Antimicrobial Stewardship Considerations during the COVID-19 Pandemic

Hayley Hodgson, PharmD, BCDIP
Clinical Pharmacist, Infectious Disease & Antimicrobial Stewardship
Rush University Medical Center
September 24th, 2021

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Disclosure

- I have no actual or potential conflicts of interest to disclose in relation to this presentation.

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Objectives

1. Recognize antimicrobial stewardship strategies that can be applied during the COVID-19 pandemic response.
2. Describe the incidence and time course of bacterial co-infections in patients with COVID-19.
3. Explain antimicrobial stewardship interventions that should be performed for patients with COVID-19.

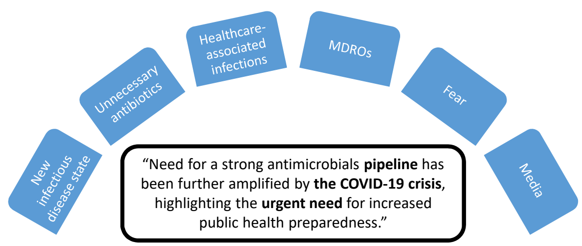
BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

I. Antimicrobial Stewardship Strategies in COVID-19 Response

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

COVID-19 Adds to Antimicrobial Resistance

10 million deaths by 2050 = $100 trillion



BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Antimicrobials Working Group. Accessed August 5, 2021.
Getahun H, et al. *Bull World Health Organ.* 2020;98:442.

Pharmacy Challenges with COVID-19

Patient Surges	Medication Delivery	Old & New Medications • Emergency Use Authorization • Compassionate Use • Off-label use
Drug Shortages	Nursing Coordination	Ethical Considerations

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Solution: Antimicrobial Stewardship

- interventions to **improve** & **measure** the appropriate use of antibiotics by promoting the **optimal** antibiotic regimen including **dosing**, **duration**, & **route**
- Goals:
  - outcomes
  - resistance
  - side effects
  - costs

"precious non-renewable resource"

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Barlam TF, et al. *Clin Infect Dis.* 2016;62:e51-e77.
Getahun H, et al. *Bull World Health Organ.* 2020;98:442.
The Society for Healthcare Epidemiology of America. Accessed August 5, 2021.

World Health Organization (WHO)

"address gaps in research to ensure that **antimicrobial stewardship** activities become an integral part of the pandemic response and beyond."

"**antimicrobial stewardship** activities should be integrated into the pandemic response across the broader health system."

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Getahun H, et al. *Bull World Health Organ.* 2020;98:442.

CDC: 7 Core Elements of Antimicrobial Stewardship

1. Leadership Commitment	IT* support, resources
2. Accountability	reporting structure
3. Drug Expertise	drug shortages, formulary
4. Action	guideline, pre-authorization
5. Tracking	CDI^, broad-spectrum antibiotics
6. Reporting	inventory, antibiotic trends
7. Education	guidelines, resources

*IT= Information Technology
^CDI= *C. difficile* Infection

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Barlam TF, et al. *Clin Infect Dis*. 2016;62:e51-e77.

"Low Hanging Fruit" of Antimicrobial Stewardship

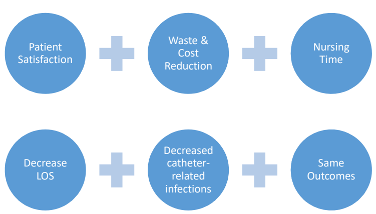
- IV to PO Conversion
- Medication Batching
- Therapeutic Substitutions
- Pre-authorization

among others.......

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Goff DA, et al. *Clin Infect Dis*. 2012;55: 87-592.

IV to PO Conversion

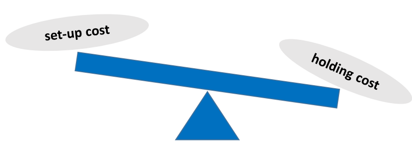


Goff DA, et al. *Clin Infect Dis*. 2012;55: 87-592.

Image removed due to copyright. Use following resource: Fischer MA, et al. *Arch Int Med. 2003;21*:2585-2589. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/216381

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Medication Batching



- Standard timing: preparation, administration
- ex. daptomycin batching --- 370 vials saved over 4 months ($83,991)

Goff DA, et al. *Clin Infect Dis*. 2012;55: 87-592.

Image removed due to copyright. Use following resource: Dobson G, et al. *Decis Support Syst. 2015;76*:53-62. https://www.sciencedirect.com/science/article/abs/pii/S0167923615000330

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Therapeutic Substitutions

PRE-COVID-19 → **COVID-19**

Therapeutic Equivalence
- Statins
- Inhalers
- Antiretrovirals

Long Acting Agents
- Metoprolol succinate
- Ertapenem

Less Monitoring
- Enoxaparin
- Daptomycin

Consolidate dosing schedules!

Goff DA, et al. *Clin Infect Dis.* 2012;55: 87-592.
Earl G, et al. *Remington.* 2020;50:849-876.

Pre-authorization

Pre-authorization → Medication Order

High cost	fidaxomicin	baricitinib
Short supply	acyclovir	remdesivir
Limited data	cefiderocol	EUA drugs
Toxicity	foscarnet	hydroxychloroquine

Predominantly drug-driven

Goff DA, et al. *Clin Infect Dis.* 2012;55: 87-592.

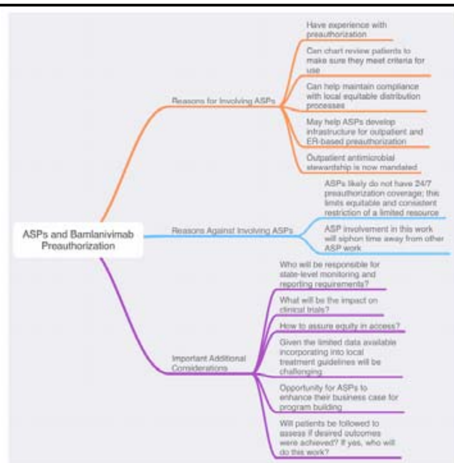


Image used with permission by: Patel PK, et al. *Infect Control Hosp Epidemiol.* 2020:1-3.

Prospective Audit & Feedback (PAF)

Medication Order → PAF

Image removed due to copyright. Please refer to:

Liew YX, et al. *Int J Antimicrob Agents.* 2015;45:168-173.
https://www.sciencedirect.com/science/article/abs/pii/S0924857914003537?via%3Dihub

More customizable targets
- Disease state
- Lab result
- Drug

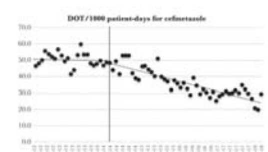


Image used with permission by:
Honda H, et al. *Open Forum Infect Dis. 2018;5:*ofy314.

Forrest GN, et al. *Clin Infect Dis. 2014;*59:S122-S133.

PAF with IT Support

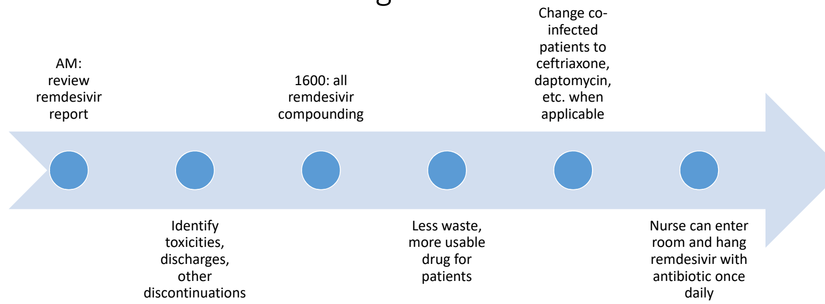
Table 1. Antimicrobial Stewardship COVID-19 Rule Logic

Name	Criteria	Display
ASP COVID-19 rule 1: negative SARS-COV-2 PCR w/ active drug order (inpatients only)	• IF negative COVID-19 PCR in last 7 days **AND** • IF active order for 1 of the following: • Chloroquine • Darunavir/ritonavir • Hydroxychloroquine • Lopinavir/ritonavir • Nitazoxanide • Remdesivir • Ribavirin • Sarilumab • Tocilizumab • Lenzilumab • IVIg • THEN fire alert	**Rule Text** • Rule name • COVID-19 medication that triggered flag • SARS-COV-2 test result, date, and time
ASP COVID-19 rule 2: positive SARS-COV-2 PCR or pending lab w/ active drug order (inpatients only)	• IF positive COVID-19 PCR in last 7 days **OR** • IF pending COVID-19 PCR in last 7 days **AND** • IF active order for 1 of the following: • Chloroquine • Darunavir/ritonavir • Hydroxychloroquine • Lopinavir/ritonavir • Nitazoxanide • Remdesivir • Ribavirin • Sarilumab • Tocilizumab • Lenzilumab • IVIg • THEN fire alert	**Rule Text** • Rule name • COVID-19 medication that triggered flag • SARS-COV-2 test result, date, and time

Image used with permission by: Stevens RW, et al. *Infect Control Hosp Epidemiol*. 2020;41:1108-1110.

Mazdeyasna H, et al. *Curr Infect Dis Rep.* 2020;22:1-6.

Combination of Strategies



Physician Perspectives on Strategies by Stewardship Program Implemented During COVID-19

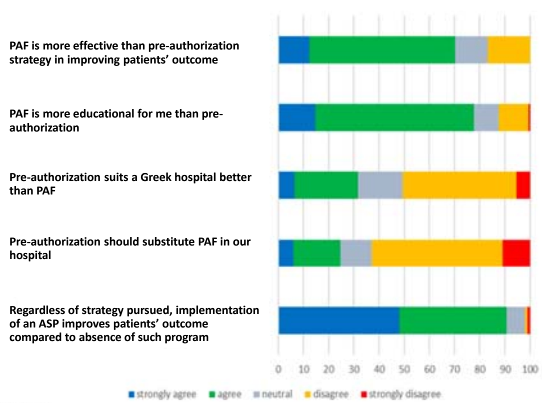


Image used with permission by: Spernovasilis N, et al. *Trop Med Infect Dis*. 2021;6:20.

	Pre-authorization	PAF
Advantages	• Initiation/empiric therapy • Direct control • Quick mechanism	• Definitive therapy • Prescriber autonomy → relationships • Hindsight/more data • Flexible
Disadvantages	• Resources: around the clock? • Limited lasting effects • Durations	• Resources: IT vs. computer surveillance • Compliance voluntary • Starting from behind

Adapted from: Goff DA, et al. *Clin Infect Dis*. 2012;55: 87-592.

Antibiotic "Time-Outs"

- Through prospective audit & feedback or electronic alerts

Image removed due to copyright. Refer to:
Wolfe JR, et al. *Infect Control Hosp Epidemiol. 2019;*40:1287-1289.
https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/impact-of-an-automated-antibiotic-timeout-alert-on-the-deescalation-of-broadspectrum-antibiotics-at-a-large-community-teaching-hospital/4CA0D7799D84CFF5D15C3EBE8F599392#

Education

- Use in combination
- High frequency
- Multi-disciplinary
- Promote guidelines, workflows

Weak recommendation, low quality evidence

Barlam TF, et al. *Clin Infect Dis.* 2016;62:e51-e77.

Which of the following drugs would be most appropriate for management via pre-authorization?

A. COVID-19 vaccine
B. IV tocilizumab
C. PO dexamethasone
D. IV ondansetron

Summary

Image removed from handout due to copyright. Refer to:

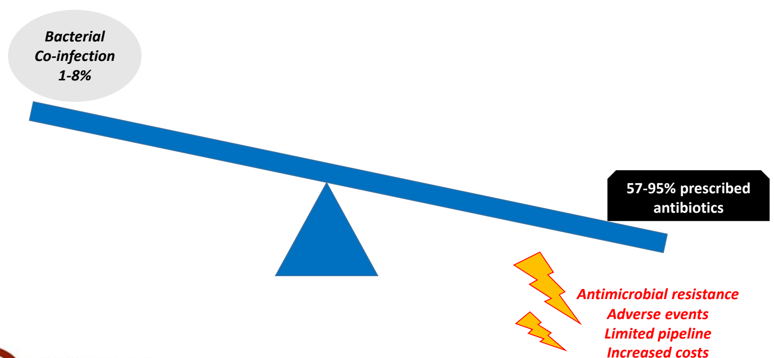
Moehring RW, et al. *Current Infect Dis Rep.* 2012;14:592-600. https://link.springer.com/content/pdf/10.1007/s11908-012-0289-x.pdf

II. Bacterial Co-infection in COVID-19

Co-infection Considerations

- Frequency of empiric antimicrobials
- Incidence
- Primary co-infection vs. secondary infection
  - Risk factors
  - Common pathogens
- Diagnostic criteria

Balance Needed



Martin AJ, et al. *J Pharm Pract.* 2021: online preprint.

International "Snapshot" of Antibiotic Use 2020

166 prescribers (50% ID)
23 countries

29% do not routinely prescribe antibiotics

Reason for antibiotics
-clinical presentation
-inflammatory markers
-radiology findings
*piperacillin/tazobactam most common

Coverage
-atypical
-*S. aureus*
-*Pseudomonas*

Mean duration (days)
All countries: 7.12

Guidelines for antibiotics in COVID-19: ~62%

Beović B, et al. *J Antimicrob Chemother.* 2020;75:3386-3390.

Co-infection in Familiar Viruses

	Influenza	SARS/MERS-CoV
Most Common Bacterial Respiratory Pathogens	1. *S. pneumoniae* 2. *S. aureus* 3. *H. influenzae* 4. *S. pyogenes*	Primary: atypical/community-acquired pneumonia (CAP) organisms Secondary: nosocomial pathogens
Bacterial Co-infection	~20%	~10-30% co-infection
Outcomes	↑ morbidity & mortality	Higher levels of care
Co-infection Guideline Recommendations	Community-acquired Pneumonia (CAP): administer antibiotics to adults with clinical and radiographically diagnosed CAP who test positive for influenza (strong recommendation, low quality of evidence)	n/a WHO refers to national guidelines for antibiotic management

Joseph C, et al. *Influenza Other Respir Viruses.* 2013;7:105-113.
Klein EY, et al. *Influenza Other Respir Viruses.* 2016;10:394-403.
Langford BJ, et al. *Clin Microbiol Infect.* 2020;26:1622-1629.
Metlay JP, et al. *Am J Respir Crit Care Med*. 2019;200:e45-e67.
Saad M, et al. *Int J Infect Dis.* 2014;29:301-306.

Limitations on Co-infection Reporting

- COVID-19: largely early 2020 data
- Difficult to group or compare reports
- Differing definitions
  - ex. community-acquired, co-infection
  - timing
- Inconsistent diagnostics

Challenges Specific to Bacterial Pneumonia in COVID-19
• COVID-19 similarities to bacterial pneumonia • Colonization • Low pathogen yield, often empiric • Abnormal inflammatory markers in COVID-19 (ex. CRP) • Limited procedures/testing, staffing *Under- vs. over-reported?*

Feldman C, et al. *Pneumonia.* 2021;13:1-15.
Lansbury L, et al. *J Infect*. 2020;81:266-275.
Musher DM. *Am J Respir Crit Care Med.* 2021; online preprint.
Rawson TM, et al. *Clin Infect Dis.* 2020;71:2459-2468.

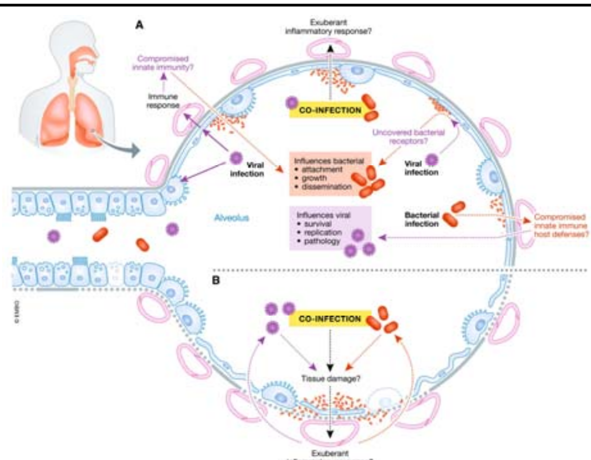


Image used with permission by: Bengoechea JA, et al. *EMBO Mol Med.* 2020;12:e12560.

Pooled Analyses of Co-infection

	Rawson (May 2020)	Langford (July 2020)
Methods	Review of 9 studies • 806 patients	Meta analysis of 24 studies • 3,338 patients
Co-infection	8%	6.9% • 3.5% co-infection • 14.3% secondary infection
Empiric Antibiotics	72%	71.8%
Pathogens Identified	*Limited:* *few atypical pathogens*	*Limited: pathogen data from 14% of patients* *Most common: Mycoplasma species, H. influenzae, & P. aeruginosa*
WARNING	*Co-infection may be misrepresented*	

Langford BJ, et al. *Clin Microbiol Infect*. 2020;26:1622-1629
Rawson TM, et al. *Clin Infect Dis.* 2020;71:2459-2468

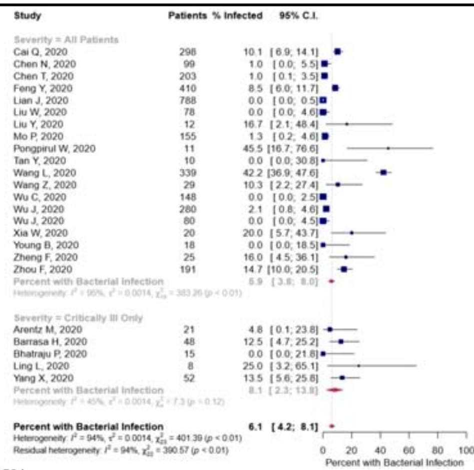
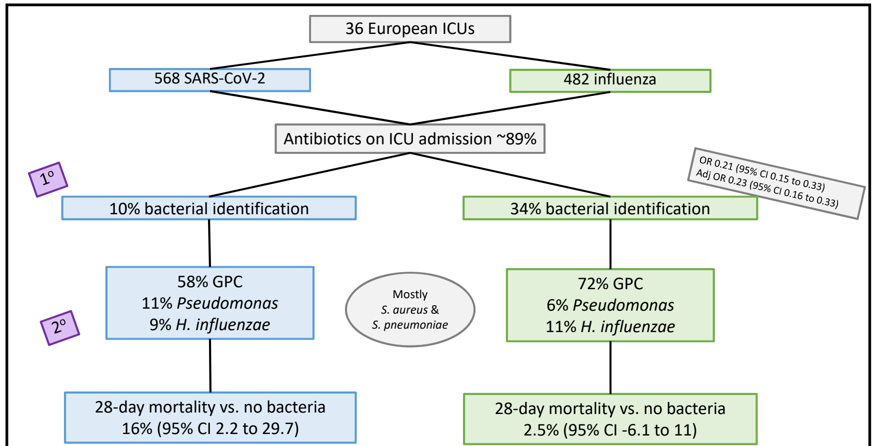


Image used with permission by: Langford BJ, et al. *Clin Microbiol Infect*. 2020;26:1622-1629.



Adapted from: Rouze A, et al. *Am J Respir Crit Care Med*. 2021; online preprint.

Early Antibiotics in Critically Ill COVID-19 Patients

Outcome (n= 48)	Antibiotics (n= 19)	No Antibiotics (n= 29)	
mortality	5 (26%)	7 (24%)	p=0.86
VAP	14 (74%)	19 (66%)	p=0.55
CRBSI	5 (26%)	7 (24%)	p=0.86
UTI	2 (11%)	8 (28%)	p=0.28

50% steroids in ICU
10% tocilizumab

Buetti N, et al. *J Infect*. 2020;81:e148–e149.

Risk Factors for Co-infection

	Incidence of Co-infection	Community-acquired Risk Factors	Hospital-associated Risk Factors
Petty LA, et al.	6.4% (141/2,205) • 3% community-acquired • 3.4% hospital-associated	• Day 1 admission to ICU • Admission from LTCF	• Median 8 days • Fever • Higher respiratory support
Vaughn VM, et al.	3.5% (59/1,705)	• Older age • Lower BMI • Mod-severe kidney disease • SNF • ICU admission • Leukocytosis	n/a
Conclusion	Consistent at <10%	Hold antibiotics at admission for non-ICU patients	Signs & symptoms of bacterial infection, timing

Petty LA, et al. *Infect Control Hosp Epidemiol*. 2021;1-10. Online preprint.
Vaughn VM, et al. *Clin Infect Dis*. 2021;72:e533-e541.

USA: Primary Co-infection at Admission

- 1,016 patients; 5 Johns Hopkins hospitals

Type of Co-infection	# of Patients (%)
Viral/atypical respiratory infection	2 (0.2)
Bacterial respiratory infection	
By any definition	497 (49)
Proven	1
Probable	11
Possible	483
Fungal Infection	
Fungal respiratory infection	0
Endemic mycoses	0
Bloodstream infection	20 (2)
Urinary tract infection	30 (3)
Clostridioides difficile colitis	2 (0.2)

71% received antibiotics

0.3% proven infection
1.1% probable infection

Proven/probable/possible bCAP more likely admitted to ICU vs. no co-infection (33% vs. 16% vs. 7%; P< .01)

Adapted from: Karaba SM, et al. *Open Forum Infect Dis.* 2021;8:ofaa578.

Bacterial Pneumonia Management Remains the Same

CAP
Duration:
5 days

HAP/VAP
Duration:
7 days

Obtain cultures!
De-escalate!
Discontinue!

Other Uncommon Co-infecting Pathogens

- Viral
  - Enterovirus/Rhinovirus
  - Influenza less common
  - Risk factor: older age
- Fungal
  - COVID-19-associated pulmonary aspergillosis (CAPA)
  - Candidiasis
  - Risk Factors: immunosuppression, corticosteroids

Fekkar A, et al. *Am J Resp Crit.* 2021;203:307-317.
Xi C, et al. *Appl Microbiol Biotechnol.* 2020;104:7777-7785.

Other Pathogens: *Clostridioides difficile* Infections (CDI)

- Incidence lower than pre-COVID-19:
  - Infection control techniques
  - Less surgeries
- Unknowns:
  - Healthcare vs. community-acquired
  - Antibiotics vs. no antibiotics

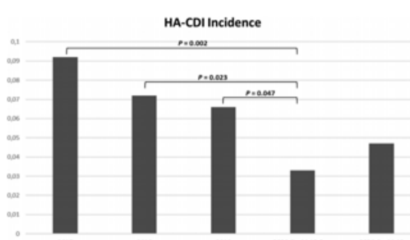


Image used with permission by: Bentivegna E, et al. *Am J Infect Control*. 2021;49:640-642.

Hazel K, et al. *Infect Control Hosp Epidemiol.* 2021:1-2. Online preprint.
Luo Y, et al. *Infect Control Hosp Epidemiol.* 2020:1-2. Online preprint.

Secondary Infection

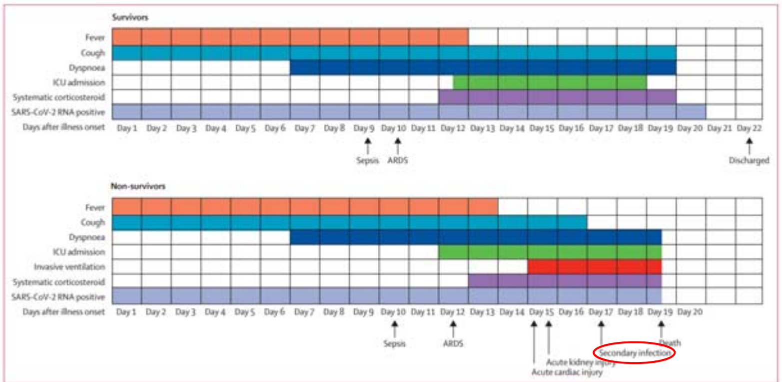


Image used with permission by: Zhou F, et al. *Lancet*. 2020;395:1054–1062.

Bacterial Co-infection Clues in Pneumonia

Respiratory Setting Trends
- Nursing
- Respiratory therapy

Sputum Gram stains
- ↑ sensitivity, specificity
- # bacteria/organisms
- Microbiology lab!

Primary vs. Secondary Infections
- ex. day of hospitalization
- central line, Foley catheter
- antibiogram

Musher DM. *Am J Respir Crit Care Med.* 2021; online preprint.

Procalcitonin (PCT) in COVID-19

- Critically ill COVID-19 patients?
- Vaughn, et al: community-onset bacterial co-infection

PCT >0.5ng/mL	PCT ≤0.1ng/mL
Positive predictive value 9.3%	Negative predictive value 98.3%

- Crotty, et al: bacterial respiratory co-infection

PCT >0.25ng/mL	PCT >0.5ng/mL
Sensitivity 73.9% Specificity 65.2%	Sensitivity 43.5% Specificity 81.3%,

- Possible role in antibiotic discontinuation and secondary infections

Crotty MP, et al. *medRxiv*. 2020: online preprint.
Vaughn VM, et al. *Clin Infect Dis*. 2021;72:e533-e541.

TA is a 48 yo F with a PMH of anxiety and hyperlipidemia who presented to the ED last night with SOB, cough, anosmia, and muscle aches. Her O2 saturations were 90% on room air and she was started on 2L nasal cannula. Upon admission to the general medicine floor, she was started on remdesivir and dexamethasone. Overnight she spiked a fever to 101°F and the covering physician ordered a one time dose of piperacillin/tazobactam.

- WBC 5.9 K/uL
- Procalcitonin 0.1 mcg/L
- Serum creatinine: 0.8 mg/dL
- Chest X-ray: mild patchy perihilar & peripheral airspace opacities
- Microbiology: blood cultures pending

Which of the following statements is most appropriate for the pharmacist to discuss with the ordering provider?

A. Patient is at risk of a secondary nosocomial infection so meropenem should be started ASAP.
B. The likelihood of bacterial co-infection is low so consider monitoring off antibiotics.
C. Procalcitonin is < 0.5 mcg/L so order piperacillin/tazobactam for 6 more days to treat bacterial pneumonia co-infection.
D. Add vancomycin to piperacillin/tazobactam to cover for resistant *S. pneumoniae*.

Guideline Recommendations

COIVD-19 Guideline	Recommendation
Surviving Sepsis, March 2020	Empiric antimicrobials over no antimicrobials in mechanically ventilated patients with
WHO, Jan 2021	Severe: clinical judgement for antibiotics, attempt de-escalation daily
NIH, April 2021	"antimicrobial stewardship is critical"
NICE	Antibiotics for suspected bacterial infection but know risks and de-escalate rapidly
IDSA, June 2021	Review of controversy in literature
IDSA Real Time Learning Network	Pre-existing antimicrobial stewardship infrastructures for guidelines

Alhazzani W, et al. *Intensive Care Med.* 2020;46:854-887
World Health Organization. Accessed August 10, 2021
National Institutes of Health. Accessed August 10, 2021
National Institute for Health and Care Excellence. Accessed August 10, 2021
Bhimraj A, et al. Infectious Diseases Society of America 2021; Version 4.4.1
COVID-19 Real-Time Learning Network. Accessed August 10, 2021

COVID-19 vs. Influenza

	COVID-19	vs. Flu
Most Common Bacterial Respiratory Pathogens	*?* *CAP organisms* *S. aureus*	=
Bacterial Co-infection	1-10%	↓
Outcomes	↑ mortality	=
Co-infection Guideline Recommendations	n/a Weak, brief summaries across multiple guidelines	↓

Co-infection Summary

- Low incidence of bacterial co-infection in COVID-19
- Distinction between co-infection and secondary infection
- Inconsistencies in reporting
- Pharmacists play an important role

III. Other Longitudinal Interventions to Enhance Care of Patients with COVID-19

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Tracking & Reporting

- Antibiogram
- Antimicrobial Utilization
  - Interventions
  - Opportunities for improvement
- Track by:
  - Institution vs. ward vs. prescriber/service
  - Drug, class, disease state

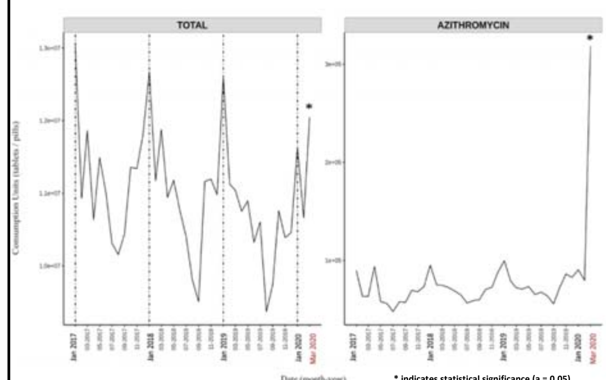
Example Metrics

- DOT/1,000 patient days
- DDD
- Costs
- Orders

DOT= days of therapy
DDD= defined daily dose

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Spain, March 2020



Other Antibiotics

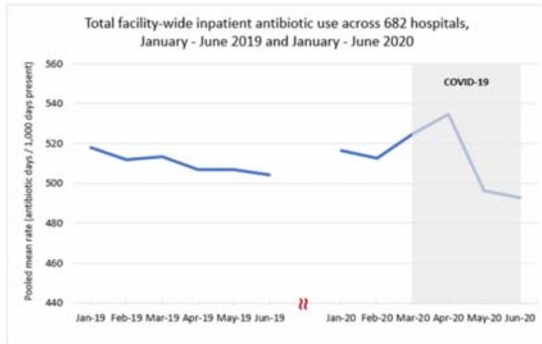
1. ceftaroline (183%)
2. ceftolozane/tazobactam (103%)
3. ceftriaxone (204%)
4. colistin (145%)
5. doxycycline (517%)
6. linezolid (189%)

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Image used with permission by: Gonzalez-Zorn B. *Clin Microbiol Infect*. 2020;27:646-647.

USA, CDC: Inpatient Antibiotic Prescribing

composite



Data Source: CDC National Healthcare Safety Network Antimicrobial Use Option

Centers for Disease Control and Prevention. Accessed August 10, 2021.

Standardized Antimicrobial Administration Ratio (SAAR)

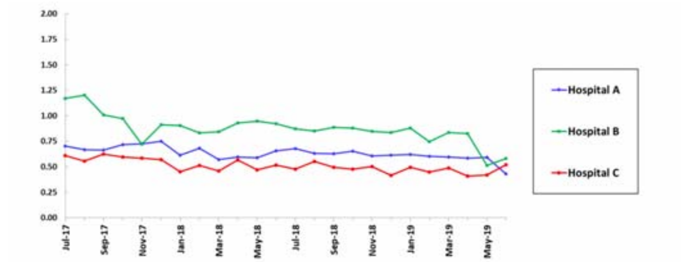
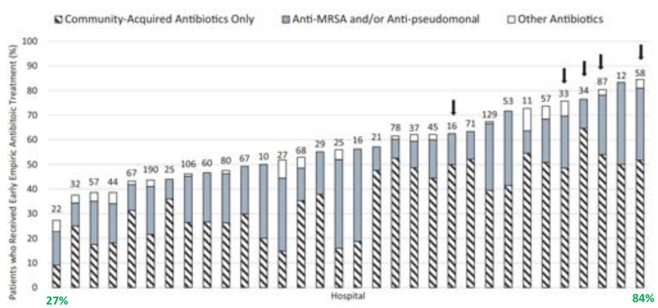


Figure 1. Standardized antimicrobial administration ratio (SAAR) trends for all antimicrobials used in adult intensive care units (ICUs), wards, step down units, and oncology units.

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Image used with permission by: Shealy S, Kohn J, Yongue E, et al. *J Pharm Pract*. 2021;9:32.

Antibiotics in Michigan Hospitals



4,628 antibacterial days/1,000 patients

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Image used with permission by: Vaughn VM, et al. *Clin Infect Dis*. 2021;72:e533-e541.

Before & After Interventions

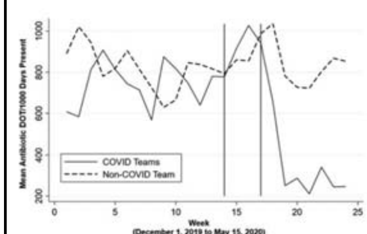


Image used with permission by: Staub MB, et al. *Infect Control Hosp Epidemiol. 2021;42*:810-816.

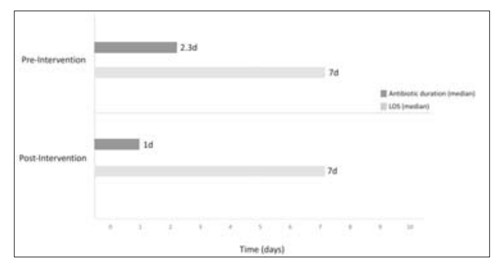


Image used with permission by: Pettit NN, et al. *BMC Infect* Dis. 2021;21:1-7.

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Tracking Tocilizumab Administration

- Viral reactivation
- Live vaccines
- Contraindications
- Shortages

The FDA has issued Emergency Use Authorization for the emergency use of tocilizumab in the treatment of COVID-19.

The primary purpose of tracking antibiotic use during the COVID-19 era is to

A. reduce the rate of healthcare-associated *Clostridiodes difficile* (CDI).
B. fulfill hospital accreditation requirements.
C. report the highest antibiotic prescribers to leadership.
D. identify and compare usage trends before COVID-19.

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

Summary

- Antimicrobial Stewardship strategies are useful for the COVID-19 response.
- Balance antibiotic use with low rates of co-infection.
- Pharmacists play an important role in multidisciplinary COVID-19 treatment teams.
- Use tracking and reporting to find and evaluate areas of opportunity.
- More antimicrobial stewardship research needed!

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

REFERENCES

1. Antimicrobials Working Group. The Antimicrobial Resistance Crisis. Available at: http://antimicrobialsworkinggroup.org/antimicrobial-resistance/. Accessed August 5, 2021.
2. Alhazzani W, Hylander Møller M, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). *Intensive Care Med.* 2020;46:854-887.
3. Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis*. 2016;62:e51-e77.
4. Bengoechea JA, Bamford CGG. SARS-CoV-2, bacterial co-infections, and AMR: the deadly trio in COVID-19?. *EMBO Mol Med*. 2020;12:e12560.
5. Bentivegna E, Alessio G, Spuntarelli V, et al. Impact of COVID-19 prevention measures on risk of health care-associated Clostridium difficile infection. *Am J Infect Control*. 2021;49:640-642.
6. Beović B, Doušak M, Ferreira-Coimbra J, et al. Antibiotic use in patients with COVID-19: a "snapshot" Infectious Diseases International Research Initiative (ID-IRI) survey. *J Antimicrob Chemother*. 2020;75:3386–3390.
7. Bhimraj A, Morgan RL, Shumaker AH, et al. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. Infectious Diseases Society of America 2021; Version 4.4.1. Available at: https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/. Accessed August 10, 2021.
8. Buetti N, Mazzuchelli T, Lo Priore E, et al. Early administered antibiotics do not impact mortality in critically ill patients with COVID-19. *J Infect*. 2020;81:e148–e149.
9. COVID-19 Real-Time Learning Network. Co-infection and Antimicrobial Stewardship. Available at: https://www.idsociety.org/covid-19-real-time-learning-network/disease-manifestations--complications/co-infection-and-Antimicrobial-Stewardship/. Accessed August 10, 2021.
10. Centers for Disease Control and Prevention. "Antibiotic Prescribing and Use in the US: The COVID-19 Pandemic and Antibiotic Prescribing. Available at: https://www.cdc.gov/antibiotic-use/stewardship-report/current.html. Accessed August 10, 2021.
11. Crotty MP, Dominguez EA, Akins R, et al. Investigation of subsequent and co-infections associated with SARS-CoV-2 (COVID-19) in hospitalized patients. *medRxiv*. 2020: online preprint.
12. Dobson G, Tilson D, Tilson V. Optimizing the timing and number of batches for compounded sterile products in an in-hospital pharmacy. *Decis Support Syst. 2015;*76:53-62.
13. Earl G, Cillessen LM, Lyons-Burney H, et al. Pharmacists' role in infectious pandemics: illustration with COVID-19. *Remington.* 2020;50:849-876.
14. Fekkar A, Lampros A, Mayaux J, et al. Occurrence of Invasive Pulmonary Fungal Infections in Patients with Severe COVID-19 Admitted to the ICU. *Am J Respir Crit Care Med*. 2021;203:307-317.
15. Feldman C, Anderson R. The role of co-infections and secondary infections in patients with COVID-19. *Pneumonia.* 2021;13:1-15.
16. Fischer MA, Solomon DH, Teich JM, et al. Conversion from intravenous to oral medications: assessment of a computerized intervention for hospitalized patients. *Arch Int Med. 2003;21:*2585-2589.
17. Forrest GN, Van Schooneveld TC, Kullar R, et al. Use of electronic health records and clinical decision support systems for antimicrobial stewardship. *Clin Infect Dis, 2014;*59:S122-S133.
18. Getahun H, Smith I, Trivedi K, et al. Tackling antimicrobial resistance in the COVID-19 pandemic. *Bull World Health Organ. 2020*;98:442.
19. Goff DA, Bauer KA, Reed EE, et al. Is the "low-hanging fruit" worth picking for antimicrobial stewardship programs?. *Clin Infect Dis*. 2012;55: 87-592.
20. Gonzalez-Zorn B. Antibiotic use in the COVID-19 crisis in Spain. *Clin Microbiol Infect.* 2020;27:646-647.
21. Hazel K, Skally M, Glynn E, et al. The other 'C': Hospital-acquired Clostridioides difficile infection during the coronavirus disease 2019 (COVID-19) pandemic." *Infect Control Hosp Epidemiol.* 2021:1-2. Online preprint.
22. Honda H, Murakami S, Tagashira Y, et al. Efficacy of a postprescription review of broad-spectrum antimicrobial agents with feedback: a 4-year experience of antimicrobial stewardship at a tertiary care center. *Open Forum Infect Dis. 2018;5:*ofy314.
23. Joseph C, Togawa Y, Shindo N. Bacterial and viral infections associated with influenza. *Influenza Other Respir Viruses.* 2013;7:105-113.
24. Karaba SM, Jones G, Helsel T, et al. Prevalence of Co-infection at the Time of Hospital Admission in COVID-19 Patients, A Multicenter Study. *Open Forum Infect Dis*. 2021;8:ofaa578.
25. Klein EY, et al. "The frequency of influenza and bacterial coinfection: a systematic review and meta-analysis." *Influenza Other Respir Viruses.* 2016;10:394-403.
26. Langford BJ, So M, Raybardhan S, et al. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. *Clin Microbiol Infect.* 2020;26:1622-1629.

BUILDING BRIDGES CONNECTING THROUGH CARE | 2021 ICHP ANNUAL MEETING

27. Lansbury L, Lim B, Baskaran V, et al. Co-infections in people with COVID-19: a systematic review and meta-analysis. *J Infect*. 2020;81:266-275.
28. Liew YX, Lee W, Tay D. Prospective audit and feedback in antimicrobial stewardship: is there value in early reviewing within 48 h of antibiotic prescription?. *Int J Antimicrob Agents. 2015;*45:168-173.
29. Luo Y, Grinspan LT, Fu Y, et al. Hospital-onset Clostridioides difficile infections during the COVID-19 pandemic. *Infect Control Hosp Epidemiol.* 2020:1-2. Online preprint.
30. Martin AJ, Shulder S, Dobrzynski D, et al. Antibiotic Use and Associated Risk Factors for Antibiotic Prescribing in COVID-19 Hospitalized Patients. *J Pharm Pract.* 2021: online preprint.
31. Mazdeyasna H, Nori P, Patel P, et al. Antimicrobial stewardship at the core of COVID-19 response efforts: implications for sustaining and building programs. *Curr Infect Dis Rep. 2020;*22:1-6.
32. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med*. 2019;200:e45-e67.
33. Moehring RW, Anderson DJ. Antimicrobial stewardship as part of the infection prevention effort. *Current Infect Dis Rep.* 2012;14:592-600.
34. Musher DM. Bacterial Coinfection in COVID-19 and Influenza Pneumonia. *Am J Respir Crit Care Med.* 2021; online preprint.
35. National Institute for Health and Care Excellence. COVID-19 rapid guideline: Managing COVID-19. Available at: https://app.magicapp.org/#/guideline/L4Qb5n/section/E5BJJj. Accessed August 10, 2021.
36. National Institutes of Health. COVID-19 Treatment Guidelines General Considerations. Available at: https://www.covid19treatmentguidelines.nih.gov/management/critical-care/general-considerations/. Accessed August 10, 2021.
37. Patel PK, Nori P, Stevens MP. Antimicrobial stewardship and bamlanivimab: Opportunities for outpatient preauthorization?. *Infect Control Hosp Epidemiol. 2020*:1-3.
38. Pettit NN, Nguyen CT, Lew, AK, et al. Reducing the use of empiric antibiotic therapy in COVID-19 on hospital admission. *BMC Infect* Dis. 2021;21:1-7.
39. Petty LA, Flanders SA, Vaughn VM, et al. Risk Factors and Outcomes Associated with Community-Onset and Hospital-Acquired Co-infection in Patients Hospitalized for COVID-19: A Multi-Hospital Cohort Study. *Infect Control Hosp Epidemiol*. 2021;1-10. Online preprint.
40. Rawson TM, Moore LSP, Zhu N, et al. Bacterial and Fungal Coinfection in Individuals With Coronavirus: A Rapid Review To Support COVID-19 Antimicrobial Prescribing. *Clin Infect Dis*. 2020;71:2459-2468.
41. Rouze A, Martin-Loeches I, Povoa P, et al. Early Bacterial Identification Among Intubated Patients with COVID-19 or Influenza Pneumonia: A European Multicenter Comparative Cohort Study. *Am J Respir Criti Care Med.* 2021; online preprint.
42. Saad M, Omrani AS, Baig K, et al. Clinical aspects and outcomes of 70 patients with Middle East respiratory syndrome coronavirus infection: a single-center experience in Saudi Arabia. *Int J Infect Dis.* 2014;29:301-306.
43. Shealy S, Kohn J, Yongue E, et al. Application of Standardized Antimicrobial Administration Ratio as a Motivational Tool within a Multi-Hospital Healthcare System. *J Pharm Pract*. 2021;9:32.
44. Spernovasilis N, Ierodiakonou D, Spanias D, et al. Doctors' Perceptions, Attitudes and Practices towards the Management of Multidrug-Resistant Organism Infections after the Implementation of an Antimicrobial Stewardship Programme during the COVID-19 Pandemic. *Trop Med Infect Dis*. 2021;6:20.
45. Staub MB, Beaulieu RM, Graves J, et al. Changes in antimicrobial utilization during the coronavirus disease 2019 (COVID-19) pandemic after implementation of a multispecialty clinical guidance team. *Infect Control Hosp Epidemiol. 2021;42:*810-816.
46. Stevens RW, Estes L, Rivera C. Practical implementation of COVID-19 patient flags into an antimicrobial stewardship program's prospective review. *Infect Control Hosp Epidemiol*. 2020;41:1108-1110.
47. The Society for Healthcare Epidemiology of America. Antimicrobial Stewardship. Available at: https://www.shea-online.org/index.php/practice-resources/priority-topics/antimicrobial-stewardship. Accessed August 5, 2021.
48. Vaughn VM, Gandhi TN, Petty LA, et al. Empiric Antibacterial Therapy and Community-onset Bacterial Coinfection in Patients Hospitalized With Coronavirus Disease 2019 (COVID-19): A Multi-hospital Cohort Study. *Clin Infect Dis*. 2021;72:e533-e541.
49. Wolfe JR, Bryant AM, Khoury JA. Impact of an automated antibiotic time-out alert on the de-escalation of broad-spectrum antibiotics at a large community teaching hospital. *Infect Control Hosp Epidemiol. 2019;*40:1287-1289.
50. World Health Organization. COVID-19 clinical management: living guidance 25 Jan 2021. Available at: https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-clinical-2021-1. Accessed August 10, 2021.
51. Xi C, Liao B, Cheng L, et al. The microbial coinfection in COVID-19. *Appl Microbiol Biotechnol.* 2020;104:7777-7785.
52. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054–1062.

Antimicrobial Stewardship Considerations during the COVID-19 Pandemic

Assessment Questions

1. Which antimicrobials stewardship strategy applicable to COVID-19 requires the most IT support?
    a. Prospective audit & feedback
    b. Therapeutic substitution
    c. Pre-authorization
    d. Guideline creation

2. Defaulting all remdesivir maintenance dose administration times to 1500 is a component of which antimicrobial stewardship strategy?
    a. Batching
    b. Prospective audit and feedback
    c. Therapeutic substitution
    d. IV to PO conversion

3. What is the estimated incidence of bacterial co-infection in COVID-19?
    a. 0%
    b. 1-10%
    c. 15-20%
    d. >25%

4. Antimicrobial utilization reports by hospital floor is an example of which Core Element of Antimicrobial Stewardship?
    a. Pharmacy Expertise
    b. Action
    c. Tracking
    d. Education

Answer key: 1. a, 2. a, 3. B, 4. c

1. Prospective audit & feedback (PAF) requires the most IT support. This is a disadvantage of PAF compared to pre-authorization. Therapeutic substitution and guideline creation do not require IT support for implementation.
2. Creating drug-specific, standard administration times for certain medications to avoid waste is a characteristic of the batching strategy. Prospective audit and feedback, therapeutic substitution, and IV to PO conversions do not affect administration times at the ordering phase of medications.
3. The estimated incidence of bacterial co-infection in COVID-19 is 1-10%. This finding is from meta analyses from limited reports in COVID-19 since the identification of the virus. This statistic varies according to country or region and the inclusion of primary vs. secondary bacterial infections.
4. Antimicrobial utilization reports by hospital floor is an example of the "Tracking" Core Element of Antimicrobial Stewardship. These reports are used to generate various "Action" or "Education" strategies. "Pharmacy Expertise" is used to interpret these reports in collaboration with other members of the antimicrobial stewardship multidisciplinary team.