

# Reflections From The Frontlines: Collateral Damage from Covid in Terms of Antimicrobial Resistance

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# Learning Objectives

- Discuss the front-line challenges of COVID-19 from a clinical and laboratory perspective
- Describe the impact of the COVID-19 pandemic on Antimicrobial Stewardship Principles
- Examine the potential longer-term consequences of a viral pandemic on emerging bacterial resistance

- Directly involved in LA County Response to Covid in Long Term Care – SNFs and LTAC
- Collaborated with Orange County Healthcare Association on Covid Outbreak Responses – over 300 outbreaks
- Infectious Disease Physician directly involved in patient care throughout the pandemic.
- The opinions expressed here are my own – mostly developed from trial and error experience with Covid.

# US Causes of Death

	2019	Deaths
<b>1</b>	Heart Disease	659,000
<b>2</b>	Cancer	599,000
<b>3</b>	Accidents	173,000
<b>4</b>	Chronic Lung Disease	157,000
<b>5</b>	Stroke	150,000

<https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm> Accessed 10/26/2021, rounded to the nearest thousand deaths.

## Seasonal Influenza 2019-2020

## COVID-19 (Feb 2020 – May 2021)

- 38 Million Infections
- 400,000 Hospitalizations
- 21,000 Deaths
- **37 Million Infections**
- **2,200,000 Hospitalizations**
- **583,596 Deaths**

[https://covid.cdc.gov/covid-data-tracker/#cases\\_casesinlast7days](https://covid.cdc.gov/covid-data-tracker/#cases_casesinlast7days) Accessed on 5/18/2021

<https://covidtracking.com/data/national> Accessed on 9/24/2020

<https://www.cdc.gov/flu/about/burden/index.html> accessed 3/10/2020

# US Causes of Death

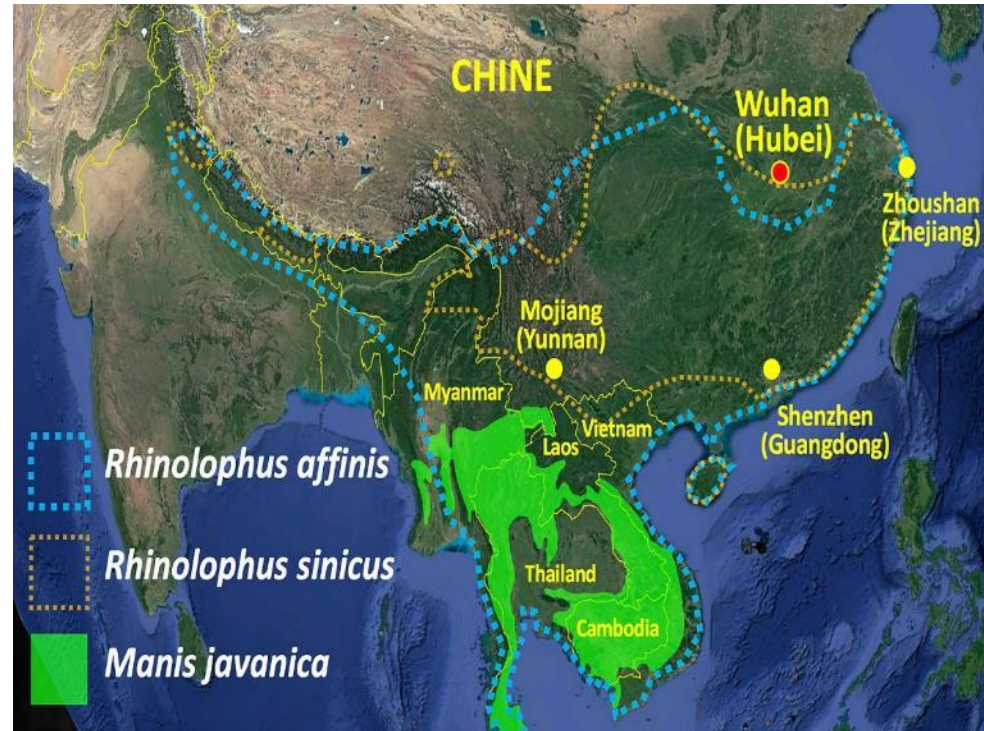
	2019	Deaths
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Accessed 9/24/2020.

What Happened?

# SARS CoV-2



- Related to Bat Coronavirus (BatCov RaTG13)
- Related to SARS CoV-1 (2003)



# SARS CoV-2

- Cross Species Recombination with Pangolin Virus
- Likely emerged in November, 2019

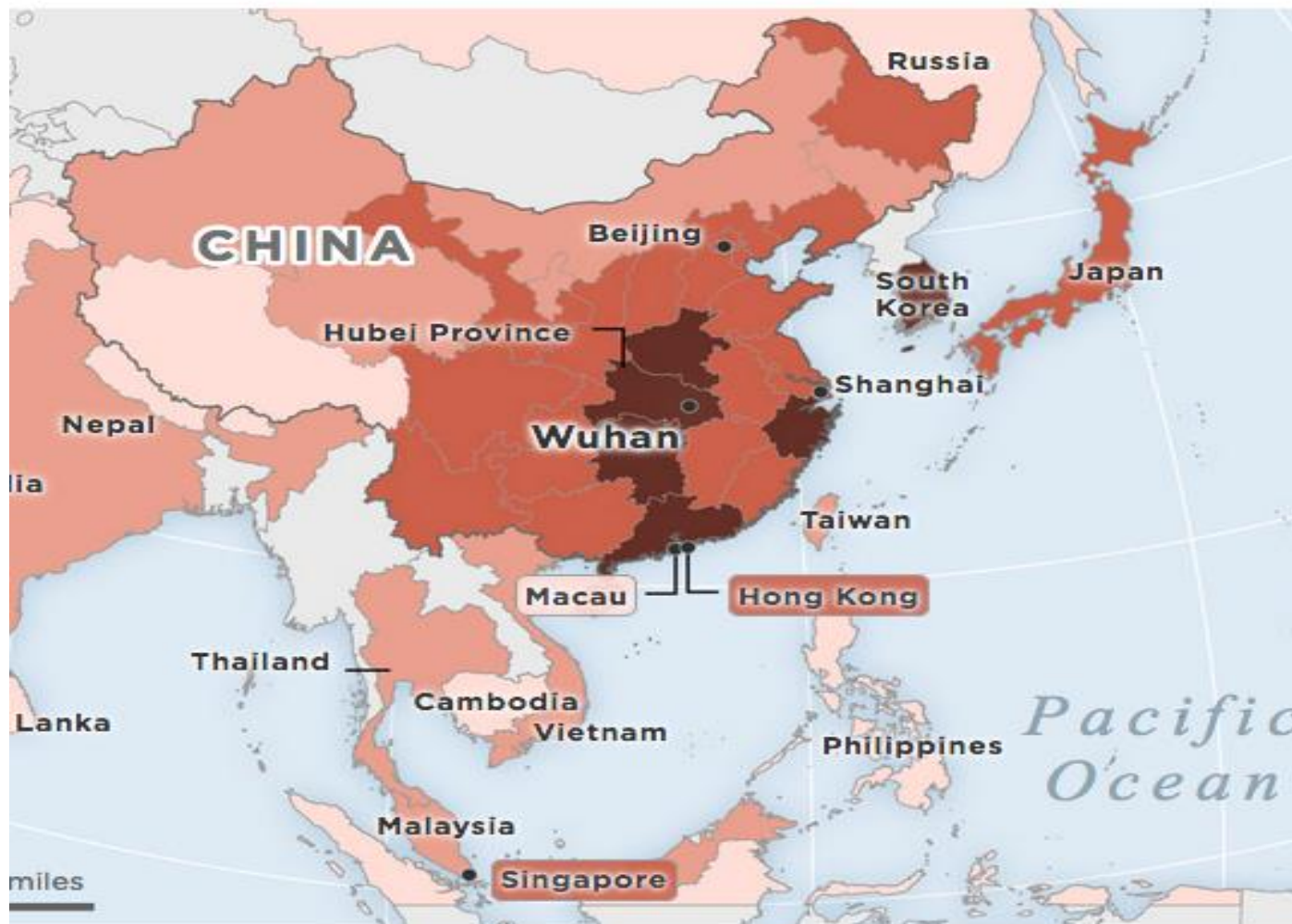
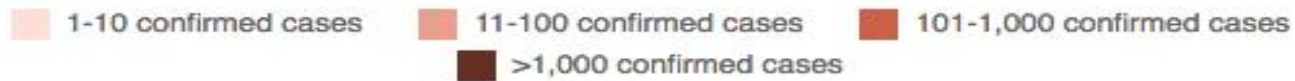


# Wuhan Market



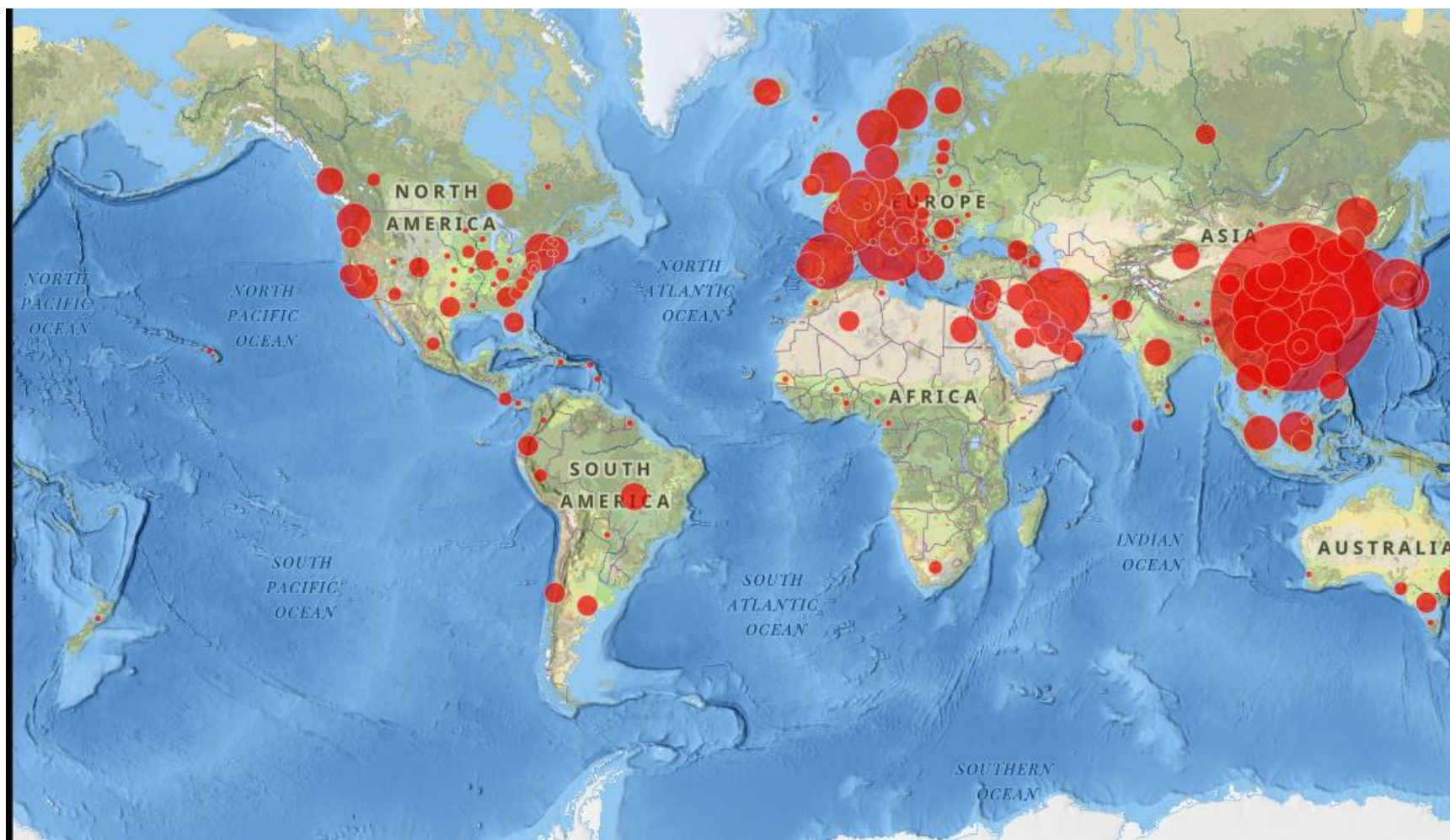


## Mapping The Spread Of COVID-19



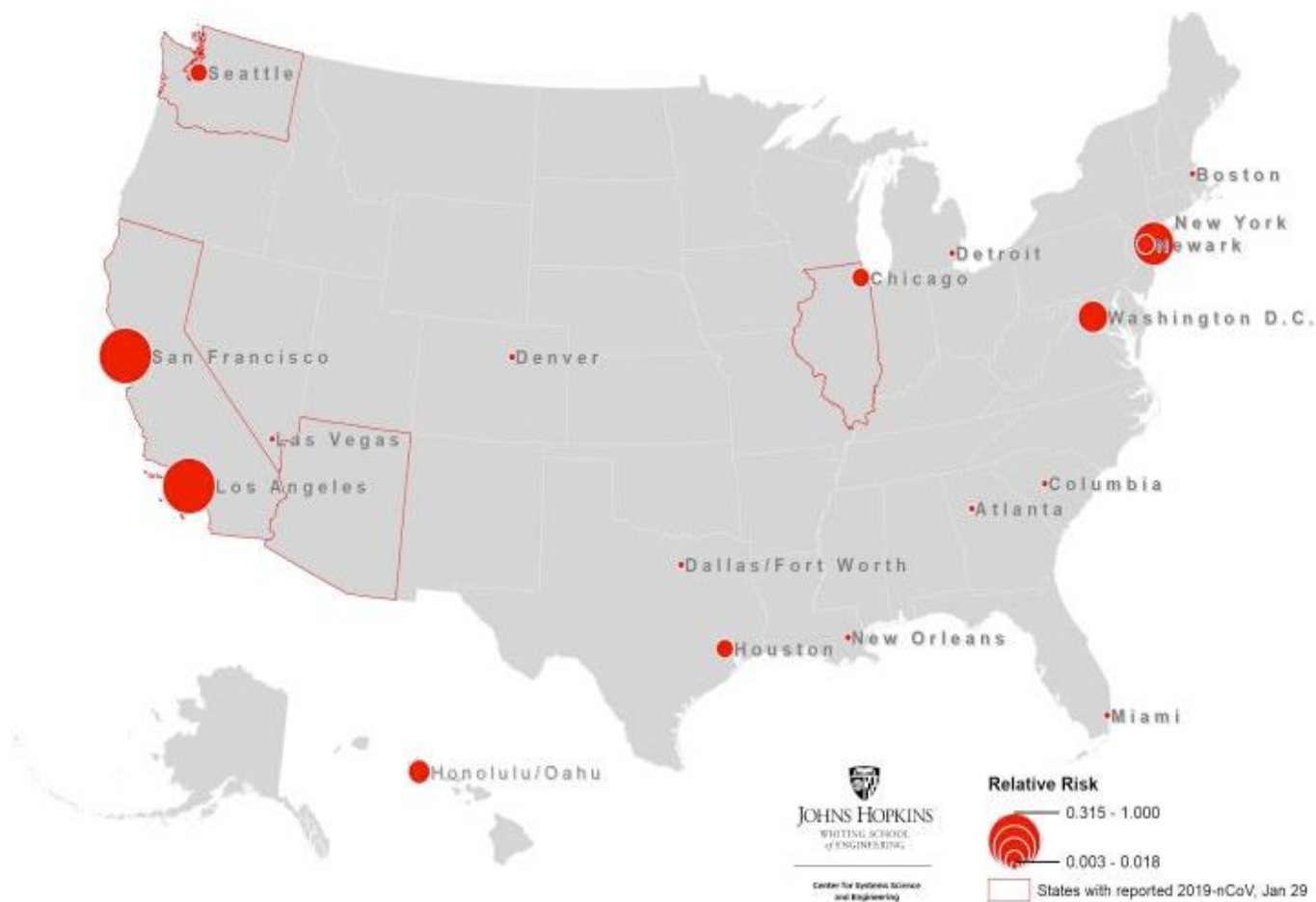
Other data as of 6 a.m. ET. Japan data excludes 696 cruise ship passengers.

# Global Distribution of Cases 3/10/20



# Importation of Coronavirus to US

Risk of 2019-nCoV Importation in U.S. Cities





# Global Distribution of Cases 3/16/20



# Three Factors For US Spread

**Social  
Distancing**

**Work  
and  
Home**

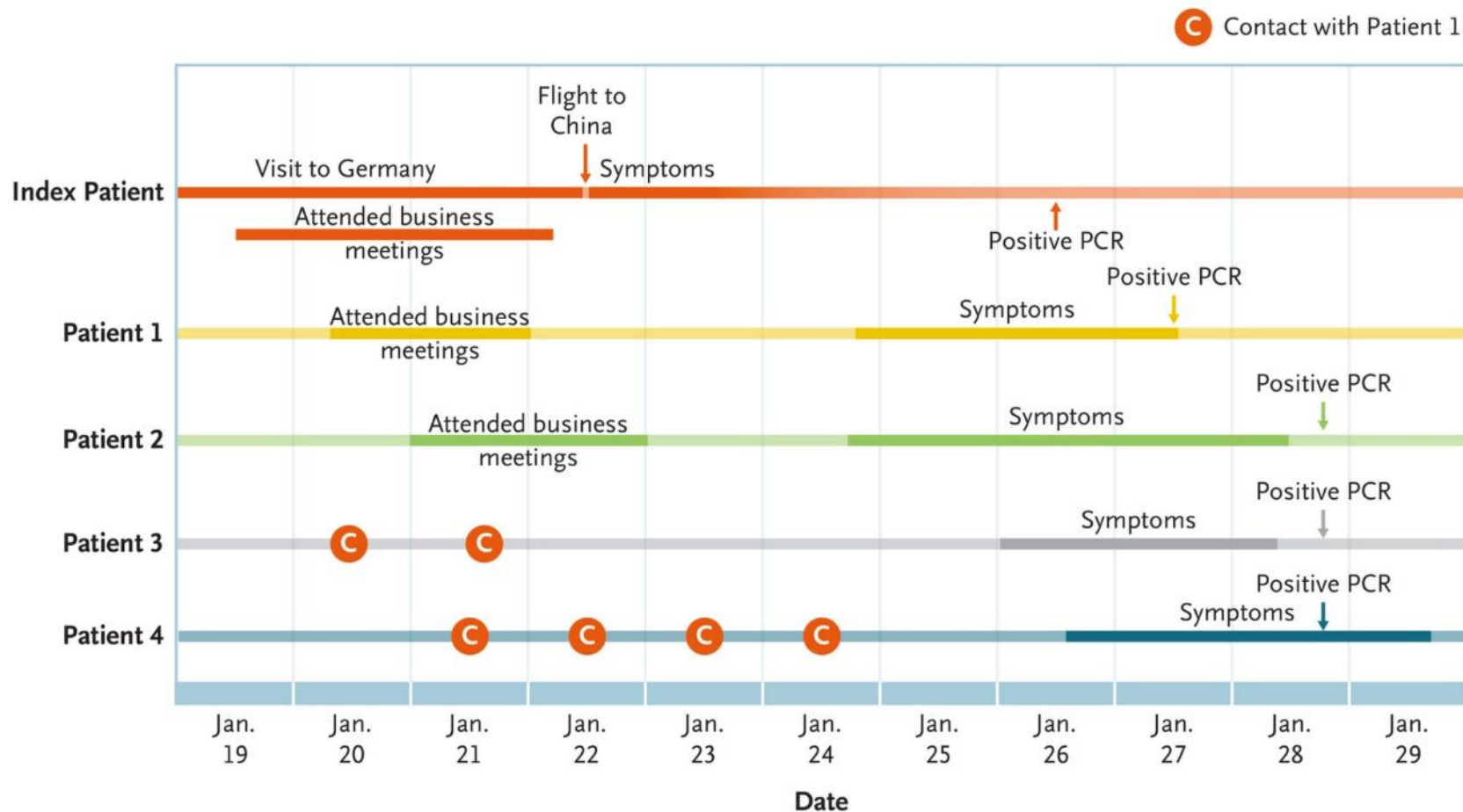
**Hand  
Hygiene**

**Properly  
And  
Timely**

**PPE**

**Proper  
Use**

# Asymptomatic transmission can occur





# Break Down in Infection Protection

**Social  
Distancing**

**Work  
and  
Home**

**Hand  
Hygiene**

**Properly  
And  
Timely**

# Hand Discipline



Wash Hands Above Shirt Collar or Below Your Belt !!

# Using Alcohol-Based Hand Rub

**Apply a squirt  
onto the palm of  
one hand**

**Rub Palms  
Together**

- **Back of Hand**
- **Between fingers**
- **Wrist**
- **Thumb**
- **Finger Tips**

# Break Down in Infection Protection

**Social  
Distancing**

**Work  
and  
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**Hand  
Hygiene**

**Properly  
And  
Timely**

**PPE**

**Proper  
Use**

# Prevent Transmission



1. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061–1069. doi:10.1001/jama.2020.1585
2. Providence-St. Joseph and Hoag Hospital unpublished data

# Prevent Transmission??





# More is not better!

## Wuhan City, China<sup>1</sup>



**29%**

## USA Hospitals<sup>2</sup>

**Eye Protection:**  
splash goggles, face shield or  
procedure mask with visor.

**Mask:**  
A fluid-resistant procedure mask  
is required.  
Staff have the option of using  
an N95 respirator.\*

**Gown:**  
yellow isolation gown,  
tied at the back.

**Gloves:**  
non-sterile  
procedure gloves



**<3%**

1. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061–1069. doi:10.1001/jama.2020.1585
2. Providence-St. Joseph and Hoag Hospital unpublished data

# What Were The Breakthroughs

- Laboratories Ramp Up Testing Capacity
- Effective Outbreak Response in SNFs



# Implementation of Rapid Testing

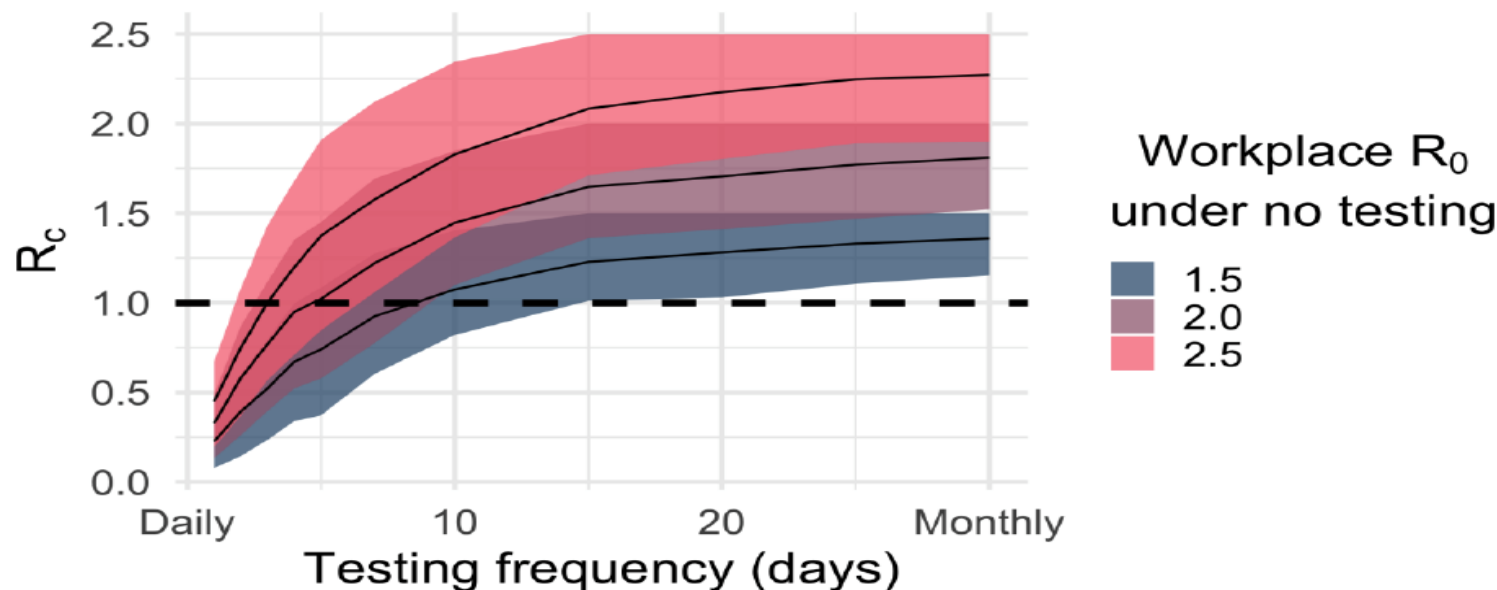


# US Develops Mass Testing Strategy

## Frequency of routine testing for COVID-19 in high-risk healthcare environments to reduce outbreaks

Elizabeth T Chin BS<sup>1†</sup>, Benjamin Q Huynh BS<sup>1†</sup>, Lloyd A. C. Chapman<sup>2</sup>,  
Matthew Murrill MD PhD<sup>2</sup>, Sanjay Basu MD PhD<sup>3,4,5</sup>, and Nathan C Lo MD PhD<sup>2</sup>

Figures



# What Were The Breakthroughs

- Laboratories Ramp Up Testing Capacity
- **Effective Outbreak Response in SNFs**

# SNF Outbreak Mitigation Strategies

- Outbreak Response Crafted around limited PPE

## **RED ZONE**

– **Confirmed Covid**

**\*PPE while on Unit**

## **YELLOW ZONE**

– **Exposed or Recovering Covid**

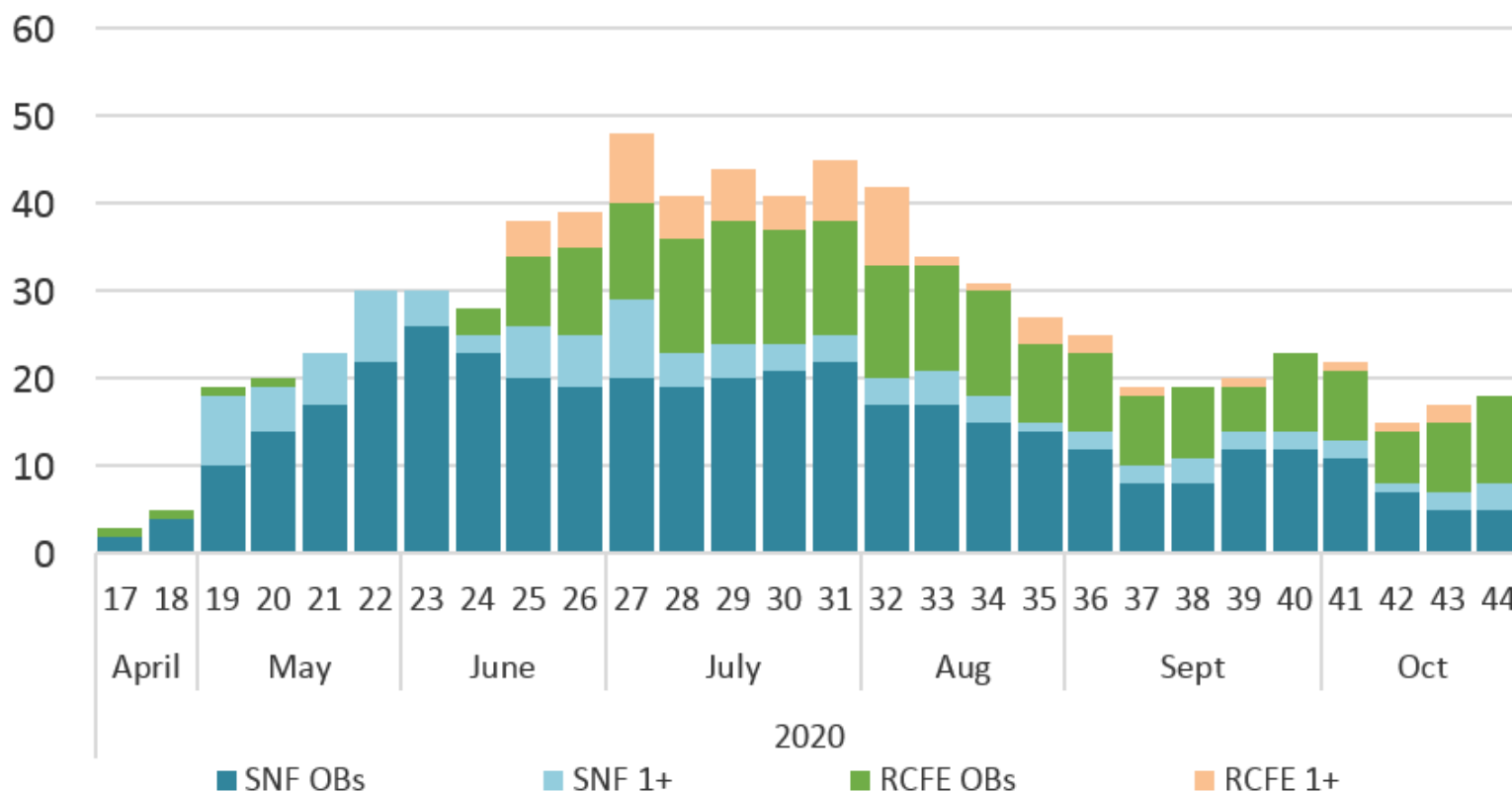
**\*Change Prior to Room Entry**

## **GREEN ZONE**

– **Unexposed**

# COVID Outbreaks in OC LTCF

## Facilities with Outbreaks



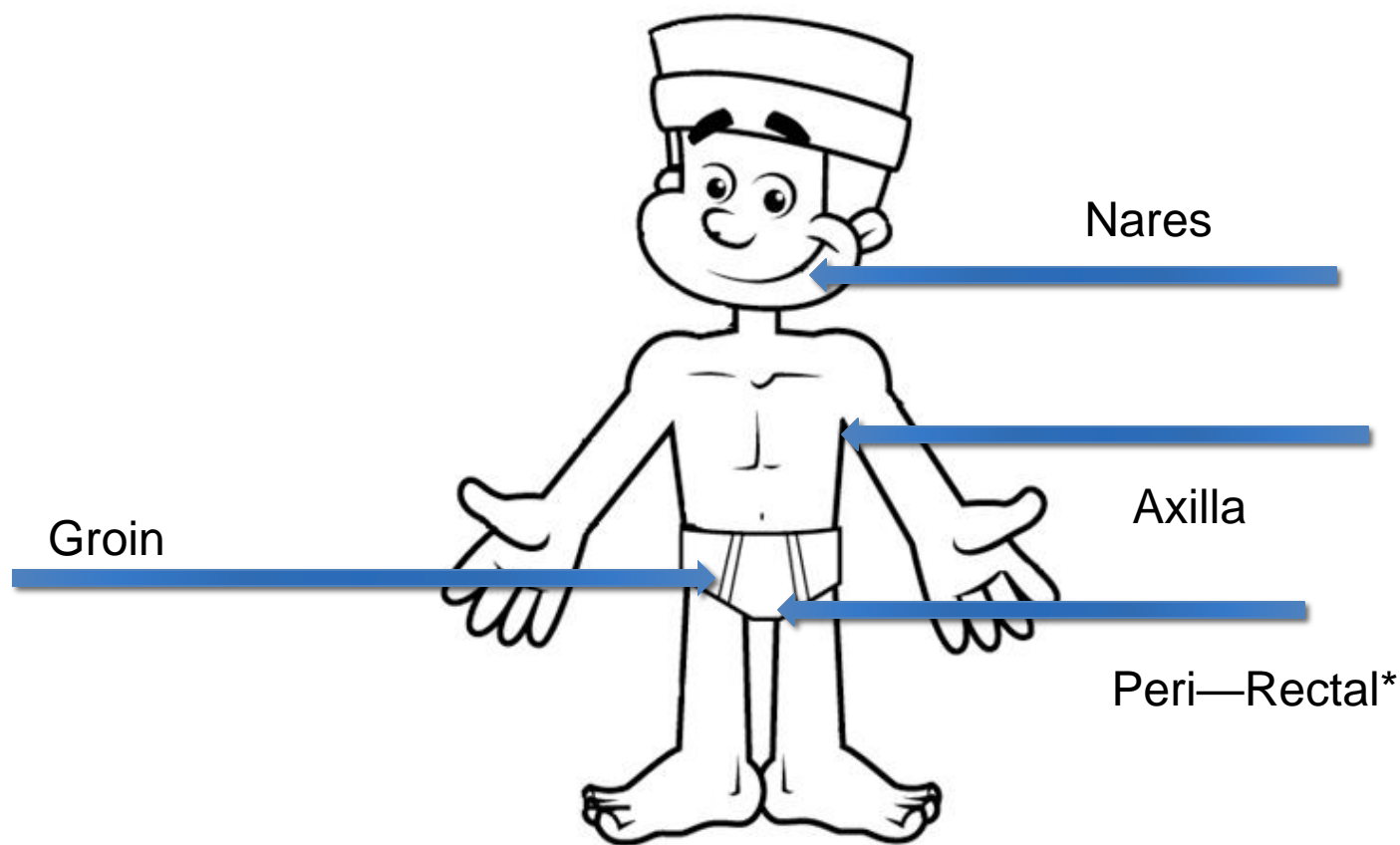
Expert Stewardship Responded to over 300 LTCF Outbreaks!

# The Red Zone Was Effective, But Problematic

# Surveillance Organisms

- Methicillin Resistant *Staphylococcus aureus* (MRSA)
- Vancomycin Resistant Enterococcus (VRE)
- Extended Spectrum Beta Lactamase Producers (ESBLs)
- Carbapenem Resistant Enterobacteriaceae (CRE)

# Surveillance Sites for MDRO



\*Peri—Rectal swabbing not done in all studies

For Expert Stewardship Use, Not for Distribution or Re-Use



# MDRO Carriage in Long Term Care

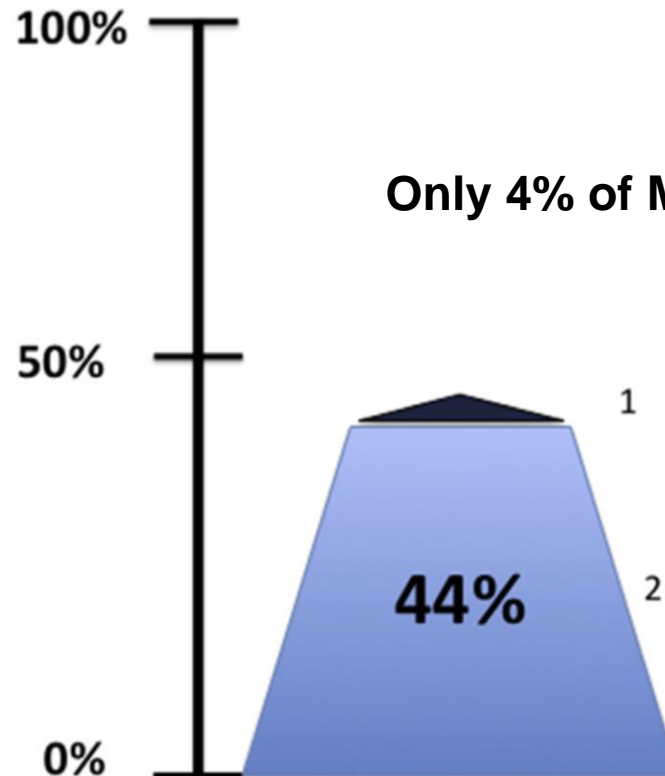
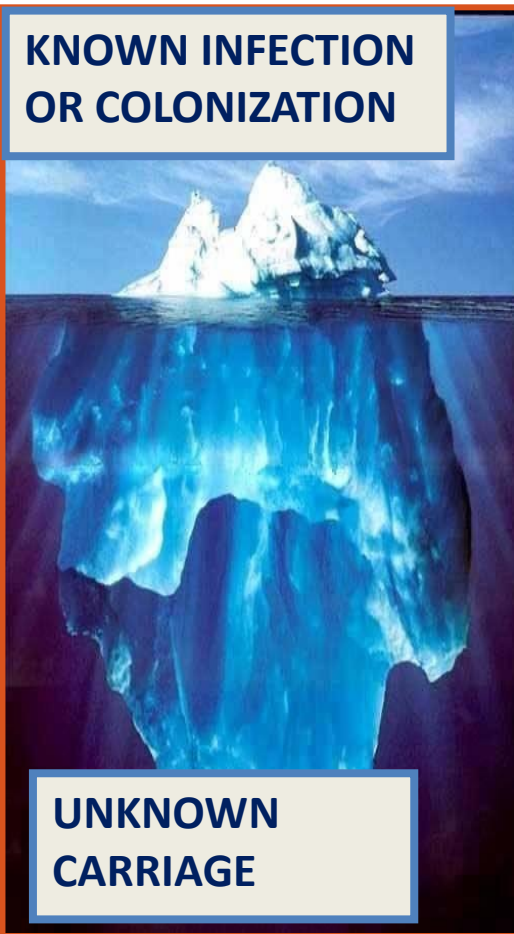
	Residents Swabbed	Any MDRO	MRSA	VRE	ESBL	CRE
Nares	1,397	29%	29%	-	-	-
Axilla/Groin	1,400	39%	24%	7%	16%	1%
All Body Sites	1,400	<b>49%</b>	37%	7%	16%	1%

**49% MDRO carriers, facility range 24-70%**

**Among MDRO pathogens detected, only 12% known to facility**

For Expert Stewardship Use, Not for Distribution or Re-Use

# Only 4% of MDRO Carriers are Known



The iceberg of MDRO colonization in skilled nursing facilities. (1) Nearly half (48%) of nursing home residents are colonized with MDRO. The top “exposed” portion of the iceberg represents the (4%) of patients for whom point prevalence survey confirmed previously known colonization status (n = 53 residents). (2) Most of the MDRO colonization is unknown to the facility, with 45% of residents representing the unknown submerged iceberg population of previously unknown MDRO colonization. Of the NH population, 39% (n = 552 residents) had no history of MDRO, but point prevalence survey identified MDRO Carriage. In addition, 5% of the NH population (n = 75 residents) had a history of an MDRO, but point prevalence survey identified an additional MDRO unknown to the facility.

For Expert Stewardship Use, Not for Distribution or Re-Use McKinnell et al. AMDA

# Environmental Contamination

- Bed Rails
- Bed Frames
- Tray Table
- Bedside Table
- Handles
- IV Poles
- BP Cuff



For Expert Stewardship Use, Not for Distribution or Re-Use

# MDRO Environmental Contamination Resident Room Objects

Object Type	# Objects Swabbed	Any MDRO	MRSA	VRE	ESBL	CRE
Bedside Table/Bedrail	84	55%	31%	29%	5%	0%
Call Button/ TV Remote/Phone	84	35%	23%	15%	1%	0%
Door Knobs	84	33%	24%	12%	1%	0%
Light Switch	84	26%	18%	8%	1%	0%
Bathroom Rail/Sink/Flush Handle	84	38%	23%	20%	5%	1%
<b>Any Object</b>	<b>420</b>	<b>37%</b>	<b>24%</b>	<b>17%</b>	<b>3%</b>	<b>0.2%</b>

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# MDRO Environmental Contamination Common Area Objects

Object Type	# Objects Swabbed	Any MDRO	MRSA	VRE	ESBL	CRE
Nursing Station Counter or Cart	28	57%	43%	32%	0%	0%
Table*	28	54%	39%	29%	4%	0%
Chair*	28	46%	29%	18%	0%	0%
Hand Rail (hallway)	28	61%	32%	32%	4%	0%
Drinking Fountain or Drinking Station	28	32%	25%	11%	0%	0%
<b>Any Object</b>	<b>140</b>	<b>50%</b>	<b>34%</b>	<b>24%</b>	<b>1%</b>	<b>0%</b>

\*Dining hall or activity room

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# Environmental Contamination with MDROs – Common Area Objects

Object Type	# Objects Swabbed	Any MDRO	MRSA	VRE	ESBL	CRE
Nursing Station Counter or Cart	28	57%	43%	32%	0%	0%
Bathroom Rail/Sink/Flush Handle	84	38%	23%	20%	5%	1%

For Expert Stewardship Use, Not for Distribution or Re-Use

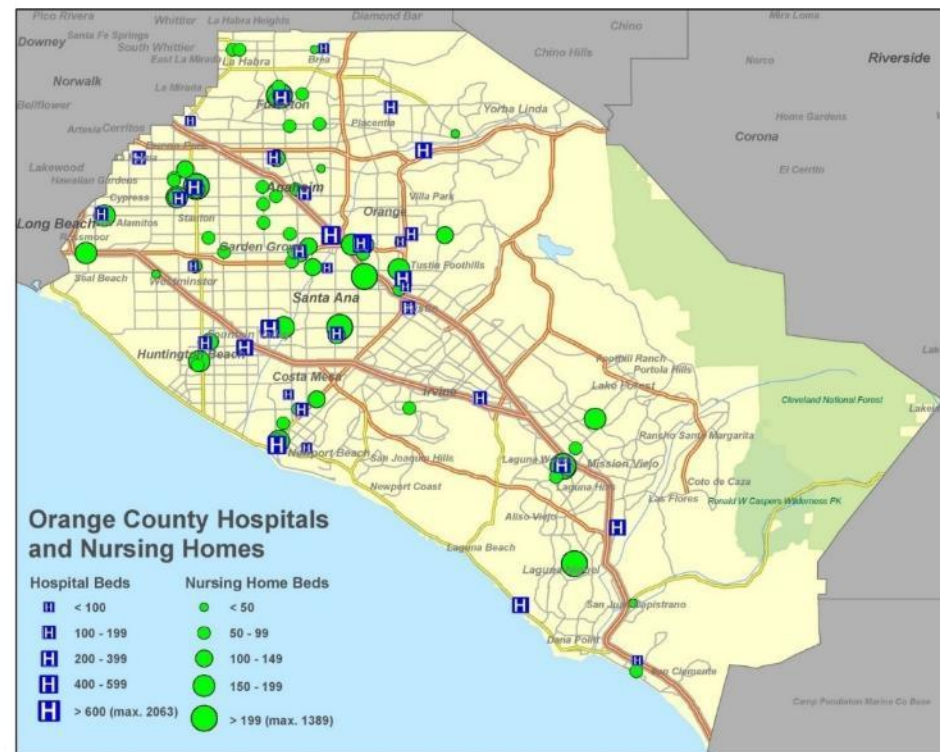
# The Red Zone Was Problematic

- Constant Use PPE Resulted in Spread of Pathogens
- CRE
- MDR Acinetobacter
- C. Auris

# Orange County, California

## Ideal Virtual Laboratory

- Relatively enclosed
  - Ocean to West
  - Forest to East
  - Undeveloped land to South
  - Traffic to North

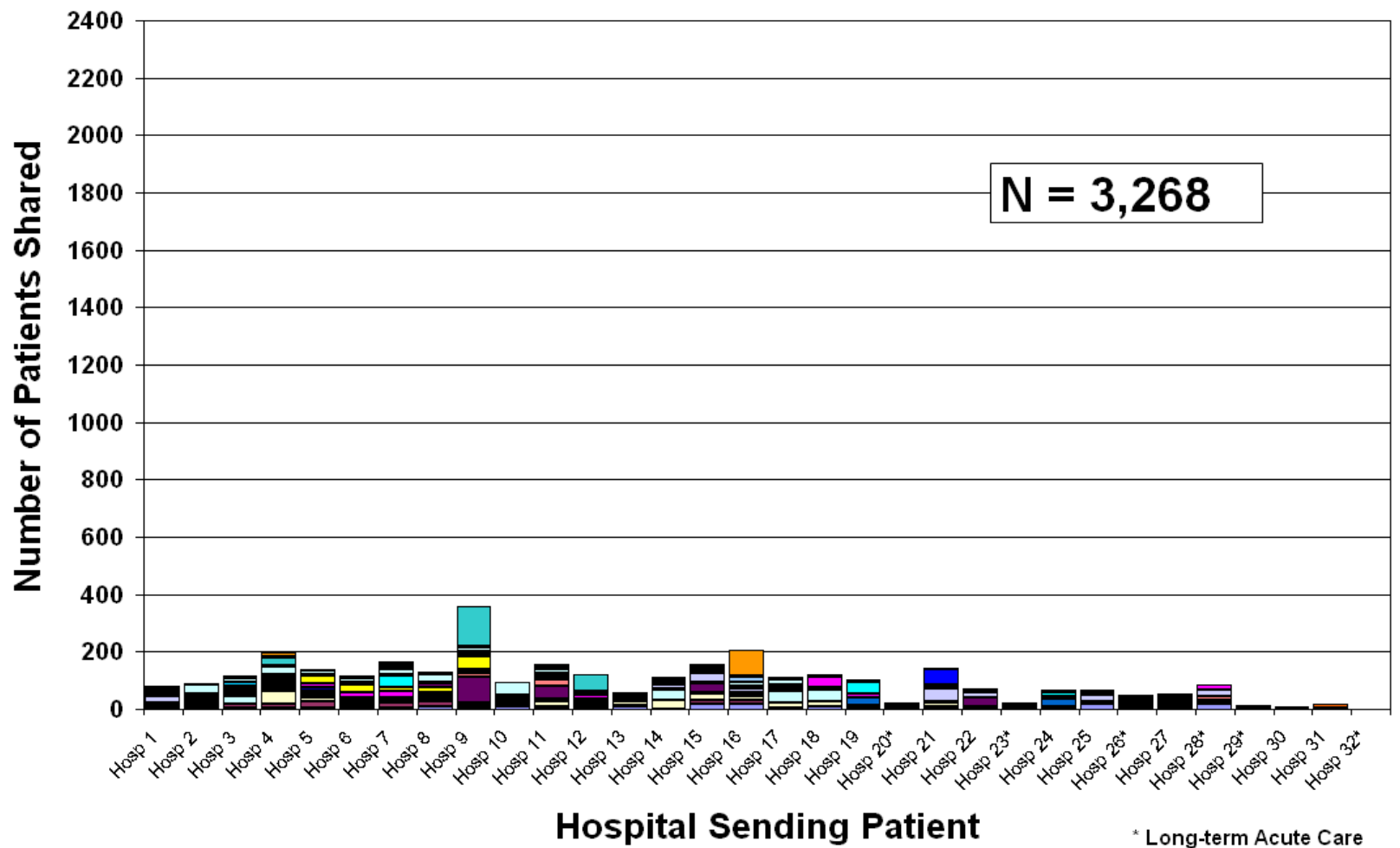




# Orange County

- 32 Acute Care Hospitals
  - 6 Long-Term Acute Care Hospitals (LTACs)
  - 2 Dedicated Children's Hospitals
- 71 nursing homes
- Serves population of 3.1 million  
(6<sup>th</sup> largest US county)
- >320,000 admissions annually

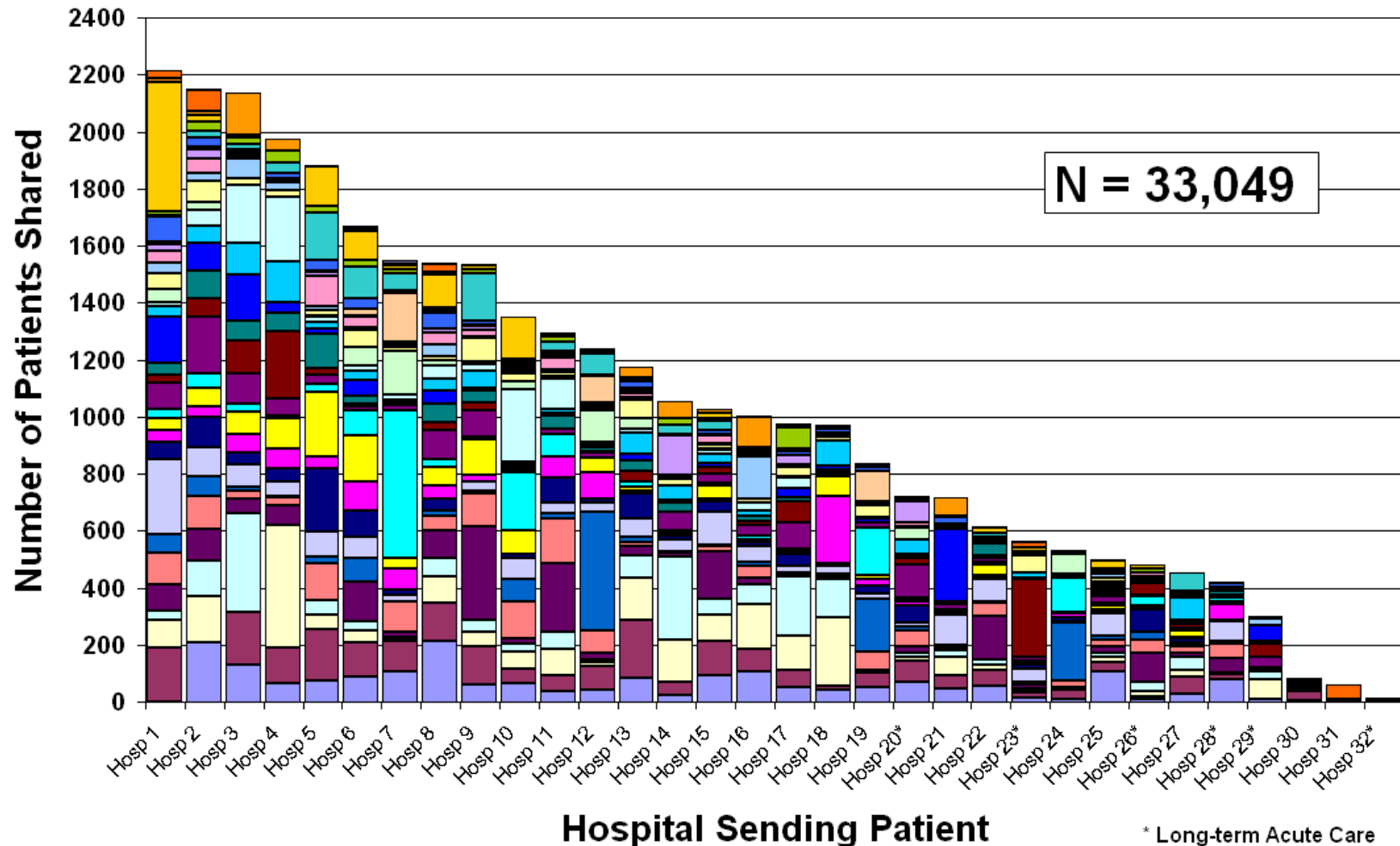
# Hospitals Share Patients – Direct



Huang SS et al. Infect Control Hosp Epidemiol 2010. 31(11):1160-9

For Expert Stewardship Use, Not for Distribution or Re-Use

# Hospitals Share Patients-Indirect



Huang SS et al. Infect Control Hosp Epidemiol 2010. 31(11):1160-9

For Expert Stewardship Use, Not for Distribution or Re-Use

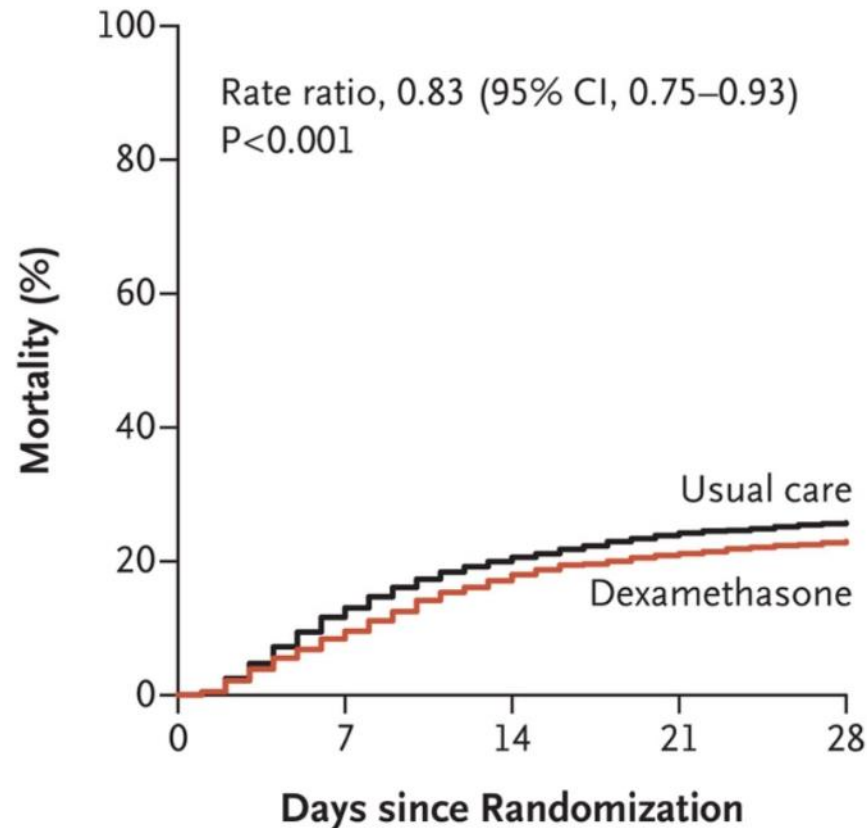


# HOSPITAL MANAGEMENT OF COVID

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# Recovery Trial of Steroids in Covid

## A All Participants (N=6425)

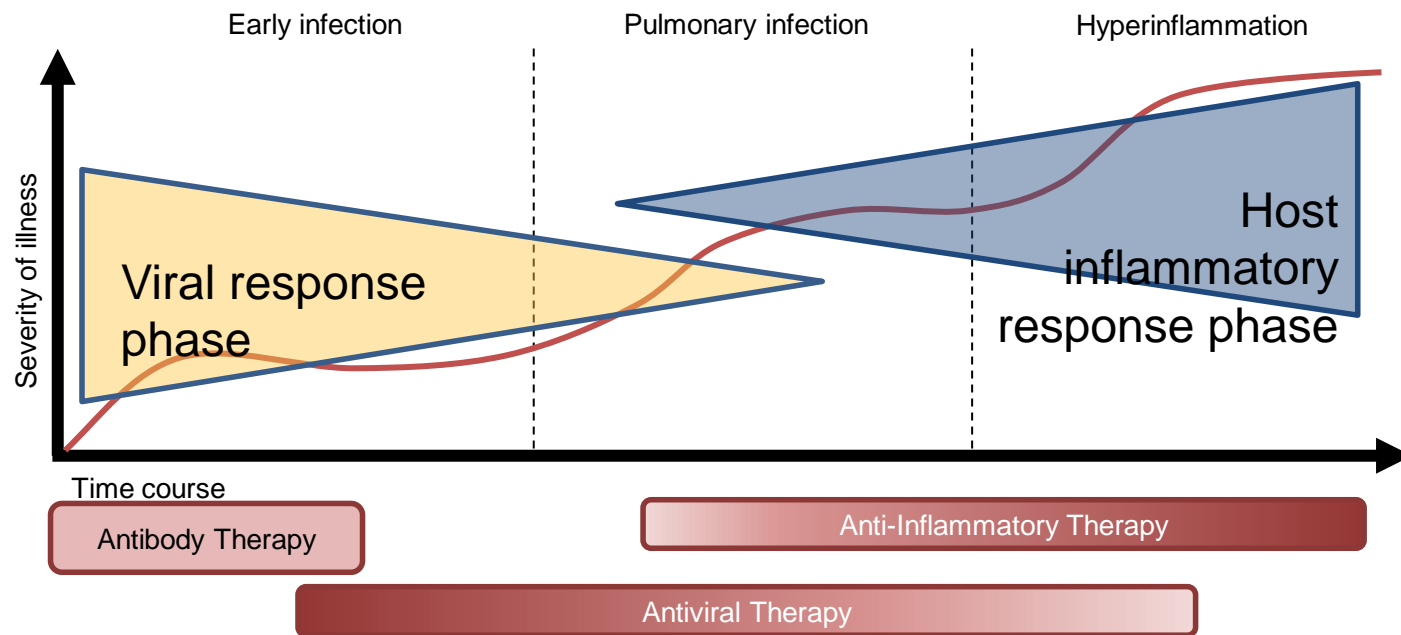


### No. at Risk

Usual care	4321	3754	3427	3271	3205
Dexamethasone	2104	1902	1724	1658	1620



# Spectrum of Disease and Therapy



Current therapies (darker gradient used to imply strength of evidence)

<https://doi.org/10.1016/j.healun.2020.03.012>



# Hospital Management Of Covid

- Anti-Viral Treatment
  - Remdesivir
- Cytokine Release Syndrome/Cytokine Storm
  - Corticosteroids
  - Tocilizumab/Baricitinib
- Hypercoaguable State
  - Prophylactic Dosing
  - “Intermediate Dose”
  - Full Dose Anticoagulation (NEJM August 2021).

# How can the Laboratory Play A Role

- Covid Testing
  - Cycle Threshold
  - SARS Specific Versus Multiplex Testing
- Procalcitonin Evaluation
  - The Infectious Disease Doctor's Crutch
- Antimicrobial Susceptibility Testing
  - Help when we really need it.

# Case Presentations

- The following descriptions are of a real cases that I managed
- I will discuss use of antibiotics that may not follow FDA approved indications, but do follow generally accepted clinical practice
- Identifying information has been changed

# LUCY

**72 year old female with fever and cough.**

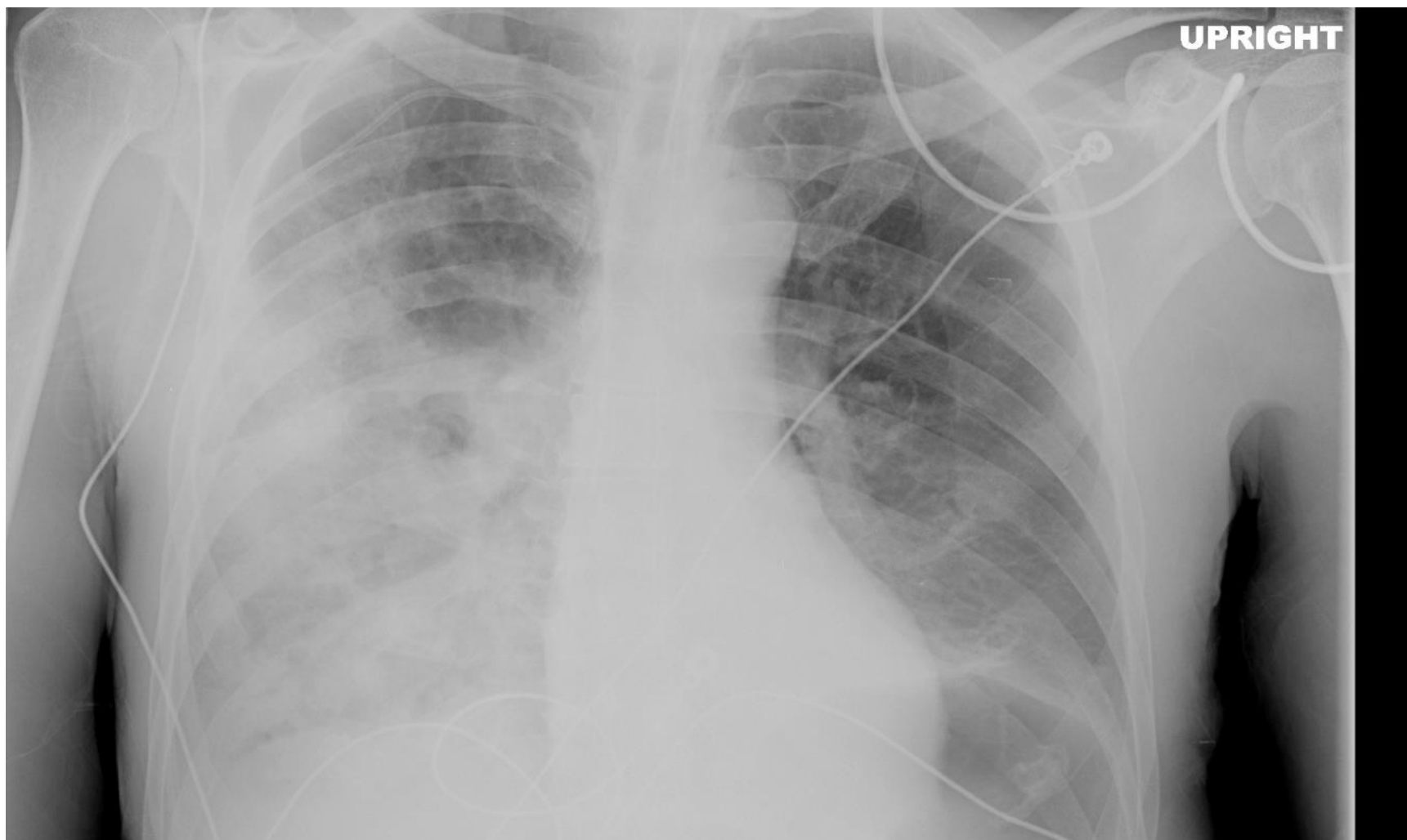
PMH: moderate dementia.

T:101.2 BP:106/62 R: 28 S:92%

- Rousable, but sleepy
- Frail, **Nasal Canula at 4 liters**
- Slight temporal wasting
- RLL Rhonchi

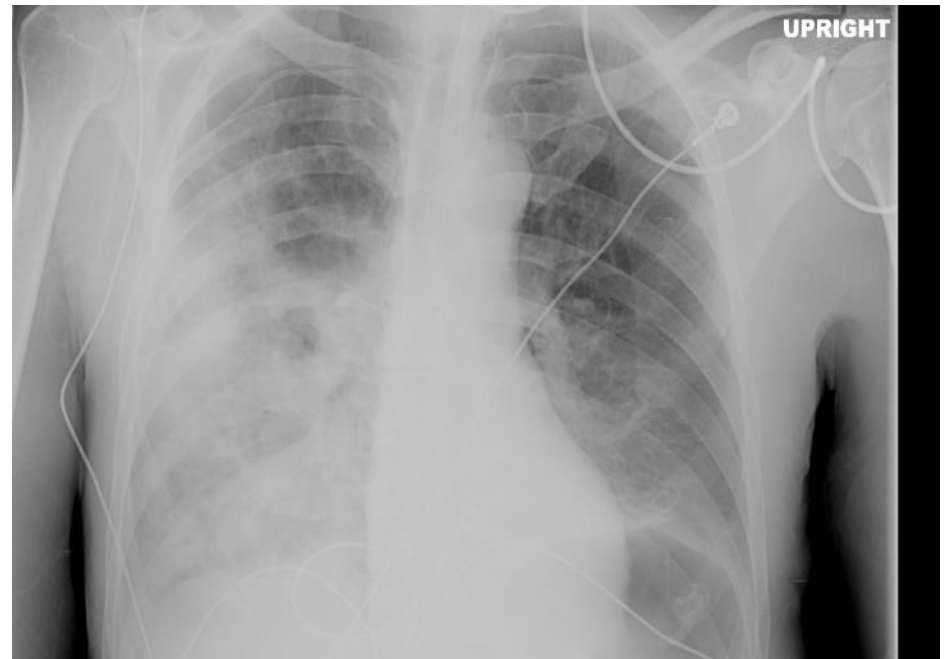


# RLL Pneumonia



# LUCY

- Bacterial Infection?
- Influenza?
- Aspiration?
- Covid?



Rapid COVID Diagnosis allows rapid initiation of treatment and improved outcomes



# LUCY

- Remdesivir
- Solumedrol 40 mg IV BID
- Prophylactic Lovenox
- Antimicrobials?



# LUCY

- Completed 5 Days Remdesivir
- Switched to Prednisone Taper
- Discharged on Day 8 to SNF.



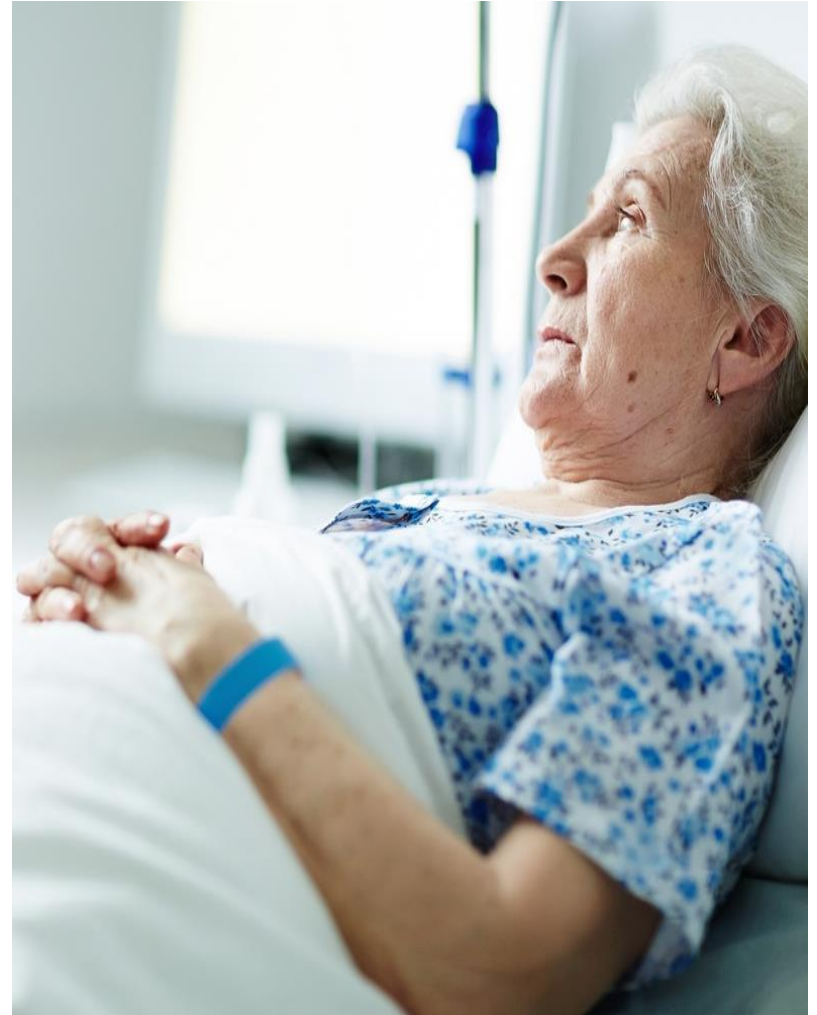
# LUCY

**72 year old female, previously treated for COVID, has a mechanical fall in her SNF.**

PMH: moderate dementia, Covid 92 days prior.

T:98.6 BP:106/62 R: 22 S:92%

- Alert
- Frail
- Slight temporal wasting
- Bruise on back of head



# LUCY

**Head CT – no Bleed**

**COVID Nares PCR positive**

**Cycle Threshold 36  
(Positive <37)**

**Repeat in AM Negative**

**Out of Isolation in Hospital**

**Isolation Required in SNF**



# Charlie

**36 year male, on PREP for HIV, admitted with fever and cough. Unvaccinated for COVID.**

PMH: none

T:102.2 BP:106/62 R: 28 S:88%

- Alert, Coughing
- **Nasal Canula at 4 liters**
- Right Mid Lung

# Faint RML Pneumonia





# Chlamydia Pneumoniae

- Obligate Intracellular Pathogen
- Azithromycin is standard treatment
- Continued Ceftriaxone/cefdinir as may be part of a polymicrobial infection.
- Patient improved on day 3 and was discharged on oral antimicrobials.

# How can the Laboratory Play A Role

- Covid Testing
  - Cycle Threshold
  - SARS Specific Versus Multiplex Testing
- **Procalcitonin Evaluation**
  - **The Infectious Disease Doctor's Crutch**
- Antimicrobial Susceptibility Testing
  - Help when we really need it.

# Linus

**78 year old male with fever and cough.**

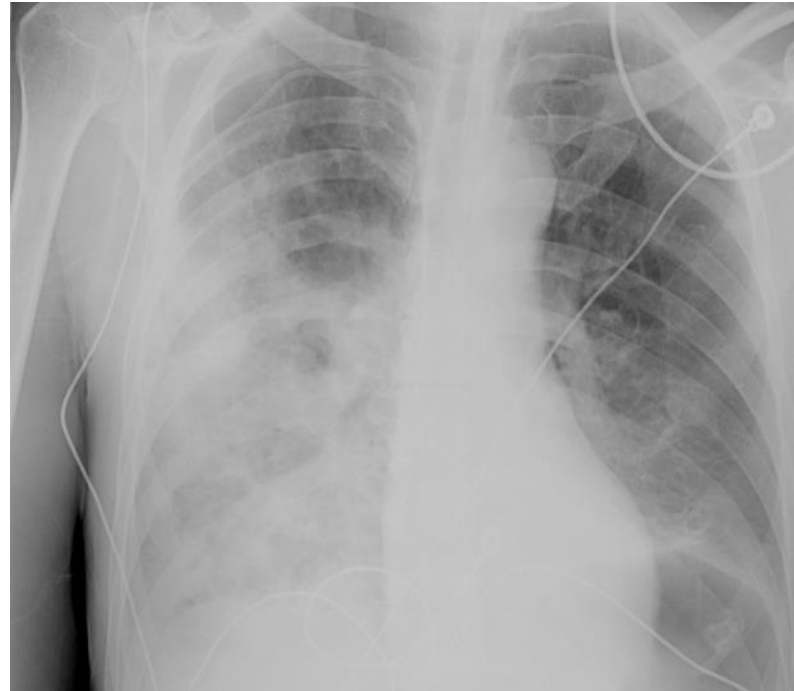
PMH: severe dementia. ESBL pyelonephritis recently completed meropenem.

T:101.2      BP:106/62   R: 28   S:78%

- Rousable, but sleepy
- Frail, **High Flow Oxygen at 30 Liters and 100%**
- Diminished Breath Sounds Bilaterally

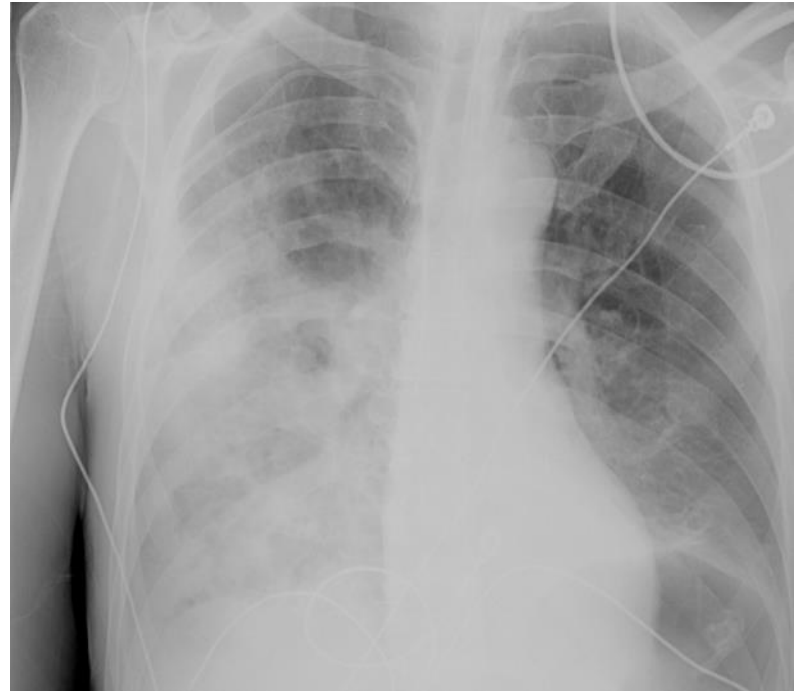
# RLL Pneumonia

- WBC 19K
- CRP 18
- D-Dimer 500
- Procalcitonin 0.2



# Linus

- Remdesivir
- Solumedrol 40 mg IV BID
- Tocilizumab
- Intermediate Dose Lovenox
- No Antimicrobials



# Linus Hospital Day 14

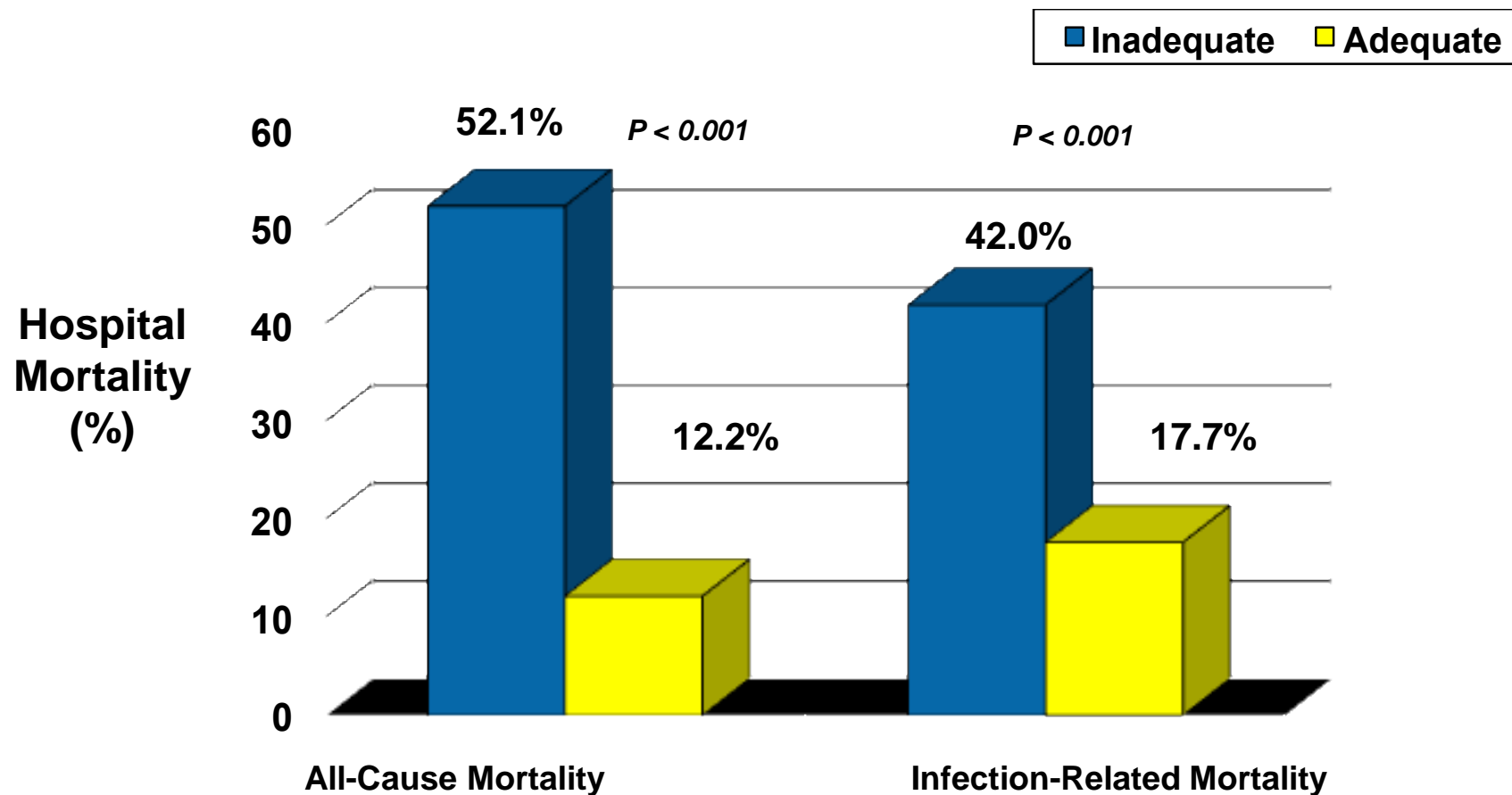
T: 102 BP:92/60 P: 115

On Pressors

- Remdesivir completed
- Solumedrol 40 mg IV BID
- Tocilizumab x2
  
- Intermediate Dose Lovenox-  
Heparin gtt?
  
- Antimicrobials?



# Inadequate antimicrobial therapy associated with higher mortality



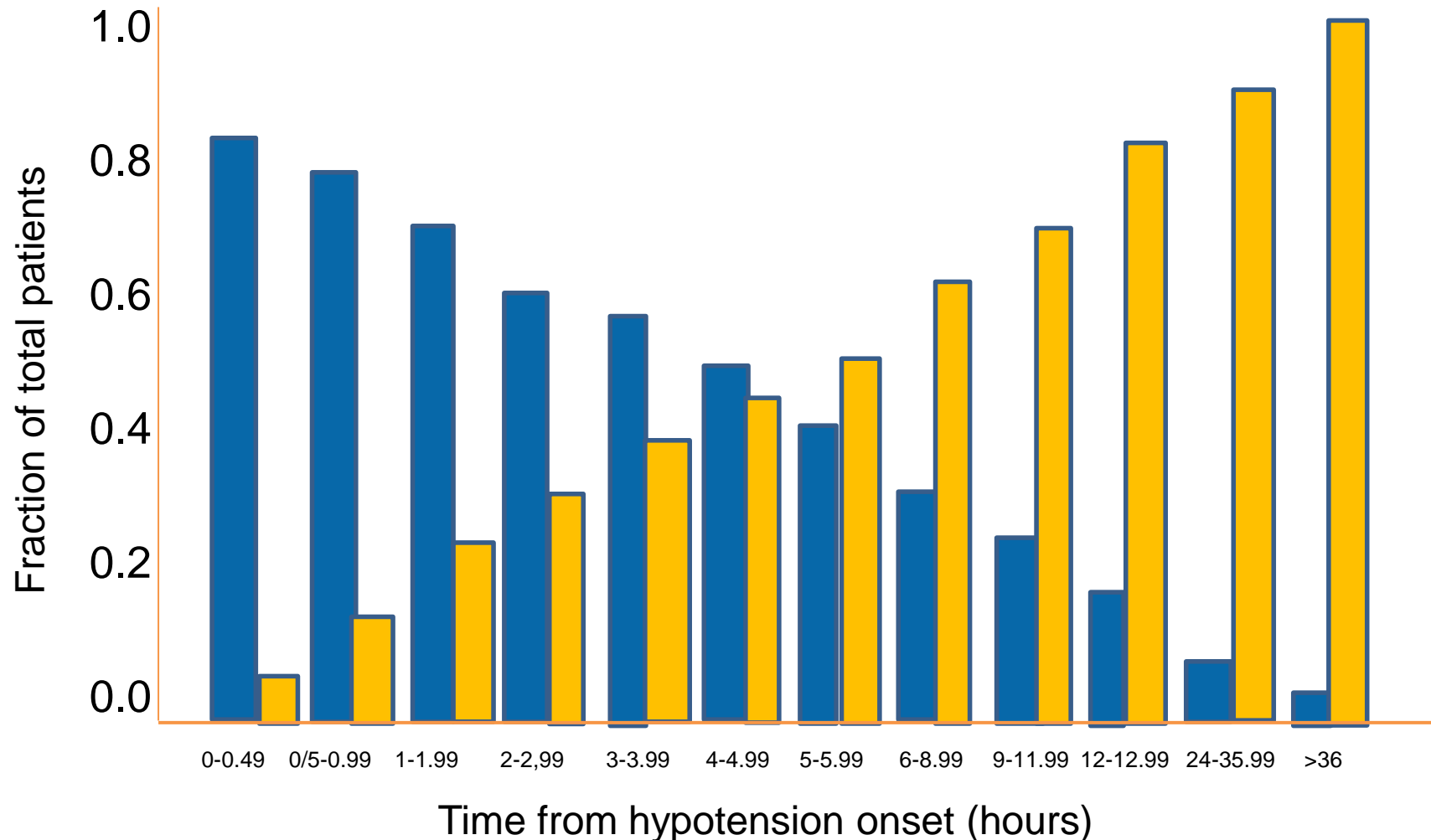
Prospective study (n=2000: 655 with infections)

25% of patients received inadequate treatment



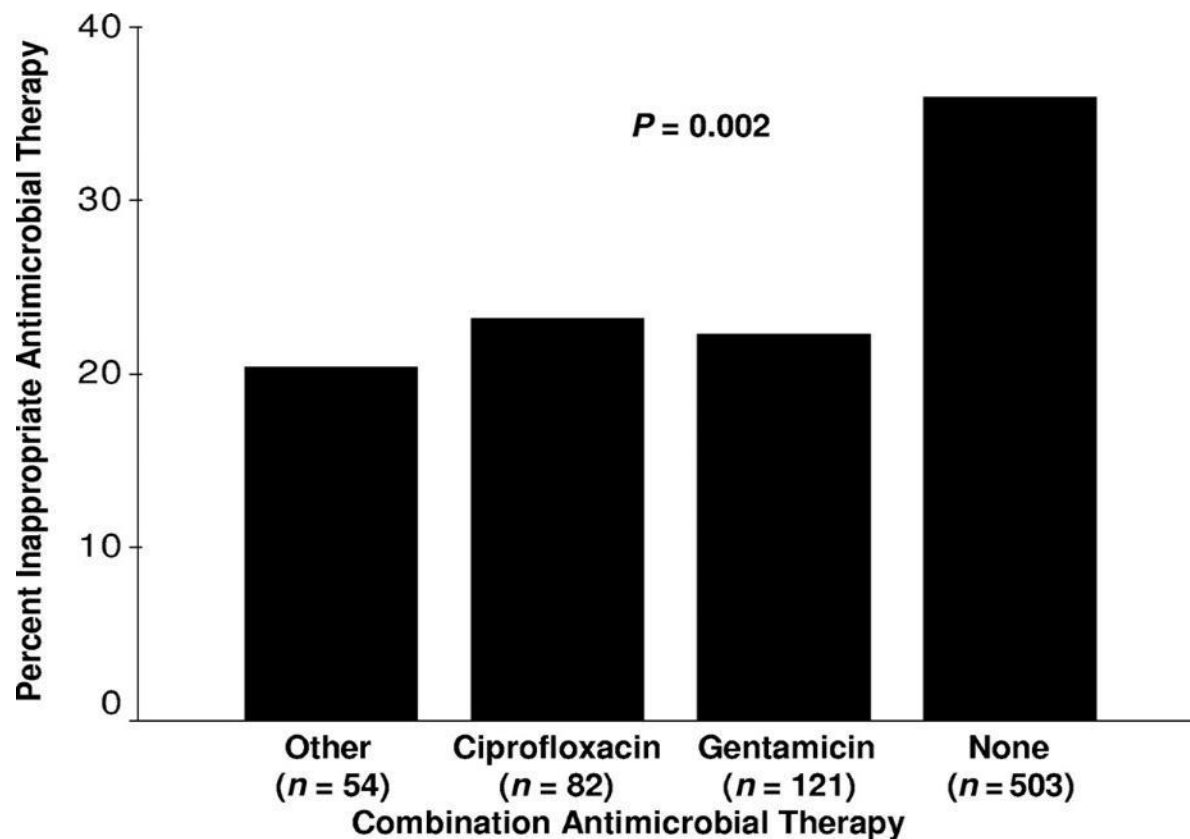
# Relationship between survival and time to effective antimicrobial treatment among patients with septic shock

Retrospective multi-center study (n=2731)



## Empiric combination therapy is associated with higher rates of early, appropriate therapy for patients with sepsis due to Gram-negatives

Retrospective study (n=760)



# **GNR: Meropenem/Gentamicin**

# *Acinetobacter baumannii.*

<b>Antimicrobial</b>	<b>Susceptibility</b>	
<b>Amikacin</b>	<b>R</b>	<b>&gt;32</b>
<b>Amp/Sulbactam</b>	<b>R</b>	<b>&gt;64</b>
<b>Ceftazidime</b>	<b>R</b>	<b>&gt;16</b>
<b>Meropenem</b>	<b>R</b>	<b>&gt;8</b>
<b>Piperacillin/Tazo</b>	<b>R</b>	<b>&gt;64</b>
<b>Tobramycin</b>	<b>R</b>	<b>&gt;8</b>

*Acinetobacter baumannii.*  
**Extended Panel**

<b>Antimicrobial</b>	<b>Susceptibility</b>	
<b>Cefiderocol</b>	<b>I</b>	<b>8</b>
<b>Ceftazidime/Avi</b>	<b>R</b>	<b>&gt;32</b>
<b>Eravacycline</b>		<b>0.5</b>
<b>Mero/Vabor</b>	<b>R</b>	<b>&gt;16</b>

# Linus

- Culture Results are Current as of Slide Presentation
- Outcome pending

# Collateral Damage From Covid

- Pathogen Spread in Nursing Homes
- Confusing and Overlapping Clinical Syndromes
- Prolonged Hospital Stays in Complex Patients with Prolonged ICU and Antibiotic Exposures



# How can the Laboratory Play A Role

- Covid Testing
  - Cycle Threshold
  - SARS Specific Versus Multiplex Testing
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Thank You for Listening!!!