objectives

Bacterial Co-Infection and Secondary Infection

- What is the prevalence of bacterial infection in patients with COVID-19?

Antimicrobial Prescribing

- How often are antibiotics prescribed in the setting of COVID-19?

Antimicrobial Resistance

- What is the prevalence of AMR in COVID-19
- Has the pandemic impacted AMR?

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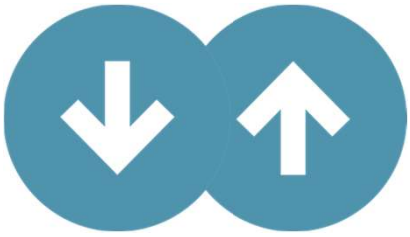
AMR in the Era of COVID-19

Factors Decreasing AMR

- Physical distancing
- Hand hygiene
- Travel restrictions
- Reduced respiratory infections and antibiotic prescribing in community



Factors Increasing AMR

- High antibiotic prescribing in patients with SARS-CoV-2 despite low rates of co-infection
- Antimicrobial stewardship and infection prevention attention shifted to COVID-19 (e.g., ARO screening halted in some facilities)

1. Rodríguez-Baño J, et al. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2021 Oct;115(10):1122-9.
2. Kitano T, et al. Open Forum Infectious Diseases 2021;8 (11):ofab533
3. Langford BJ, et al. Lancet Microbe. 2023; 4(3):e179-e191.

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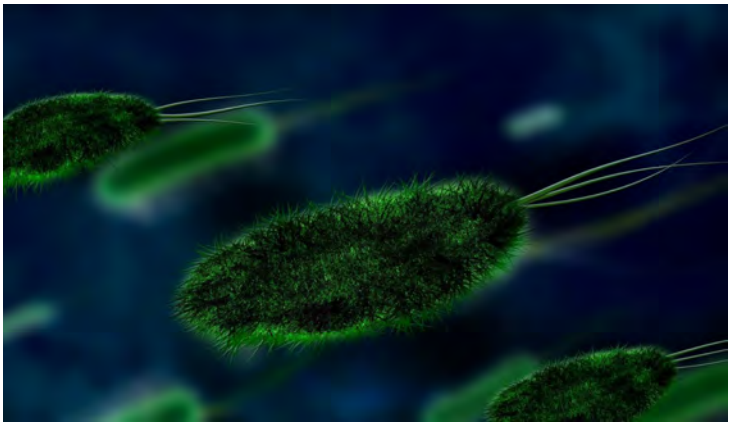
Bacterial Co-Infections and Secondary Infections in COVID-19



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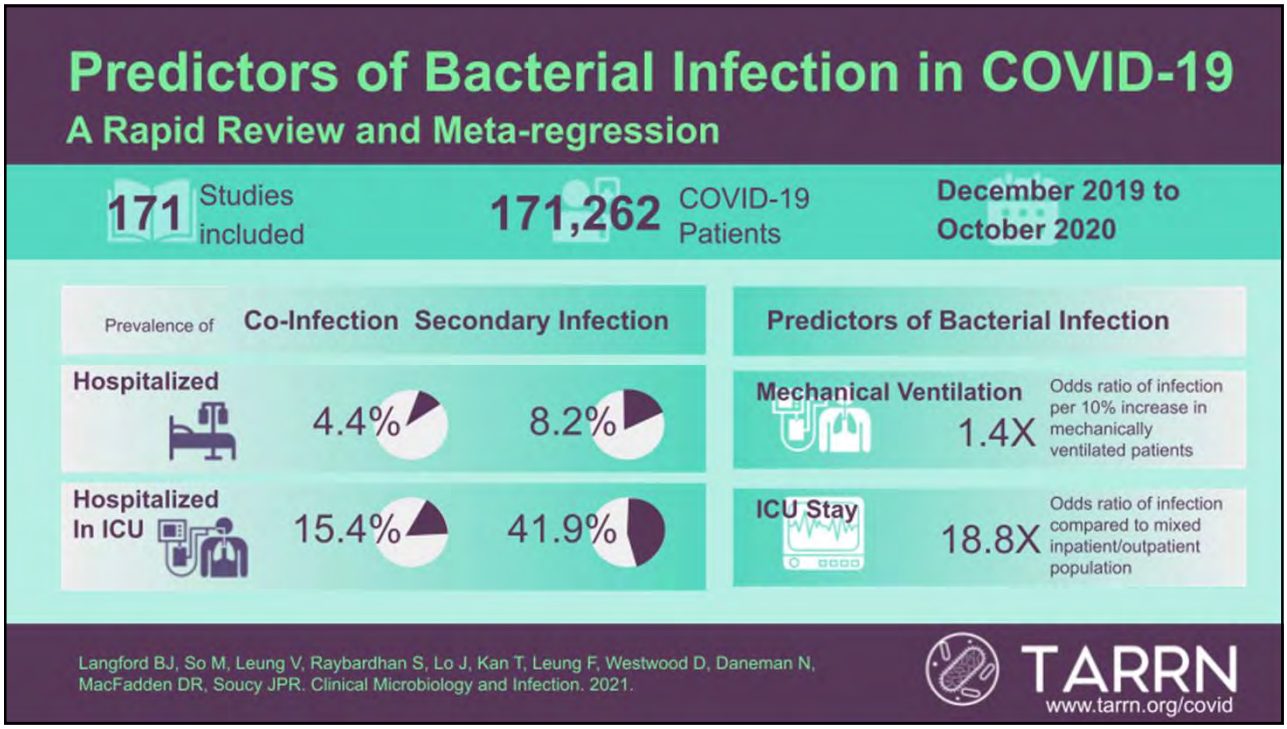

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Antibiotic Use and Overuse in COVID-19

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Role of Antibiotics in COVID-19

Guideline	Recommendation based on COVID-19 Severity: Mild	Moderate	Severe	Statement
World Health Organization 2021	✗	✗	⚠	"Do not prescribe antibiotics to suspected or confirmed COVID-19 patients with low suspicion of a bacterial infection, In patients admitted to ICU, the frequency of bacterial secondary infections is high, therefore empiric antibiotic therapy should be considered in this population".
Surviving Sepsis Campaign 2021	-	-	-	No recommendation
National Institute for Health and Care Excellence (NICE) 2020	✗	✗	✗	"If there is confidence that the clinical features are typical for COVID-19, it is reasonable not to start empirical antibiotics"
Infectious Diseases Society of America 2020	-	-	-	No definitive recommendation
National Institutes of Health (NIH) 2021	-	-	-	"insufficient evidence for the Panel to recommend either for or against empiric broad-spectrum antimicrobial therapy"
Dutch Working Party on Antibiotics 2020	✗	✗	⚠	"We generally suggest restrictive use of antibacterial drugs in patients with proven or a high likelihood of COVID-19. This especially applies for patients who are mildly to moderately ill"
Ontario Clinical Practice Guidelines 2022	✗	✗	✗	Bacterial co-infection is uncommon in COVID-19 pneumonia at presentation. Do not add empiric antibiotics for bacterial pneumonia unless bacterial infection is strongly suspected.

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Antibiotic Prescribing in Patients with COVID-19 Rapid Review and Meta-Analysis

Objective: to estimate the prevalence and associated factors of antibiotic prescribing in patients with COVID-19

- Across all healthcare settings
- Across all age groups
- Pooled proportion data using random effects meta-analysis.

- 154 Studies included
- 30,623 patients with COVID-19
- Study period:

December 2019 to May 2020

- Most studies from China (n=115), US (n=12), South Korea (n=4)

Langford BJ, So M, Raybardhan S, Leung V, Soucy JP, Westwood D, Daneman N, MacFadden DR. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. Clinical Microbiology and Infection.Langford BJ, So M, Raybardhan S, Leung V, Soucy JP, Westwood D, Daneman N, MacFadden DR. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. Clinical Microbiology and Infection. 2021.

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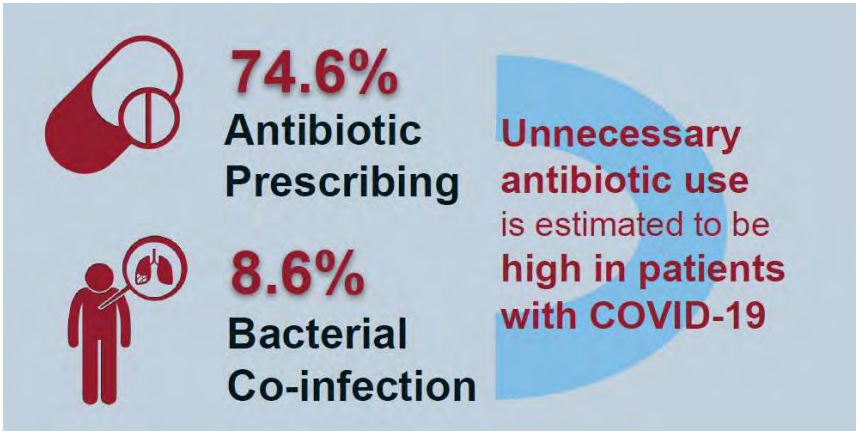
Antibiotic Use Far Exceeds Bacterial Infection Prevalence



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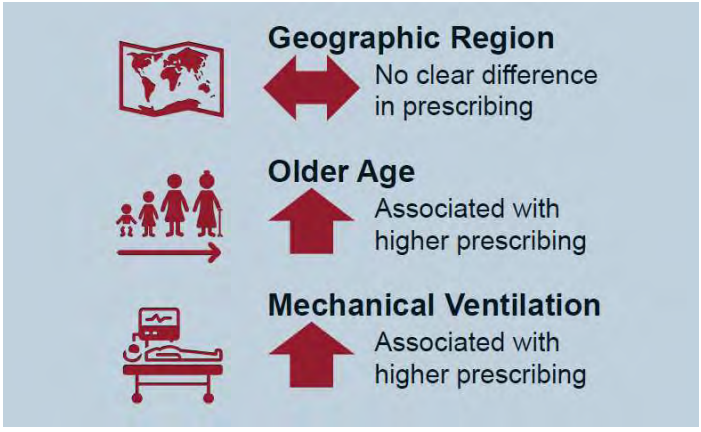
Antibiotic Use Higher in Older Age Groups and Critically Ill



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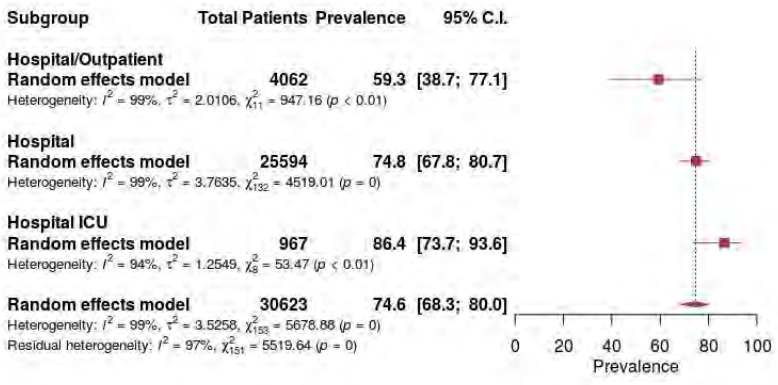
Results: Antibiotic Prescribing by Healthcare Setting

Overall **74.6%** of patients with COVID-19 received at least one antibiotic



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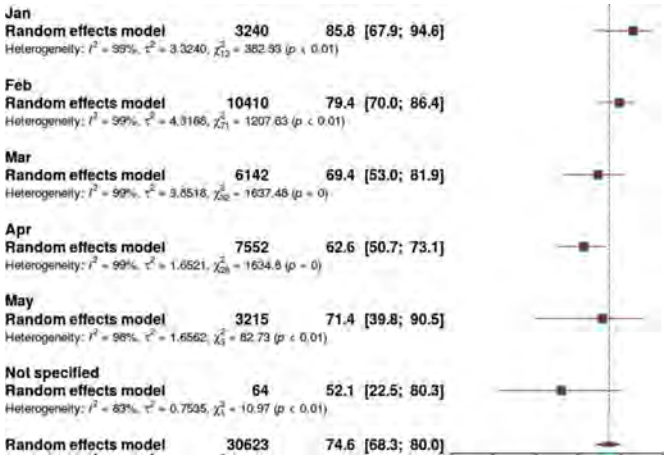
Results: Antibiotic Prescribing by Month in 2020

Trend toward reduced antibiotic use with each month of the pandemic



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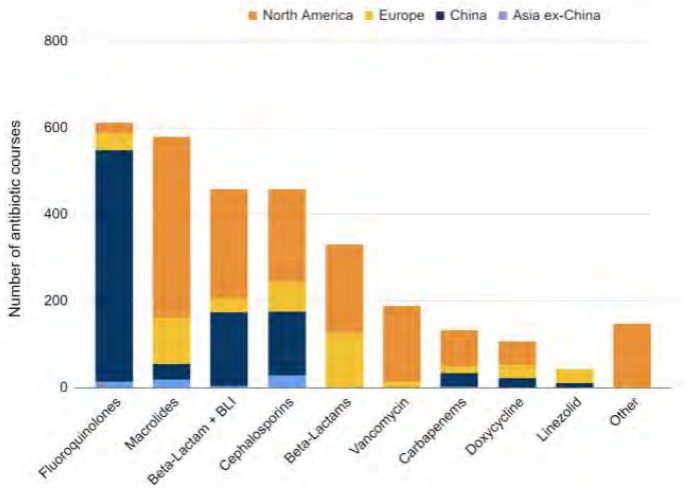
Antibiotic Classes Prescribed in Patients with COVID-19



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Antibiotic Prescribing in Patients with COVID-19

Rapid Review and Meta-analysis

154 Studies included

30,623 COVID-19 Patients

December 2019 to May 2020

74.6% Antibiotic Prescribing

8.6% Bacterial Co-infection

Unnecessary antibiotic use is estimated to be **high in patients with COVID-19**

Geographic Region
No clear difference in prescribing

Older Age
Associated with higher prescribing

Mechanical Ventilation
Associated with higher prescribing

Langford BJ, So M, Raybardhan S, Leung V, Soucy JPR, Westwood D, Daneman N. MacFadden DR, Clinical Microbiology and Infection. 2021.

TARRN

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Impact of COVID-19 on Antibiotic Use in Hospitals

Study	Setting	Direction	Details
Vaughn VM 2020	Hospital (MI, USA)	?	38 hospitals. 56.6% were prescribed early empiric antibiotics, range between hospitals prescribing empiric antibiotics (27-84%) Median duration was 3 days, 55% had antibiotics DC within 1 day of negative result. 65% of those who did not have bacterial infection received >5 days antibiotics. Vaughn VM et al. Clinical Infectious Diseases. 2021 May 15;72(10):e533-41.
Buehrle DJ 2020	Hospital (PA, USA)	↑	Single-centre. Non-epi-center. Initial increase in DOT/1000 bed days of 8.1/month. Buehrle DJ, Antimicrobial agents and chemotherapy. 2020 Oct 20;64(11):e01011-20.
Abelenda-Alonso2020	Hospital (Spain)	↑	Single-centre, epicentre referral hospital. Increase in amoxicillin-clavulanate and "broad spectrum" as a result of empiric recommendations to use antibiotics in all patients COVID-19. Abelenda-Alonso G, et al. Infection Control & Hospital Epidemiology. 2020 Nov;41(11):1371-2.
Calderón-Parra J 2020	Hospital (Spain)	↑	Registry of COVID-19 patients in 150 hospitals. 21.6% were prescribed no antibiotics, 43.9% were appropriately prescribed antibiotics, and 34.2% were inappropriately prescribed antibiotics. ADEs more frequent in patients who received antibiotics (4.9% vs 2.7%, $p < .001$). Calderón-Parra J, et al. PLoS One. 2021 May 11;16(5):e0251340.
So M 2021	Hospital (ON, Canada)	↑	Single centre, COVID+ on General internal medicine compared with historical CAP controls (2019, 2020). 70.2% of patients with COVID-19 received antibiotics. So M et al. JAMMI. 2022
Henig O 2021	Hospital (Israel)	↓	Single centre, tertiary centre with ongoing ASP. During COVID-19, 30.9% received at least 1 dose of antibiotic. Comparing COVID-19 wave to the same previous calendar months, proportion of hospitalized patients receiving antibiotics was lower, DOT/1000 PDs were lower, and time to starting antibiotics was longer (p < 0.001) Henig O et al. Antibiotics. 2021 Sep;10(9):1056.
Elligsen M 2022	Hospital (ON, Canada)	↑↓	Multi-centre, 3 hospitals retrospective interrupted time series. Respiratory antibiotic utilization DOT/1000 PD, initial increase in antibiotic use RR 1.76 medical ward, RR 1.30 ICU (wave 1), but use returned to baseline by wave 3 (for wards), wave 2 (for ICU) Elligsen M, Antimicrobial Stewardship & Hospital Epidemiology. 2022;2(1):E128

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Credit. Dr. Elizabeth Leung

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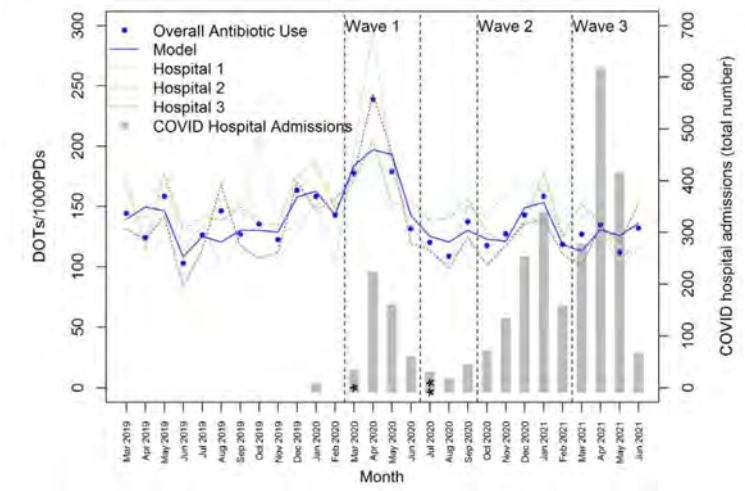
Antibiotic Use in Inpatient General Medicine Wards



* Regional guidelines released discouraging antibiotic prescribing in COVID-19 in absence of bacterial infection

** publication of systematic review reporting low co-infection rate in hospitalized patients with COVID-19

Elligsen M, Wan M, Lam PW, Lo J, Taggart LR, Chan AJ, Downing M, Gough K, Seah J, Leung E. Trends in hospital antibiotic utilization during the coronavirus disease 2019 (COVID-19) pandemic: A multicenter interrupted time-series analysis. Antimicrobial Stewardship & Healthcare Epidemiology. 2022;2(1):e128.

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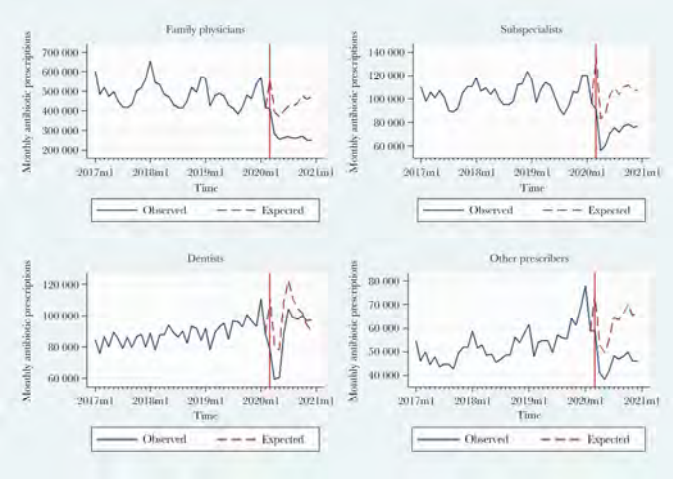
Impact of COVID-19 on Antibiotic Use in Community

Study	Setting	Direction	Details
Thompson W 2022	Community HIC Dental	↑	UK (NHS). increase 22% from April 2020-March 2021 vs previous year Thompson W et al. British Dental Journal. 2022;233:653-658.
Sulis G 2021	Community LMIC	↑	India - IQVIA data from January 2018 to December 2020. Estimated 216 million excess adult formulation antibiotic usage. Sulis G, et al. PLOS Medicine. 2021 Jul 1;18(7):e1003682.
Zhong X 2023	Community HIC	↓↑	UK (NHS England) decrease in overall prescribing, temporary increase in proportion of broad-spectrum antibiotics (e.g., amox-clav, FQ) Zhong X, et al. The Lancet Regional Health–Europe. 2023.
Armitage R 2021	Community HIC	↓	UK (NHS England). 15% decrease April-Aug 2020 compared to previous year, but also decreased # of visits (increased Rx/visit) Armitage R, Nellums LB. Lancet ID. 2021;21:E144.
PHAC 2020	Community HIC	↓	Canada-wide antibiotic dispensing data from Canadian CompuScript database (IQVIA). 30% decrease in Apr/May 2020 vs 2019 Public Health Agency of Canada. 2020.
Buehrle DJ 2020	Community HIC	↓	USA-wide antibiotic dispensing data from National Prescription Audit database (IQVIA). Antibiotic use decreased by 13-56% for top 10 antibiotics. Buehrle DJ et al. Antimicrobial agents and chemotherapy. 2020 Oct 20;64(11):e01011-20.
King LM 2021	Community HIC	↓	USA - IQVIA data from January 2017 to May 2020. Antibiotic use decreased 33% points compared to seasonal prediction King LM, et al. Clinical Infectious Diseases. 2021 Aug 1;73(3):e652-60.
Ha D 2022	Community HIC	↓	USA - Urgent care clinics January 2019 to December 2020, 17% of encounters received antibiotics before, 11% during COVID-19 Ha D, et al. Open Forum Infectious Diseases. 2022; 9(2): ofab662
Kitano T 2021	Community HIC	↓	Canada - Using IQVIA linked to aggregated outpatient visit data based on OHIP billings from ICES from January 2017 - December 2020. 31.2% relative reduction in total antibiotic prescriptions and total antibiotic prescriptions/1000 visits (-27.5%), likely related to decreased outpatient visits, especially visits for respiratory infections. Kitano T, Open Forum Infectious Diseases 2021

Credit. Dr. Elizabeth Leung

Antibiotic Prescribing in the Community Decreased Early in Pandemic

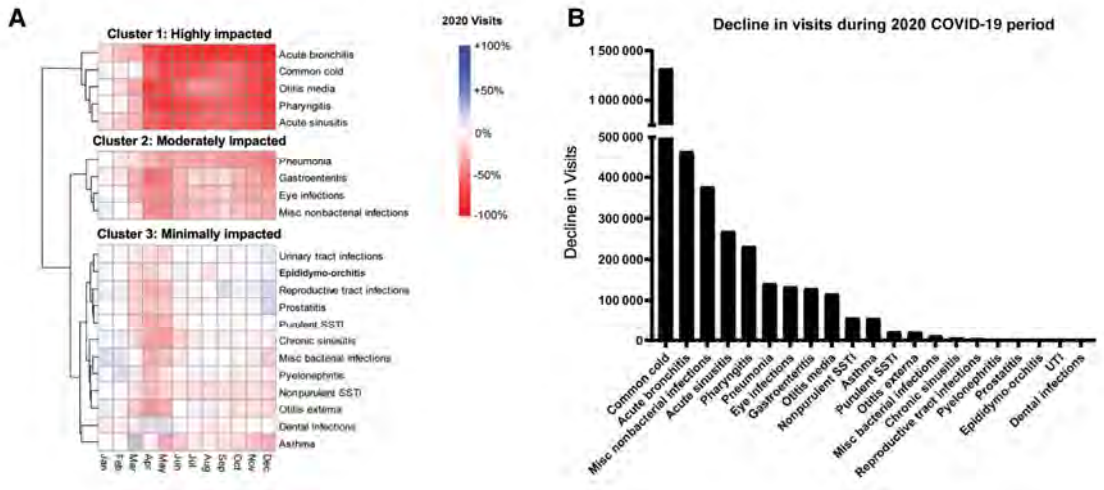


31% reduction in total antibiotic prescribing during COVID-19 period March – December 2020

Largely explained by decreased visits for respiratory tract infections

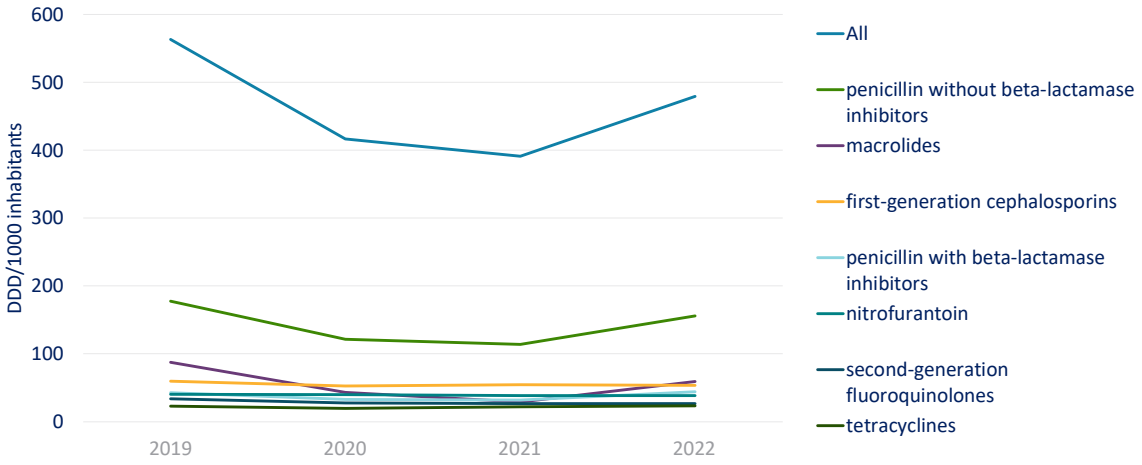
Kitano T, Brown KA, Daneman N, MacFadden DR, Langford BJ, Leung V, So M, Leung E, Burrows L, Manuel D, Bowdish DM. The impact of COVID-19 on outpatient antibiotic prescriptions in Ontario, Canada; an interrupted time series analysis. InOpen Forum Infectious Diseases 2021 Nov (Vol. 8, No. 11, p. ofab533). US: Oxford University Press.

Decline in Infectious Diseases Visits Due to Respiratory Infection



Zhang A, et al. The Collapse of Infectious Disease Diagnoses Commonly Due to Communicable Respiratory Pathogens During the Coronavirus Disease 2019 Pandemic: A Time Series and Hierarchical Clustering Analysis. Open forum infectious diseases 2022 Jul (Vol. 9, No. 7, p. ofac205)..

Rebound in Outpatient Antibiotic Prescribing As Pandemic Progressed



Source ASP/AMR Comparison Tool. 2023. www.publichealthontario.ca/ASP

Predictors of Antibiotic Prescribing in Outpatients with COVID-19

- **Design.** Population-wide retrospective study (Ontario, Canada) evaluating timing and risk factors for outpatient antibiotic prescribing in COVID-19
- **Population.** Nursing home and community-dwelling residents (66+)
  - Dates: Jan 1 2020 – Dec 31 2021
- **Eligibility.** First PCR-confirmed SARS-CoV-2 Diagnosis
- **Outcome.** Antibiotic Prescribing (Rates and Incidence Rate Ratios):
  - Pre-diagnosis (7 days before); Post-diagnosis (7 days after); Peri-diagnosis = Pre+Post Diagnosis; Control (4-8 weeks pre diagnosis)
- **Predictors**. Sociodemographic, clinical, COVID-19 Vaccine (>= 2 doses)

MacFadden DR, Maxwell C, Bowdish D, Bronskill S, Brooks J, Brown K, Burrows LL, Clarke A, Langford B, Leung E, Leung V. COVID-19 Vaccination is Associated with Reduced Outpatient Antibiotic Prescribing In Older Adults with Confirmed SARS-CoV-2: A Population Wide Cohort Study. Clinical Infectious Diseases. 2023 Mar 31:ciad190.

Slide c/o Dr. D. MacFadden

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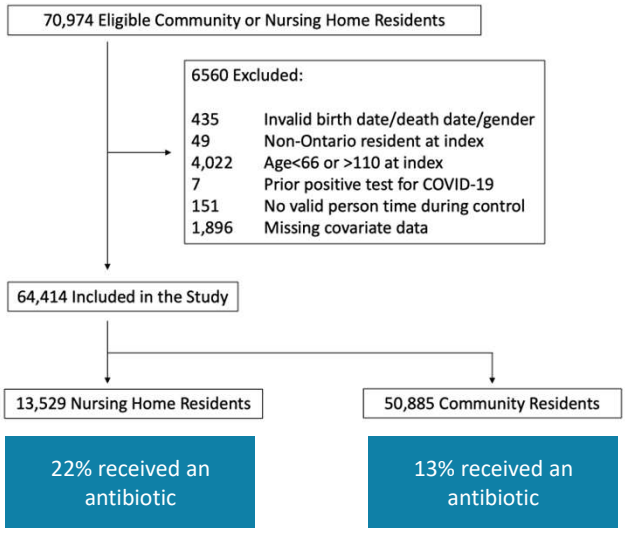
Predictors of Antibiotic Prescribing in Outpatients with COVID-19

- Of 13,529 nursing home residents
  - 3,020 (22%) received an antibiotic
  - Mean age of 85 yrs, 69% female
  - Large homes (85%) in urban settings (96%)
  - Diabetes (29%) and COPD (5%)
- Of 50,885 community residents
  - 6,372 (13%) received an antibiotic
  - Mean age of 75 yrs, 52% female
  - Diabetes (35%) and COPD (6%)



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Predictors of Antibiotic Prescribing in Outpatients with COVID-19

Antibiotic Prescribing Rates per 1000 PD and IRR in Nursing Homes

	Pre-Diagnosis		Post-Diagnosis		Control Period	
Variable	**Rate**	**IRR**	**Rate**	**IRR**	**Rate**	**IRR**
All	14.97	3.52 (3.28 - 3.77)	20.92	4.92 (4.59 - 5.27)	4.25	Ref
Age (years)						
65 to 74	15.92	3.41 (2.83 - 4.10)	22.02	4.71 (3.89 - 5.70)	4.67	Ref
75 to 84	15.76	3.57 (3.15 - 4.06)	20.33	4.61 (4.05 - 5.24)	4.41	Ref
85 or more	14.37	3.52 (3.21 - 3.86)	20.99	5.14 (4.70 - 5.63)	4.08	Ref
Sex						
Female	13.98	3.29 (3.03 - 3.58)	19.06	4.49 (4.13 - 4.88)	4.24	Ref
Male	17.13	4.01 (3.53 - 4.55)	25.14	5.88 (5.20 - 6.65)	4.27	Ref
COVID-19 Vaccine						
< 2 doses	15.00	3.59 (3.34 - 3.85)	21.43	5.12 (4.77 - 5.50)	4.19	Ref
>= 2 doses	14.56	2.81 (2.18 - 3.63)	14.40	2.78 (2.13 - 3.64)	5.18	Ref
Index Period						
January - June 2020	18.33	4.31 (3.86 - 4.83)	18.71	4.40 (3.91 - 4.96)	4.25	Ref
July - December 2020	12.75	3.11 (2.75 - 3.51)	20.58	5.02 (4.45 - 5.66)	4.10	Ref
January - June 2021	13.34	3.14 (2.71 - 3.63)	26.54	6.24 (5.46 - 7.14)	4.25	Ref
July - December 2021	13.95	2.66 (2.03 - 3.50)	13.17	2.52 (1.87 - 3.38)	5.23	Ref

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Predictors of Antibiotic Prescribing in Outpatients with COVID-19

Antibiotic Prescribing Rates per 1000 PD and IRR in Community Residents

	Pre-Diagnosis		Post-Diagnosis		Control Period	
Variable	**Rate**	**IRR**	**Rate**	**IRR**	**Rate**	**IRR**
All	10.47	4.12 (3.92 - 4.33)	9.78	3.84 (3.65 - 4.04)	2.54	Ref
Age (years)						Ref
65 to 74	9.38	4.68 (4.37 - 5.01)	8.60	4.29 (4.00 - 4.60)	2.00	Ref
75 to 84	11.73	4.30 (3.92 - 4.71)	10.62	3.89 (3.54 - 4.28)	2.73	Ref
85 or more	12.68	2.80 (2.50 - 3.14)	13.79	3.05 (2.73 - 3.41)	4.52	Ref
Sex						Ref
Female	10.69	3.91 (3.66 - 4.19)	10.08	3.69 (3.45 - 3.95)	2.73	Ref
Male	10.23	4.37 (4.06 - 4.70)	9.45	4.04 (3.74 - 4.35)	2.34	Ref
COVID-19 Vaccine						Ref
< 2 doses	11.34	4.48 (4.24 - 4.73)	10.82	4.27 (4.04 - 4.52)	2.53	Ref
>= 2 doses	6.74	2.60 (2.30 - 2.93)	5.64	2.17 (1.92 - 2.46)	2.60	Ref
Index Period						Ref
January - June 2020	18.38	4.53 (3.84 - 5.33)	13.15	3.24 (2.70 - 3.89)	4.06	Ref
July - December 2020	11.90	4.67 (4.19 - 5.19)	9.62	3.77 (3.37 - 4.21)	2.55	Ref
January - June 2021	9.93	4.15 (3.86 - 4.46)	10.60	4.43 (4.12 - 4.76)	2.39	Ref
July - December 2021	8.17	3.31 (2.97 - 3.69)	7.44	3.02 (2.71 - 3.36)	2.47	Ref

Slide c/o Dr. D. MacFadden

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Predictors of Antibiotic Prescribing in Outpatients with COVID-19

Multivariable Regression Analysis by Time Period and Population (IRR, 95%CI)

	Nursing Home Residents			Community Residents		
Variable	**Pre-diagnosis**	**Post-diagnosis**	**Control Period**	**Pre-diagnosis**	**Post-diagnosis**	**Control Period**
Demographics						
Age	0.99 (0.99 - 1.00)	1.00 (1.00 - 1.01)	1.00 (0.99 - 1.01)	1.01 (1.01 - 1.02)	1.02 (1.01 - 1.02)	1.02 (1.01 - 1.02)
Female	0.84 (0.75 - 0.95)	0.74 (0.67 - 0.82)	1.02 (0.91 - 1.15)	1.00 (0.93 - 1.07)	0.99 (0.92 - 1.07)	1.07 (0.98 - 1.16)
COVID-19 Vaccinated (>=2 doses)	1.18 (0.78 - 1.78)	0.66 (0.44 – 0.99)	1.09 (0.67 - 1.76)	0.43 (0.37 - 0.51)	0.31 (0.26 - 0.37)	1.18 (0.95 - 1.46)
Healthcare Utilization						
Physician Visits Prior 12-mo	1.01 (1.00 -1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.01 (1.01 - 1.02)	1.01 (1.01 - 1.01)	1.02 (1.02 - 1.03)
Hospitalizations Prior 12-mo	0.94 (0.86 - 1.02)	1.02 (0.95 - 1.09)	1.24 (1.16 - 1.33)	0.92 (0.87 - 0.98)	0.99 (0.93 - 1.05)	1.26 (1.20 - 1.34)
Receipt of Antibiotics Prior 6-mo	2.23 (1.94 - 2.57)	1.41 (1.26 - 1.57)	3.49 (3.06 - 3.97)	1.89 (1.76 - 2.03)	1.71 (1.59 - 1.85)	4.28 (3.94 - 4.64)

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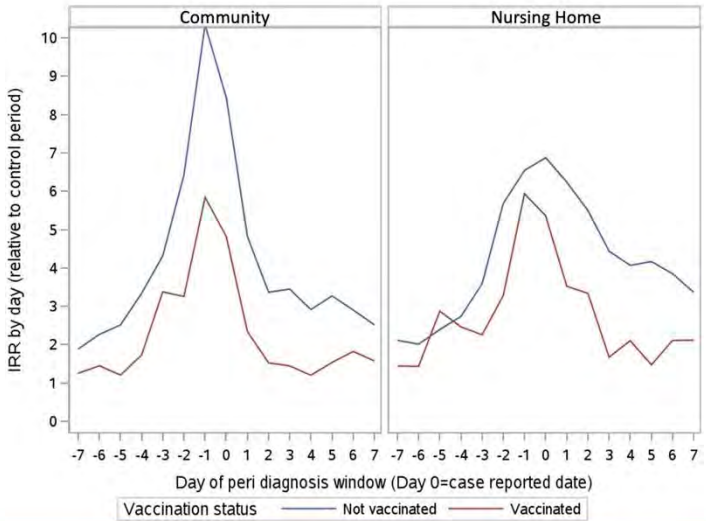
Predictors of Antibiotic Prescribing in Outpatients with COVID-19

Incidence Rate Ratio by Day in Peri-diagnosis Period



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Antimicrobial Resistance and COVID-19

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Antibiotic Resistance in COVID-19

A Rapid Systematic Review

148 Studies included

362,976 COVID-19 Patients

December 2019 to May 2021

Antibiotic resistance was inconsistently reported

63% of studies reported AMR for ≥1 species

28% of studies reported AMR for ≥4 species

High Prevalence of antibiotic resistance

95.9% carbapenem-resistance *Acinetobacter* spp.

69.2% carbapenem-resistance *Klebsiella* spp.

41.1% methicillin-resistance *Staphylococcus aureus*

Predictors for antibiotic resistance

- Low and middle-income countries
- ICU Setting
- Diabetes
- IL-6 inhibitors

Langford BJ, So M, Simeonova M, Leung V, Lo J, Kan T, Raybardhan S, Sapin ME, Mponponsuo K, Farrell A, Leung E, Soucy J-PR, Cassini A, MacFadden D, Daneman N, Bertagnolio S. The Lancet Microbe. 2023.

TARRN
www.tarrn.ca/covid

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What is the impact of the COVID-19 pandemic on AMR at the population level?

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Systematic Review Methodology

- **Search:** World Health Organization (WHO) COVID-19 Research Database searched for published literature on 'bacterial infection' in any language from January 2019-December 2021. Forward citation search to June 2022.
- **Inclusion:** study reports on AMR before vs. during pandemic or associated with COVID-19 cases, any patient population.
- **Outcomes:** incidence rate ratio of AMR *OR* risk ratio of AMR. Pooled across Gram-positive and Gram-negative organisms, stratified by the reporting of enhanced IPAC measures and/or antimicrobial stewardship programs
- **Quality:** assessed using a risk of bias tool for prevalence studies

Langford BJ, et al. Clinical Microbiology and Infection. 2022.
Hoy D, et al. Journal of Clinical Epidemiology. 2012;65(9):934-9.

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Definition of AMR

AMR includes any of the following pathogens and resistance phenotypes, as defined by study authors:

- methicillin resistant *Staphylococcus aureus* (MRSA),
- vancomycin-resistant enterococci (VRE),
- extended-spectrum beta-lactamase (ESBL)-producing (or third-generation cephalosporin-resistant) Enterobacterales,
- carbapenem-resistant Enterobacterales (CRE),
- carbapenem-R or multi-drug resistant (MDR) *Pseudomonas aeruginosa*,
- carbapenem-R or MDR *Acinetobacter baumannii*

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Results

28 studies included

6036 studies screened
18 via full text
9 via forward citation search
1 expert identified
23 evaluable for meta-analysis

Mostly Hospitalized

Hospitalized n=17
ICU only n=5
Other/mixed n= 5
Community n=1

Mostly Clinical Specimens

Clinical n=20
Clinical/screening n=6
Screening n=2

Global Representation

Most common countries:
United states n=4
Italy n=4
Brazil n=3

Variable Risk of Bias

Moderate n=18
Low n=5
High n=5

Langford BJ, et al. Clinical Microbiology and Infection. 2022

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High Variability
in AMR metrics used

Incidence Density
Cases of resistant infection per patient days

Proportions
Proportion of isolates with resistance

Cumulative Incidence
Resistant cases per admission or discharge

Other metrics
Standardized infection ratio, point prevalence

Langford BJ, et al. Clinical Microbiology and Infection. 2022

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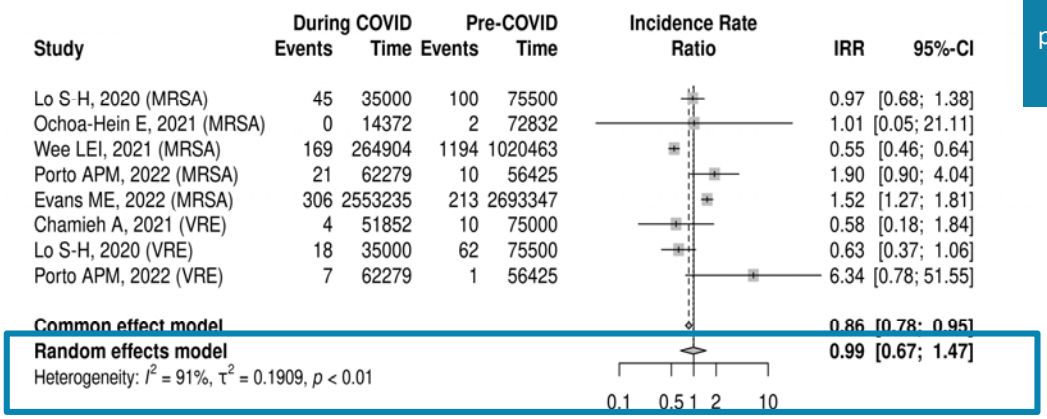
Gram-Positive AMR: Incidence Rate Ratio

High heterogeneity - No change in Gram-positive AMR identified



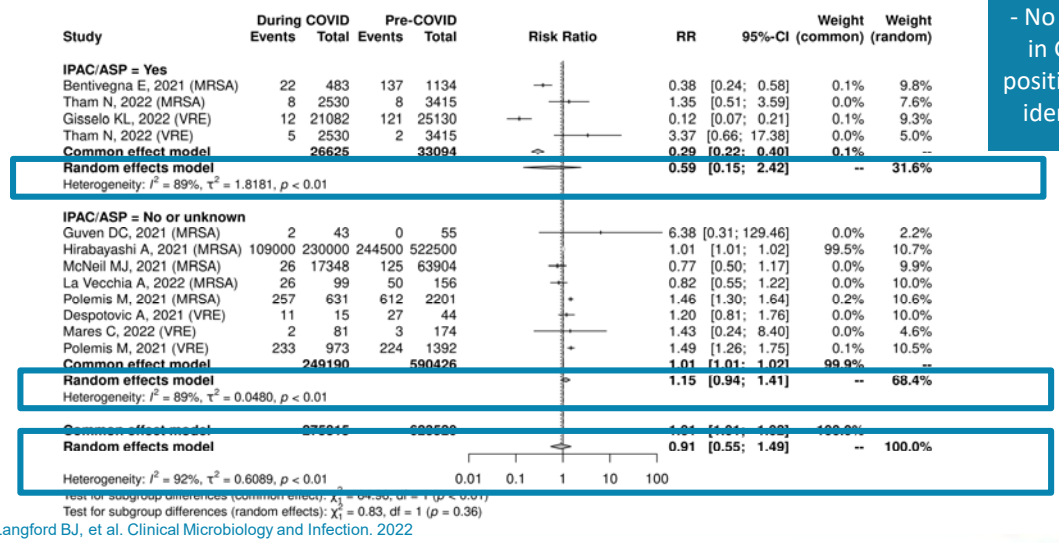
Langford BJ, et al. Clinical Microbiology and Infection. 2022

All included studies reported infection prevention and control/antimicrobial stewardship program initiatives

34

Gram-Positive AMR: Risk Ratio

High heterogeneity - No change in Gram-positive AMR identified



Langford BJ, et al. Clinical Microbiology and Infection. 2022

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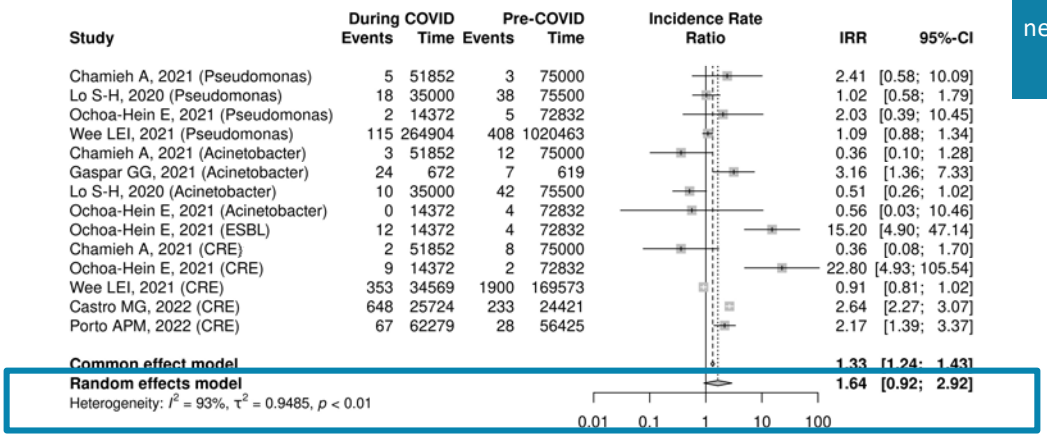
Gram-Negative AMR: Incidence Rate Ratio

High heterogeneity - Increase Gram-negative AMR signal



Langford BJ, et al. Clinical Microbiology and Infection. 2022

All included studies reported infection prevention and control/antimicrobial stewardship program initiatives

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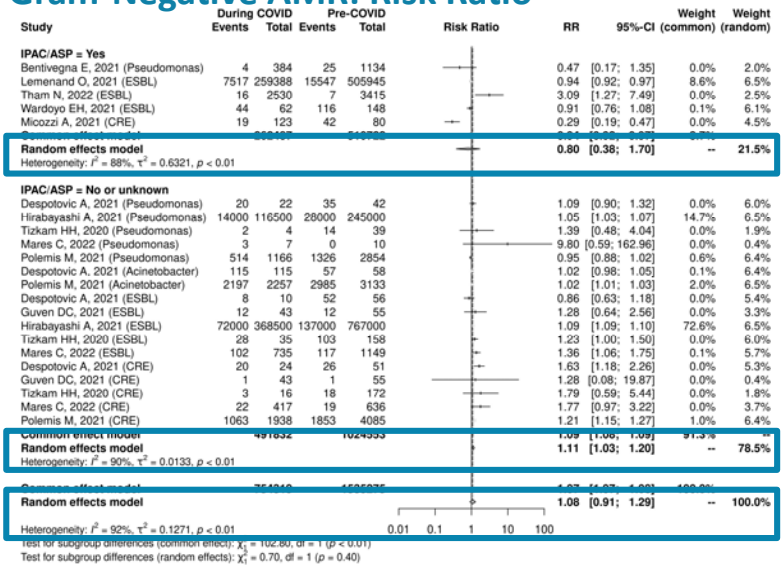
Gram-Negative AMR: Risk Ratio



High heterogeneity - Increase Gram-negative AMR signal

Particularly in settings without enhanced IPAC/ASP

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Antibiotic Resistance Associated with the COVID-19 Pandemic
A Rapid Systematic Review

28 Studies included

96% Compared AMR during vs. before pandemic

89% In hospital settings

High Variability
in AMR metrics used

- **Incidence Density** — Cases of resistant infection per patient days
- **Proportions** — Proportion of isolates with resistance
- **Cumulative Incidence** — Resistant cases per admission or discharge
- **Other metrics** — Standardized infection ratio, point prevalence

Impact of pandemic on AMR
High heterogeneity in AMR. Non-significant increase in Gram- negative AMR, particularly in studies that did not report enhanced ASP/IPAC

Gram-positive AMR
0.99 **Incidence Rate Ratio**
95%CI: 0.67 to 1.47, I^2=91%
0.91 **Risk Ratio**
95%CI: 0.55 to 1.49, I^2=92%

Gram-negative AMR
1.64 **Incidence Rate Ratio**
95%CI: 0.92 to 2.92, I^2=93%
1.08 **Risk Ratio**
95%CI: 0.91 to 1.29, I^2=92%

Langford BJ, Soucy J-PR, Leung V, So M, Kwan ATH, Portnoff JS, Bertagnolio S, Raybardhan S, MacFadden D, Daneman N. Clinical Microbiology and Infection. 2022.

TARRN
www.tarrn.ca/covid

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US Data on AMR Associated with COVID-19

Because of pandemic impacts, 2020 data are delayed or unavailable for 9 of the 18 antimicrobial resistance threats.

- *Clostridioides difficile (C. diff)*
- Drug-resistant *Neisseria gonorrhoeae*
- Drug-resistant *Campylobacter*
- Drug-resistant nontyphoidal *Salmonella*
- Drug-resistant *Salmonella* serotype Typhi
- Drug-resistant *Shigella*
- Drug-resistant *Streptococcus pneumoniae*
- Erythromycin-resistant group A *Streptococcus*
- Clindamycin-resistant group B *Streptococcus*

Available data show an alarming increase in resistant infections starting during hospitalization, growing at least 15% from 2019 to 2020.

- Carbapenem-resistant *Acinetobacter* (↑78%)
- Antifungal-resistant *Candida auris* (↑60%)*
- Carbapenem-resistant Enterobacterales (↑35%)
- Antifungal-resistant *Candida* (↑26%)
- ESBL-producing Enterobacterales (↑32%)
- Vancomycin-resistant Enterococcus (↑14%)
- Multidrug-resistant *P. aeruginosa* (↑32%)
- Methicillin-resistant *Staphylococcus aureus* (↑13%)

*_Candida auris_ was not included in the hospital-onset rate calculation of 15%. See Data Table and Methods for more information on this pathogen.

US Centers for Disease Control and Prevention. COVID-19: U.S. Impact on Antimicrobial Resistance, Special Report 2022

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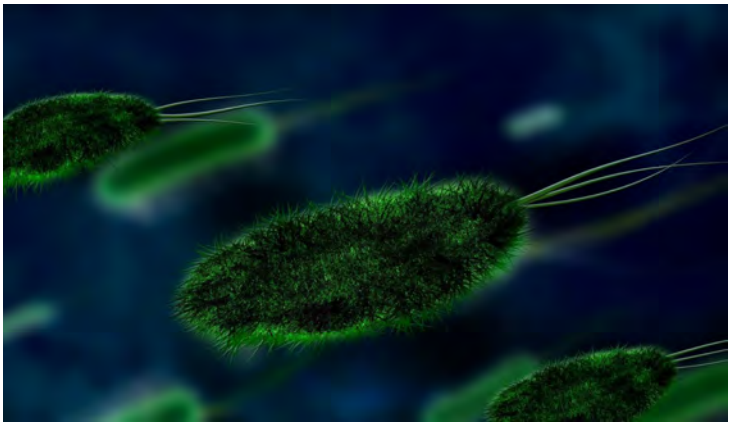
Implications to Antimicrobial Stewardship in the Context of Future Pandemics



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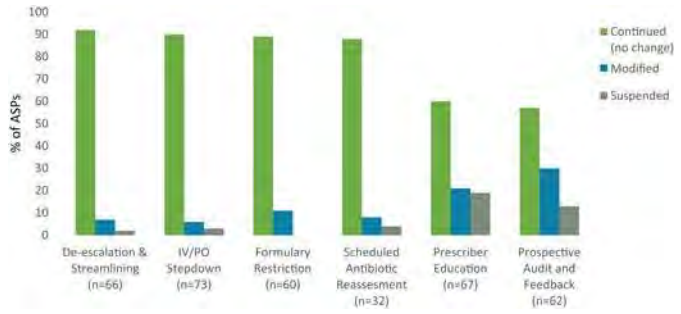
Antimicrobial Stewardship in the Context of COVID-19… and Future Pandemics

- Sustained antimicrobial stewardship efforts are vital
  - Competing priorities for antimicrobial stewards (guidelines, shortages, access, vaccination)
  - impact on conventional ASP activities
  - adequate resourcing and capacity building is key to ensure ASP preparedness for future pandemics



Leung V, Quirk J, Muir S, Daneman N, Schwartz KL, Langford BJ. A cross-sectional study of hospital antimicrobial stewardship programmes in the COVID-19 era. JAC-Antimicrobial Resistance. 2023 Feb;5(1):dlac134.

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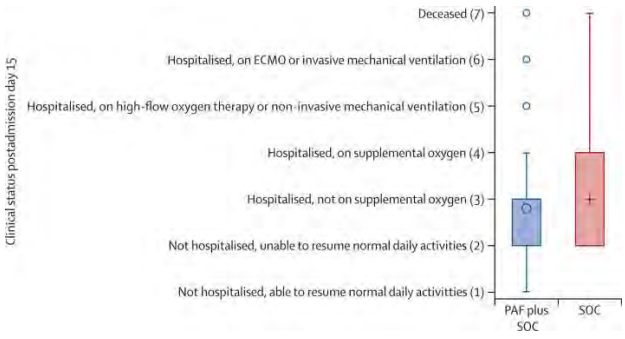
Antimicrobial Stewardship in the Context of COVID-19… and Future Pandemics

- Prospective audit and feedback works in COVID-19 too!
  - Cluster RCT of over 800 hospitalized patients with COVID-19 found 5% decrease in antibiotic use with no change in clinical status or adverse outcomes
  - 544·5 (PAF) *vs* 561·2 (control) days of therapy per 1000 patient days, p=0·0060



Chen JZ, Hoang HL, Yaskina M, Kabbani D, Doucette KE, Smith SW, Lau C, Stewart J, Remtulla S, Zurek K, Schultz M. Efficacy and safety of antimicrobial stewardship prospective audit and feedback in patients hospitalised with COVID-19 (COVASP): a pragmatic, cluster-randomised, non-inferiority trial. The Lancet Infectious Diseases. 2023 Jan 27.

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Antimicrobial Stewardship in the Context of COVID-19… and Future Pandemics

- Vaccination = Antimicrobial Stewardship
- Influenza vaccine
  - High certainty in adults RR 0.72 (95% CI 0.62–0.84)
  - Moderate-certainty evidence in children aged 6 months to 14 years RR 0·62 (95% CI 0·54–0·70)
  - Moderate certainty in children aged 3–15 years RR 0·69 (95% CI 0·58–0·83)
- Pneumococcal vaccination
  - Moderate certainty in children aged 6 weeks to 6 years, RR 0·93 (95% CI 0·87–0·99)
- COVID-19 vaccination
  - 70% reduction in community and 30% reduction in long-term care residents receiving a primary series of vaccination

- Buckley BS, Henschke N, Bergman H, Skidmore B, Klemm EJ, Villanueva G, Garritty C, Paul M. Impact of vaccination on antibiotic usage: a systematic review and meta-analysis. Clinical Microbiology and Infection. 2019 Oct 1;25(10):1213-25.
- MacFadden DR, Maxwell C, Bowdish D, Bronskill S, Brooks J, Brown K, Burrows LL, Clarke A, Langford B, Leung E, Leung V. COVID-19 Vaccination is Associated with Reduced Outpatient Antibiotic Prescribing In Older Adults with Confirmed SARS-CoV-2: A Population Wide Cohort Study. Clinical Infectious Diseases. 2023 Mar 31:ciad190.

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Conclusions

- Antimicrobial use is generally high in COVID-19 patients while rates of co-infection and secondary infection outside of the ICU are low
- Antimicrobials use is highly heterogeneous but there is overuse in patients with COVID-19 in all settings
- The impact of the pandemic on antibiotic use for non COVID-19 indication depended on a variety of factors (prevailing respiratory infection, access to care)
- COVID-19 may exacerbate AMR particularly in hospital settings, for Gram-negative organisms, and in low-resource settings
- These findings reinforce the need for bolstered infection prevention, antimicrobial stewardship, and AMR surveillance in the context of the COVID-19 pandemic and beyond

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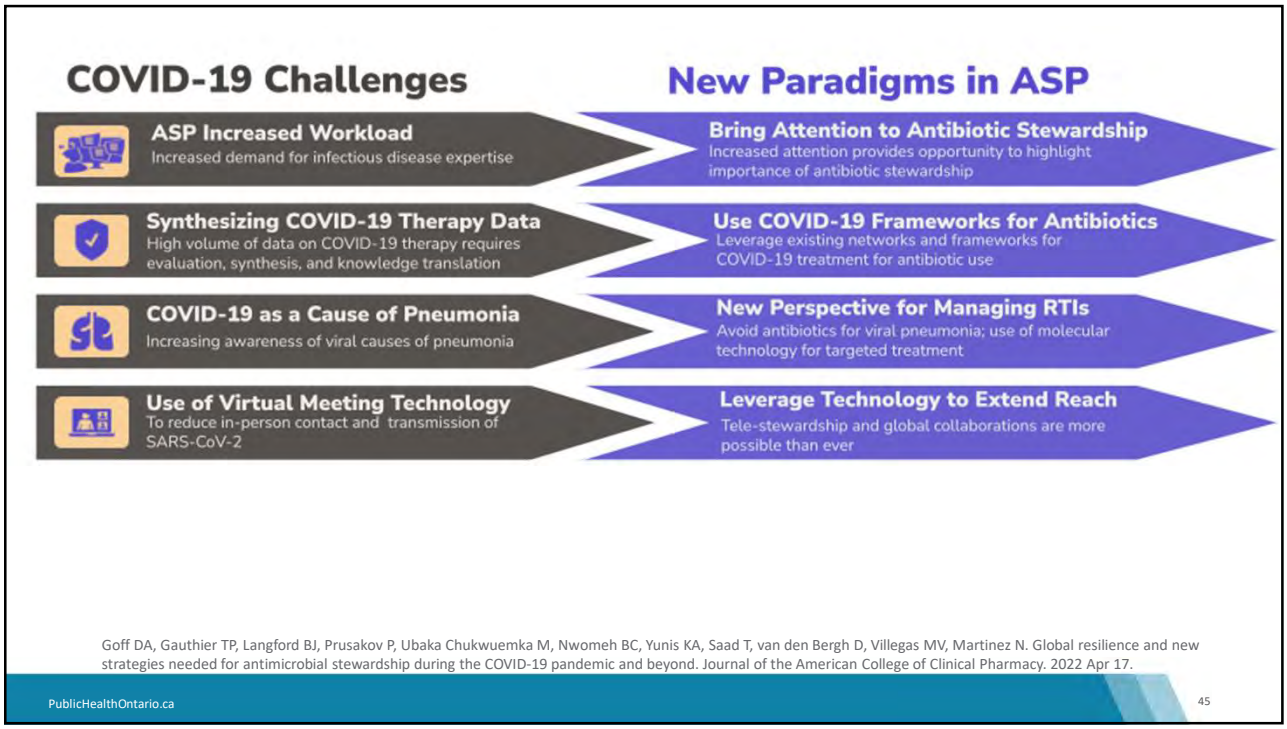

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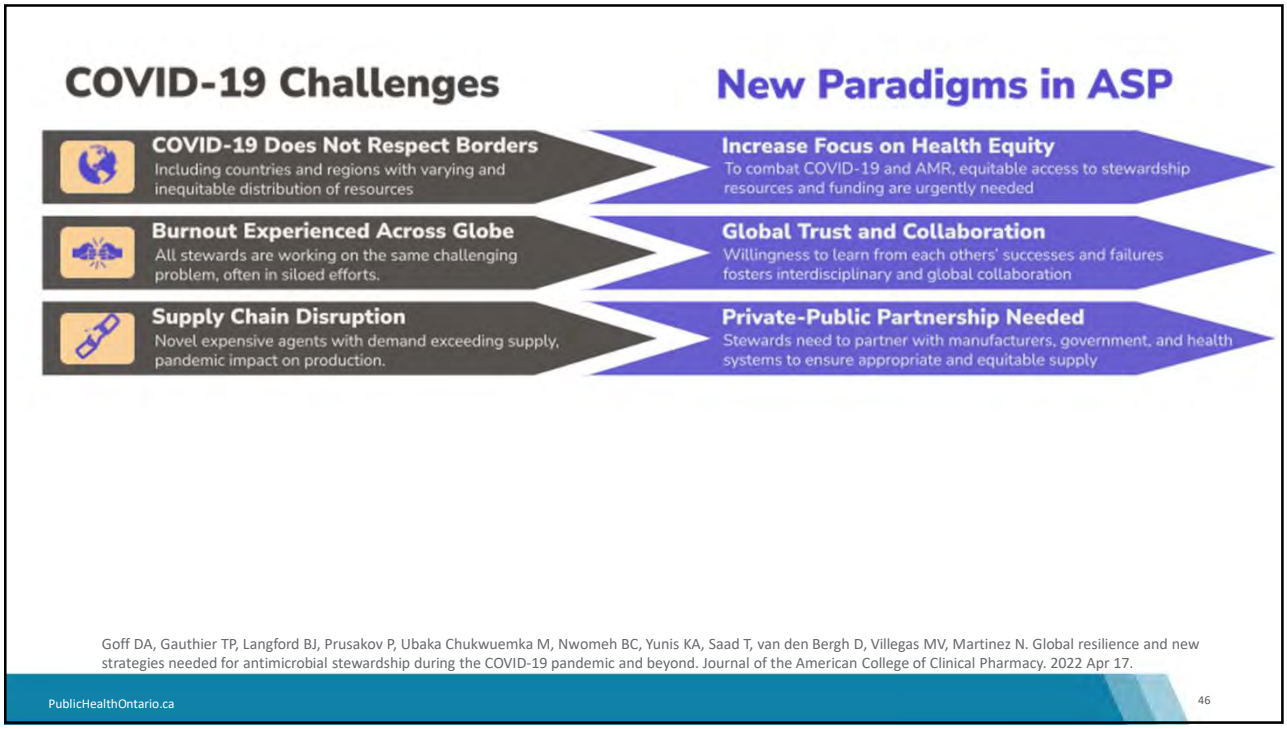

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