FRIDAY, MARCH 20, 2025

PREVENTION OF RESPIRATORY PATHOGENS

JUSTIN ORTIZ, MD, MS

University of Maryland

KEYNOTE ADDRESS – PREVENTING RSV: PROVIDING OLDER PATIENTS WITH THE INFORMATION THEY NEED

Friday, March 21, 2025 8:10 am - 8:55 am

Dr. Ortiz is a pulmonologist at the Center for Vaccine Development and Global Health at the University of Maryland. He is the PI on the NIH-funded Collaborative Influenza Vaccine Innovation Centers (CIVICs) Clinical Core at UMSOM. During the COVID-19 pandemic, he contributed to most of the CVD SARS-CoV-2 prevention trials, and he was the site PI on the NIH ACCT trial which demonstrated the efficacy of remdesivir for COVID-19. His greatest contribution within CIVICs has been to help reestablish influenza challenge studies within the United States, as they had been halted outside NIH for nearly 20 years. He co-chairs the American Thoracic Society vaccines and immunization working group and advises the Society on a CDC-funded initiative to increase vaccine coverage among persons with chronic lung disease.

MICHELE MAISON-FOMOTAR, MD, MSC

UCSF Fresno

PREVENTING COMMUNITY ACQUIRED RESPIRATORY VIRUSES THROUGH VACCINATION

Friday, March 21, 2025 8:55 am - 9:20 am

Dr. Maison-Fomotar received her medical degree from the University of Yaoundé I in Cameroon. She later earned her Master of Science in Tropical Medicine and International Health at the London School of Hygiene and Tropical Medicine. She then completed an internal medicine residency and infectious disease fellowship at UCSF Fresno. Currently, she serves as an Assistant Professor of Medicine and Assistant Program Director for the Infectious Disease Fellowship program at UCSF Fresno.

SAIRAM PARTHASARATHY, MD

University of Arizona

PREVENTION AND TREATMENT OF VENTILATOR ASSOCIATED PNEUMONIA

Friday, March 21, 2025 9:20 am - 9:45 am

Dr. Sairam Parthasarathy is the Murray and Clara Walker Endowed Chair and Chief of the Division of Pulmonary, Allergy, Critical Care and Sleep Medicine, Founding Director of the UAHS Center for Sleep, Circadian and Neurosciences Research Center at the University of Arizona. He has a broad background in translational and clinical research with emphasis on intervention-based approaches in sleep, COVID, and health disparities. His current research work is focused on as Principal investigator for the following research: (a) community engaged research alliance against COVID-19 related health disparities (NIH-CEAL Alliance); that is Arizona statewide endeavor (Arizona-CEAL); (b) RECOVER long-COVID Adult Cohort study and RECOVER Clinical Trials that is aimed at studying the epidemiology, etiology, and treatment of post-acute sequelae of SARS-CoV-2 infection; (c) health-services research in sleep medicine with emphasis on patient-centered approaches and dissemination and implementation aspects of interventions aimed to promote treatment adherence in health disparate populations and a nationwide peer-driven intervention for promoting treatment adherence and training the trainers during the COVID- 19 pandemic that is funded by PCORI; and (d) A NIH-funded training grant that aims to train individuals underrepresented in biomedical and behavioral research in lung and sleep disorders. He is board- certified in Pulmonary, Critical Care and Sleep Medicine and practices at Banner University Medical Center Tucson, Arizona

ACUTE RESPIRATORY DISTRESS SYNDROME

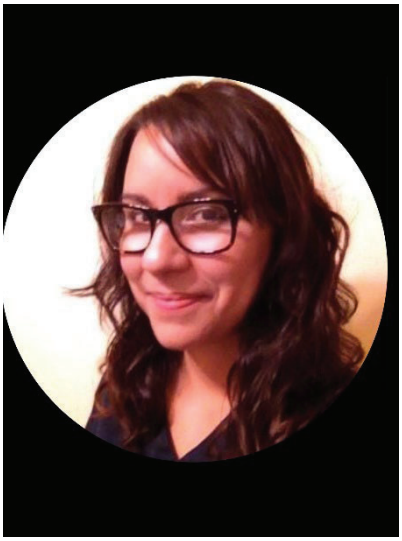
JEFFREY E. GOTTS, MD, PhD

Kaiser San Francisco

UPDATE ON ARDS MANAGEMENT STRATEGIES AND THE ROLE OF STEROIDS IN SEVERE CAP AND ARDS

Friday, March 21, 2025 10:25 am - 10:50 am

Dr. Gotts completed MSTP training at UCLA, did residency and fellowship at UCSF, and was on the UCSF faculty for 6 years studying mechanisms of bacterial and viral acute lung injury and sepsis in animal models while serving as the co-medical director of the MICU. He currently works as a cardiac intensivist at KP-San Francisco, maintaining an adjunct appointment at UCSF.



THERSA CANTU, MSRC RRT-NPS

Valley Children's Healthcare/San Joquin College

PEDIATRIC ACUTE LUNG INJURY MANAGEMENT

Friday, March 21, 2025 10:50 am - 11:15 am

Theresa Cantu is a pediatric clinical respiratory specialist with a passion for improving pediatric health outcomes in her community. As a member of Valley Children's Healthcare, she focuses her research efforts on quality improvement to enhance patient outcomes through innovative technologies, evidence-based protocols, and simulation. Her work is deeply rooted in addressing the challenges at the intersection of socioeconomic disadvantages and healthcare access, particularly in serving a vast rural population of 1.3 million children across 250 square miles. Through her commitment to advocacy, research, and innovation, Theresa strives to create equitable healthcare solutions that improve the lives of children in underserved communities.

BRIAN SMITH, MSC, RRT

UC Davis

OXYGEN TARGETS IN RESPIRATORY FAILURE

Friday, March 21, 2025 11:15 am - 11:40 am

Brian J Smith is currently serving as Children's hospital Respiratory care educator and QI Coordinator at UC Davis Health, specializing in neonatal and pediatric critical care. He holds an adjunct faculty position at Butte College. Brian serves on the AARC Education Advisory council and RT led research advancement committee. Brian has academic interest and research pursuits in HFNC, mechanical ventilation including high frequency, transcutaneous C02 monitoring, pediatric aerosol deposition and RT burnout.

CHRISTIANA HAYWARD, MD

UCLA-Harbor

PRO: EARLY INTUBATION IS PREFERENTIAL FOR THE PATIENT WITH ARDS ON HFNC

Friday, March 21, 2025 11:40 am - 11:55 am

Dr. Christiana Hayward is an Assistant Clinical Professor of Medicine, David Geffen School of Medicine at UCLA, and a recent addition to the faculty at Harbor-UCLA Medical Center. A Louisiana native and a graduate of Louisiana State University Shreveport, she attended Baylor College of Medicine for her Internal Medicine residency, completing a year as Chief Medical Resident. She then completed her fellowship in Pulmonary Critical Care Medicine at the University of California, Los Angeles. While a senior fellow, she completed the prestigious David Geffen Medical Education Fellowship, focusing on the creation of a novel simulated mechanical ventilation curriculum for residents rotating in the West Los Angeles VA Medical ICU. Her academic interests include airways disease and medical education, with a focus on curriculum development.

KATHRYN BILELLO, MD

UCSF-Fresno

CON: LATE INTUBATION IS PREFERENTIAL FOR THE PATIENT WITH ARDS ON HFNC

Friday, March 21, 2025 11:55 am - 12:10 pm

Dr. Kathryn Bilello received her medical degree from New York University. She did her internal medicine residency at the University of Maryland, Baltimore and William Beaumont Army Medical Center and then completed fellowship training in pulmonary and critical care medicine at Walter Reed Army Medical Center. She is a Clinical Professor of Medicine at UCSF School of Medicine and is the Program Director for the Pulmonary and Critical Care Medicine Fellowship at UCSF-Fresno. She currently serves as a Governance Member on the ABIM Pulmonary Disease Board.

HANDS ON SESSION

JOE VAN VLEET, BSRC, RRT

UCLA

HANDS-ON SESSION: AIRWAY CLEARANCE

Friday, March 21, 2025 1:40 pm - 2:40 pm

Joseph Van Vleet is a full-time clinician and Pulmonary Navigator in the Respiratory Therapy Department at University of California Los Angeles. He graduated from the Los Angeles Valley College Respiratory Therapy Program. He received his bachelor's degree in respiratory care at the University of Missouri. He has over 7 years of clinical experience at UCLA working in the NICUs, ICUss, Emergency Department, the Post-ICU Clinic and assists with performance improvement projects on both campuses. He helped develop the POST-ICU Recovery Clinic at UCLA and assists with recruitment and post discharge navigation for that population. As pulmonary navigator, he provides education to pulmonary patients during their hospitalizations, assists with optimizing patients' home RT regimen by ordering DME and optimizing home care plans, and follows up with patients after discharge.

JUSTIN PHILLIPS, RRT-ACCS

UCSF-Zuckerberg

HANDS-ON SESSION: VENT MANAGEMENT IN ARDS

Friday, March 21, 2025 1:40 pm - 2:40 pm

Justin Phillips is an Adult Critical Care Respiratory Therapist for the University of California San Francisco, Department of Anesthesia at Zuckerberg San Francisco General Hospital and Trauma Center (ZSFG). There, he currently serves as a bedside therapist and educator. Justin is a lecturer for the Critical Care Residency Program at ZSFG and has spoken nationally at several respiratory and critical care conferences. Additionally, he is Adjunct Faculty for the Respiratory Care Program at Ohlone College for Health Sciences and Technology. Justin's clinical interests include enhancing mechanical ventilation delivery through innovation and strategic ventilator practices.

GAURAV SINGH, MD

Stanford

HANDS-ON SESSION: NON-INVASIVE VENTILATION

Friday, March 21, 2025 1:40 pm - 2:40 pm

Dr. Gaurav Singh received his Doctor of Medicine degree from the University of California San Francisco and Master of Public Health degree from the University of California Berkeley. He completed residency training in Internal Medicine and subsequent fellowship trainings in Pulmonary and Critical Care Medicine as well as Sleep Medicine at Stanford University. He is a Staff Physician at the VA Palo Alto Health Care System, where he serves as the Pulmonary and Critical Care Lead for the VA Sierra Pacific Network. Dr. Singh is also an Affiliated Clinical Assistant Professor in the Division of Pulmonary, Allergy, and Critical Care Medicine at Stanford University, and he is an Associate Program Director for the fellowship training program. Dr. Singh has been involved in the California Thoracic Society since 2018. He served as the Conference Co-Chair of the Northern California Annual Educational Conference from 2022 to 2024. He was elected to the CTS Executive Committee as Treasurer in 2024, and he will serve as Secretary this year. His primary vocation is providing clinical care for Veterans and teaching medical students, residents, and fellows. He also engages in some clinical research and scholarly activities, with an emphasis on obstructive lung diseases, sleep related breathing disorders, ventilatory support for chronic respiratory failure, and the intersection of sleep medicine and critical care. He has authored several reviews and books chapters in these subspecialized fields.

NAOMI BUGAYONG, MSRC, RRT

UC Davis

HANDS-ON SESSION: HIGH FLOW NASAL CANNULA

Friday, March 21, 2025 1:40 pm - 2:40 pm

Naomi Bugayong has been a respiratory therapist since 2007 receiving her graduate degree from Boise State University. She currently works at UC Davis Health as an Adult Clinical Educator and serves on the California Society for Respiratory Care Board of Directors as the Secretary.

NEUROMUSCULAR DISORDERS

CHAMINDRA LAVERTY, MD

Rady Children's/UCSD)

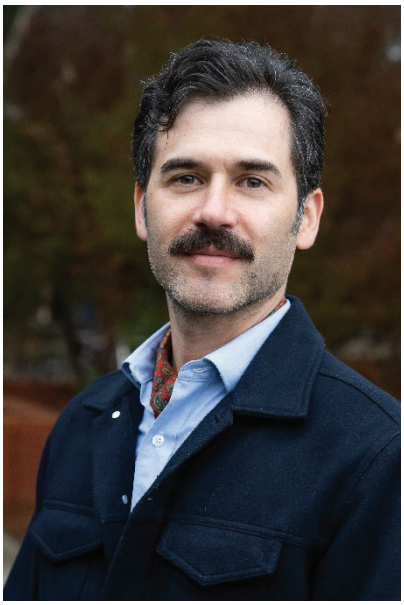
UNDERSTANDING THE SPECTRUM OF NEUROMUSCULAR DISEASES

Friday, March 21, 2025 3:10 pm - 3:35 pm

Chamindra G. Laverty, M.D. is a board-certified neurologist with neuromuscular certification that specializes in the management and treatment of hereditary and acquired neuromuscular disease. As a Clinical Professor of Neurosciences at the UC San Diego School of Medicine, Dr. Laverty is the principal investigator for 17 interventional and natural history clinical trials in various muscular dystrophies and neuropathies. She is the Director of both the pediatric and adult Multidisciplinary Neuromuscular clinics. Her special interest is bringing disease modifying therapy including gene replacement therapy, cell therapy and anti-sense oligonucleotides, to her complex patients, exceeding a p. In collaboration with colleagues, Dr. Laverty has described several new muscle diseases.

Dr. Laverty is the program director for the ACGME-accredited Neuromuscular Medicine Fellowship at UCSD, training the next generation of neuromuscular specialists. She received accreditation and launched the Fellowship in 2019.

She completed her neurology residency training and Neuromuscular fellowship training at the University of California, Los Angeles, after earning her medical degree from Drexel University, College of Medicine.



JACOB BAILEY, MD

UCSD

MANAGEMENT CONSIDERATIONS INPATIENTS WITH NEUROMUSCULAR DISORDERS

Friday, March 21, 2025 3:35 pm - 4:00 pm

Dr. Jacob Bailey received his medical degree from the UC San Diego School of Medicine, a master's degree in education at UCLA, and completed his residency in Internal Medicine and Pediatrics at Los Angeles County + University of Southern California Medical Center. Dr. Bailey returned to UC San Diego to complete his fellowship in Pulmonary and Critical Care Medicine where he subsequently stayed as faculty.

JOE VAN VLEET, BSRC, RRT

UCLA

AIRWAY CLEARANCE MODALITIES

Friday, March 21, 2025 4:00 pm – 4:25 pm

Joseph Van Vleet is a full-time clinician and Pulmonary Navigator in the Respiratory Therapy Department at University of California Los Angeles. He graduated from the Los Angeles Valley College Respiratory Therapy Program. He received his bachelor's degree in respiratory care at the University of Missouri. He has over 7 years of clinical experience at UCLA working in the NICUs, ICUss, Emergency Department, the Post-ICU Clinic and assists with performance improvement projects on both campuses. He helped develop the POST-ICU Recovery Clinic at UCLA and assists with recruitment and post discharge navigation for that population. As pulmonary navigator, he provides education to pulmonary patients during their hospitalizations, assists with optimizing patients' home RT regimen by ordering DME and optimizing home care plans, and follows up with patients after discharge.

HUGO PAZ Y MAR, MD

UC Irvine

NON-INVASIVE VENTILATION BASICS

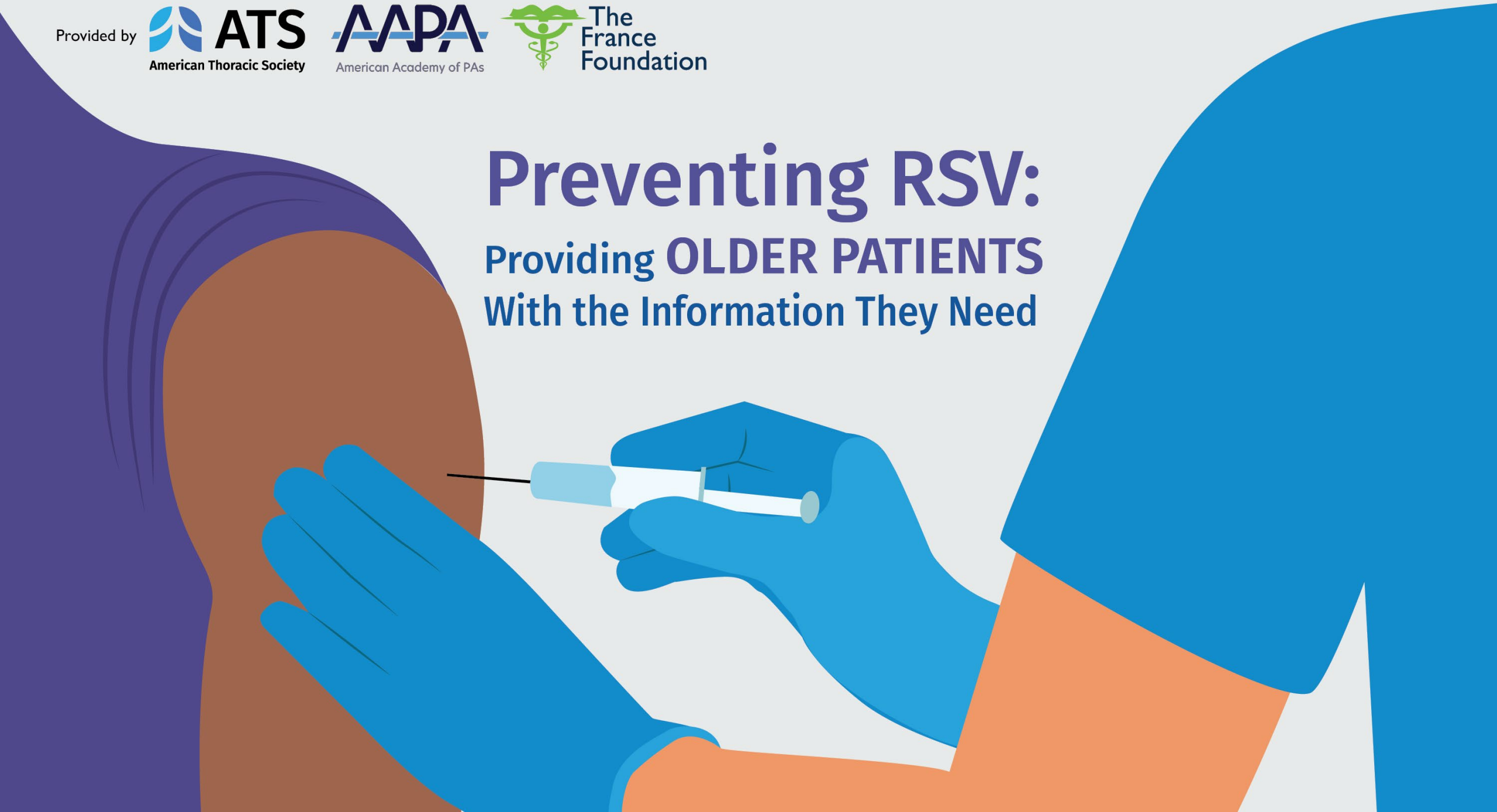
Friday, March 21, 2025 4:25 pm - 4:50 pm

Dr. Hugo Paz received his medical degree from The University of Tamaulipas Mexico. He completed his Internal Medicine, Sleep, Pulmonary and Critical Care Medicine at the Cleveland Clinic. Dr. Paz is an Associate Professor of Medicine at UC Irvine and currently serves as the Associate Program Director for the Pulmonary and Critical Care Medicine fellowship program.

Provided by ATS American Thoracic Society · AAPA American Academy of PAs · The France Foundation

Preventing RSV:

Providing OLDER PATIENTS With the Information They Need



Provided by the
American Academy of PAs
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Supported by an educational grant from
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AAPA
American Academy of Physician Associates

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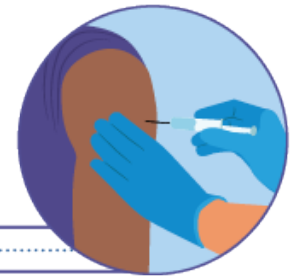
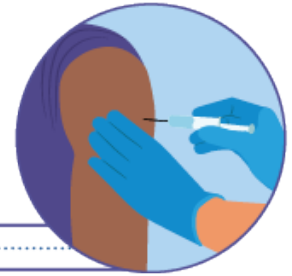


Expert Faculty

Justin R. Ortiz, MD, MS
Pulmonary Critical Care,
Infectious Diseases
Professor of Medicine
University of Maryland School of Medicine
Baltimore, MD

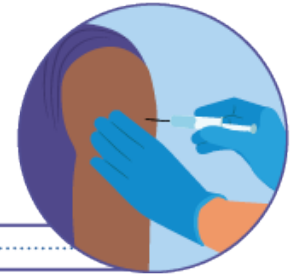


Disclosures

Financial Relationships with “ineligible companies” within the past 24 months.

Company name, type of relationship:

- Advarra DSMB member (personal)
- BlueWillow clinical trial assay research support (institution)
- GSK Vaccine Virtual Days Steering Committee member (personal)
- Moderna Scientific Advisory Committee member (personal)
- Pfizer Scientific Advisory Committee member (personal)
- The Vaccine Company clinical trial research support (institution)

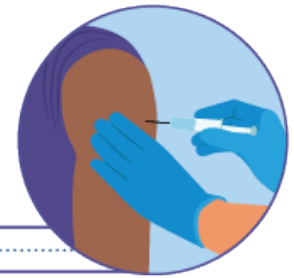


Steering Committee

Sarah McQueen, PA-C
Family Medicine Physician Associate
Dayspring Health
Williamsburg, KY

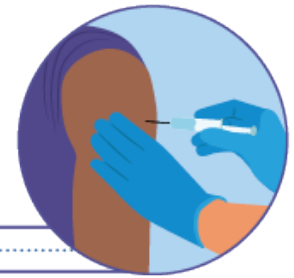
Justin R. Ortiz, MD, MS
Pulmonary Critical Care, Infectious Diseases
Professor of Medicine
University of Maryland School of Medicine
Baltimore, MD

Pamela Rockwell, DO, FAAFP
Professor
Medical Director, Family Medicine at Domino's Farms
University of Michigan
Ann Arbor, MI



Learning Objectives

- Describe the mechanism of RSV illness in adults, as well as its overall incidence in this population
- Summarize the disease burden of RSV illness in US adults, with a focus on hospitalizations, comorbidities, and health disparities
- Evaluate the data on performance of RSV vaccines to assess their potential role in prevention strategies for older adults



Knowledge Checks 1-2

Answer via QR code →

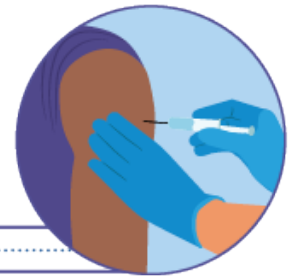
1. Your 75-year-old patient describes having a cold that "seems to have gotten really bad." They think they caught it from their 2-year-old grandchild, who recently had nasal congestion, a runny nose, and a fever. However, your patient has symptoms of lower respiratory tract disease (LRTD), with coughing, substantial mucus production, and shortness of breath.

Which change in affected airways has been associated with development of an RSV-related illness?

A. Airway hyporeactivity
B. Debris accumulation
C. Greater surfactant production
D. Increased mucociliary transport
E. Neutrophil sloughing

2. What is the estimated annual rate of RSV-related illness in healthy older adults (≥ 65 years old)?

A. Less than 1%
B. 3%-7%
C. 9%-12%
D. 15%-17%
E. Greater than 20%



Knowledge Checks 3-4

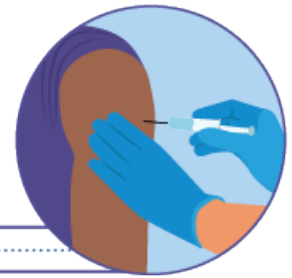
Answer via QR code →

3. You have 4 adult patients scheduled for annual wellness exams this morning. According to recent recommendations from the Centers for Disease Control and Prevention (CDC), which of the following people should receive an RSV vaccine?

A. The healthy 45-year-old patient who requests an RSV vaccine so her record is up to date for travel
B. The patient who is 65 years old and lives with grandchildren who are 10-12 years old
C. The patient who is 77 years old and lives in a long-term care facility
D. The patient who is 70 years old, generally healthy, and has no cardiovascular or pulmonary conditions

4. In the US, the number of RSV-associated hospitalizations per year for children < 5 years of age is 58,000-80,000. What is the approximate number of RSV-associated hospitalizations per year for older adults (≥ 65 years of age) in the US?

A. 300
B. 1,550
C. 68,000
D. 177,000
E. 2,200,000

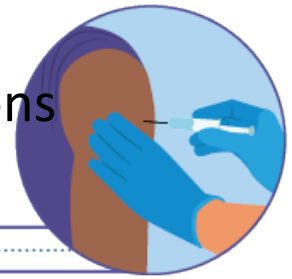


Knowledge Check 5

Answer via QR code →

A healthy 60-year-old patient with knee osteoarthritis and hearing impairment, but no other chronic medical conditions, has an office visit for a wellness check. Their youngest grandchild was very ill with RSV last winter, so they'd like to learn more about the vaccines they've heard advertised. Which of the following is correct and appropriate to share with the patient, based on product prescribing information and evidence-based recommendations from the Centers for Disease Control and Prevention (CDC)?

A. The best time to get vaccinated is early winter, when RSV infections typically peak
B. If the vaccine is given in spring or summer, a booster is recommended in early winter
C. RSV vaccines are recommended for people who are 60 years old only if they are at risk for severe RSV-related illness
D. RSV vaccines should not be administered with other vaccines
E. RSV vaccines are only indicated for individuals with chronic cardiopulmonary conditions



Chimpanzee Coryza Agent

544

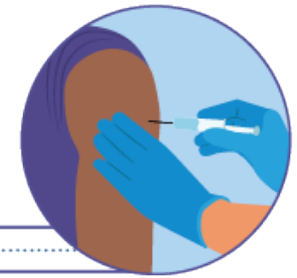
Recovery of Cytopathogenic Agent from Chimpanzees with Coryza. (22538)

J. A. Morris, R. E. Blount, Jr. and R. E. Savage. (Introduced by J. E. Smadel.)
Department of Virus Diseases, Walter Reed Army Institute of Research, Washington, D.C.

During October, 1955, a respiratory illness characterized by coughing, sneezing and mucopurulent nasal discharge occurred in a colony of 20 "normal" chimpanzees at the Walter Reed Army Institute of Research. The present paper describes the isolation of a virus of apparent etiologic significance in the epizootic, establishes an etiologic association between the chimpanzee coryza agent and respiratory illness in a laboratory worker and finally, presents serologic data suggesting that a number of human beings have experienced infection with the chimpanzee coryza virus or an agent closely related to it.

Materials and methods. Chimpanzees and cm) in nutrient medium consisting of 8 parts Eagle's basal medium(2), 2 parts inactivated horse serum, and 0.2 part L-glutamine. Penicillin (100 units/ml) and streptomycin (20 μg/ml) were added to control adventitious bacterial contaminants. Tubes and bottles contained 1 ml and 15 ml of nutrient fluid, respectively. The cells were fed on the 3rd or 4th day by replacing the old nutrient fluid with an equal amount of fresh nutrient. Cultures were incubated at 36°C and at the time of use were usually 4 to 6 days old. *Isolation of coryza agent.* A fresh (within the hour of collection) throat swab from a chimpanzee (Sue) involved in the epizootic was

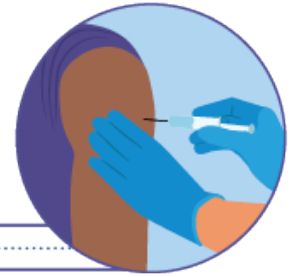
- In 1956, a new pathogen isolated 14 chimpanzees with colds and coryza at Walter Reed
- Named Chimpanzee Coryza Agent in first publication
- In 1957, CCA recovered from two children with respiratory infections



Morris JA, Blount JA, & Savage RE. Recovery of cytopathogenic agent from chimpanzees with coryza. Proc Soc Exp Biol Med. 1956 Jul;92(3):544-9.

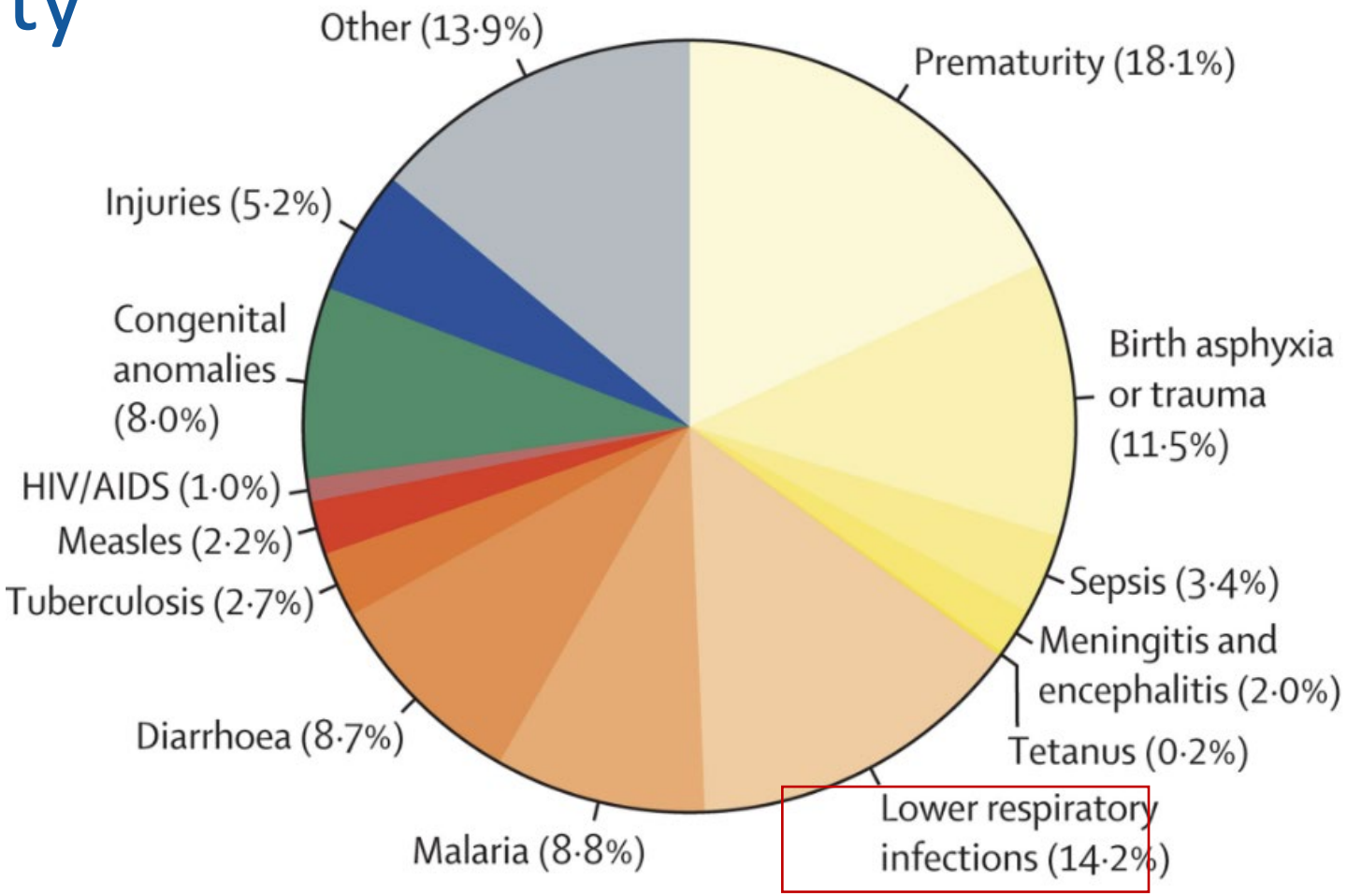
Epidemiology of RSV in Children

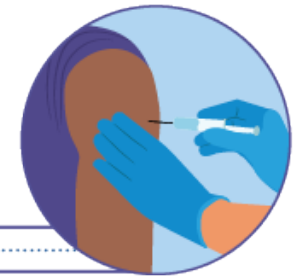
- When specific neutralizing antibody to CCA was found to be present in most school-aged children, renamed respiratory syncytial virus (RSV) to denote its clinical and laboratory manifestations
- After its discovery, RSV quickly determined to be an important pathogen in children
- All children are infected by RSV early
  - 68% infected by first birthday
  - 97% by second birthday



Suh et al. JID 2022. Glezen et al, Arch Dis Child, 1986; Hall et al, Pediatrics, 2013; Langley & Anderson, PIDJ, 2011; CDC NVSN data

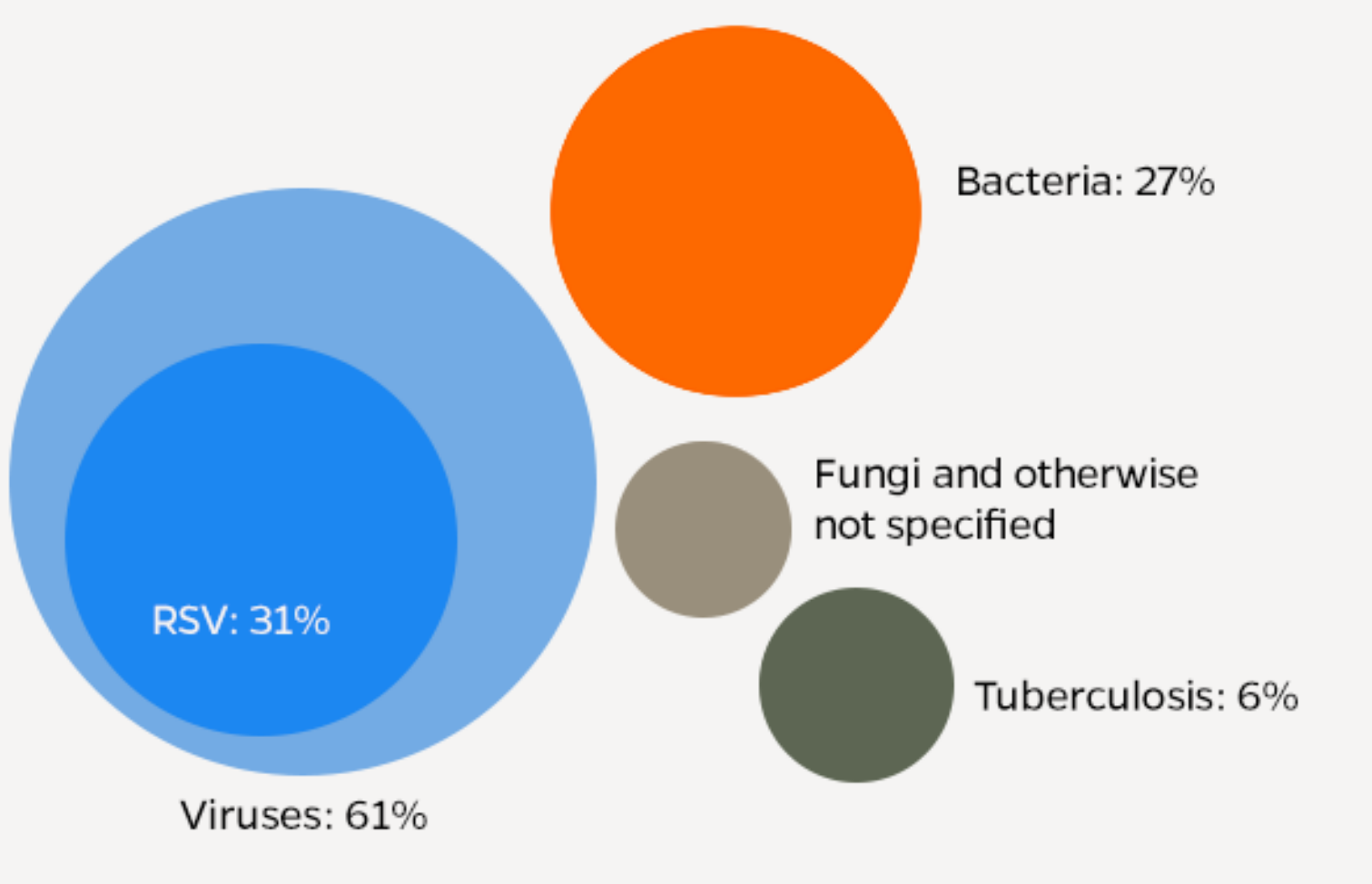
After complications of prematurity, lower respiratory infections are most important cause of <5 mortality



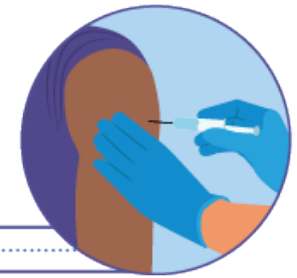


Villavicencio F, et al. Lancet Glob Health. 2024

Among early childhood LRTI, RSV is the most common etiology

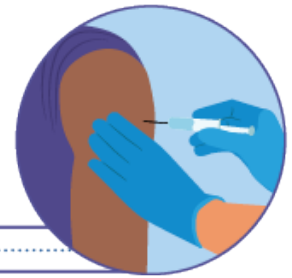


Pneumonia Etiology Research for Child Health (PERCH) Study Group. Lancet. 2019, https://hub.jhu.edu/2019/06/27/viruses-cause-pneumonia-rsv-vaccines-needed/



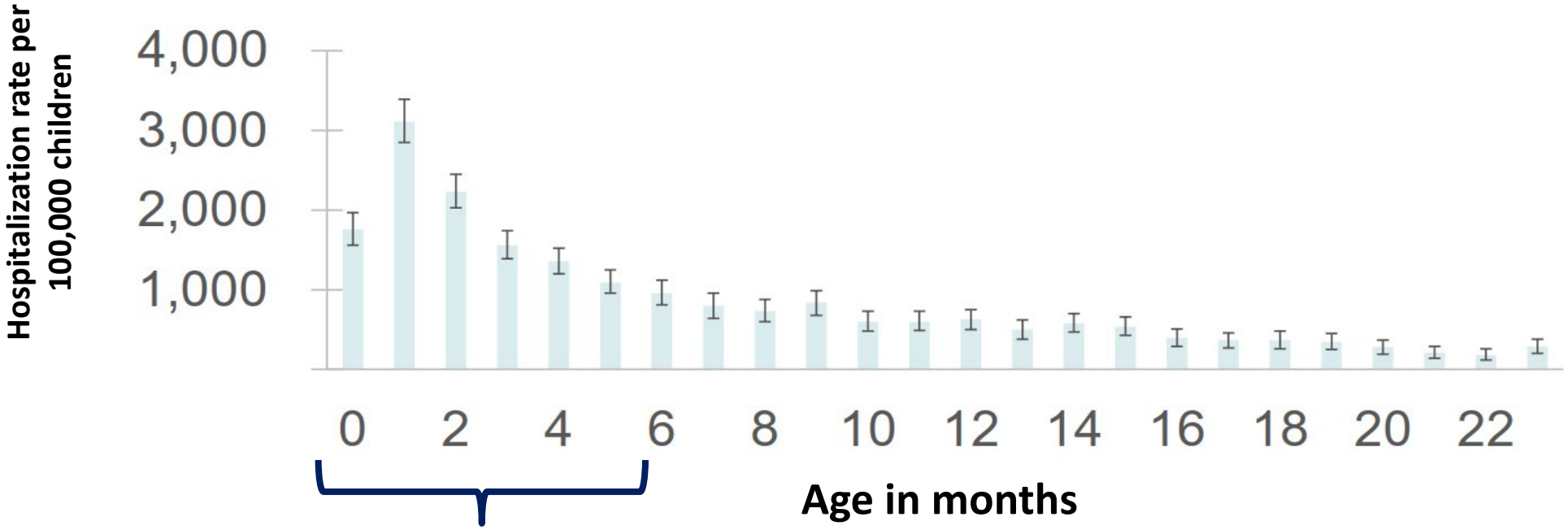
Pediatric RSV Burden in the United States

- Annually, 2-3% of US infants are hospitalized for RSV
  - Most frequent cause of hospitalization in infants (58,000-80,000)
  - no reduction in this statistic in last 2 decades
  - 1 in 5 go to ICU
  - 100-300 deaths annually
- Premature babies <30 weeks GA:
  - ~3x risk of hospitalization
- 79% of all hospitalized infants w/RSV have no underlying problems



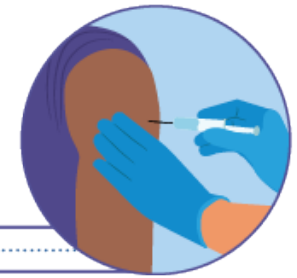
Suh et al. JID 2022. Glezen et al, Arch Dis Child, 1986; Hall et al, Pediatrics, 2013; Langley & Anderson, PIDJ, 2011; CDC NVSN data

US RSV-LRTI hospitalizations in kids

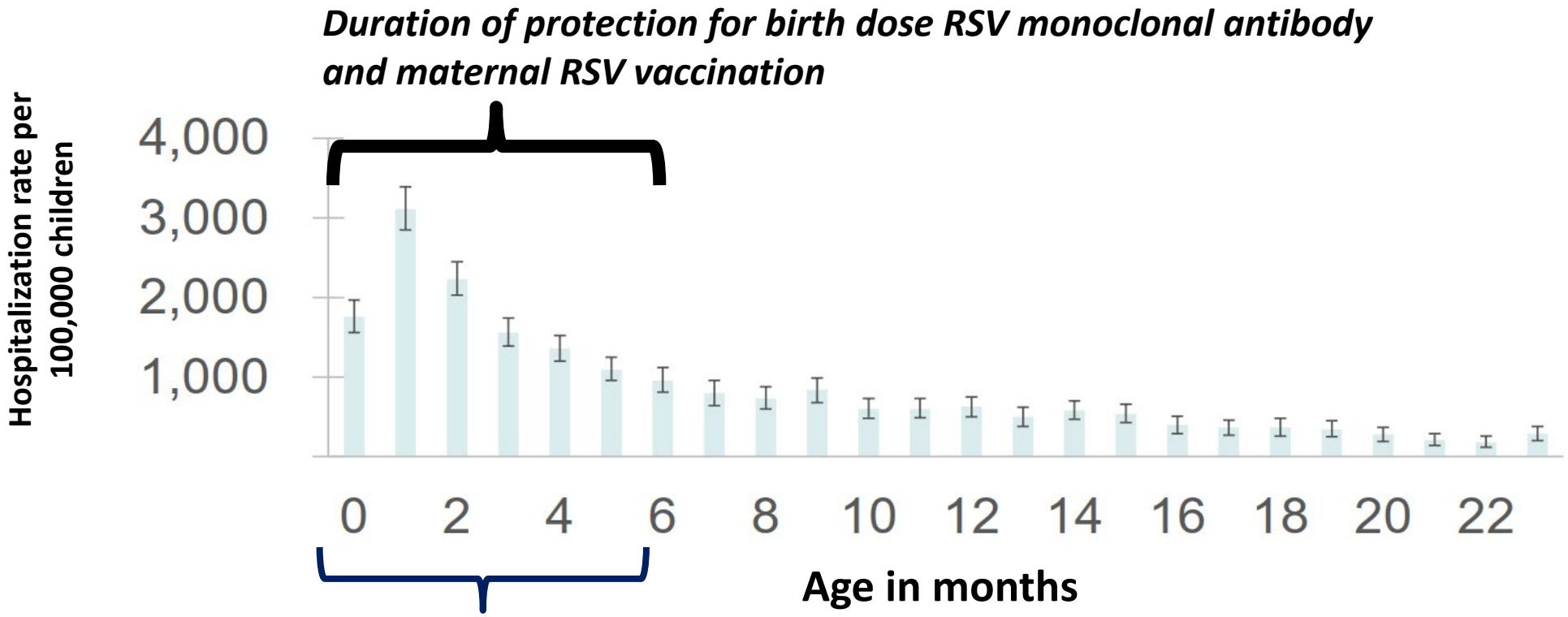


58% of pediatric RSV hospitalizations occur in < 6 months

CDC NVSN data



US RSV-LRTI hospitalizations in kids



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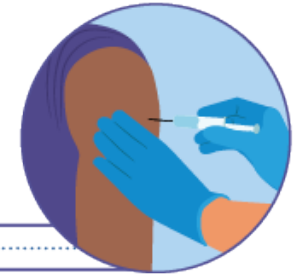
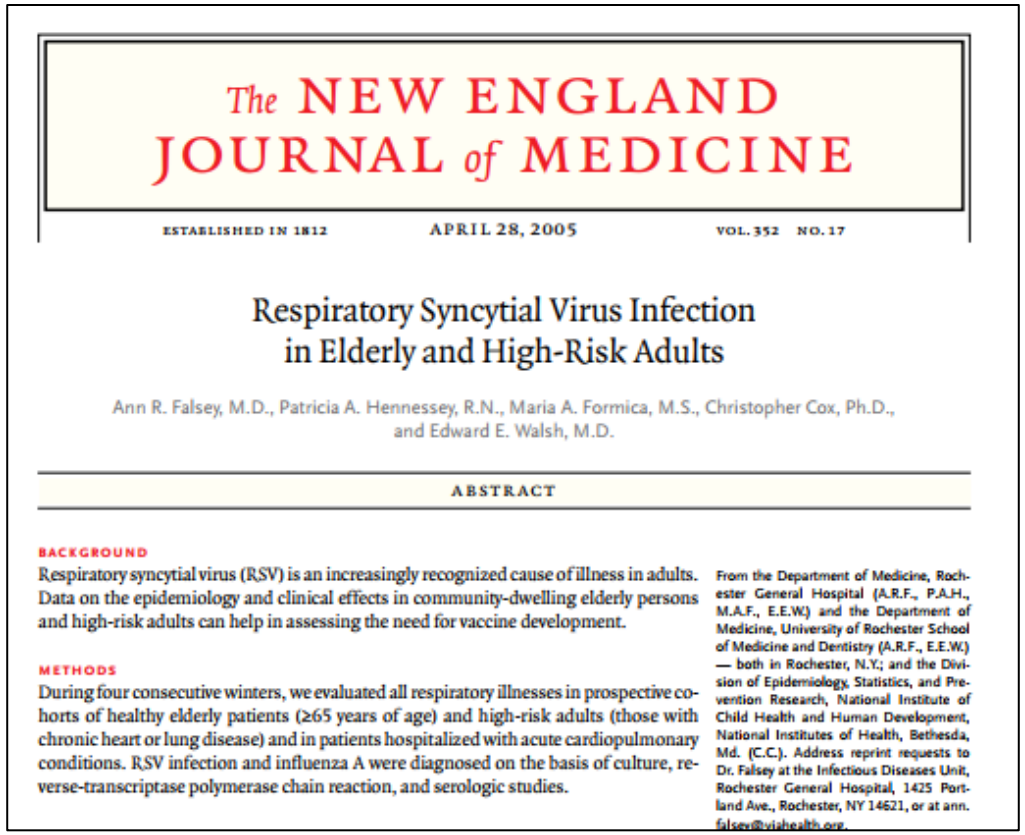


Recognition of RSV burden in adults



The NEW ENGLAND JOURNAL of MEDICINE

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Respiratory Syncytial Virus Infection in Elderly and High-Risk Adults

Ann R. Falsey, M.D., Patricia A. Hennessey, R.N., Maria A. Formica, M.S., Christopher Cox, Ph.D., and Edward E. Walsh, M.D.

ABSTRACT

BACKGROUND

Respiratory syncytial virus (RSV) is an increasingly recognized cause of illness in adults. Data on the epidemiology and clinical effects in community-dwelling elderly persons and high-risk adults can help in assessing the need for vaccine development.

METHODS

During four consecutive winters, we evaluated all respiratory illnesses in prospective cohorts of healthy elderly patients (≥65 years of age) and high-risk adults (those with chronic heart or lung disease) and in patients hospitalized with acute cardiopulmonary conditions. RSV infection and influenza A were diagnosed on the basis of culture, reverse-transcriptase polymerase chain reaction, and serologic studies.

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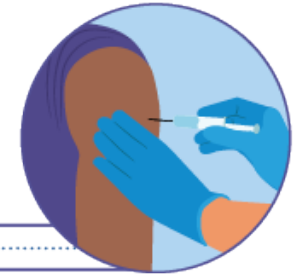
- RSV in adults was generally underappreciated until this landmark surveillance study at Rochester General Hospital
- In this 4-year study, RSV-associated hospitalizations similar to influenza in >65 years



Falsey AR, at al. N Engl J Med. 2005 Apr 28;352(17):1749-59.

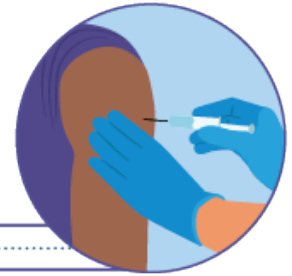
RSV-Associated Hospitalization and Death: Older Adults and Young Children in the US

Outcome	Young Children, <5 years of age	Older Adults, ≥65 years of age
Hospitalizations/year	58,000 – 80,000	≈177,000
Deaths/year	100 – 300	6,000 – 10,000

In the United States

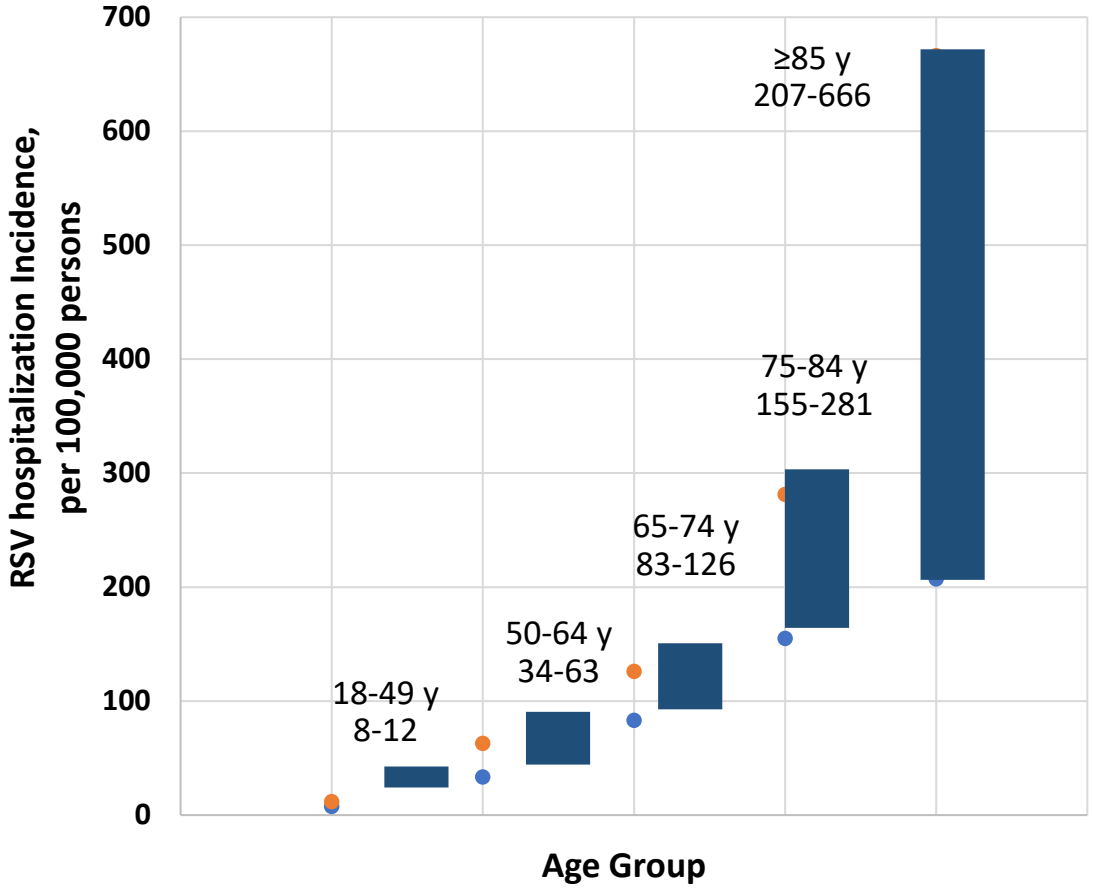
- Highest infection rates are in infants and young children
- Highest mortality is among older adults

Havers F. Presented at the Advisory Committee on Immunization Practices meeting on June 23, 2022. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-06-22-23/04-RSV-Havers-508.pdf; Falsey AR, et al. *N Engl J Med*. 2005;352(17):1749-1759; Hall CB, et al. *N Engl J Med*. 2009;360(6):588-598; McLaughlin JM, et al. *J Infect Dis*. 2022;225(6):1100-1111; Thompson WW, et al. *JAMA*, 2003;289(2):179-186; Hansen CL, et al. *JAMA Netw Open*. 2022;5(2):e220527; Tong S, et al. *J Glob Health*. 2020;10(2):020422.. https://emergency.cdc.gov/han/2023/han00498.asp.



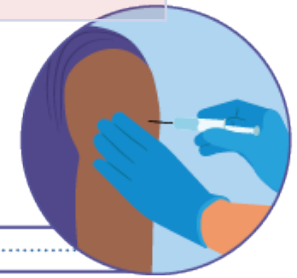
RSV and Hospitalizations Among US Adults

Results of RSV Surveillance in Hospitalized Patients (NY, USA, 2017-2020)



Characteristics and Outcomes Among Adults ≥60 Years Old Hospitalized with RSV (RSV-NET, July 2022-June 2023)

- ≥75 years of age: 54.1%
- Underlying medical condition: 95.5%
- Intensive care admission: 17.0%
- Mechanical ventilation: 4.8%
- Death: 4.7%



RSV-NET, Respiratory Syncytial Virus-Associated Hospitalization Surveillance Network. Branche A, et al. *Clin Infect Dis*. 2022;74(6):1004-1011; Havers FP, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72(40):1075-1082.

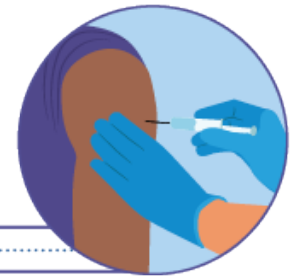
RSV Illness in Long-Term Care Facilities

Adults ≥60 years old residing in a long-term care facility have been found to be high risk for RSV complications.

17.2% of RSV hospitalizations in adults ≥60 years old occurred in long-term care facility residents.

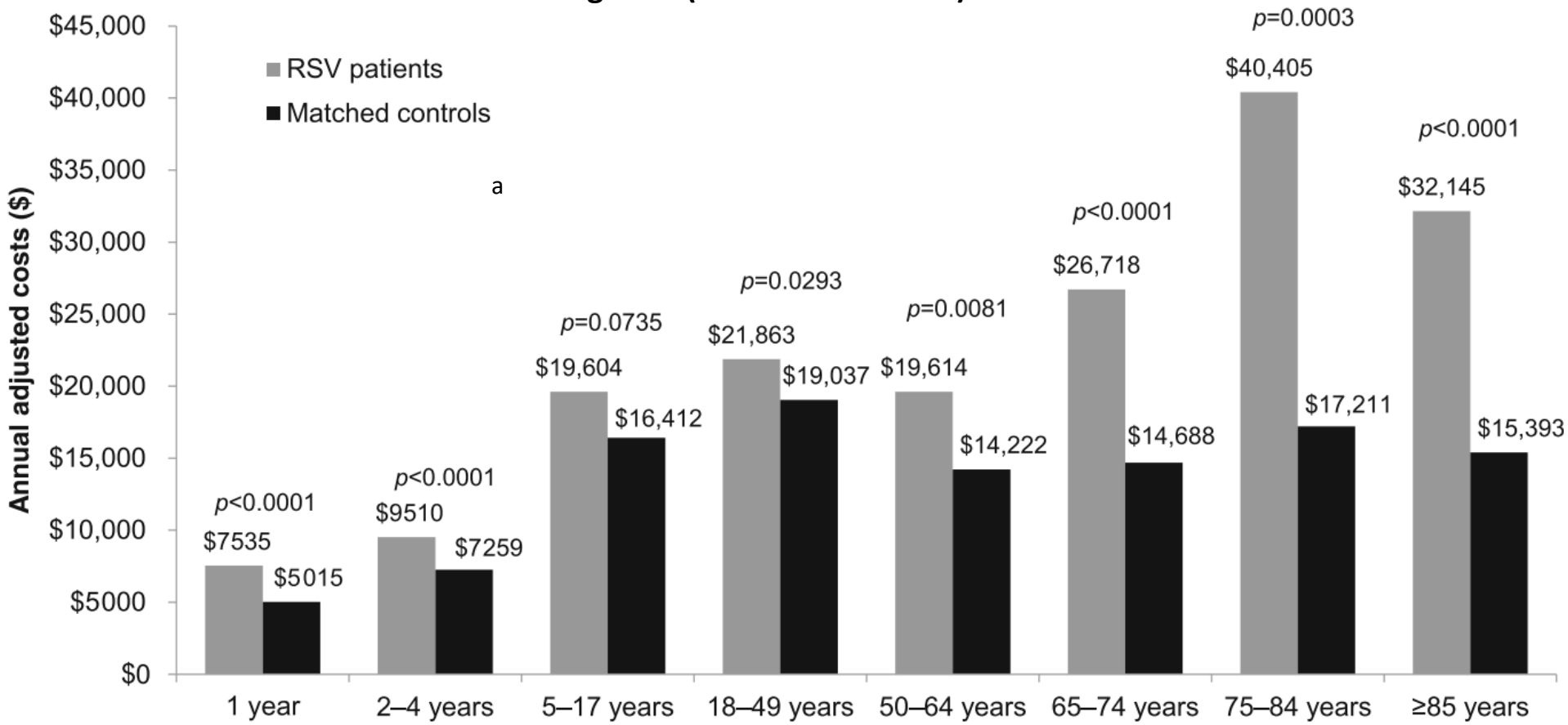
In November 2024, vaccine coverage among reporting nursing homes was 18% for RSV and 58% for influenza.

Havers FP, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72(40):1075-1082; Reses HE, et al. *https://www.cdc.gov/mmwr/volumes/73/wr/mm7346a2.htm*



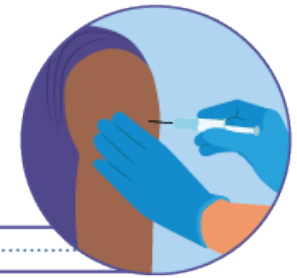
US RSV Economic Burden

Adjusted Annual Healthcare Costs for Index Event and 12-Month Follow-up (2014 US Dollars) in Patients With an RSV Diagnosis (2012-2013 season)



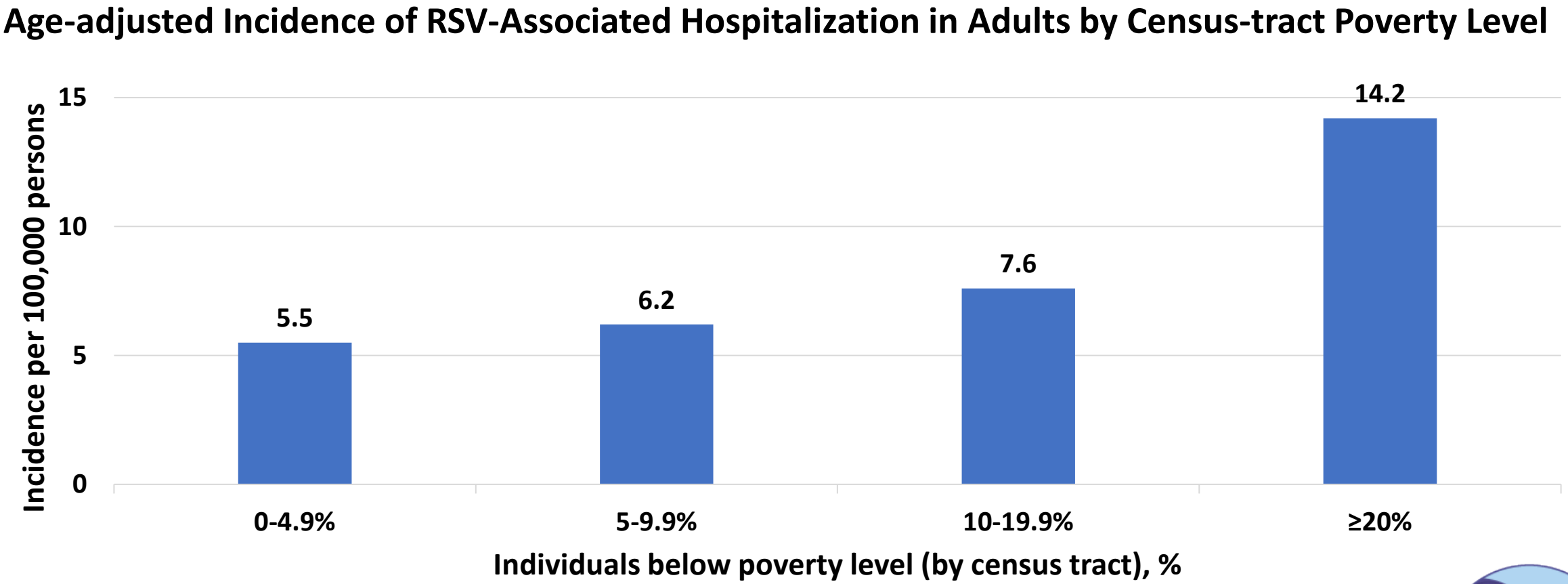
Patients without RSV matched based on age, sex, region, health plan, and index date

Costs include inpatient visits, ED and urgent care visits, Ambulatory visits, Outpatient visits, Pharmacy prescriptions

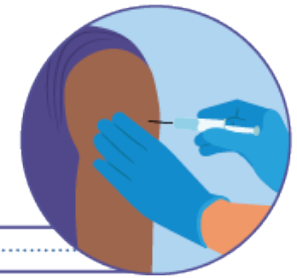


Amand C, et al. *BMC Health Serv Res*. 2018;18(1):294.

Relationship Between RSV-Associated Hospitalizations and Poverty Level in Adults

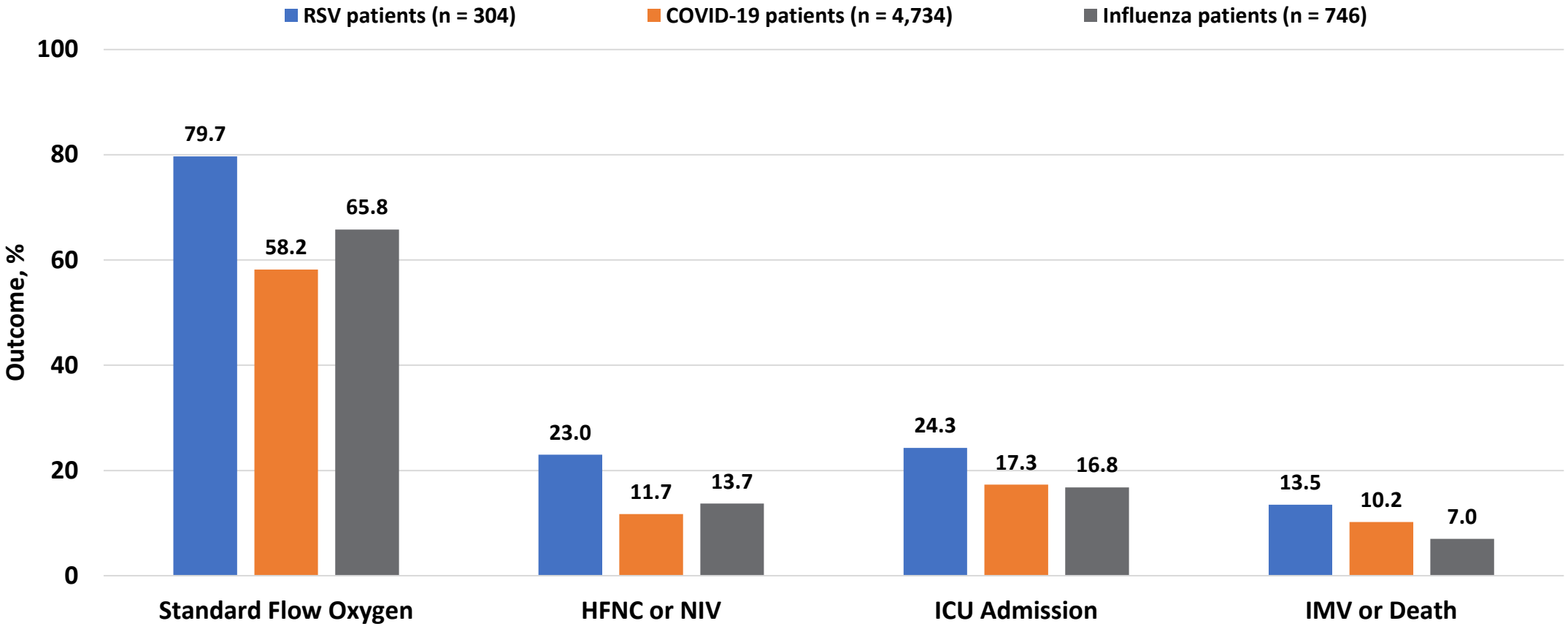


P <.005 for trend

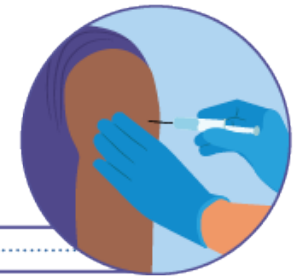


Holman JE, et al. *BMC Infect Dis*. 2021;21:293.

Outcomes in Hospitalized Older Adults With RSV, COVID-19, or Influenza (February 2022 – May 2023)



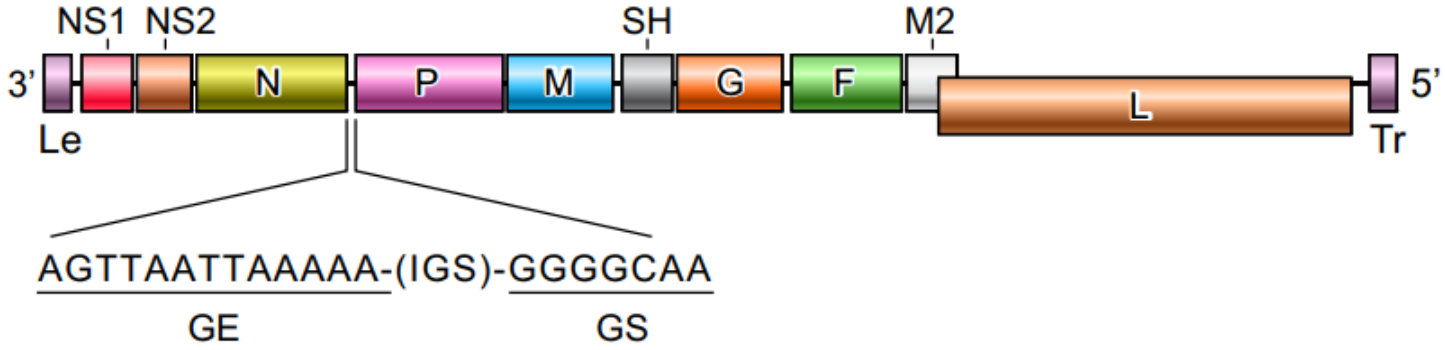
HFNC=high-flow nasal cannula; ICU=intensive care unit; IMV=invasive mechanical ventilation; NIV=noninvasive ventilation



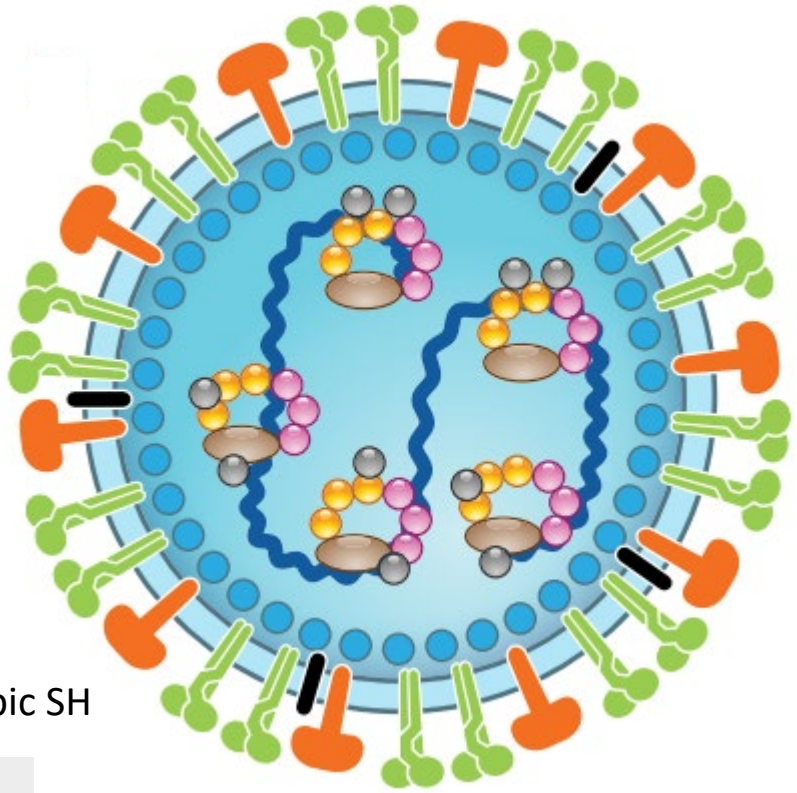
Surie D, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72:1083-1088.

RSV Components

RSV Genomic RNA



RSV Virus Particle



Nucleocapsid Proteins

- Nucleoprotein N
- Phosphoprotein P
- Large polymerase subunit L
- Transcription anti-termination factor M2-1

SS RNA

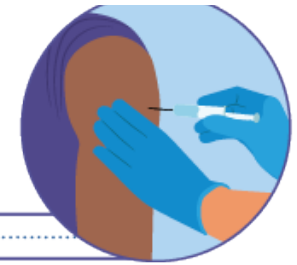
Viral Assembly Factor

- Matrix protein M

Membrane Envelope Glycoproteins

- Attachment G
- Fusion F
- Small hydrophobic SH

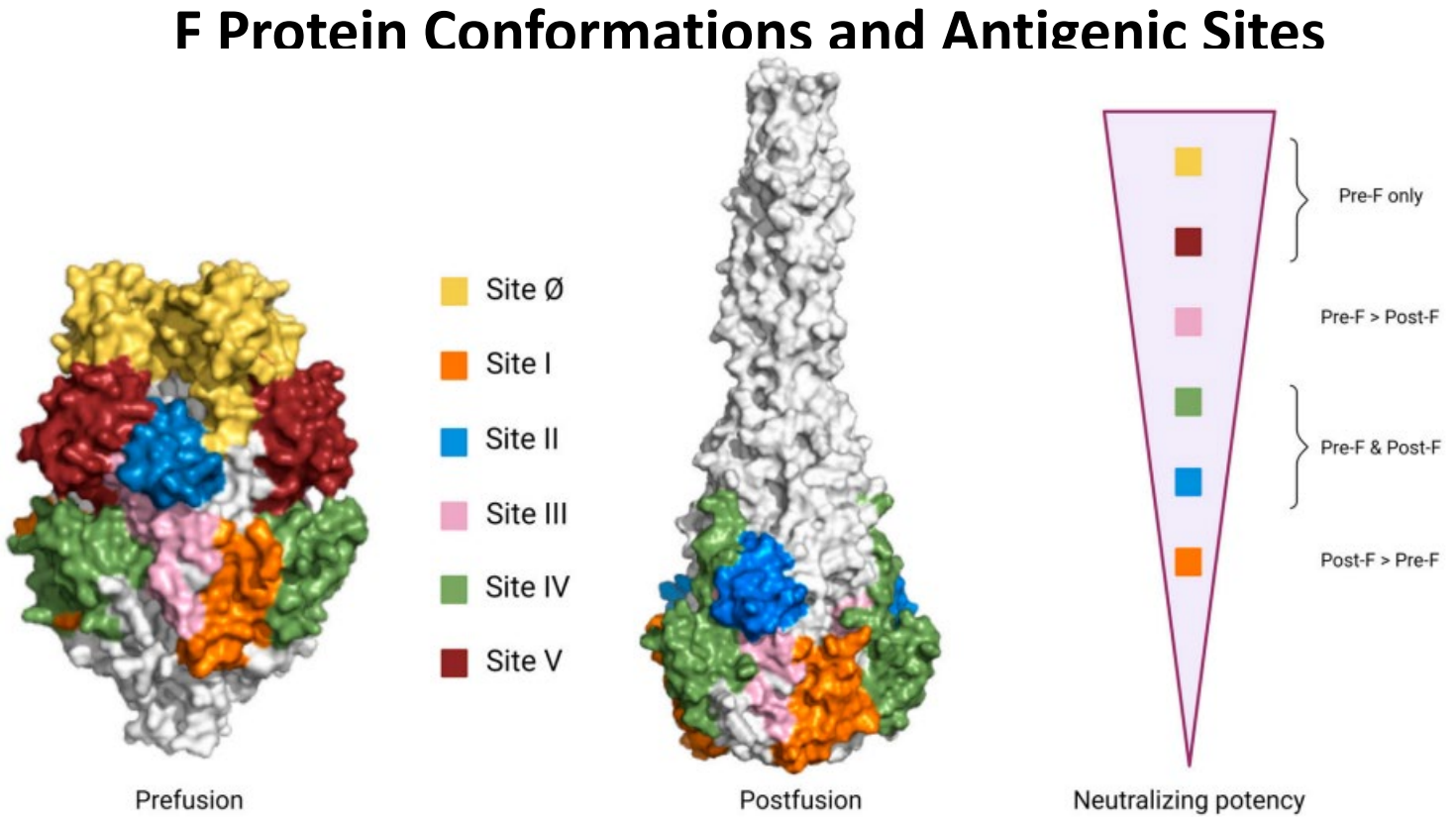
Viruses classified in A and B subgroups based on reactivity to monoclonal antibodies against surface proteins

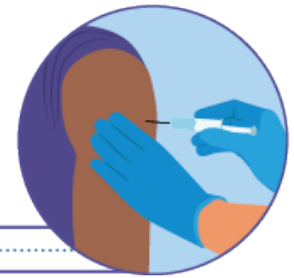


Hu M, et al. *Physiol Rev*. 2020;100:1527-1594.

The RSV F Protein: Membrane Fusion and Vaccine Target

- Conformational changes in the F protein facilitate membrane entry
- The F protein (pre-fusion conformation) is the target of FDA-approved adult vaccines





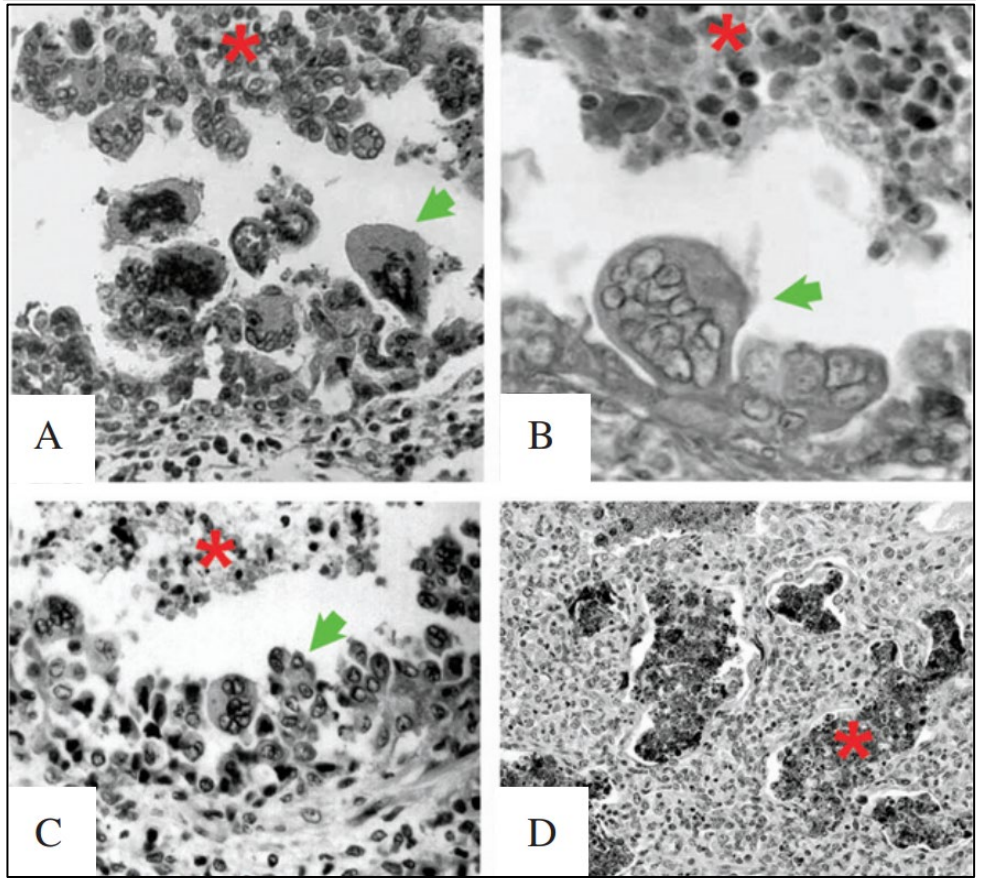
Hu M, et al. *Physiol Rev*. 2020;100:1527-1594; GSK. https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Arexvy/pdf/AREXVY.PDF; Pfizer. https://labeling.pfizer.com/ShowLabeling.aspx?id=19589; Schaerlaekens S, et al. *Vaccines*. 2024;12:97.

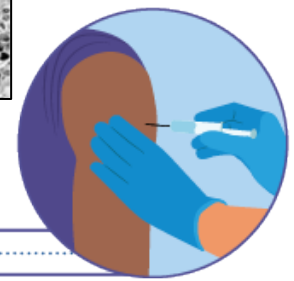
RSV: Infection Cycle

- Viral attachment and entry
  - Upper respiratory tract first (nasal epithelium), with potential to move to the lower respiratory tract
  - Main targets: ciliated epithelial cells, alveolar type II cells
- Viral transcription and replication
- Viral assembly and budding
- Pathological changes with lower respiratory tract infection may include
  - Syncytia formation
  - Epithelial cell sloughing
  - Debris accumulation in lumen

Histopathology of RSV-Infected Small Airways

- Epithelial cells retained in lumen (arrows)
- Giant cell/polyploid formation (asterisks)

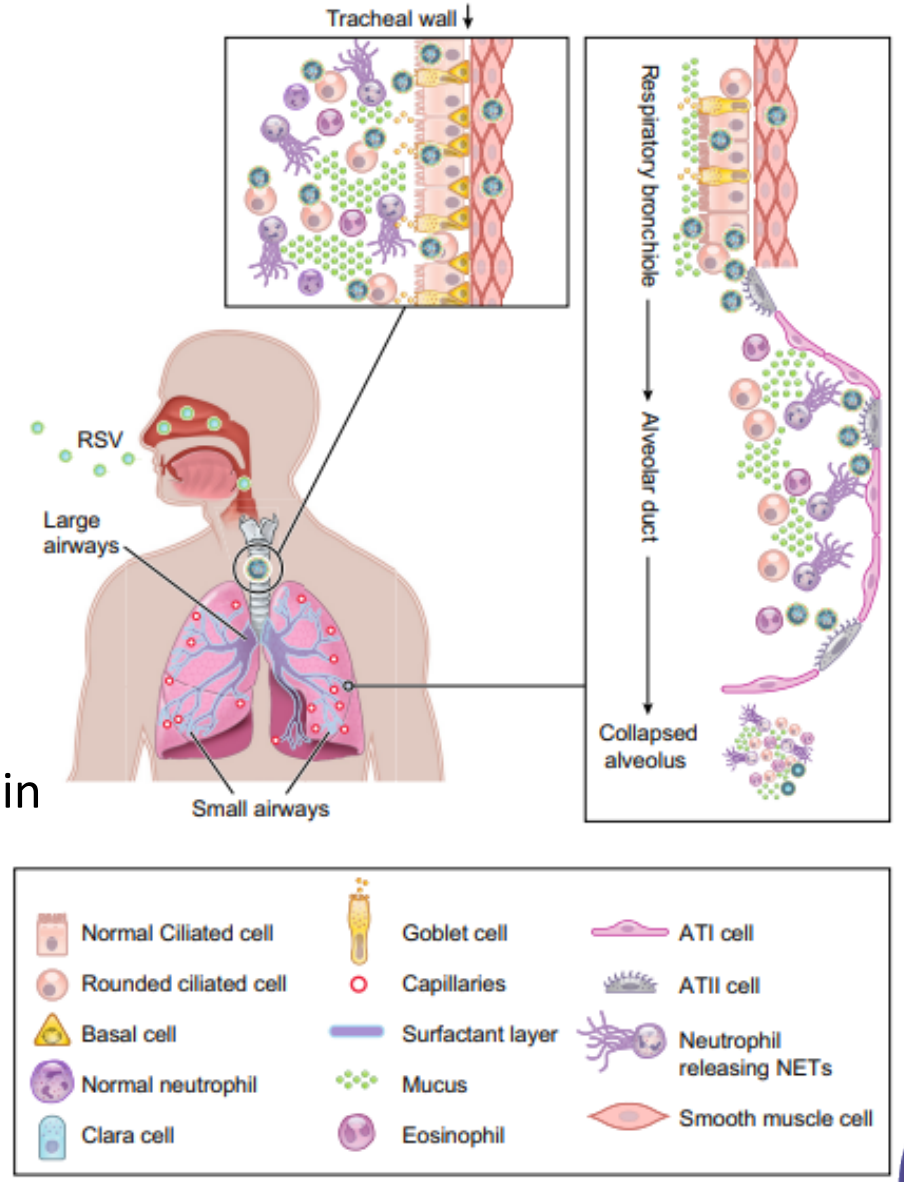


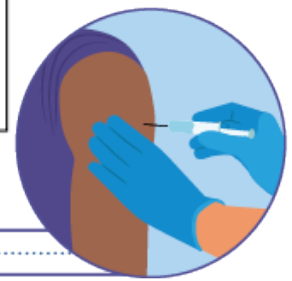


Hu M, et al. *Physiol Rev.* 2020;100:1527-1594; Pickles RJ, DeVincenzo JP. *J Pathol*. 2015;235:266-276.

RSV Pathology

- Usually, self-limited URI in healthy adults
- Pathological changes due to RSV
  - Epithelial cell sloughing lumenal debris accumulation
  - Lower airway obstruction and plugging
  - Pro-inflamatory mediators
  - Decrease surfactant production
  - Increased mucus production
  - Airway hyperreactivity
  - Impaired mucociliary transport
- The presence of potent bronchoconstrictor and pro-inflammatory mediators lead to the clinical symptoms
- The pathogenesis of the disease is very well described in young children, less so in older adults
- Among adults, exacerbations of underlying chronic condition more common than primary LRTI





Hu M, et al. *Physiol Rev.* 2020;100:1527-1594; Villanueva D, et al. *Ther Adv Infect Dis*. 2022;9:1-13.

Time Course of RSV illness

People are usually shedding virus for 3-8 days*

Exposure

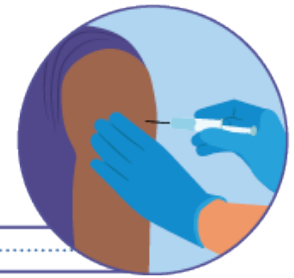
Individuals may transmit 1-2 days before symptoms appear

Symptoms typically develop 4-6 days after exposure

Typical disease duration (mild, acute respiratory illness):

- <5 days in adults
- 1-2 weeks in young children

*Some people, including infants and people with weakened immune systems (e.g., individuals on immunosuppressant medications) can spread the virus for up to 4 weeks, even if they no longer have symptoms



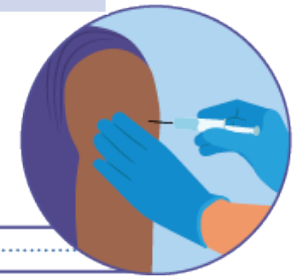
CDC. Respiratory syncytial virus infection (RSV): Symptoms & Care, Transmission, Healthcare Professionals. https://www.cdc.gov/rsv/index.html;
Melgar M, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72(29):793-801.

RSV: Ability to Establish Infection

Increasing ability to establish infection

Virus	Secondary Attack Rate (proportion infected among susceptible individuals in contact with the primary case), %
Measles virus	52.0 – 84.6
Varicella zoster virus	61.0 – 78.1
Parainfluenza virus	36.0 – 67.0
Rhinovirus	28.0 – 58.0
Respiratory syncytial virus	11.6 – 39.3
Influenza virus	1.4 – 38.0
Human coronavirus	0 – 38.2

Values are range of reported estimates of mean or median.

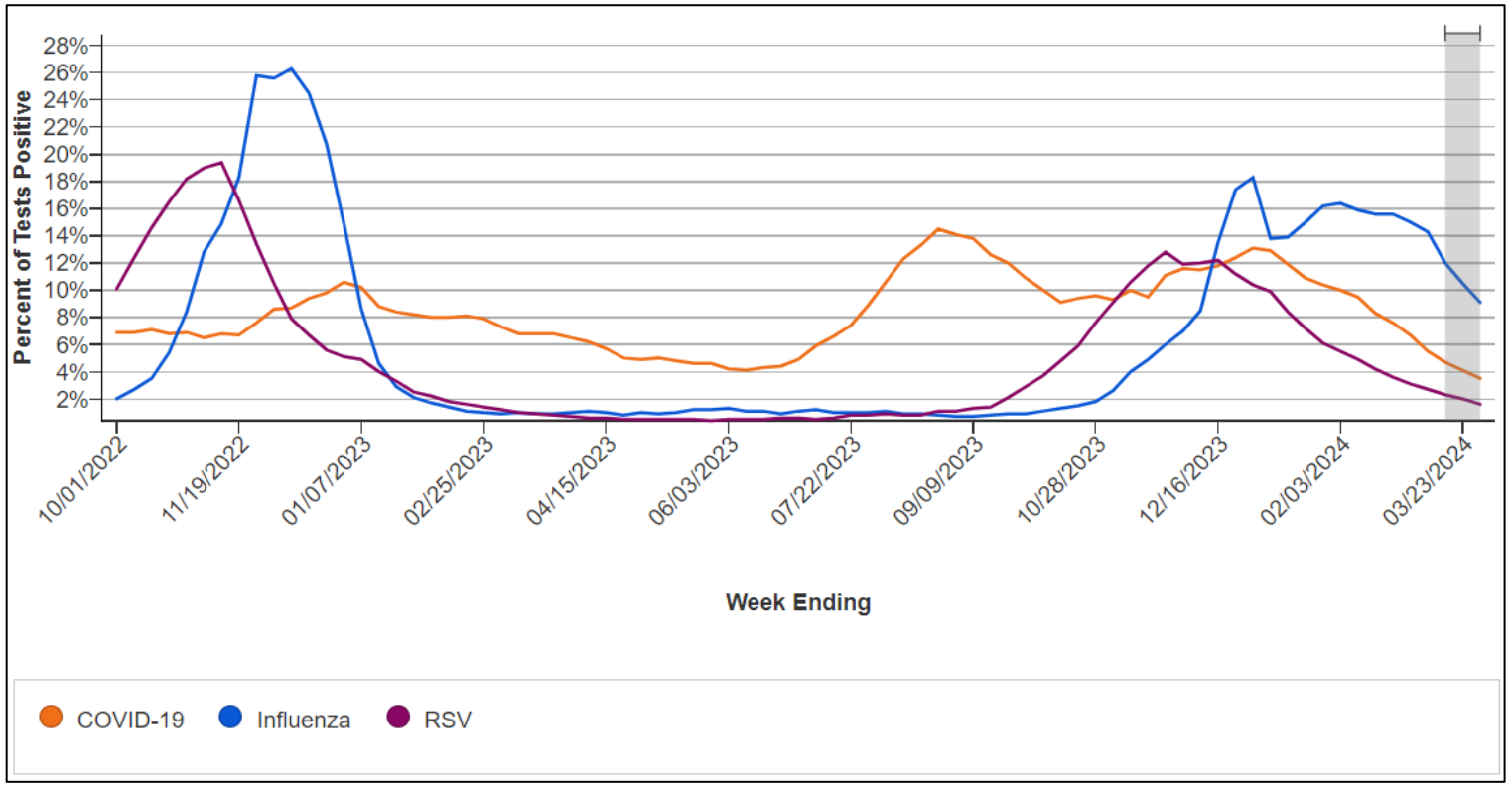


Leung NHL. Nat Rev Microbiol. 2021;19(8):528-545.

Seasonality of RSV Cases

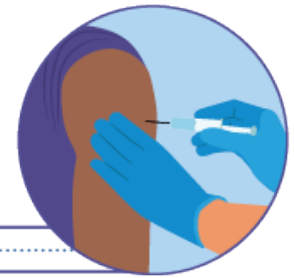
- Data from sentinel network of laboratories throughout the US, reported weekly to Centers for Disease Control and Prevention
- Impact of COVID-19 pandemic
  - RSV seasonality was disrupted by COVID-19 pandemic (2020-2022)
  - 2022-2023 data suggest return to pre-pandemic seasonality

Percent of Tests Positive for Respiratory Viruses, October 2022 to March 2024



Data Sources

- COVID-19, RSV: National Respiratory and Enteric Virus Surveillance System (NREVSS)
- Influenza: NREVSS and U.S. World Health Organization collaborating laboratories



CDC. Respiratory virus activity levels. https://www.cdc.gov/respiratory-viruses/data-research/dashboard/activity-levels.html; Hamid S, et al. MMWR Morb Mortal Wkly Rep. 2023;72(14):335-361.

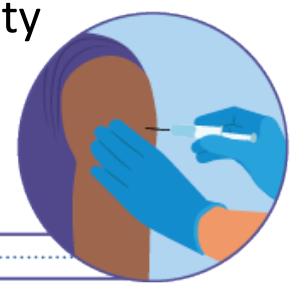
RSV Symptoms and Disease Course in Older Adults

Most Common RSV Symptoms in Older Adults, Present in >50% of Patients

Symptoms: Upper respiratory tract infection	Symptoms: Lower respiratory tract infection	Other symptoms
•Runny nose •Nasal congestion •Sore throat	•Cough •Sputum production •Dyspnea •Wheezing •Tachypnea	•Fatigue/ weakness •Lethargy •Headache

- Symptoms of respiratory disease caused by different viruses are similar
- Time to care/diagnosis is longer than for infants – symptoms often attributed to another cause (e.g., influenza)
- Factors associated with increased risk of severe illness
  - Older age (>60-65 years)
  - Chronic heart or lung disease
  - Weakened immune system (e.g., patients taking immunosuppressive medications for cancer, transplant)
  - Nursing home/long-term care facility residence

Kenmoe S, Nair H. *Curr Opin Infect Dis*. 2024;37:129-136; Kaler J, et al. *Cureus*. 2023;15(3):e36342; Hu M, et al. *Physiol Rev*. 2020;100:1527-1594; CDC. https://www.cdc.gov/rsv/high-risk/older-adults.html; Melgar M, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72(29):793-801.



RSV Diagnosis and Treatment in Adults

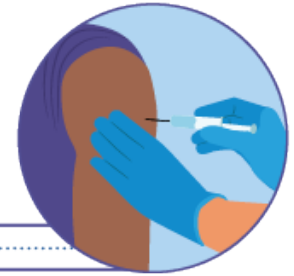
Identifying RSV as the Cause of Respiratory Illness

- Often unrecognized
  - Indistinguishable from other viral respiratory infections – testing needed to confirm
  - People often admitted to the hospital for exacerbations of complications, even when RSV may be precipitating cause
  - No motivation to test because no treatments are available
- Respiratory pathogen panels available
  - RSV, influenza, and SARS-CoV-2
  - Also available in at-home versions

Treatment

- No specific treatments
- Supportive care
  - Fever/pain management
  - Hydration
  - Management of exacerbated illness (e.g., change in medication dose for asthma, COPD)
  - Oxygen
  - Supportive therapy (e.g., mucus clearance)
- Ribavirin (aerosolized)
  - Approved only for hospitalized infants/young children
  - Not recommended for routine use

Hurley L. https://clinicaloptions.com/CE-CME-program/rsv-in-older-adults/100002577; NLM. Medline Plus. https://medlineplus.gov/lab-tests/respiratory-syncytial-virus-rsv-tests/; Boukli N, et al. *Front Med (Lausanne)*. 2023;10:1161268; American Lung Association. https://www.lung.org/lung-health-diseases/lung-disease-lookup/rsv/rsv-in-adults; Hu M, et al. *Physiol Rev.* 2020;100:1527-1594; Cleveland Clinic. https://my.clevelandclinic.org/health/diseases/rsv-in-adults; Ribavirin for inhalation. Prescribing information. https://pi.bauschhealth.com/globalassets/BHC/PI/Virazole-PI.pdf.; American Academy of Pediatrics. https://publications.aap.org/redbook/book/347/chapter-abstract/5755493/Respiratory-Syncytial-Virus?redirectedFrom=fulltext.



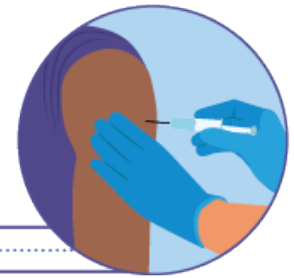
RSV Infection in Children and Older Adults

Incidence in Infants and Children	Incidence in Older Adults
• 69% with illness by one year and 97% with illness by two years	• Annual rates of illness 3%-7% in healthy older adults
• In children under five years, associated with – 15% of office visits for ARI – 20% of hospitalizations for ARI – 100 to 300 deaths	• In adults ≥60-65 years, associated with – 11% of outpatient visits for ARI – 6% of hospitalizations for ARI – 6,000-10,000 deaths

- Studies demonstrate increasing incidence of RSV illness with age in people ≥65 years old
- Infection can recur throughout life

ARI = acute respiratory infection; LRTI = lower respiratory tract infection

Glezen WP, et al. *Am J Dis Child*. 1986;140(6):543-546; Hall CB, et al. *N Engl J Med*. 2009;360(6):588-598; Falsey AR, et al. *N Engl J Med*. 2005;352:1749-1759; Belongia EA, et al. *Open Forum Infect Dis*. 2018;5(12):ofy316; Nowalk MP, et al. *Vaccine*. 2022;40(31):4121-4127; Tong S, et al. *J Glob Health*. 2020;10(2):020422. doi: 10.7189/jogh.10.020422; Kenmoe S, Nair H. *Curr Opin Infect Dis*. 2024;37:129-136; Hu M, et al. *Physiol Rev.* 2020;100:1527-1594. https://emergency.cdc.gov/han/2023/han00498.asp



Indications of Licensed RSV Vaccines for Adults

FDA-Approved Vaccines	Population	Indication(s)
GSK 's Arexvy (RSV vaccine, Adjuvanted)	**Older adults**	Active immunization for prevention of LRTD caused by RSV in • **individuals ≥60 years of age** • **Individuals 50-59 years at increased risk**
Pfizer's Abrysvo (RSV vaccine)	**Older adults**	Active immunization for prevention of LRTD caused by RSV in • **individuals ≥60 years of age** • **Individuals 18-59 years who are at increased risk**
	Maternal	Active immunization of **pregnant individuals** at 32-36 weeks gestational age for prevention of LRTD caused by RSV in infants from birth through 6 months of age
Moderna's Mresvia	**Older adults**	Active immunization for prevention of LRTD caused by RSV in **individuals ≥60 years of age**

Only vaccine approved for use in pregnant individuals

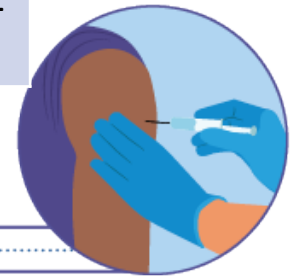
Note that this is not the same as public health recommendations

ARD = acute respiratory disease; LRTD = lower respiratory tract disease.

PATH. https://www.path.org/our-impact/resources/rsv-vaccine-and-mab-snapshot/;
GSK. https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Arexvy/pdf/AREXVY.PDF; Pfizer. https://labeling.pfizer.com/ShowLabeling.aspx?id=19589; Moderna. https://finance.yahoo.com/news/moderna-expands-field-mrna-medicine-103000511.html;
GSK. https://www.gsk.com/media/10948/press-release-arexvy-file-acceptance-us-50-59.pdf.

Features of Published Phase 3 Efficacy Trials for RSV Vaccines for Older Adults

Feature	RSVPreF3 OA (GSK) AReSVi-006 (NCT04886596)	RSVpreF (Pfizer) RENOIR (NCT05035212)	mRNA-1345 (Moderna) ConquerRSV (NCT05127434)
Control	Placebo	Placebo	Placebo
Participants, N	24,966	34,284	35,541
Randomization ratio	1:1 (single vaccine dose:placebo)	1:1 (single vaccine dose:placebo)	1:1 (single vaccine dose:placebo)
Mean age, y	69.5	68.3	68.1
High risk, %	Vaccine: 33.9[b] Placebo: 33.1[b]	Vaccine: 51.5[c] Placebo: 51.7[c]	Vaccine: 6.9[d] Placebo: 7.0[d]
Mean follow-up	6.7 months	7 months	112 days
Primary endpoint(s)/ outcome(s)	Efficacy preventing RSV-related LRT disease, confirmed by RT-PCR	Efficacy preventing RSV-associated LRT illness (confirmed by RT-PCR) with ≥2 or ≥3 signs or symptoms	Efficacy preventing RSV-associated LRT disease (confirmed by RT-PCR) with ≥2 or ≥3 signs or symptoms



Papi A, et al. *N Engl J Med*. 2023;388(7):595-560; Walsh EE, et al. *N Engl J Med*. 2023;388(16):1465-1477; Wilson E, et al. *N Engl J Med*. 2023;389(24): 2233-2244.

GSK RSVPreF3 OA Efficacy: Incidence of RSV-Related Lower Respiratory Tract Disease (LRTD)

Efficacy against LRTD

82.6% (96.95% CI, 57.9 to 94.1)

Episodes

- Vaccine group: 7/12,466
- Placebo group: 40/12,494

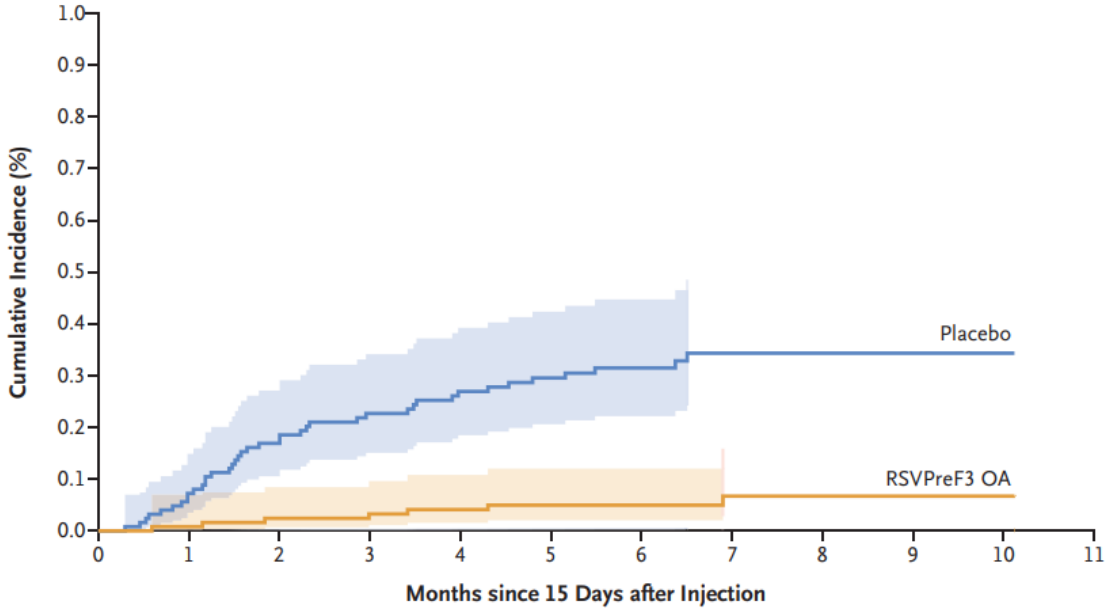
Efficacy against severe LRTD

94.1% (95% CI, 62.4 to 99.9)

Episodes

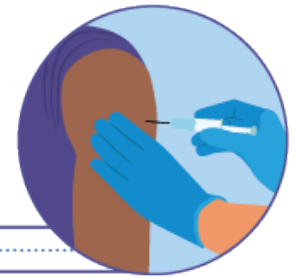
- Vaccine group: 1/12,466
- Placebo group: 17/12,494

Cumulative Incidence of RSV-Related LRTD



No. at Risk												
Placebo	12,494	12,403	12,290	11,887	11,640	11,022	8291	5464	2709	559	2	0
RSVPreF3 OA	12,466	12,392	12,286	11,892	11,655	11,046	8320	5495	2727	571	2	0

Cumulative No. of Cases												
Placebo	0	9	21	28	33	36	38	40	40	40	40	40
RSVPreF3 OA	0	1	3	4	5	6	6	7	7	7	7	7

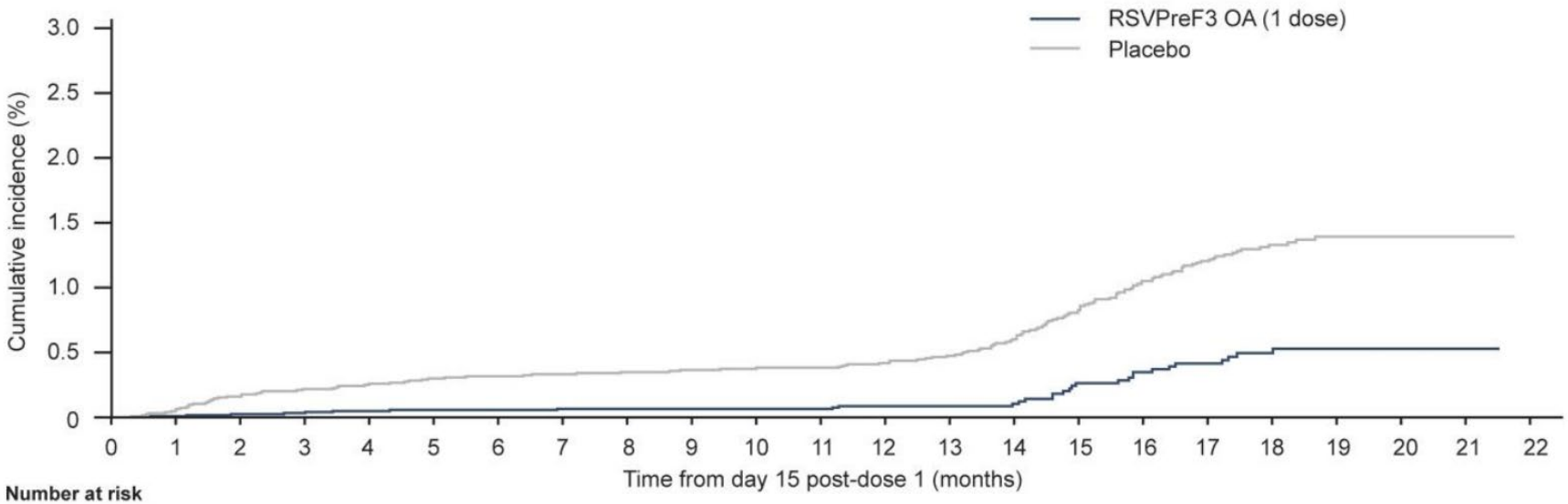


Papi A, et al. *N Engl J Med*. 2023;388(7):595-560; 2. Melgar M. Presented at the Advisory Committee on Immunization Practices meeting on February 23, 2023. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-02/slides-02-23/rsv-adults-04-melgar-508.pdf

GSK RSVPreF3 OA: Cumulative RSV Lower Respiratory Tract Disease (LRTD) Incidence with One Dose vs Revaccination Over 2 Seasons

- Efficacy in season 2 was similar with one dose in season 1 and second dose (revaccination) in season 2
- Revaccination within one year does not seem to provide additional efficacy benefit

RSV-LRTD After a Single Dose of RSVPreF3 OA

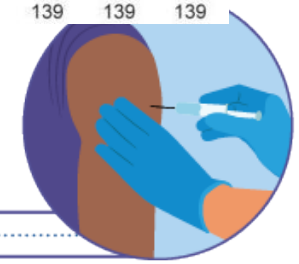


Number at risk

RSVPreF3 OA	12,469	12,393	12,339	12,294	12,255	12,213	12,160	12,115	12,006	11,876	11,266	10,020	8011	6540	5363	4836	4635	4046	2909	1652	685	49	0
Placebo	12,498	12,403	12,342	12,276	12,225	12,183	12,138	12,077	11,977	11,846	11,631	11,332	10,869	10,469	9857	9497	9219	8054	5761	3278	1382	95	0

Cumulative number of cases

RSVPreF3 OA	0	1	3	5	6	7	7	8	8	8	8	8	10	10	11	19	23	26	29	30	30	30	30
Placebo	0	8	20	27	32	37	39	41	43	45	47	47	51	57	70	92	113	127	136	139	139	139	139

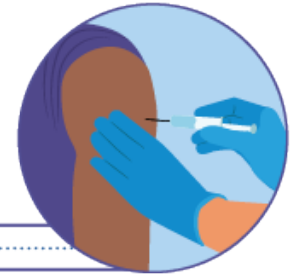


Ison MG, et al. *Clin Infect Dis*. 2024 Jan 22:ciae010. doi: 10.1093/cid/ciae010.

GSK RSVPreF OA: Safety and Tolerability

- No reported RSV- or treatment-related deaths in the clinical trial
- In the exposed group
  - More reported adverse events related to vaccine vs placebo (24.9% vs 5.8%)
    - Most were due to injection site reactions (pain, erythema swelling) or systemic reactions (fever, headache, fatigue, myalgia, arthralgia)
    - Most adverse events events were mild-to-moderate
  - Serious adverse events were balanced between groups
- Most common (≥10%) adverse reactions
  - Local: **injection site pain** (60.9%)
  - Systemic: **fatigue** (33.6%), **myalgia** (28.9%), **headache** (27.2%), **arthralgia** (18.1%)

Papi A, et al. *N Engl J Med*. 2023;388(7):595-560;
GSK. https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Arexvy/pdf/AREXVY.PDF.



Pfizer RSVpreF Efficacy: Prevention of RSV-Associated Lower Respiratory Tract Infection (LRTI)

Efficacy against LRTI with ≥2 signs or symptoms
66.7% (96.66% CI, 28.8 to 85.8)

Episodes

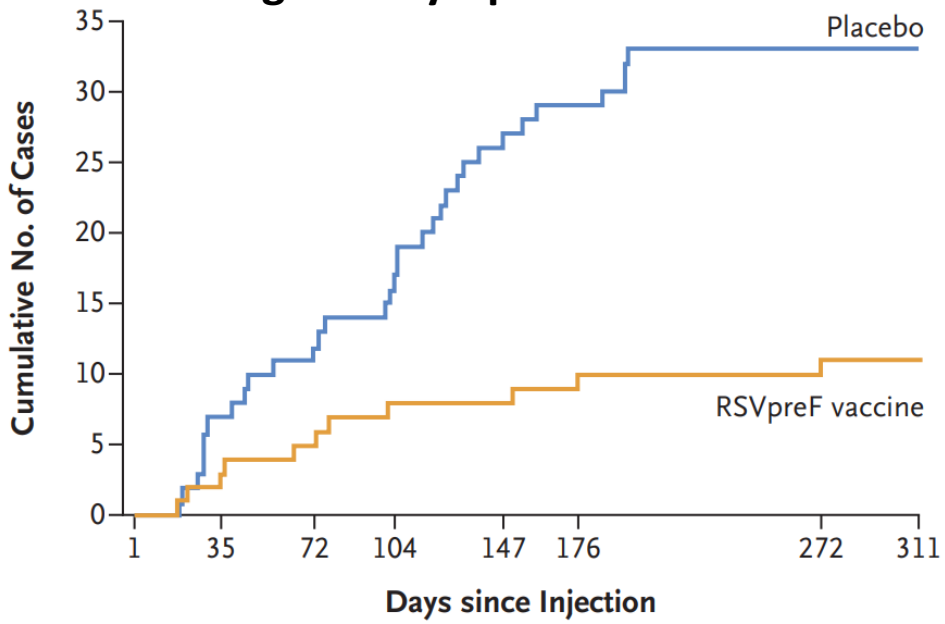
- **Vaccine group: 11**/17,215
- **Placebo group: 33**/17,069

Efficacy against severe LRTI ≥3 signs or symptoms
85.7% (96.6% CI, 32.0 to 98.7)

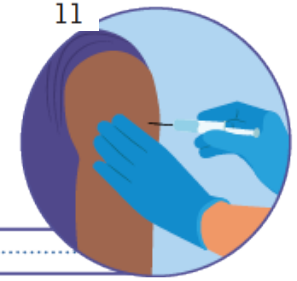
Episodes

- Vaccine group: 2/17,215
- Placebo group: 14/17,069

RSV-Associated Lower Respiratory Tract Illness with ≥2 Signs or Symptoms



Cumulative No. of Cases								
Placebo	0	7	12	17	27	29	33	33
RSVpreF vaccine	0	3	5	8	8	10	11	11

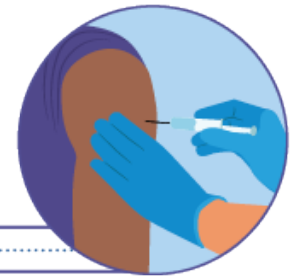


Walsh EE, et al. *N Engl J Med*. 2023;388(16):1465-1477; Melgar M. Presented at the Advisory Committee on Immunization Practices meeting on February 23, 2023. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-02/slides-02-23/rsv-adults-04-melgar-508.pdf

Pfizer RSVpreF: Safety and Tolerability

- No trial intervention-related deaths were reported
- In the exposed population
  - More reported local reactions with vaccine vs placebo (12% vs 7%)
  - Similar systemic event for vaccine vs placebo (27% vs 26%)
  - Balance in serious adverse events between groups (2.3% in each group)
- Most common (≥10%) adverse reactions in older adults
  - Older individuals: **fatigue** (15.5%), **headache** (12.8%), **injection site pain** (10.5%), **muscle pain** (10.1%)

Walsh EE, et al. *N Engl J Med*. 2023;388(16):1465-1477; Pfizer. https://labeling.pfizer.com/ShowLabeling.aspx?id=19589.



Moderna mRNA-1345: Prevention of RSV-Associated Lower Respiratory Tract Disease (LRTD)

Efficacy against LRTD with ≥2 signs or symptoms

83.7% (95.88% CI, 66.0 to 92.2)

Episodes

- Vaccine group: 9/17,572
- Placebo group: 55/17,516

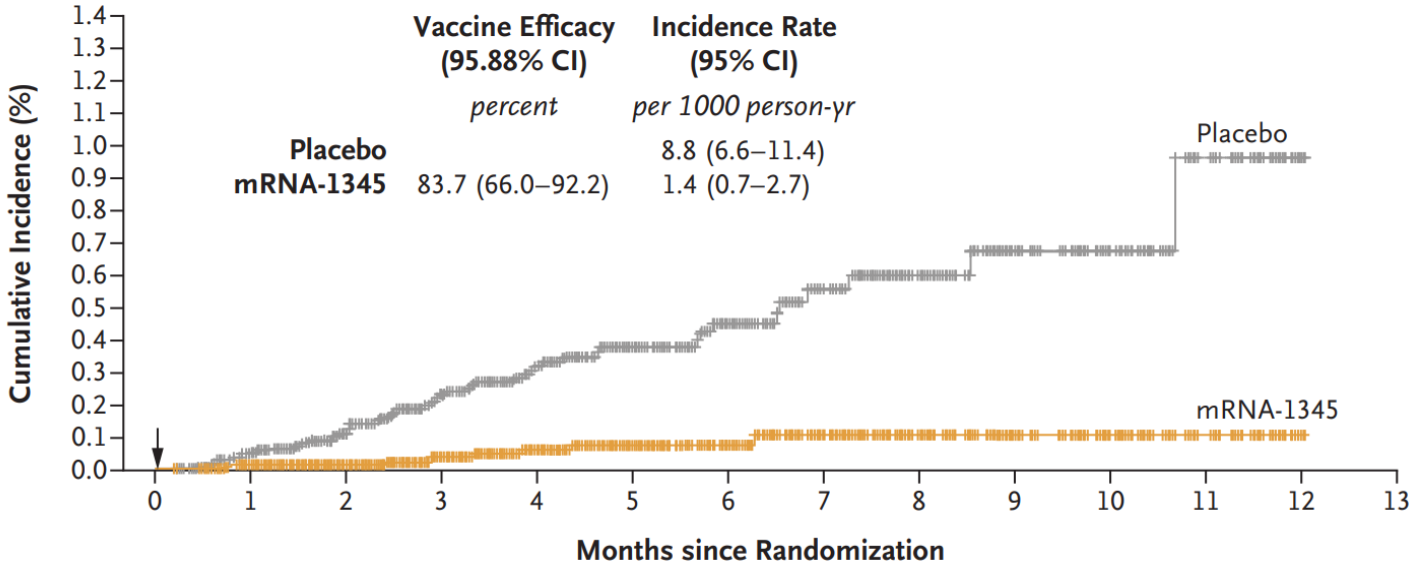
Efficacy against severe LRTD ≥3 signs or symptoms

82.4% (96.36% CI, 34.8 to 95.3)

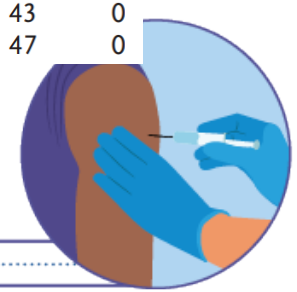
Episodes

- Vaccine group: 3/17,572
- Placebo group: 17/17,516

RSV-Associated Lower Respiratory Tract Disease with ≥2 Signs or Symptoms



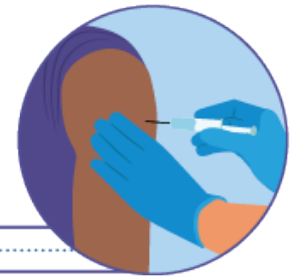
No. at Risk														
Placebo	17,516	17,433	14,735	11,275	7866	5314	3657	2384	1682	1058	629	267	43	0
mRNA-1345	17,572	17,514	14,783	11,293	7892	5333	3648	2389	1694	1062	645	273	47	0



Wilson E, et al. *N Engl J Med*. 2023;389(24): 2233-2244.

Moderna mRNA-1345: Safety and Tolerability

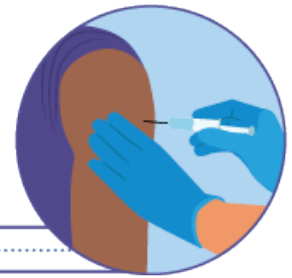
- No trial intervention-related deaths were reported
- In the safety population
  - More reported local reactions with vaccine vs placebo (58.7% vs 16.2%)
  - Systemic adverse reactions were reported in 47.7% of participants in the vaccine group vs 32.9% of participants in the placebo group
  - Balance in all unsolicited adverse events (20.4% in the vaccine group and 18.8% in the placebo group within 28 days after injection)
- Most common adverse reactions
  - Local: **injection site pain** (56.3% of vaccine participants, 13.7% of placebo participants)
  - Systemic: **fatigue, headache, myalgia, arthralgia**



Wilson E, et al. *N Engl J Med*. 2023;389(24): 2233-2244.

Guillain-Barré Syndrome (GBS) and RSV vaccines

- Guillain-Barre syndrome (GBS) is a rare neurological disorder that occurs when the body's immune system attacks the peripheral nerves, causing muscle weakness, numbness, and sometimes paralysis
  - In Pfizer trials: 20,255 recipients ≥60 years, 2 cases of Guillain-Barré syndrome (GBS) were observed within 42 days of vaccination
  - In GSK trials: 18,304 recipients ≥60 years, 1 case of GBS was within 42 days of vaccination
  - Moderna trials: no cases of GBS
  - Cases occurred in age groups at increased risk for this syndrome
  - There are too little data to determine whether there is a link between Guillain-Barre and RSV vaccine
- Post-licensure safety monitoring is ongoing and has found no conclusive evidence of a causal association
- Based on the available data, ACIP and CDC continue to conclude that the *"benefits of RSV vaccination, in terms of preventable hospitalizations and deaths, outweigh the potential risk for GBS, among adults ages 75 years and older and among adults ages 60-74 years at increased risk of severe RSV disease"*

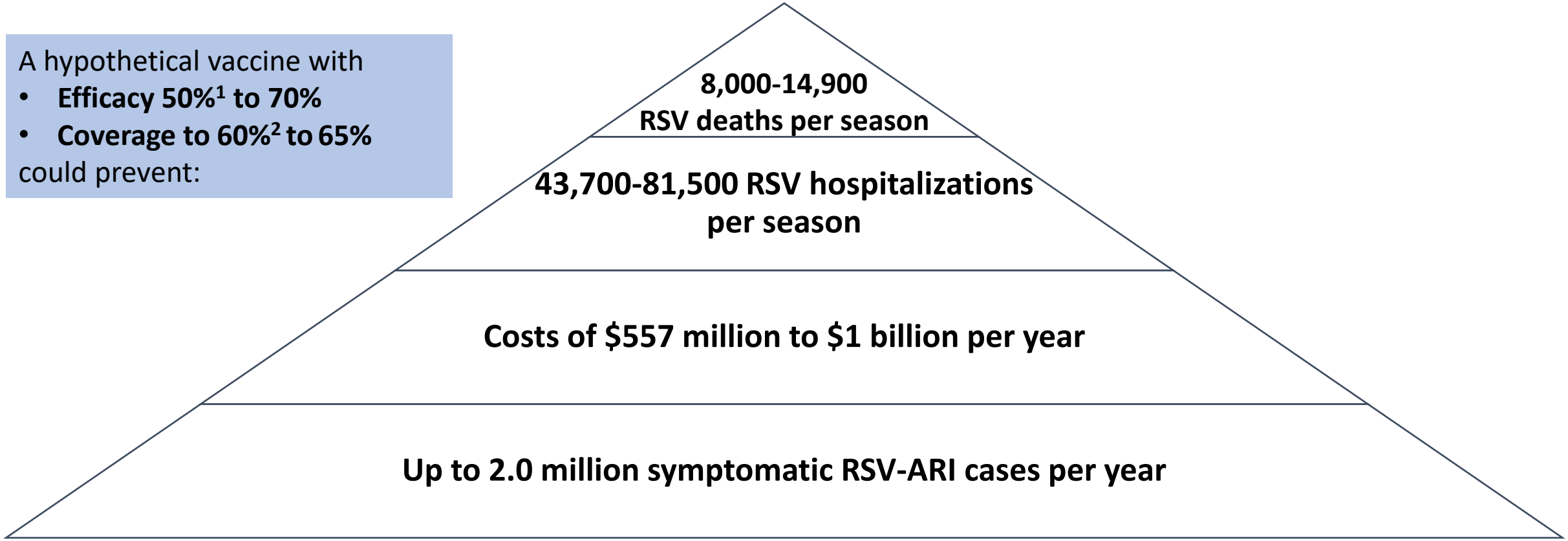


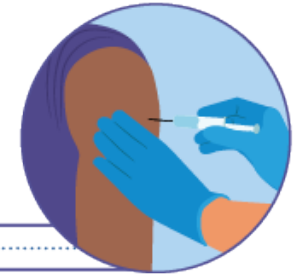
https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2024-02-28-29/05-RSV-Adults-Shimabukuro-508.pdf

Estimated Benefits of US RSV Vaccination in Older Adults (≥ 60 Years Old)

A hypothetical vaccine with
- **Efficacy 50%[1] to 70%**
- **Coverage to 60%[2] to 65%**

could prevent:

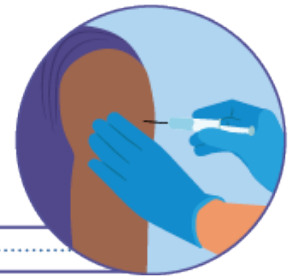




Herring WL, et al. *Vaccine*. 2022;40:483-493; 2. Van Effelterre T, et al. *Clin Infect Dis*. 2023;77(3):480-489.

ACIP RSV Vaccine Recommendations

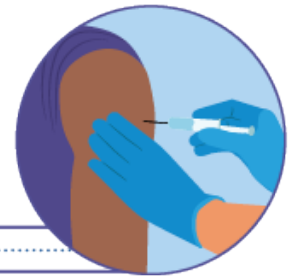
- Three RSV vaccines are licensed by the U.S. Food and Drug Administration for use in adults ages 60 and older in the United States and in adults 18 and older with risk factors
  - CDC recommends everyone ages 75 and older get an RSV vaccine.
  - CDC recommends adults ages 60–74 who are at increased risk of severe RSV disease get an RSV vaccine.
- If you have already received an RSV vaccine, you do not need to get another one at this time.
  - Continued evidence of protection into the third year and studies continue
- You can be vaccinated at any time, but the best time is in late summer and early fall
- One dose is all that is recommended at this time



https://www.cdc.gov/rsv/vaccines/older-adults.html

Which adults 60–74 are at increased risk of severe RSV?

- Conditions that increase your risk for severe illness include:
- Chronic heart or lung disease
- Weakened immune system
- Certain other medical conditions, including some people with diabetes and some people with obesity
- Living in a nursing home
- ***Patient attestation is sufficient evidence of the presence of a risk factor. Vaccinators should not deny RSV vaccination to a person because of lack of medical documentation.***

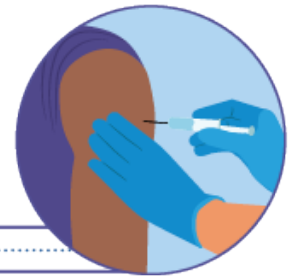


https://www.cdc.gov/rsv/vaccines/older-adults.html

Who Pays for RSV Vaccines for Older Adults

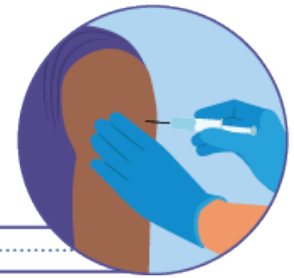
- **Private health plans** are required to cover new ACIP vaccine recommendations in the next plan year (some may in this year).
  - Health Insurance Marketplace plans and most other private insurance plans must cover recommended RSV vaccine without charging a copayment or coinsurance when provided by an in-network provider.
  - This is true even for patients who have not met a yearly deductible.
- **Medicare Part D**: all adult vaccines recommended by ACIP (except those covered by Part B) available at no cost
- **Medicaid**: all adult vaccines recommended by ACIP (except those covered by Part B) available at no cost
- **Military**: all vaccines are covered
- **No insurance**: Some health departments make vaccine available. Otherwise, an example of costs (CVS website): $295.00 for Pfizer ABRYSVO & $280.00 for GSK Arexvy

https://www.cdc.gov/vaccines-adults/recommended-vaccines/how-to-pay-adult-vaccines.html



Who should not get an RSV vaccine?

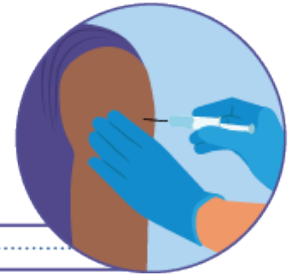
- You should not get an RSV vaccine if you've ever had a severe allergic reaction to any component of the vaccine.
- Information about the three available RSV vaccines can be found in the manufacturer's package inserts for GSK's Arexvy, Moderna's mResvia, and Pfizer's Abrysvo.



https://www.cdc.gov/rsv/vaccines/older-adults.html

When and how often to vaccinate

- One dose of RSV vaccine provides protection against RSV disease for at least two years.
- Because Arexvy and Abrysvo were licensed by FDA in May 2023 and mResvia was licensed in June 2024, we are still learning about how long they protect
- Vaccine can be given any time, but the best time to get vaccinated is in late summer and early fall before RSV usually starts to spread in the community.
  - moderate or severe illness: wait until recover
  - minor illness: ok to vaccinate
- The RSV vaccine is not currently an annual vaccine, one dose is all that is recommended at this time



https://www.cdc.gov/rsv/vaccines/older-adults.html

Knowledge ReChecks 1-2

Answer via QR code →

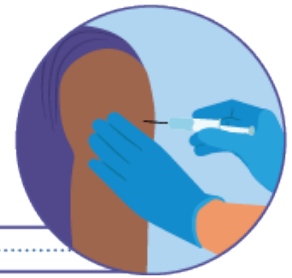
1. Your 75-year-old patient describes having a cold that "seems to have gotten really bad." They think they caught it from their 2-year-old grandchild, who recently had nasal congestion, a runny nose, and a fever. However, your patient has symptoms of lower respiratory tract disease (LRTD), with coughing, substantial mucus production, and shortness of breath.

Which change in affected airways has been associated with development of an RSV-related illness?

A. Airway hyporeactivity
B. Debris accumulation
C. Greater surfactant production
D. Increased mucociliary transport
E. Neutrophil sloughing

2. What is the estimated annual rate of RSV-related illness in healthy older adults (≥ 65 years old)?

A. Less than 1%
B. 3%-7%
C. 9%-12%
D. 15%-17%
E. Greater than 20%



Knowledge ReChecks 3-4

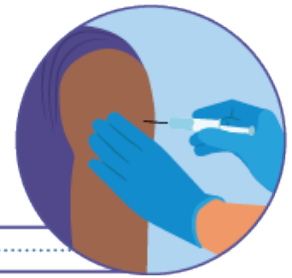
Answer via QR code →

3. You have 4 adult patients scheduled for annual wellness exams this morning. According to recent recommendations from the Centers for Disease Control and Prevention (CDC), which of the following people should receive an RSV vaccine?

A. The healthy 45-year-old patient who requests an RSV vaccine so her record is up to date for travel
B. The patient who is 65 years old and lives with grandchildren who are 10-12 years old
C. The patient who is 77 years old and lives in a long-term care facility
D. The patient who is 70 years old, generally healthy, and has no cardiovascular or pulmonary conditions

4. In the US, the number of RSV-associated hospitalizations per year for children < 5 years of age is 58,000-80,000. What is the approximate number of RSV-associated hospitalizations per year for older adults (≥ 65 years of age) in the US?

A. 300
B. 1,550
C. 68,000
D. 177,000
E. 2,200,000

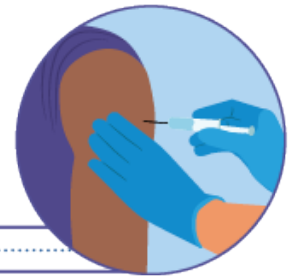


Knowledge ReCheck 5

Answer via QR code →

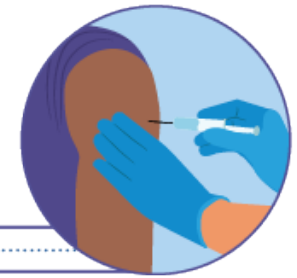
A healthy 60-year-old patient with knee osteoarthritis and hearing impairment, but no other chronic medical conditions, has an office visit for a wellness check. Their youngest grandchild was very ill with RSV last winter, so they'd like to learn more about the vaccines they've heard advertised. Which of the following is correct and appropriate to share with the patient, based on product prescribing information and evidence-based recommendations from the Centers for Disease Control and Prevention (CDC)?

A. The best time to get vaccinated is early winter, when RSV infections typically peak
B. If the vaccine is given in spring or summer, a booster is recommended in early winter
C. RSV vaccines are recommended for people who are 60 years old only if they are at risk for severe RSV-related illness
D. RSV vaccines should not be administered with other vaccines
E. RSV vaccines are only indicated for individuals with chronic cardiopulmonary conditions



Thank You!

Please provide feedback on this session here



Preventing Community Acquired Respiratory Viruses Through Vaccination

Michele Maison-Fomotar, MD, MSc TMIH, DTMH

Assistant Clinical Professor

Infectious Diseases

UCSF Fresno

Disclosures

- I have the following relationships with ACCME defined ineligible companies:
- **None**
- I **WILL NOT** discuss off-label use and/or investigational use of any drugs or devices.

Objectives

Describe

Describe the impact of respiratory viruses on health with emphasis on RSV, COVID 19 and influenza viruses

Review

Review updated recommendations for RSV, COVID 19 and influenza vaccinations and nirsevimab use for RSV

Discuss

Discuss the role of vaccine hesitancy in vaccination uptake and recommend counter strategies

Covid and flu rates rise across the US, according to the CDC

Less than half of Americans planned to get Covid vaccine in 2024, and slightly more than half planned to get flu shot

'ang

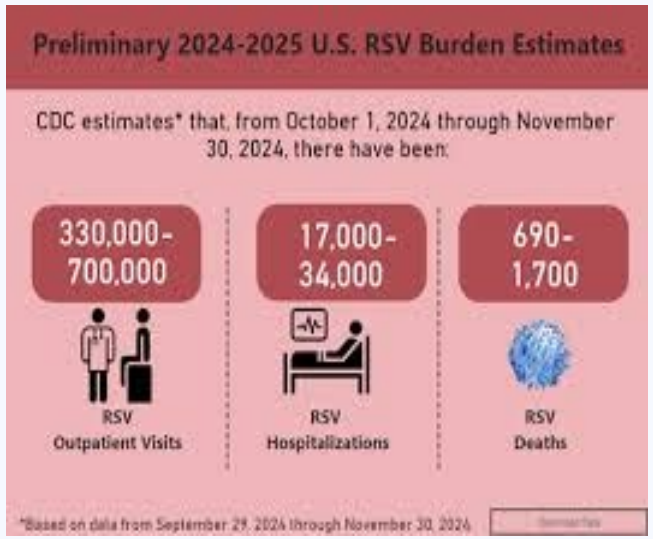
2025 13.56 EST

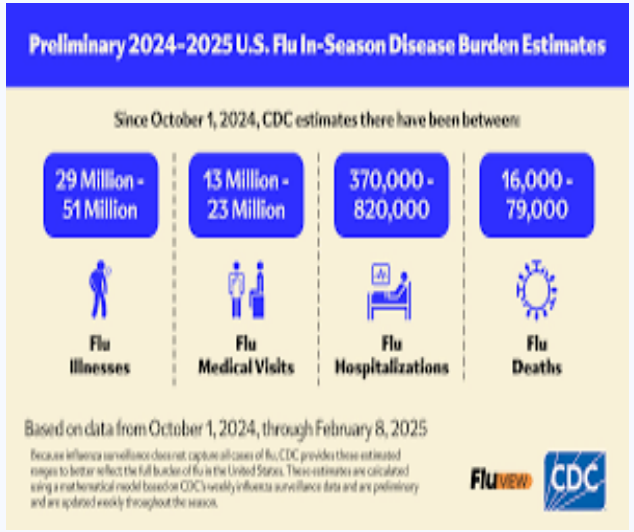
hare

The CDC recommends the seasonal flu shot and the Covid vaccine for everyone aged six months and older. Photograph: Xinhua/Rex/Shutterstock

• Theguardian.com

Burden of respiratory infections





- Major cause of illness, hospitalizations and deaths; especially COVID-19, RSV, Influenza
- Severe disease more likely in infants and older patients
- Strain on healthcare resources, especially during seasonal outbreak
- Importance of understanding this burden is key for better prevention and management

• Ramirez JA et al. Clin Infect Dis 2017, CDC. gov

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Respiratory viruses - overview

Orthomyxoviridae

- Influenza viruses A and B

Pneumoviridae

- Respiratory syncytial virus (RSV)
- Human metapneumovirus

Paramyxoviridae

- Parainfluenza

Corona viruses – SARS, MERS

Rhinoviruses

Adenoviruses

Bocaviruses

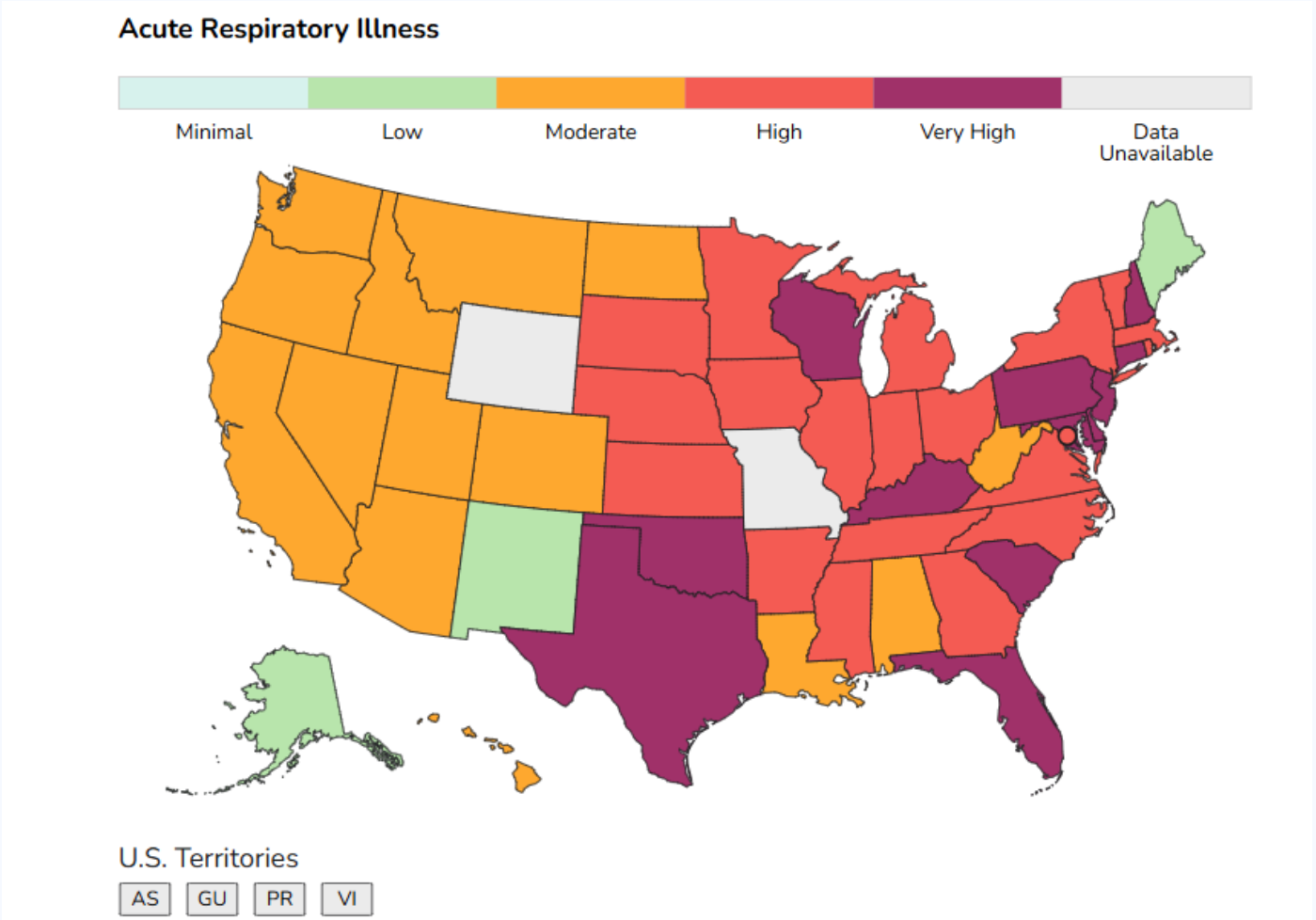
• Boncristiani HF, et al.. Encyclopedia of Microbiology. 2009

Significant impact in patients with underlying heart and lung disease

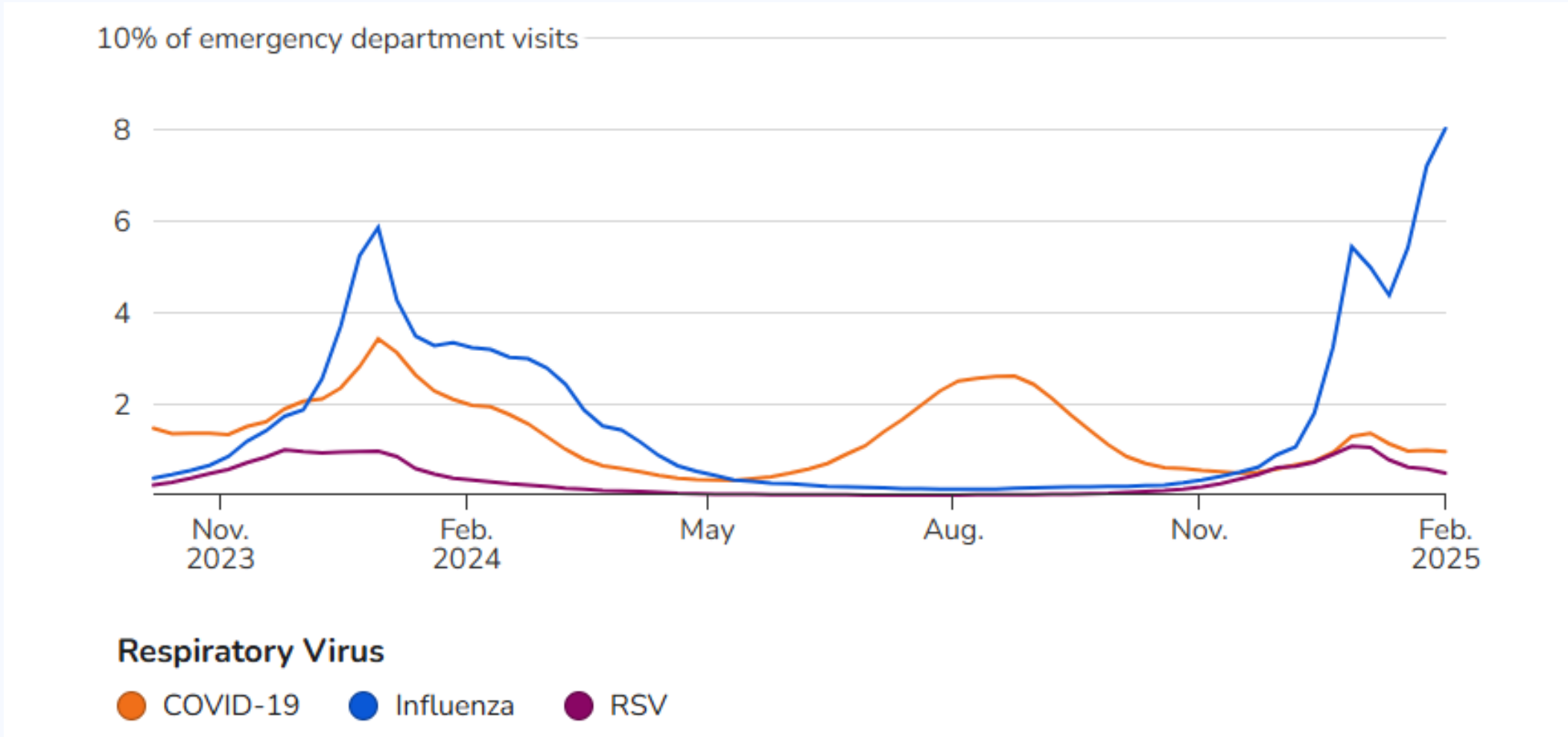
- Burden in patients with cardiovascular disease:
  - Higher risk of severe complications and mortality
  - Increased incidence of heart attacks and strokes post-infection
  - Common infections (influenza, COVID-19) contribute to heart failure exacerbations

- Burden in patients with pulmonary disease:
  - COPD and asthma patients experience worsened symptoms and increased hospitalizations.
  - Pneumonia and RSV cause prolonged exacerbations and lung function decline.
  - Increased ventilatory support and ICU admissions

• Modin D et al. Circulation, 2009; Panhwar MS et al. *JACC Heart Fail* 2019, CDC.gov



- data.cdc.gov. Accessed February 12th 2025



• data.cdc.gov. Accessed February 12th 2025

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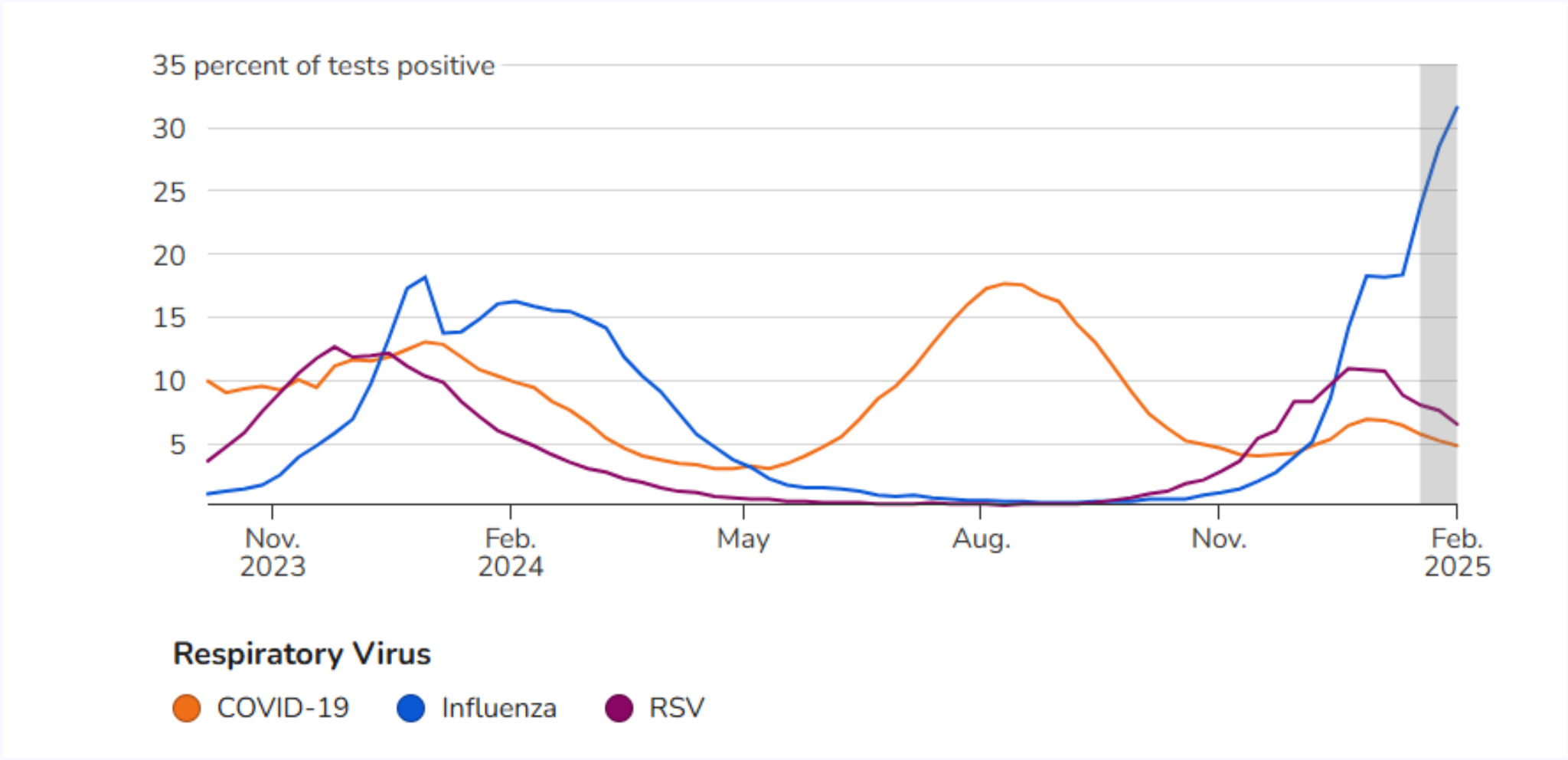

• data.cdc.gov. Accessed February 12th 2025

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Strategies to avoid respiratory infections

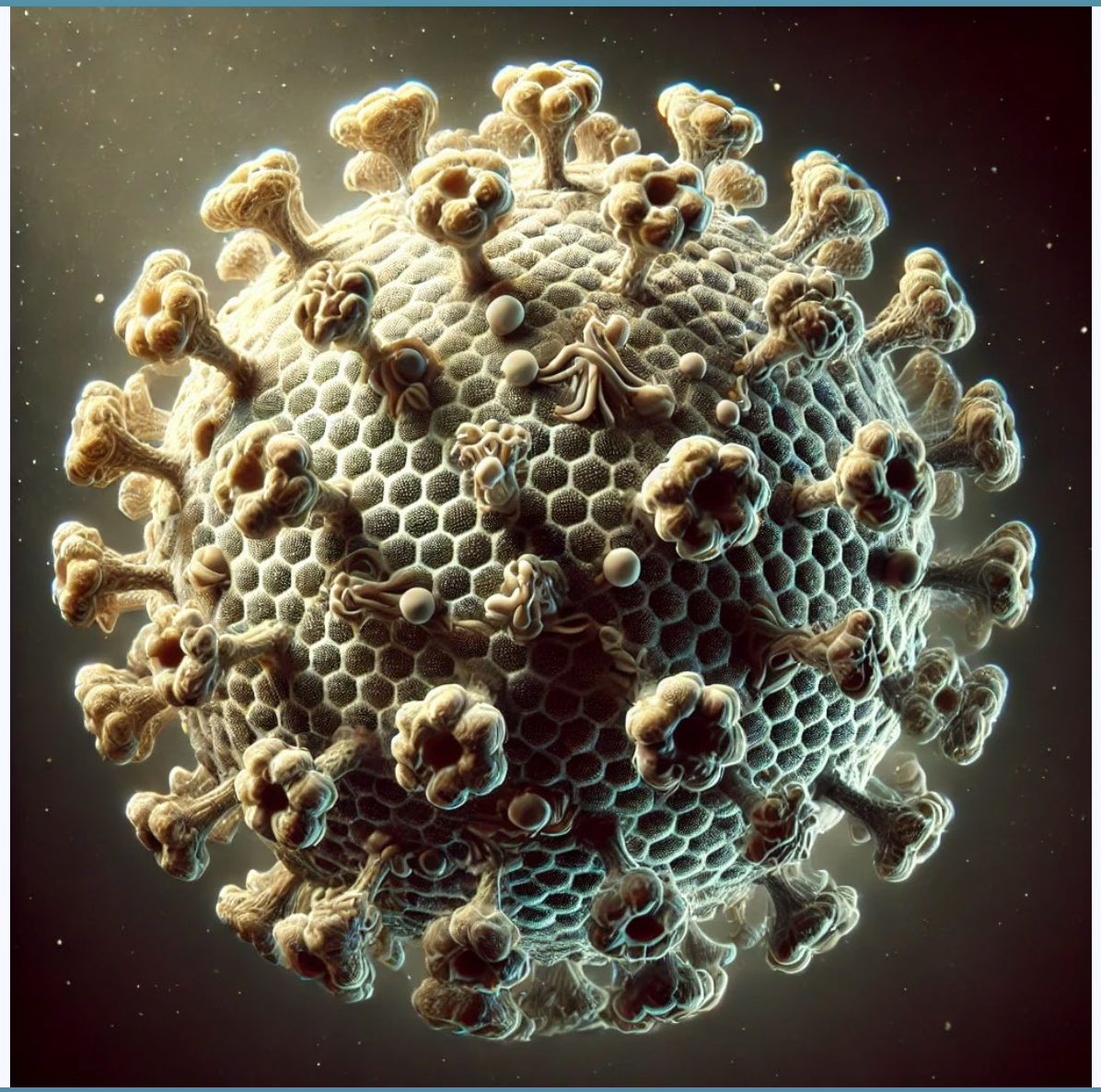
Avoid exposure

Vaccination

Symptom-triggered medication

• Cerrato P, Mawhorter S. Cleve Clin J Med 2025

Influenza



Influenza

About 5% to 20% of all US residents have influenza every year.

120,000 to 710, 000 hospitalizations/ year for influenza-related complications

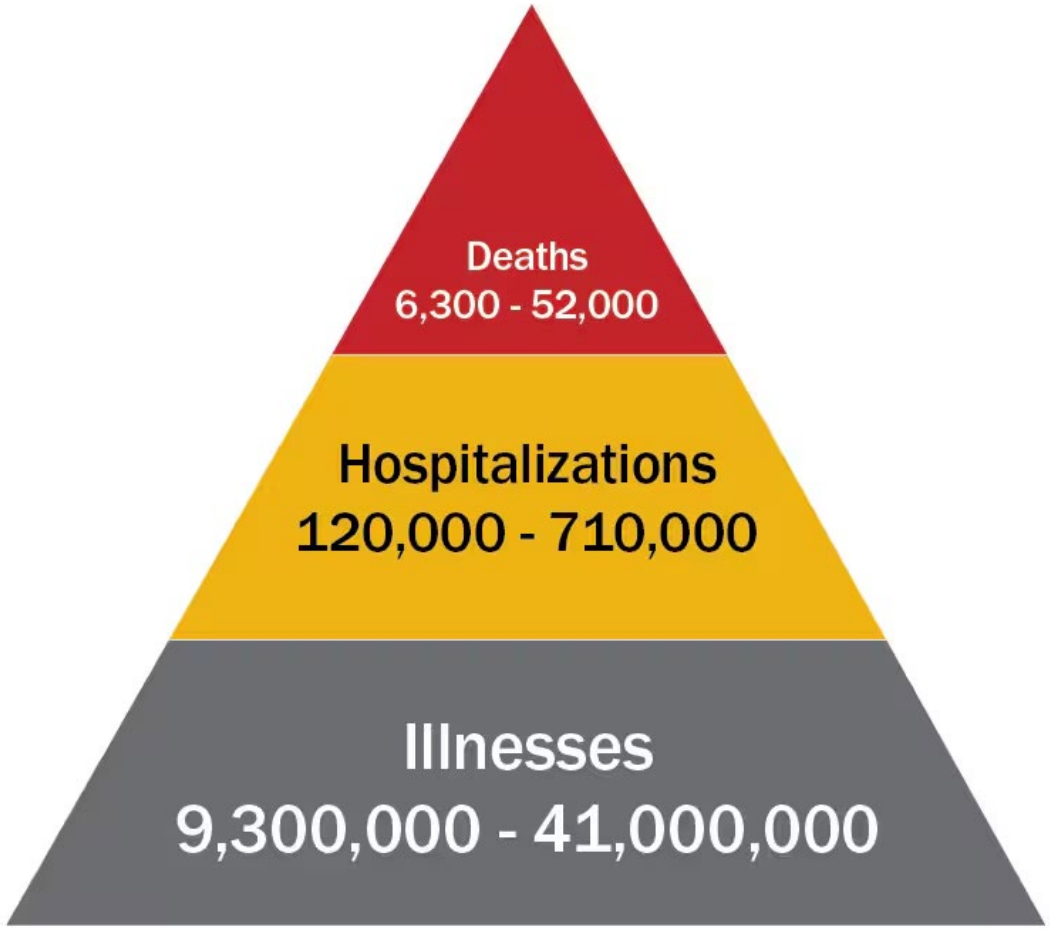
Nearly $90 billion/year in medical expenses, lost workdays due to illness, and deaths

Influenza vaccine reduces risk of serious complications and possibly death

ACC/AHA- Influenza vaccination is recommended as part of secondary prevention in children and adults with coronary and other atherosclerotic vascular disease

Four genera of influenza viruses:

- Influenza A- Most virulent; infect mammalian and avian species
- Influenza B viruses- Less severe; exclusive to humans
- Influenza C- mainly human reservoir; causes mild illness
- Influenza D- swine reservoir



- CDC.gov, ACC.gov

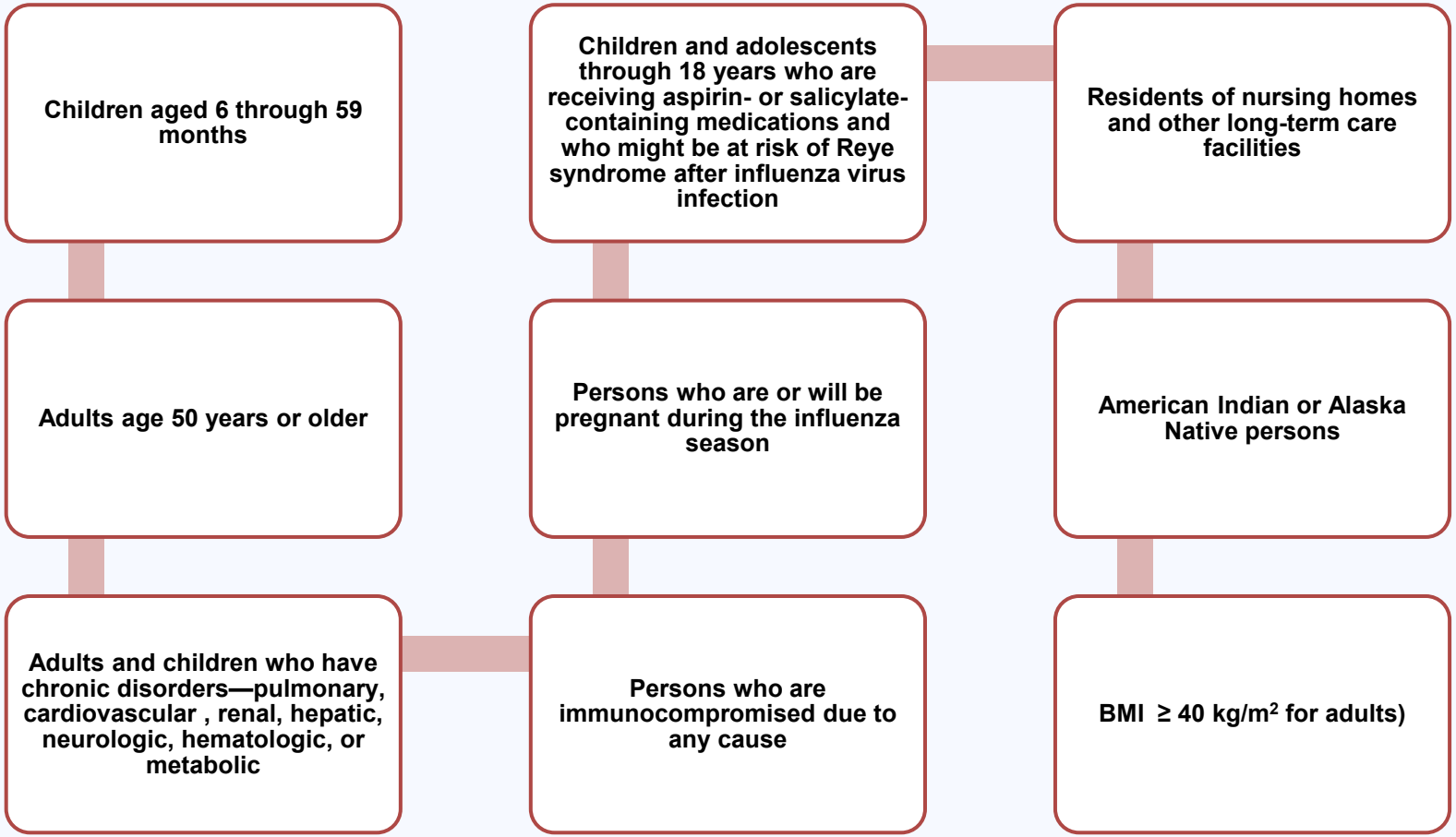
Four genera of influenza viruses:

- Influenza A- Most virulent; infect mammalian and avian species
- Influenza B viruses- Less severe; exclusive to humans
- Influenza C- mainly human reservoir; causes mild illness
- Influenza D- swine reservoir

Influenza A	Influenza B
• Subtypes based on 2 main surface proteins: **Hemagglutinin (HA)** and **Neuraminidase (NA)** • Antibody response mostly directed towards HA • NA antibodies do not prevent infection but can mitigate disease severity • Main circulating strains: **H1N1** and **H3N2**	• B/Victoria • B/Yamagata **The B/Yamagata strain has been removed from current vaccines as no longer detected globally since March 2020**

Wolff T, Veit M. Encyclopedia of Virology. 2021;
cdc.gov/flu

Groups at high risk for severe influenza



Influenza Vaccine products

The 2024-2025 seasonal influenza vaccine is trivalent, with hemagglutinin from 3 strains:

- Influenza A/Victoria/4897/2022 (H1N1) or influenza A/Wisconsin/67/2022 (H1N1)
- Influenza A/Thailand/8/2022 (H3N2) or influenza A/Massachusetts/18/2022 (H3N2)
- Influenza B/Austria/1359417/2021 (Victoria lineage)

Quadrivalent influenza vaccine is no longer used. The B/Yamagata strain has been removed as no longer detected globally since March 2020

- Three types of influenza vaccines are available:
- Inactivated vaccine (egg-based)
- Recombinant vaccine (not egg-based)
- Live attenuated vaccine (Inhaled)

Influenza Vaccine Products for the 2024–2025 Influenza Season

Manufacturer	Trade Name (vaccine abbreviation)[1]	How Supplied	Mercury Content (mcg Hg/0.5mL)	Age Range	CVX Code	Vaccine Product Billing Code[2] CPT
AstraZeneca	FluMist (LAIV3)	0.2 mL (single-use nasal spray)	0	2 through 49 years	111	90660
GSK	Fluarix (IIV3)	0.5 mL (single-dose syringe)	0	6 months & older[3]	140	90656
	FluLaval (IIV3)	0.5 mL (single-dose syringe)	0	6 months & older[3]	140	90656
Sanofi	Flublok (RIV3)	0.5 mL (single-dose syringe)	0	18 years & older	155	90673
	Fluzone (IIV3)	0.5 mL (single-dose syringe)	0	6 months & older[3]	140	90656
		0.5 mL (single-dose vial)	0	6 months & older[3]	140	90656
		5.0 mL multi-dose vial (0.25 mL dose)	25	6 through 35 months[3]	141	90657
		5.0 mL multi-dose vial (0.5 mL dose)	25	6 months & older	141	90658
	Fluzone High-Dose (HD-IIV3)	0.5 mL (single-dose syringe)	0	65 years & older[4]	135	90662
CSL Seqirus	Afluria (IIV3)	5.0 mL multi-dose vial (0.25 mL dose)	24.5	6 through 35 months[3]	141	90657
		5.0 mL multi-dose vial (0.5 mL dose)	24.5	3 years & older[5]	141	90658
		0.5 mL (single-dose syringe)	0	3 years & older[3]	140	90656
	Fluad (aIIV3)	0.5 mL (single-dose syringe)	0	65 years & older[4]	168	90653
	Flucelvax (ccIIV3)	0.5 mL (single-dose syringe)	0	6 months & older[3]	153	90661
		5.0 mL multi-dose vial (0.5 mL dose)	25	6 months & older[3]	320	90661

Influenza vaccine recommendation

- Routine annual influenza vaccination is recommended for all persons aged ≥6 months who do not have contraindications.
- Timing:
  - Most adults and pregnant women in first 2 trimesters of pregnancy: Start September or October, continue throughout flu season
  - Pregnant women in 3rd trimester- can consider in July and August
- Live attenuated influenza vaccine is not recommended in pregnancy or for immunocompromised persons
- Children 6 months to 8 years who need 2 doses: Receive 1st dose as soon as vaccine is available
- **It is never too late to get the flu shot! Vaccinate throughout the season as long as influenza viruses are circulating**

Influenza vaccination- older adults

- Adults 65 and older should receive an enhanced influenza vaccine (i.e. either a high-dose formulation of inactivated or recombinant influenza vaccine, or adjuvanted influenza vaccine), if these are available

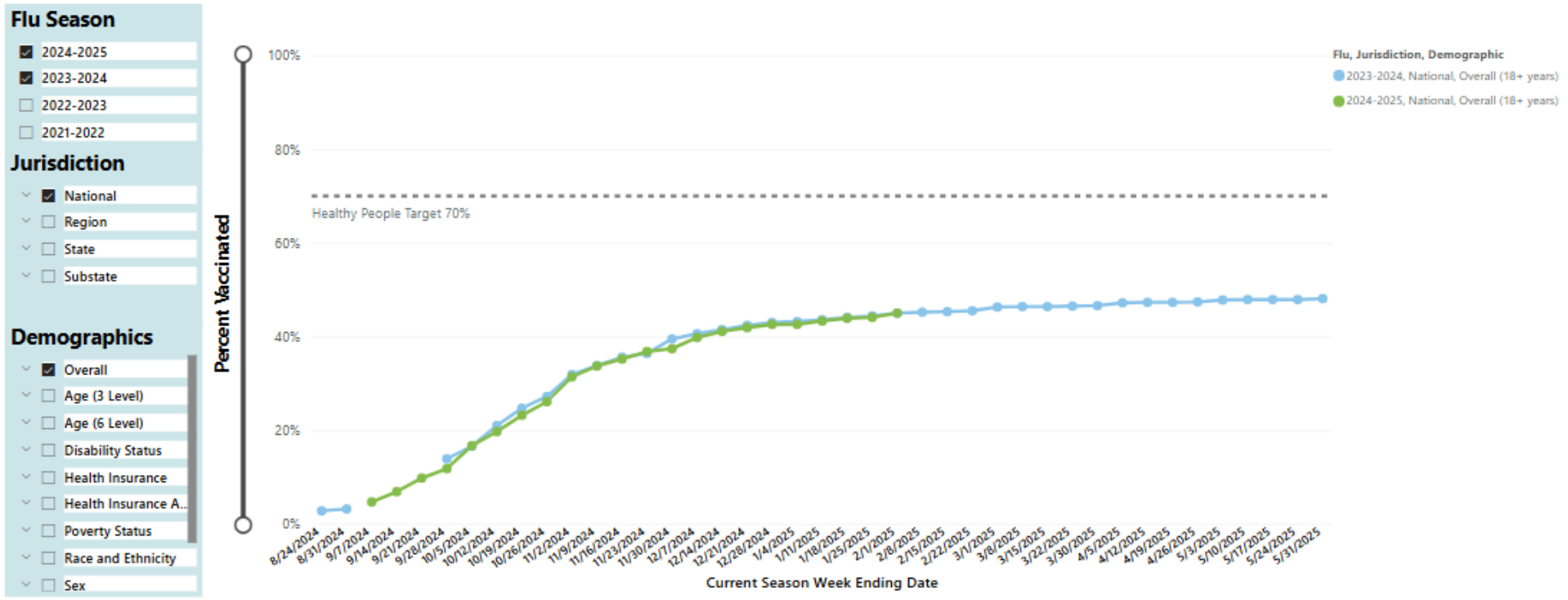
- Live attenuated influenza vaccine is not recommended for immunocompromised persons.

Grohskopf LA,, et al. United States, 2024–25 Influenza Season. MMWR Recomm Rep 2024;73(No. RR-5):1–25

Influenza vaccination coverage

Figure 4A. Influenza Vaccination Coverage, Overall by Selected Demographics, 2024-25 and Jurisdiction, Among Adults 18 Years and Older *,†,‡,§,±

Data Source: National Immunization Survey–Adult COVID Module



- https://www.cdc.gov/fluvaxview/dashboard/adult-coverage.html

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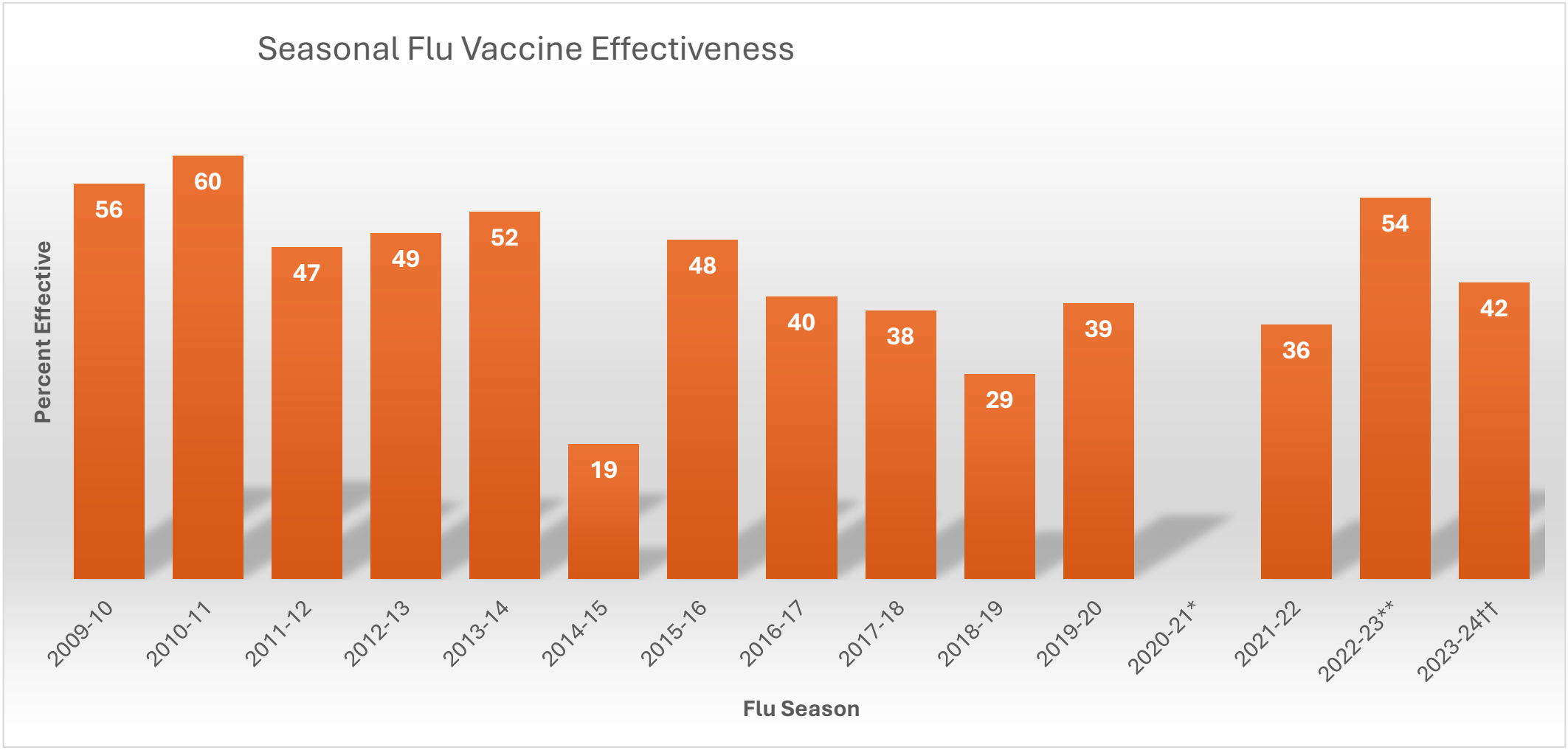
Effectiveness of Seasonal Flu Vaccines from the 2005 – 2024 Flu Seasons



Source: https://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm

*2020-21 flu vaccine effectiveness was not estimated due to low flu virus circulation during the 2020-2021 flu season.
**In a Wisconsin study among patients aged 6 months to 64 years, VE was 54% against medically attended outpatient acute respiratory illness (ARI) associated with laboratory-confirmed influenza A.
†† VE estimates for 2022-2023 flu season are preliminary.

Common myths with the flu vaccine

- Influenza is not serious so I don't need the vaccine
- The flu vaccine can give me the flu
- The flu vaccine can cause severe side effects
- I had the vaccine and still got the flu, so it doesn't work
- I am pregnant so shouldn't get the flu vaccine

Flu vaccine and egg allergies

- Individuals with egg allergies:
  - Any influenza vaccine (egg-based or non-egg based) can be used
  - Egg allergy alone does not need any additional safety measures for flu vaccination of people beyond those recommended for receipt of any vaccine, **regardless of the severity of previous reaction to egg**

Grohskopf LA,, et al. United States, 2024–25 Influenza Season. MMWR Recomm Rep 2024;73(No. RR-5):1–25

Guillain-Barre Syndrome

- Individuals with history of Guillain-Barre Syndrome (GBS) within 6 weeks of getting an influenza vaccine have a "**precaution for influenza vaccine**" and should discuss potential risks and benefits before getting any future influenza vaccine doses
  - As an alternative to vaccination, providers might consider using influenza antiviral chemoprophylaxis for these persons

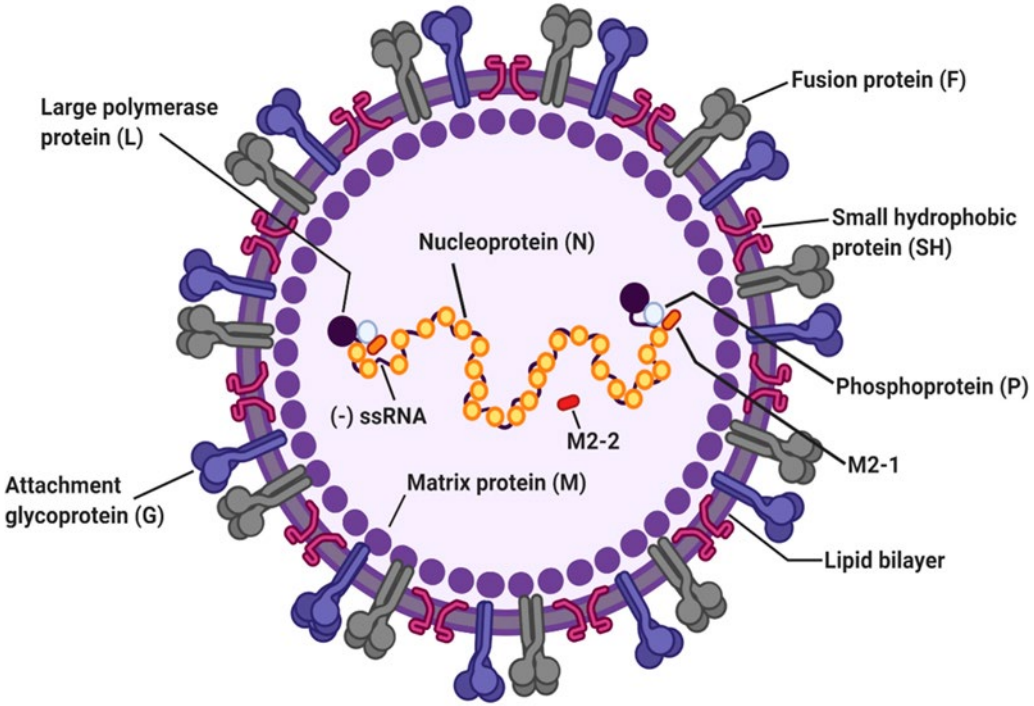
- History of GBS NOT associated with an influenza vaccine is neither a precaution nor a contraindication for influenza vaccine

Grohskopf LA,, et al. United States, 2024–25 Influenza Season. MMWR Recomm Rep 2024;73(No. RR-5):1–25

Respiratory Syncytial Virus (RSV)

RSV

- Very common and highly infectious virus
- Most common cause of acute lower respiratory tract infections and hospitalizations in children under 2 years
- 33 million cases of acute lower respiratory tract infections
- 3.6 million hospitalizations, mostly in infants under 6 months
- Over 100,000 deaths in children under 5 years
- The annual attack rate for older adults generally ranges between 3% to 10%, resulting in an estimate of over 177,000 hospitalization and 14,000 deaths in older adults in the United States every year



- Li Y, et al. Lancet,2022; Landi SN et al. JAMA Netw Open. 2024 ; WHO.int, Jung, H.E. et al. *Viruses* **2020**

Severe disease risk in infants and young children:

- Age < 6 months
- Premature infants
- Suppressed or weakened immune systems
- Neuromuscular disorders or congenital anomaly
- Severe cystic fibrosis

Severe disease risk on adults 60 and older:

- Chronic cardiovascular disease (e.g. Heart failure, coronary artery disease, congenital heart disease)
- Chronic lung disease (COPD, asthma, cystic fibrosis)
- End stage renal disease
- Diabetes complicated by CKD, neuropathy, end organ damage
- Neurologic conditions causing impaired airway clearance
- Chronic liver disease
- Chronic hematologic disease
- Severe obesity
- Residence in a nursing home

• CDC.gov

RSV vaccination timeline

May 2023:

RSV vaccines by GSK (Arexvy) and Pfizer (Abrysvo) were approved by the FDA in for adults 60 years and older

June 2023:

Advisory Committee on Immunization Practices (ACIP) recommended RSV vaccines for people 60 years and older

May 2024:

FDA approved Mresvia (Moderna) for use in adults 60 years and older

June 2024:

Arexvy licensed by FDA for use in people 50-59; no vote yet by ACIP to recommend Arexvy for this population

• ACIP

RSV vaccine products

- **Abrysvo, Pfizer**
  - Recombinant RSV F protein antigen
  - Vaccine Efficacy (VE): 66.7%;(96.66% [CI], 28.8 to 85.8)

Arexvy, GSK

- Recombinant RSV F protein antigen and AS01 adjuvant
- VE: Overall, 82.6%, older adults with underlying medical condition 94.6%

mRESVIA, Moderna

- Unadjuvanted modified mRNA encoding RSV F protein
- VE: 83.7%

CDC does not have a preferential recommendation for adults 60 years and older; they may receive whichever vaccine is available

- Papi A et al. NEJM 2023; Walsh EE et al. NEJM 2023; Wilson E et al. NEJM 2023; CDC.gov

RSV vaccination for adults

- Prior ACIP recommendation:

  "Adults aged ≥60 years may receive a single dose of RSV vaccine, using shared clinical decision-making."

Current recommendation (Update August 2024)

CDC recommends **a single dose of RSV vaccine :**

- For all adults ages **75 and older** , and
- For adults ages **60–74 who are at increased risk of severe RSV**

RSV immunization in pregnant women and infants

- Pregnant women for are between 32 – 36 weeks 6 days gestation:
  - Recommend 1 dose of Pfizer's Abrysvo (from September through January)

- Pregnant women 37 weeks pregnant:
  - DO NOT VACCINATE (not enough time for antibodies to develop, cross the placenta and protect infant)
  - Give monoclonal antibody **(Nirsevimab)** to the infant just before or at the start of the RSV season

- No need to re-vaccinate for subsequent pregnancies once appropriate maternal RSV vaccine has been given

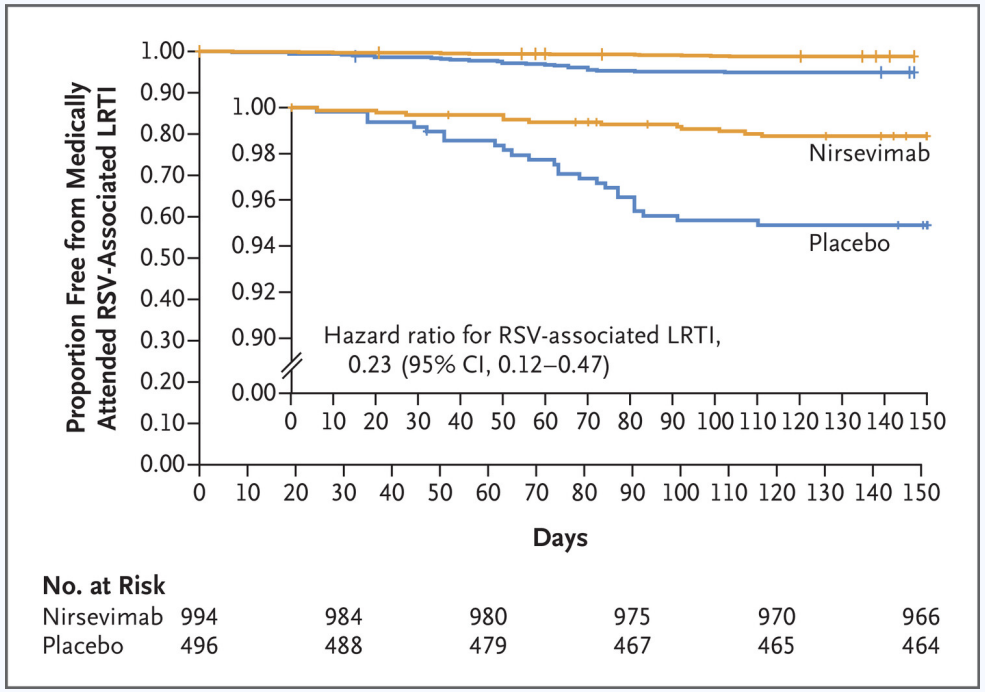
Pfizer's Abrysvo is the only RSV vaccine recommended for pregnant women. **GSK's Arexvy and Moderna's mResvia are NOT approved for use during pregnancy**

• CDC.gov

Nirsevimab

Monoclonal antibody against RSV

- Target: pre-fusion form of the RSV F protein
- Indicated age:
  - All infants < 8 months
  - High risk up to 19 months
  - Associated with 75% decrease in all medically attended lower respiratory tract infections (with a statistically insignificant trend to decrease in hospitalizations by 60% (MELODY Trial)



• Hammitt LL et al. NEJM 2022

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COVID 19

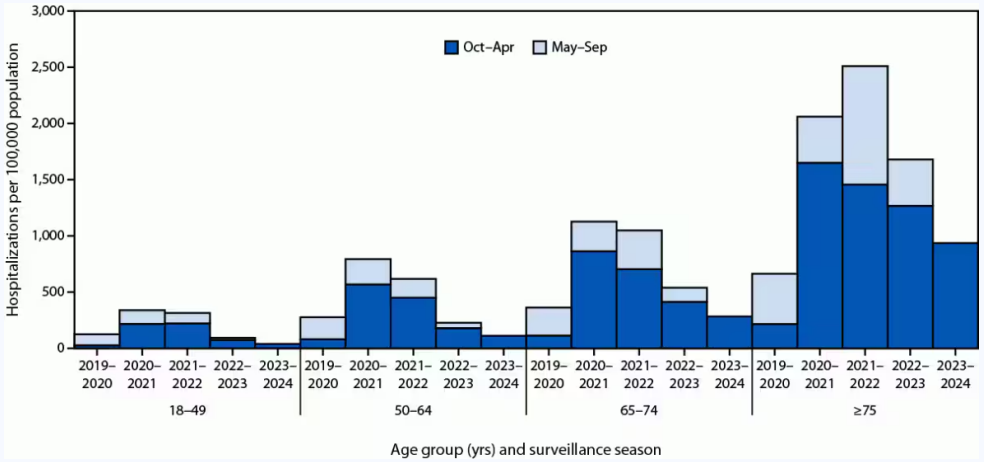
COVID-19

COVID-NET Surveillance Data across 12 states:

- Cumulative rates of COVID 19 hospitalizations from October 2023 through April 2024 were the lowest for all adult age groups since the 1st year of the pandemic

- 70% of all adult COVID-associated hospitalizations are in adults 65 and older

- Among a sample of 1,320 adults hospitalized for COVID-19, 88.1% had not received the 2023-24 COVID-19 vaccine and 57.7% had not received the 2022-23 vaccine



• Taylor CA,, et al. Morb Mortal Wkly Rep 2024;73:869–875

COVID-19 vaccine products

- Monovalent vaccines against circulating JN.1 variant with KP.2 strain if feasible
- 2 types of COVID-19 vaccines
  - **messenger RNA (mRNA)–based**
    - ➢ Moderna (Spikevax)
    - ➢ Pfizer- BioNTech (Comirnaty)

  - **Adjuvant protein subunit vaccine**
    - ➢ Novavax (Nuvaxovid, Covovax)

• CDC.gov

Current COVID-19 Vaccination Recommendations

- **Primary Series:** Initial two-dose mRNA vaccines (Pfizer-BioNTech, Moderna) or single-dose Johnson & Johnson.
- **Booster Doses:**
  - Updated boosters (bivalent) targeting Omicron variants recommended.
  - Frequency depends on age, health conditions, and prior vaccination.
- **Children & Adolescents:** Vaccination recommended from 6 months and older.

COVID-19 vaccine- primary vaccination series

- **All individuals aged 6 months and older** are recommended to get an FDA-approved 2024–2025 COVID-19 vaccine for all persons aged 6 months and older (Pfizer-BioNTech, Moderna, Novovax)

- For those receiving the Novavax vaccine for the first time, **a two-dose series** is required, spaced 3–8 weeks apart

COVID 19 vaccine- Booster doses

- **Adults 65 years and older:**

- Recommend 2 doses of **ANY** 2024-2025 COVID vaccine (Moderna, Novovax, Pfizer-BioNTech) separated by 6 months (minimum interval 2 months) **regardless of vaccination history**

  - Exception: Unvaccinated people who initiate vaccination with 2024–2025 Novavax COVID-19 vaccine: Recommend **2 doses of Novavax followed by a third dose of any COVID-19 vaccine** 6 months (minimum interval 2 months) later.

• CDC.gov

COVID-19 vaccine - immunocompromised

People 6 months and older who are moderately or severely immunocompromised:

- Unvaccinated: A multidose initial series with an age-appropriate COVID-19 vaccine and 1 dose 6 months (minimum interval 2 months) after completion of the initial series; may receive additional doses under shared clinical decision making

- Previously vaccinated: Recommend 2 age-appropriate doses of 2024–2025 COVID-19 vaccine 6 months (minimum interval 2 months) apart; may receive additional doses under shared clinical decision making

COVID-19 Vaccine Timing if Moderately/Severely Immunocompromised

Vaccinate ALL 58

Children and Adolescents (Ages 6 months–17 years)

Age	Vaccine	If unvaccinated*§:	If had prior monovalent doses give bivalent (B) doses*§:
6 months–4 years	**Pfizer** Bivalent–Infant/Toddler	1st Dose → 3 weeks → 2nd Dose → ≥8 weeks → 3rd Dose → ≥2 months → Optional Dose*	1 Monovalent → 3 w → B → ≥8 w → B 2-3 Monovalent → ≥8 w → B → ≥2 m → Optional Dose*
5–11 years 12+ years	**Pfizer** Bivalent–Pediatric **Pfizer** Bivalent–Adol/Adult	1st Dose → 3 weeks → 2nd Dose → ≥4 weeks → 3rd Dose → ≥2 months → Optional Dose* Use orange cap for 5-11 years and gray cap for 12+ years.	1 Monovalent† → 3 w → B → ≥4 w → B 2 Monovalent† → ≥4 w → B 3 Monovalent† → ≥8 w → B → ≥2 m → Optional Dose* Orange cap: 5-11 yrs, Gray cap: 12+ yrs
6+ months	**Moderna** Bivalent	1st Dose → 4 weeks → 2nd Dose → ≥4 weeks → 3rd Dose → ≥2 months → Optional Dose* Use blue cap vial, 6 months-11years: 0.25mL, 12+ years: 0.5mL	1 Monovalent^ → 4 w → B → ≥4 w → B 2 Monovalent^ → ≥4 w → B 3 Monovalent^ → ≥8 w → B Blue cap: 5+ yrs; B Pink cap: 6 m-4 yrs → ≥2 m → Optional Dose* Blue cap: 6+ yrs, Pink (or Blue) cap: 6 m-5 yrs
12+ years	**Novavax** Monovalent	1st Dose → 3 weeks → 2nd Dose →	If 1 or 2 prior doses, then: ≥8 weeks → **Bivalent** (Moderna/Pfizer) → ≥2 m → Optional Dose* (Moderna/Pfizer)

Figure 3A. COVID-19 Vaccination Coverage, Overall and by Selected Demographics and Jurisdiction, Among Adults 18 Years and Older, 2023–24 Through 2024–25*,†,‡,§

Data Source: National Immunization Survey–Adult COVID Module

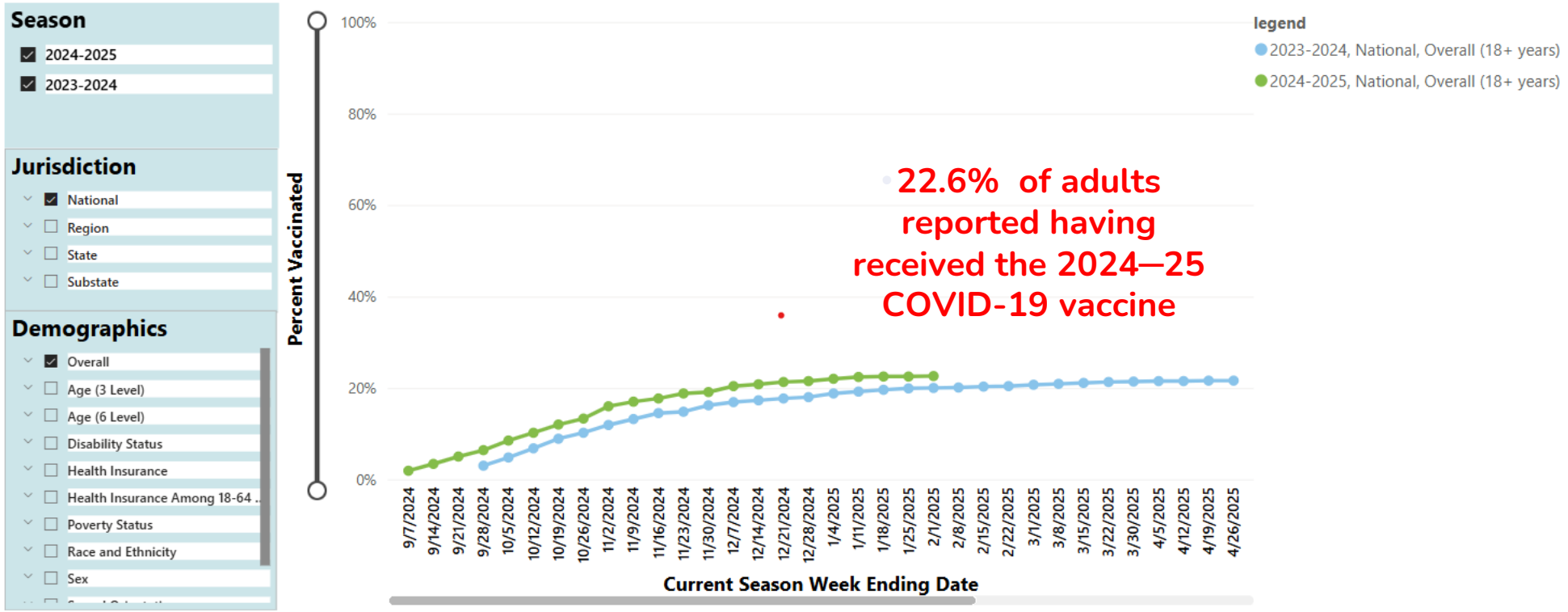
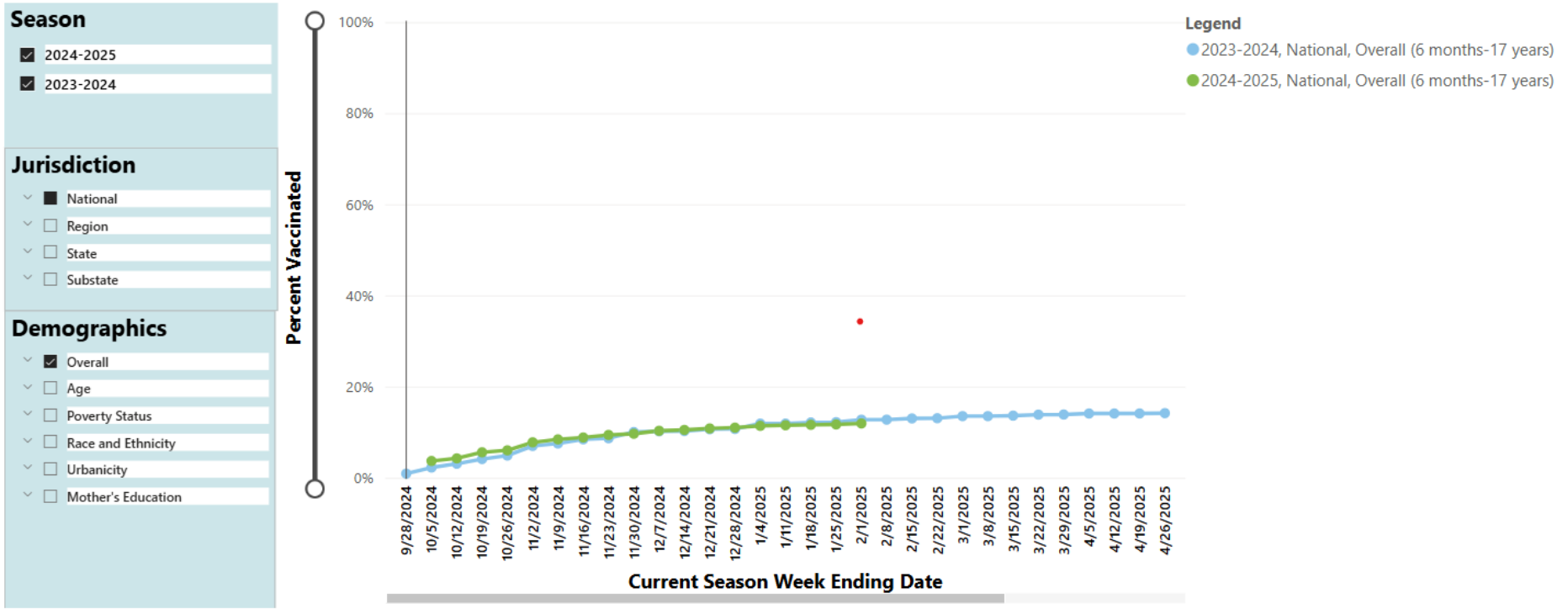
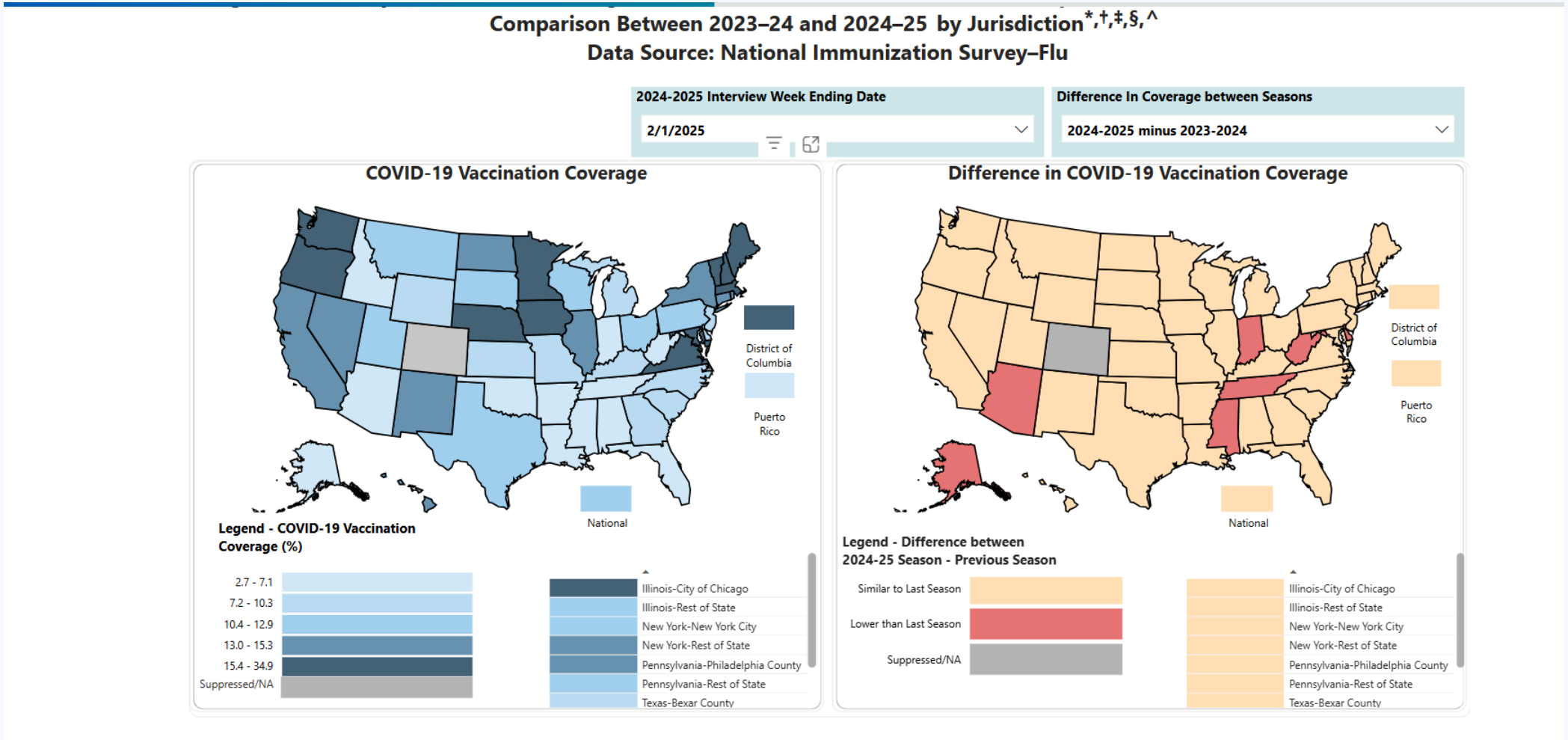


Figure 1A. Weekly Cumulative Percentage of Children 6 Months–17 Years Who Are Up to Date with COVID-19 Vaccines by Season*,†,‡,§
Data Source: National Immunization Survey–Flu



- https://www.cdc.gov/covidvaxview/weekly-dashboard/child-coverage-vaccination.html



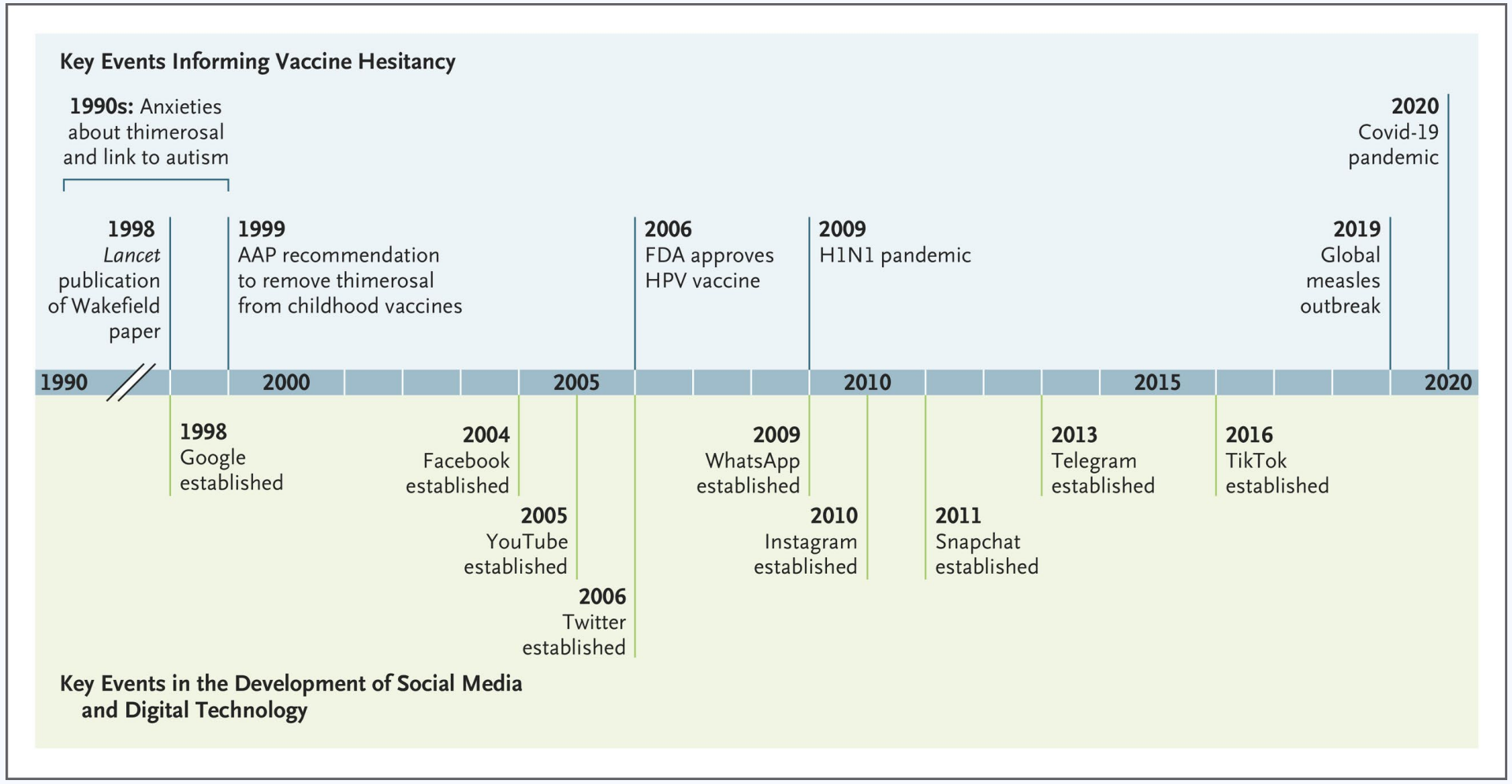
- https://www.cdc.gov/covidvaxview/weekly-dashboard/child-coverage-vaccination.html

Vaccine hesitancy

Vaccine Hesitancy

- "Vaccine hesitancy [is] a state of indecision and uncertainty that precedes a decision to become (or not become) vaccinated"
- One of WHO's top 10 major global health threats in 2019, along with the influenza pandemic
- Impact: Resurgence of preventable diseases, increased healthcare costs, herd immunity decline
- Importance of addressing vaccine hesitancy to prevent disease outbreaks

- WHO, 2019; Larson HJ et al. NEJM 2022



• ; Larson HJ et al. NEJM 2022

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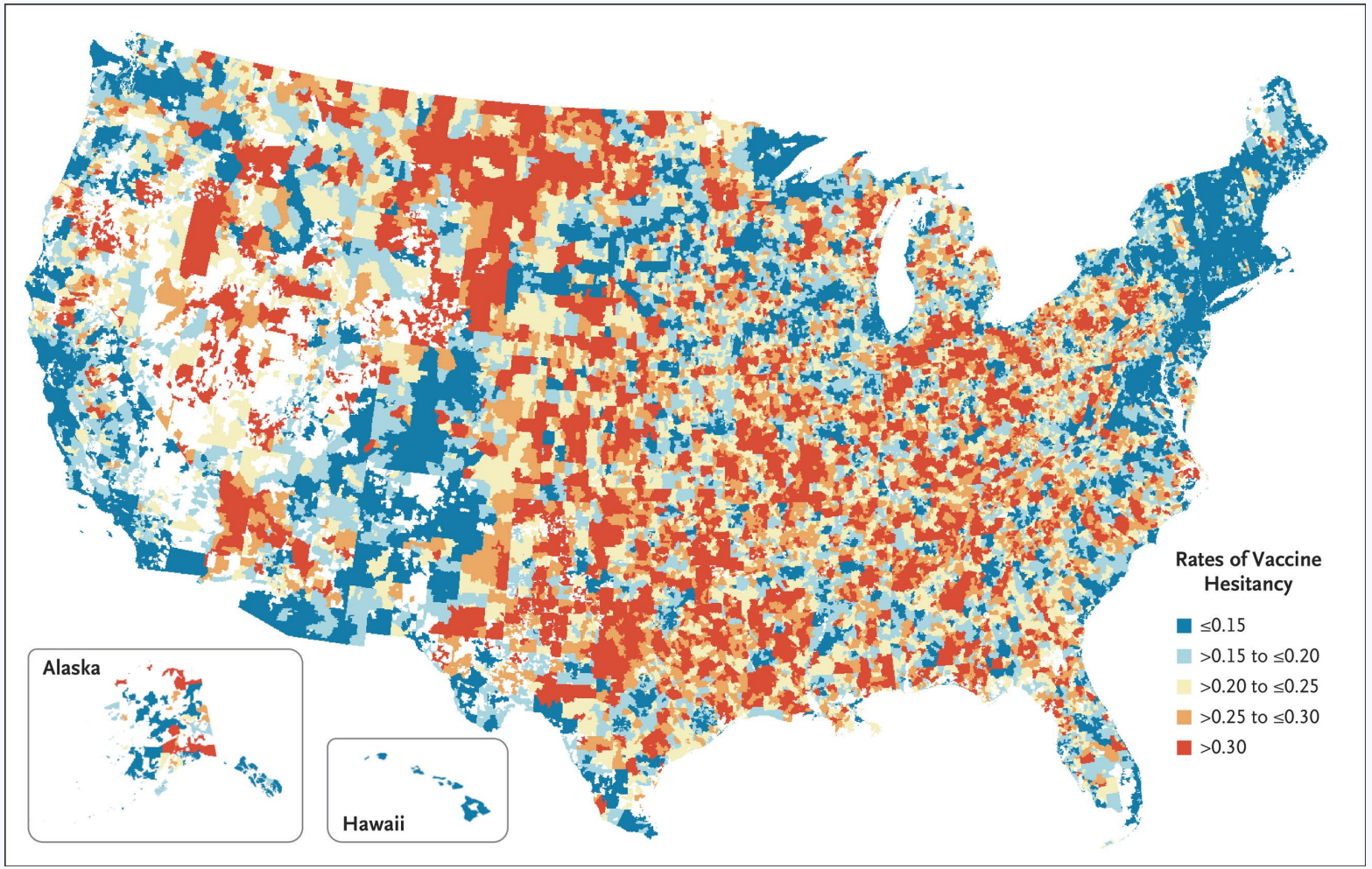

• Larson HJ et al. NEJM 2022

Determinants of vaccine hesitancy

Environmental factors:	• Socioeconomic level; access to vaccination services, complacency, lack of information, resistance to vaccine mandates
Personal factors:	• individual beliefs, cultural beliefs, perception of risk of vaccine related to risk of disease; trust in healthcare institutions; historical trauma and segregation
Social factors:	• Social network/peer influence; media and information sources; stigma associated with vaccines, misinformation about vaccines
Safety and vaccine-related factors:	• Vaccine safety concerns, concerns about vaccine efficacy; vaccine ingredients, vaccine administration concerns

• WHO.int;
• Goje O, Kapoor A. Cleve **Clin J Med 2024; 91(9 suppl 1)**

Examples of vaccine hesitancy

- **Influenza Vaccine:**
- Misconception that the flu shot causes the flu
- Belief that flu is not serious enough to warrant vaccination
- Low uptake among young adults and certain ethnic groups
- **RSV Vaccine:**
- Newer vaccine leads to skepticism about safety.
- Concern over long-term side effects.
- Limited public awareness compared to flu and COVID-19 vaccines.

• ; Larson HJ et al. NEJM 2022

Strategies to counter vaccine hesitancy

Education and clear communication

Community engagement

Legislation and policy

Address misinformation and disinformation

Research and innovation

Incorporate vaccination into routine prenatal care

• Goje O, Kapoor A. Cleve **Clin J Med 2024**; **91(9 suppl 1)**

Applying the SHARE Model

SHARE the reasons:

- "This vaccine can protect you and your family from getting sick from flu. By getting the vaccine today, you'll be helping to protect yourself and the people around you who are more vulnerable to serious flu illness, like your children and parents."

HIGHLIGHT positive experiences:

- "CDC recommends that everyone over 6 months of age get a flu vaccine each year. I always get one myself to minimize the chance that I will pass along flu to my patients and my family members."

ADDRESS patient questions:

- "To answer your question, a flu vaccine cannot cause flu illness. There can be some mild side effects, but this is not flu illness. There are different side effects that may be associated with getting a flu shot or a nasal spray flu vaccine."

REMIND patients that flu vaccines protect them and their loved ones:

- "Flu activity is going to start to pick up, and CDC says to expect more cases in the coming months. That is why I want to make sure I help protect you and your loved ones."

EXPLAIN the potential costs of flu:

- "It's important to get vaccinated this season because flu vaccination can reduce potential flu illnesses, doctor visits, and missed work or school due to flu."

NCIRD FLU 2020-2021 www.cdc.gov/flu/professionals/vaccination/flu-vaccine-recommendation.htm

Key takeaway points

- Viral respiratory infections continue to have an important impact on morbidity and mortality, especially in high-risk populations (elderly, children, pregnant women)
- Vaccination is a key player for prevention and should be recommended and administered
- CDC and ACIP have updated recommendations for vaccination against RSV, COVID 19 and influenza for the 2024-2025 season
- Vaccine hesitancy is an ongoing challenge, and multiple strategies are needed to improve vaccine uptake

Thank you!

PREVENTION AND TREATMENT OF VENTILATOR ASSOCIATED PNEUMONIA

Sairam Parthasarathy, MD

Murray and Clara Walker Endowed Chair for Emphysema

Professor and Chief, Division of Pulmonary Allergy Critical Care & Sleep Medicine

University of Arizona, Tucson, AZ

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RELEVANT FINANCIAL DISCLOSURES

- I have the following relationships with ACCME defined ineligible companies:

- Consultant: Abbvie, Inc., April Healthcare Inc., and Jazz Pharmaceuticals, Inc.
- Research grants to Institution: Philips, Inc. and Verily Lifesciences, Inc.
- Royalties: UpToDate, Inc.

- I WILL/WILL NOT discuss off-label use and/or investigational use of any drugs or devices.

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OBJECTIVES

- **Prevention**
- **Treatment**
- **Future research**

DEFINITIONS

Why define?

Ventilator-associated pneumonia (VAP) is a type of HAP that develops in intubated patients on mechanical ventilation for more than 48 hours. VAP also includes HAP that occurs within 48 hours of extubation.

Hospital Acquired Pneumonia

Non-ventilator associated HAP (NV-HAP)

~~**Healthcare Associated Pneumonia (HCAP)**~~

MDR/XDR/PDR Pathogens ⬆️ Mortality

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Intubation
- **Prolonged**
- **Reintubation**
- **Frequent Circuit changes**

Increased gastric pH
Older Age
Chronic Lung Disease
Aspiration
Microaspiration
Prior antibiotic exposure
Multiple trauma
AUD/Opioids
Paralysis and Deep Sedation

# of surgeries/central lines
Muscle relaxants
Glucocorticoids
Malnutrition
Burns
Hypothermia
Poor oral hygiene
Chronic renal failure
Previous hospitalization

Prevention Bundles

Intubation
- **Early extubation**
- **Avoid reintubation (HFNC / NIV)**
- **Reduce Circuit changes**

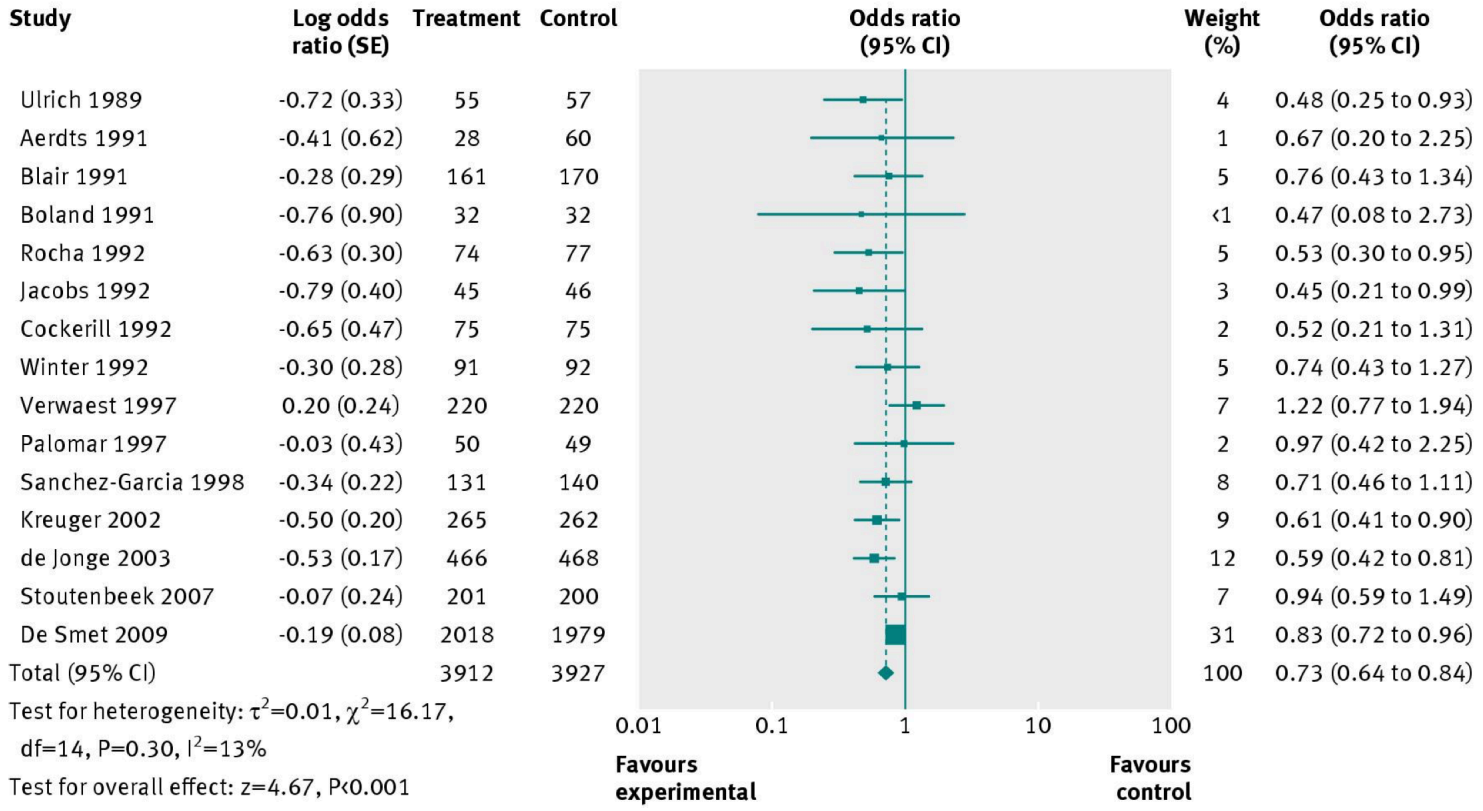
Sucralfate

30° to 45 ° head angle elevation; post-pyloric feeding
ETT cuff pressure / subglottic drainage / early trach (7d)
Antibiotic stewardship

Minimize sedation / sedation intervals / days of paralysis
(reduces delirium, deconditioning, atelectasis, and aspiration)
Early mobilization and exercise
Avoid muscle relaxants
Limit glucocorticoids
Avoid parenteral feeding

Avoid Hypothermia
Provide Oral Care & toothbrushing
Selective decontamination of digestive tract (SDD/SOD)*
Colistin, tobra, nystatin, quinolone, cephalosporin

SELECTIVE DIGESTIVE DECONTAMINATION REDUCES MORTALITY



Study	Log odds ratio (SE)	Treatment	Control	Weight (%)	Odds ratio (95% CI)
Ulrich 1989	-0.72 (0.33)	55	57	4	0.48 (0.25 to 0.93)
Aerdts 1991	-0.41 (0.62)	28	60	1	0.67 (0.20 to 2.25)
Blair 1991	-0.28 (0.29)	161	170	5	0.76 (0.43 to 1.34)
Boland 1991	-0.76 (0.90)	32	32	<1	0.47 (0.08 to 2.73)
Rocha 1992	-0.63 (0.30)	74	77	5	0.53 (0.30 to 0.95)
Jacobs 1992	-0.79 (0.40)	45	46	3	0.45 (0.21 to 0.99)
Cockerill 1992	-0.65 (0.47)	75	75	2	0.52 (0.21 to 1.31)
Winter 1992	-0.30 (0.28)	91	92	5	0.74 (0.43 to 1.27)
Verwaest 1997	0.20 (0.24)	220	220	7	1.22 (0.77 to 1.94)
Palomar 1997	-0.03 (0.43)	50	49	2	0.97 (0.42 to 2.25)
Sanchez-Garcia 1998	-0.34 (0.22)	131	140	8	0.71 (0.46 to 1.11)
Kreuger 2002	-0.50 (0.20)	265	262	9	0.61 (0.41 to 0.90)
de Jonge 2003	-0.53 (0.17)	466	468	12	0.59 (0.42 to 0.81)
Stoutenbeek 2007	-0.07 (0.24)	201	200	7	0.94 (0.59 to 1.49)
De Smet 2009	-0.19 (0.08)	2018	1979	31	0.83 (0.72 to 0.96)
Total (95% CI)		3912	3927	100	0.73 (0.64 to 0.84)

Test for heterogeneity: τ^2=0.01, χ^2=16.17, df=14, P=0.30, I^2=13%

Test for overall effect: z=4.67, P<0.001

Fig 2 Forest plot of intervention-control pairwise meta-analysis of selective digestive decontamination v control in adult patients in intensive care

Price et al, BMJ. 2014 Mar 31;348:g2197.

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SELECTIVE OROPHARYNGEAL DECONTAMINATION REDUCES MORTALITY

Study	Log odds ratio (SE)	Treatment	Control	Weight (%)	Odds ratio, IV random (95% CI)
Pugin 1991	-0.03 (0.49)	38	41	2	0.97 (0.37 to 2.55)
Bergmans 2001	-0.42 (0.28)	87	139	6	0.65 (0.38 to 1.13)
Rios 2005	-0.19 (0.38)	47	49	3	0.83 (0.39 to 1.75)
De Smet 2009	-0.15 (0.07)	1886	1979	88	0.86 (0.74 to 0.99)
Total (95% CI)		2058	2208	100	0.85 (0.74 to 0.97)

Test for heterogeneity: τ^2=0.00, χ^2=0.99, df=3, P=0.80, I^2=0%

Test for overall effect: z=2.39, P=0.22

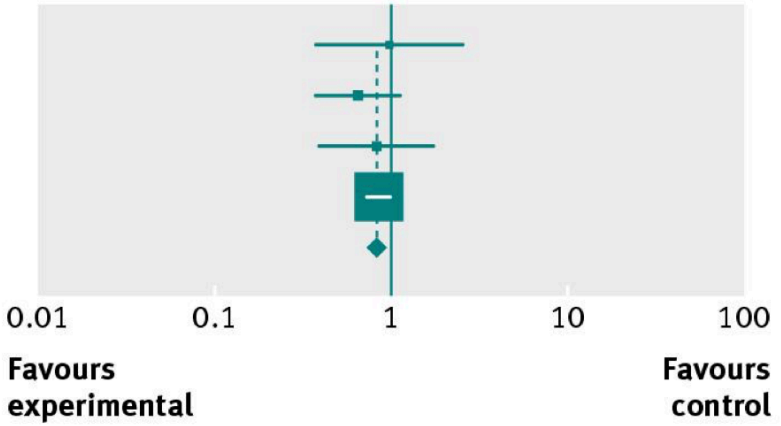

Fig 3 Forest plot of intervention-control pairwise meta-analysis of selective oropharyngeal decontamination v control in adult patients in intensive care

Price et al, BMJ. 2014 Mar 31;348:g2197.

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NASCENT Trial: VAP reduced but NO reduction in LOMV, ICU stay, LOS, & mortality

~~Chlorhexidine~~

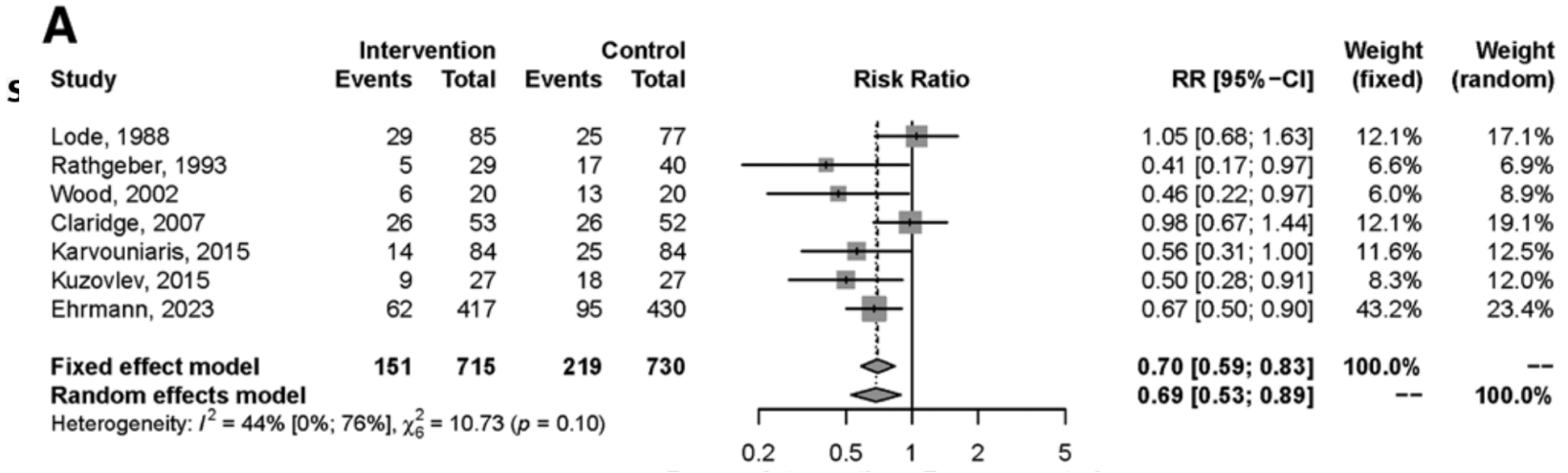
~~Probiotics~~

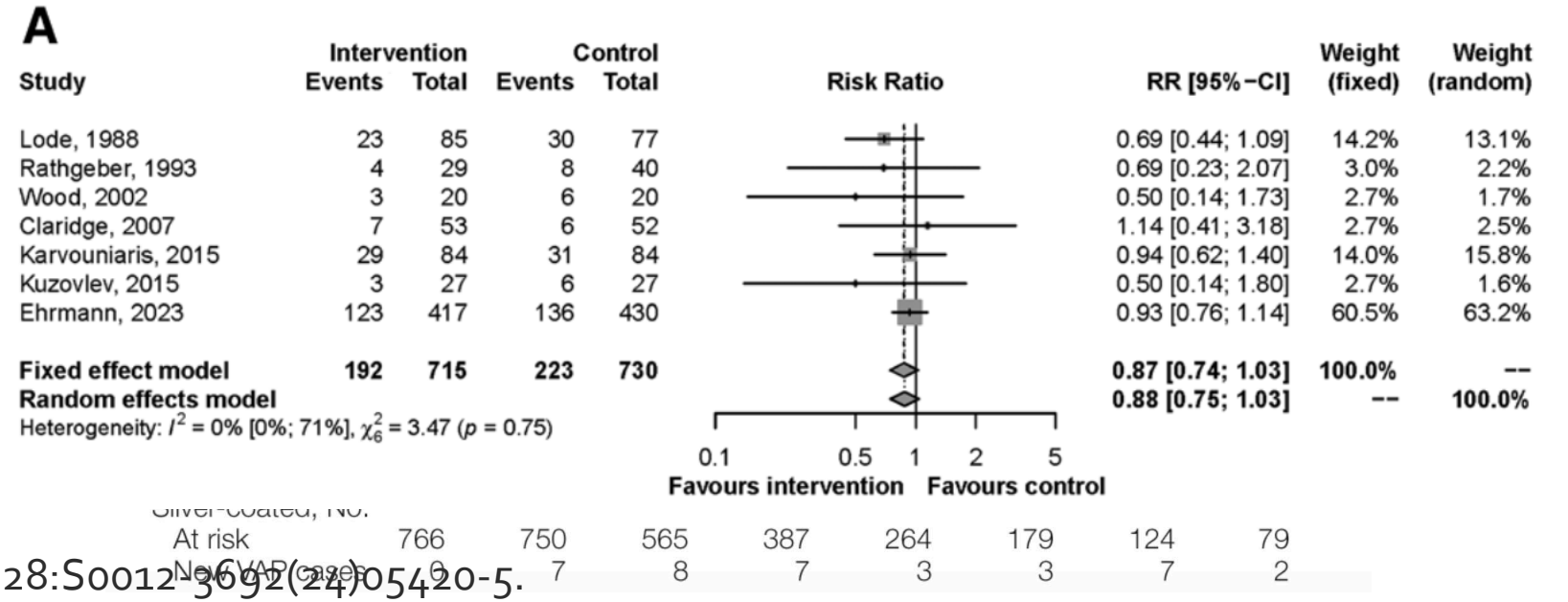
~~Ag-coated ETT~~

~~Systemic antibio~~

~~Inhaled antibiotic~~

~~Gastric residual~~





Li et al, Crit Care Med. 2024 Oct 1;52(10):1612-1623.

Hadley-Brown et al, Chest. 2024 Oct 28:S0012-3692(24)05420-5.

Kollef et al, JAMA. 2008 Aug 20;300(7):805-13.

Johnstone et al, JAMA. 2021 Sep 21;326(11):1024-1033

Price et al, BMJ. 2014 Mar 31;348:g2197.

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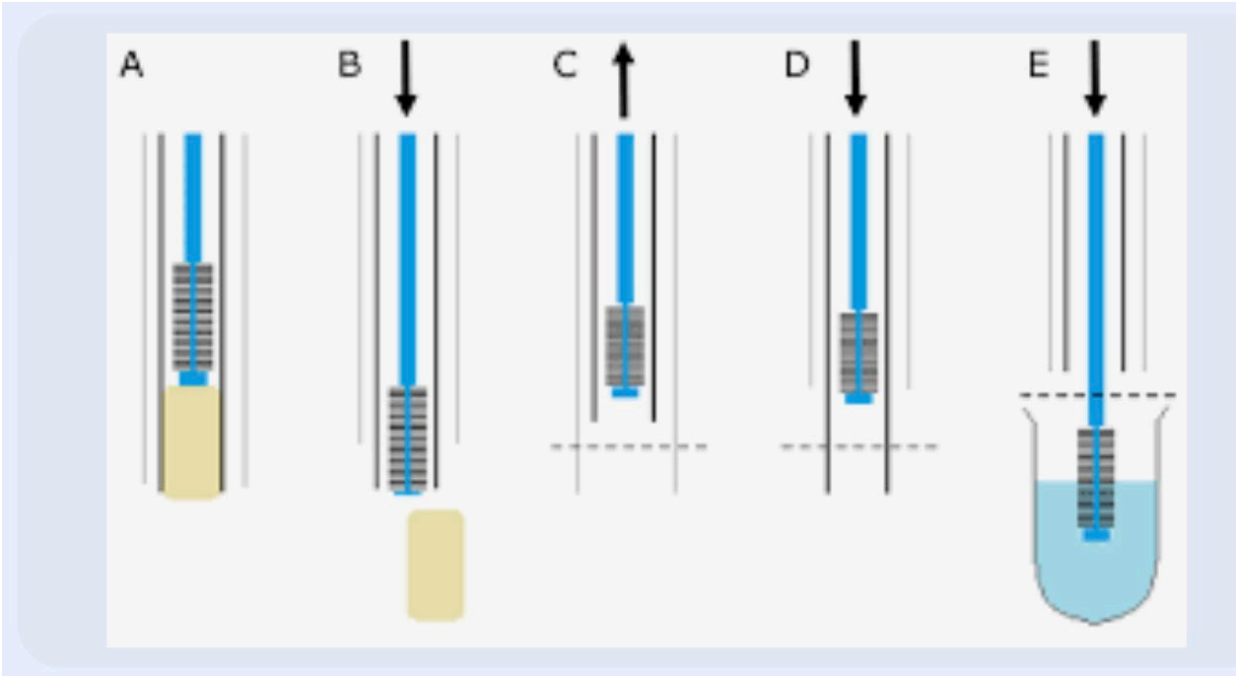
DIAGNOSIS

New or evolving pulmonary infiltrate on imaging + clinical findings of infection (eg, fever, secretions, leukocytosis, etc.)

Imaging: CXR, non-contrast CT Chest, USN

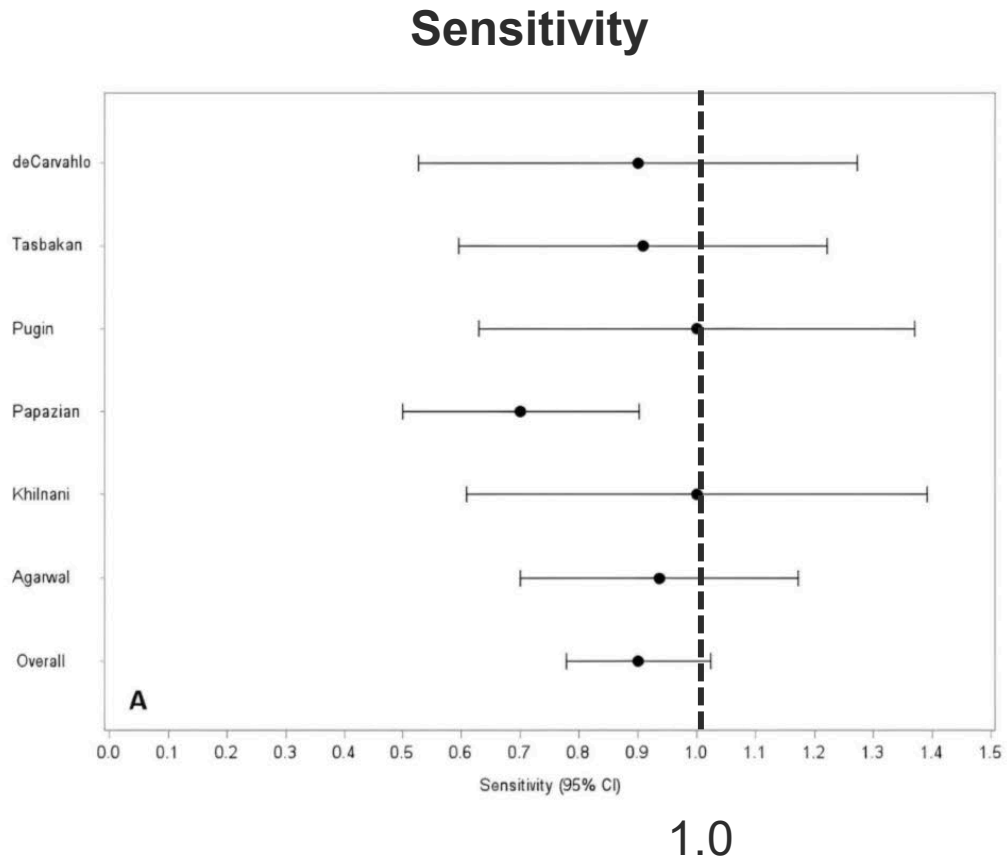
Invasive sample collection: mini-BAL, **BAL****, or protected specimen brush [PSB] with quantitative cultures are better than tracheal aspirate

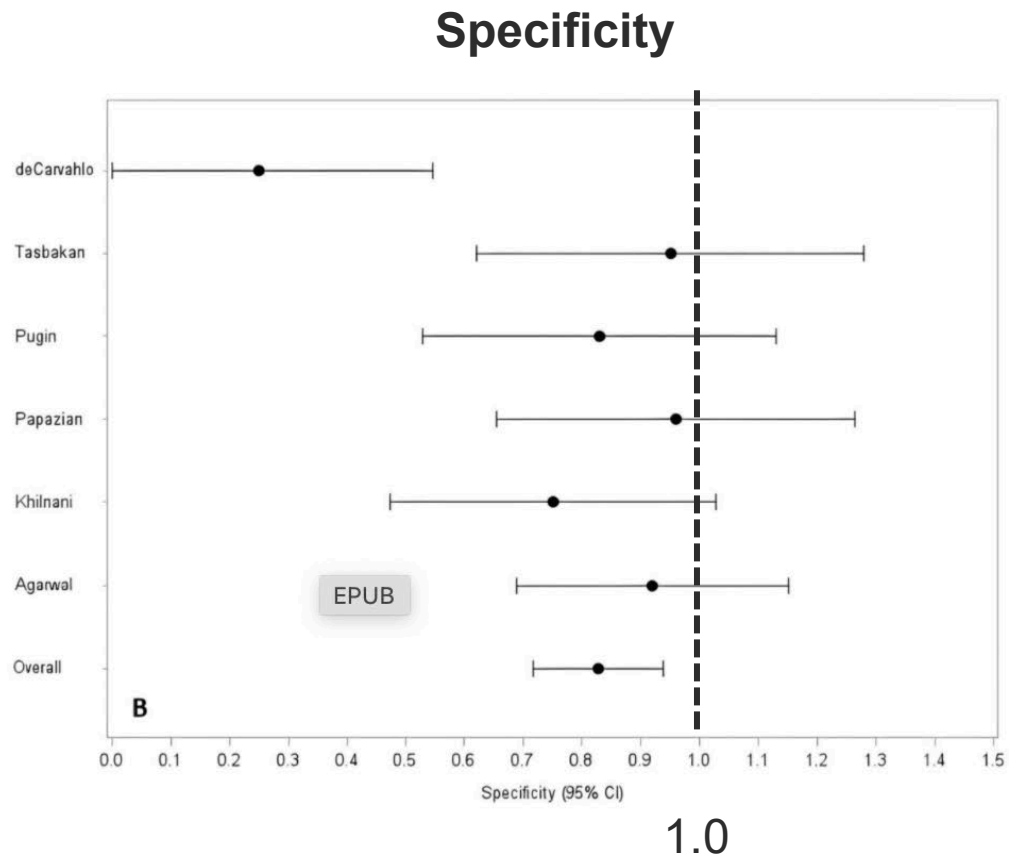


Tracheal aspirates ≥1,000,000 cfu/mL
BAL – 10,000 cfu/mL
PSB – 1000 cfu/mL

** immunocompromised

Sensitivity and specificity with confidence intervals for the mini-BAL compared to the bronchoscopic BAL for diagnosing VAP





There is a high degree of both sensitivity and specificity of mini-BAL for the diagnosis of pneumonia in ventilated patients

Tepper et al, J Intensive Care Med. 2023;38(12):1099.

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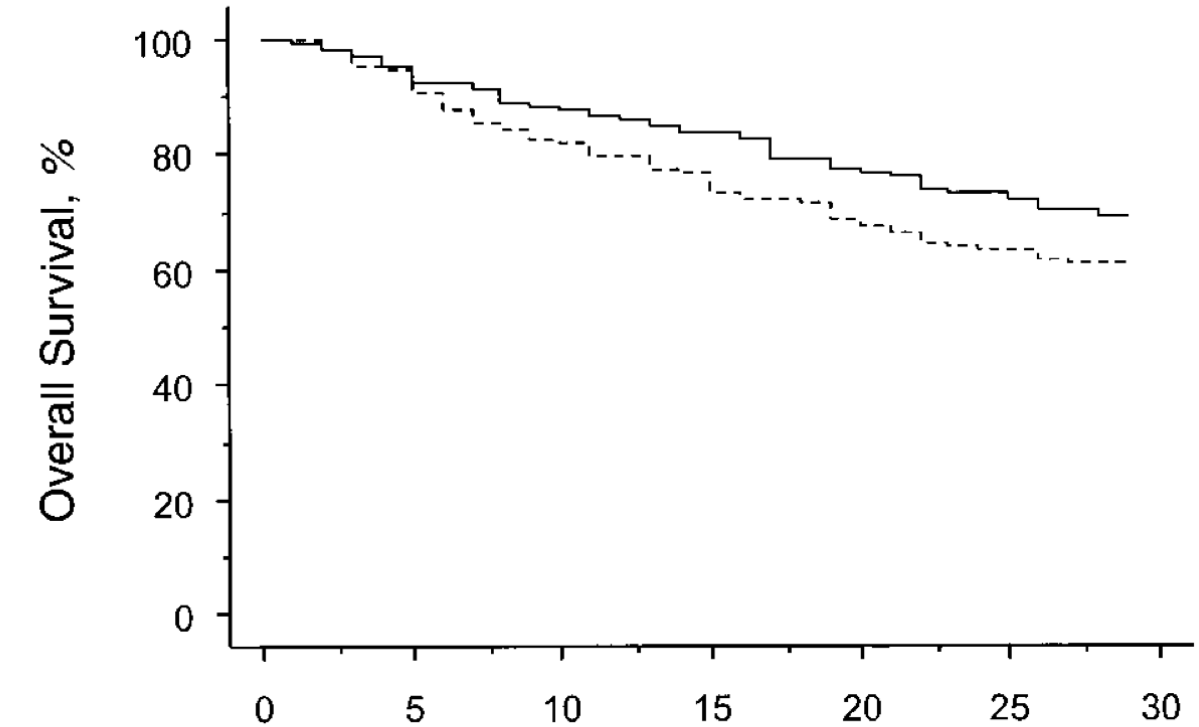
Actuarial 28-day survival among 413 patients assigned to the invasive (*solid line*) or clinical (*dashed line*) management strategy

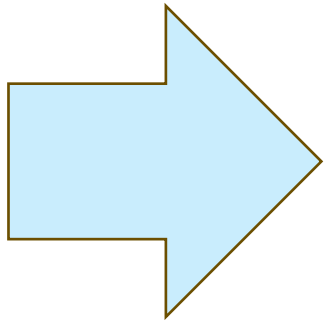


Patients at Risk, *n*						
Invasive therapy	204	193	179	170	157	149
Clinical therapy	209	197	172	159	142	132

Fagon et al, Ann Intern Med. 2000 Apr 18;132(8):621-30.

RISK FACTORS FOR MDR → ABX REGIMEN

Prior IV antibiotics (< 30 days)
ARDS
Acute RRT
Septic Shock
> 5 days of hospitalization
Prior colonization*
Antibiogram or lack thereof*
Structural lung disease (Bronchiectasis / Cystic Fibrosis)



Known pathogens (Antibiogram)
Colonization (MRSA, Pseudomonas aeruginosa)
Recent antibiotics
Prior MDR infection
Adverse reactions
Organ dysfunction
DDRs
Severity of illness (timing)
Good quality gram-stain
PCR multiplex
Cost

Pip-Tazo 4.5 gm IV q6 or Cefepime 2 gm IV q8h

Meropenem / Imipenem

Vancomycin / Ceftazidime

Ceftazidime / Avibactam *
Ceftolozane / Tazobactam *

*** Carbapenem resistance**

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TAILORING OF THERAPY

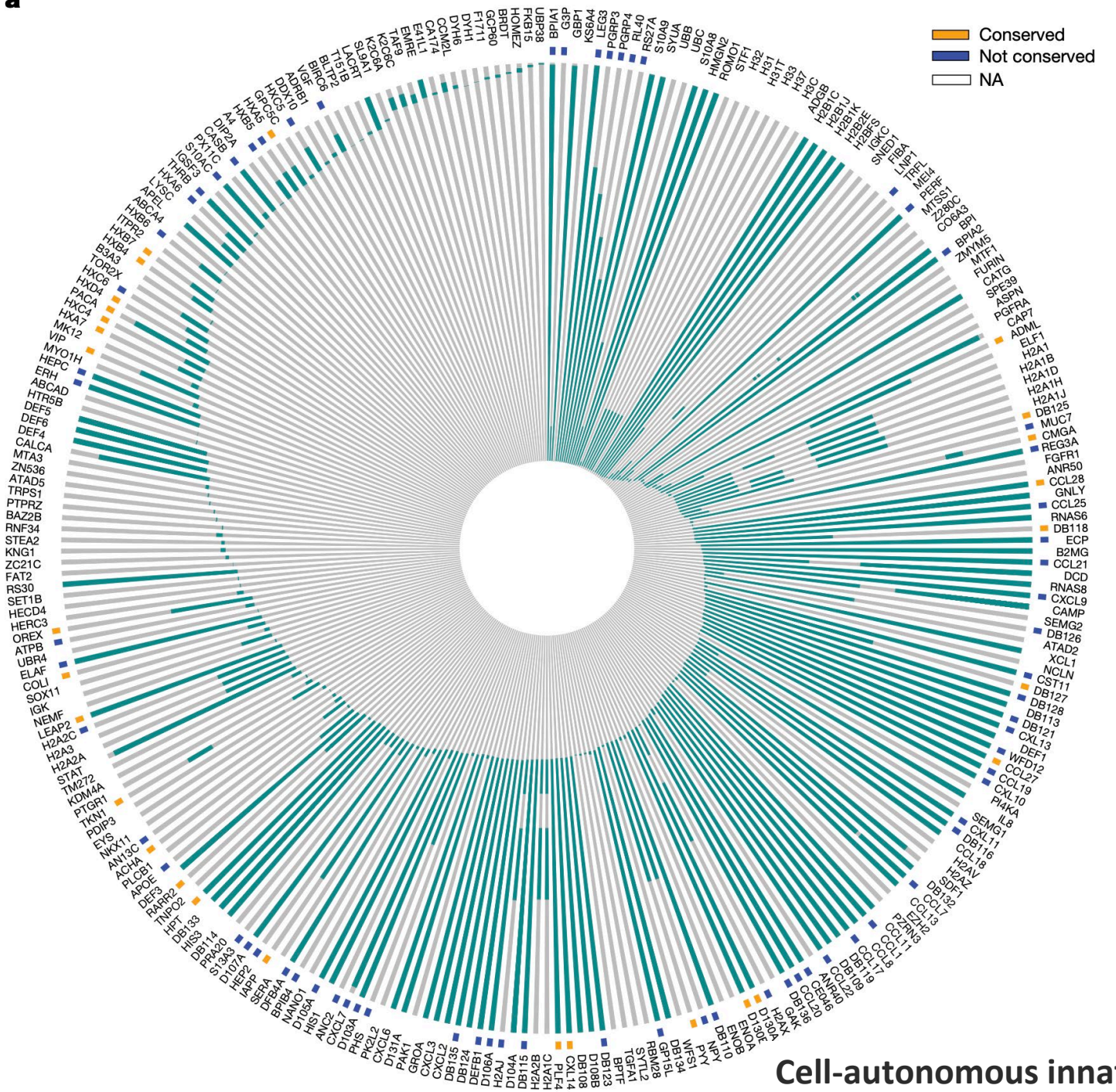
MRSA swabs for culture / PCR

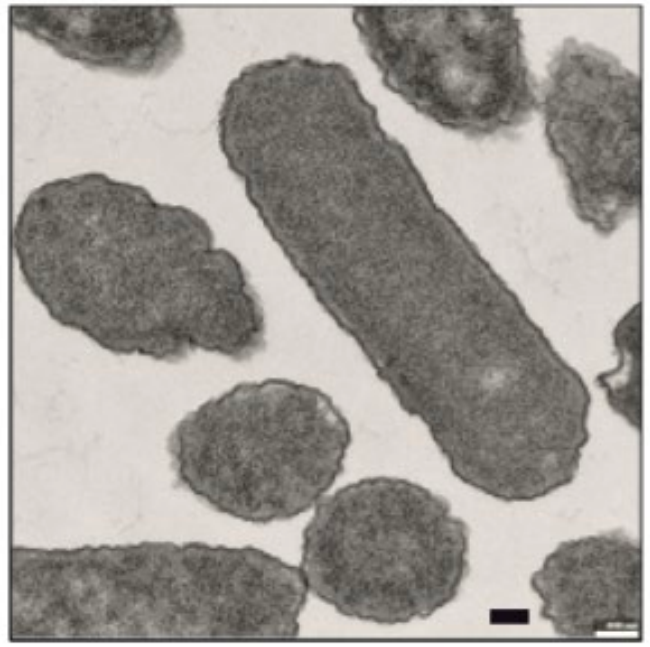
Reassess in 48-72 hours

- Cultures & sensitivities – high quality sputum or BAL/sputum
- Discontinuation of anti-MRSA, Pseudomonas, or other MDRs

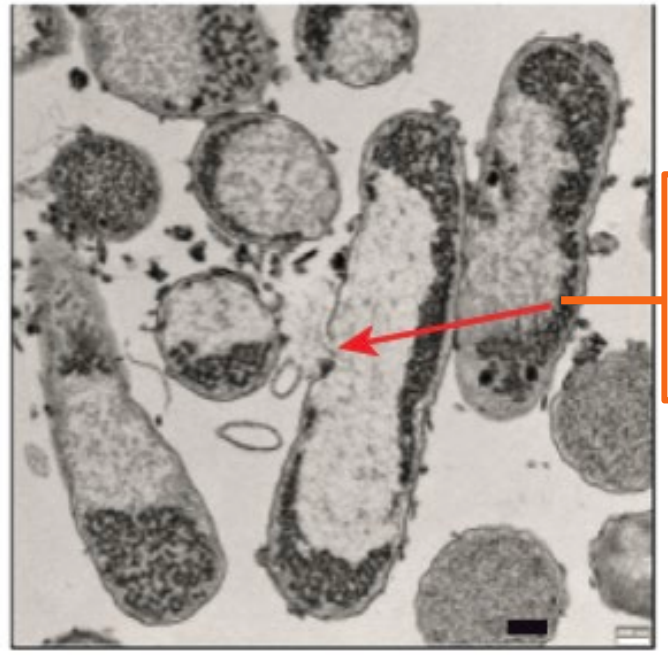
Discontinue antimicrobials targeting MDR organisms if cultures are negative

Consider alternate diagnosis or complications (e.g., empyema) if not improving





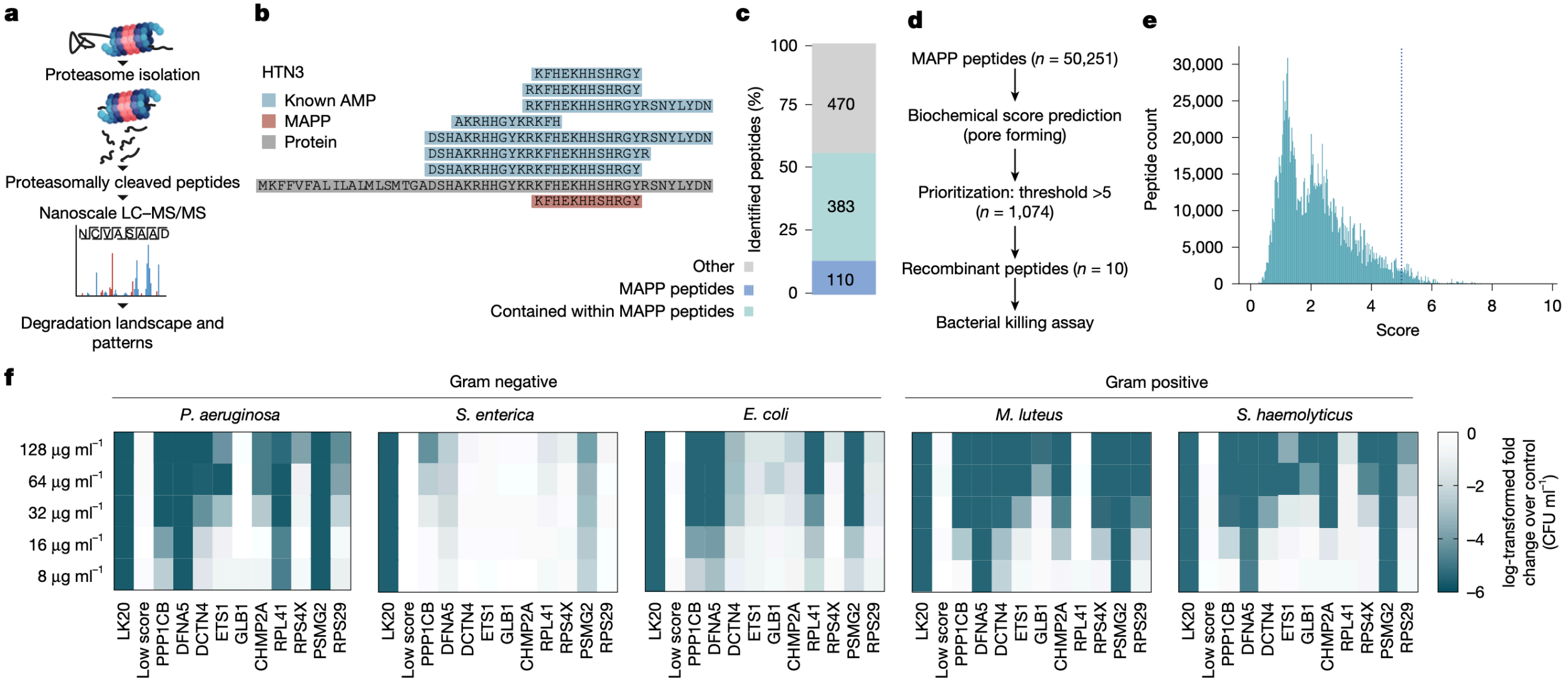
E. coli



Morphological Disruption & Cytoplasmic release

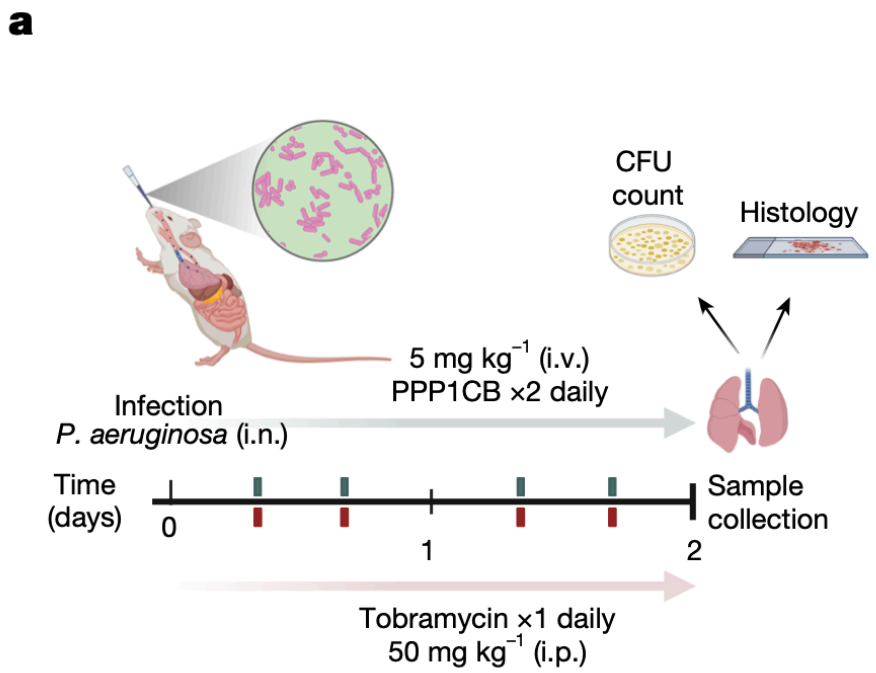
Goldberg et al, Nature 2025
https://doi.org/10.1038/s41586-025-08615-w

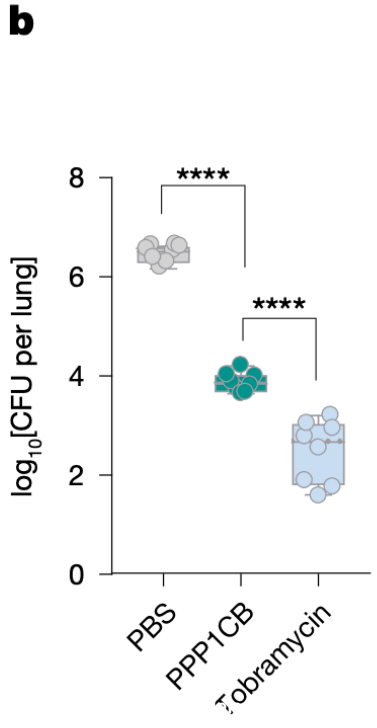
Cell-autonomous innate immunity by proteasome-derived defence peptides

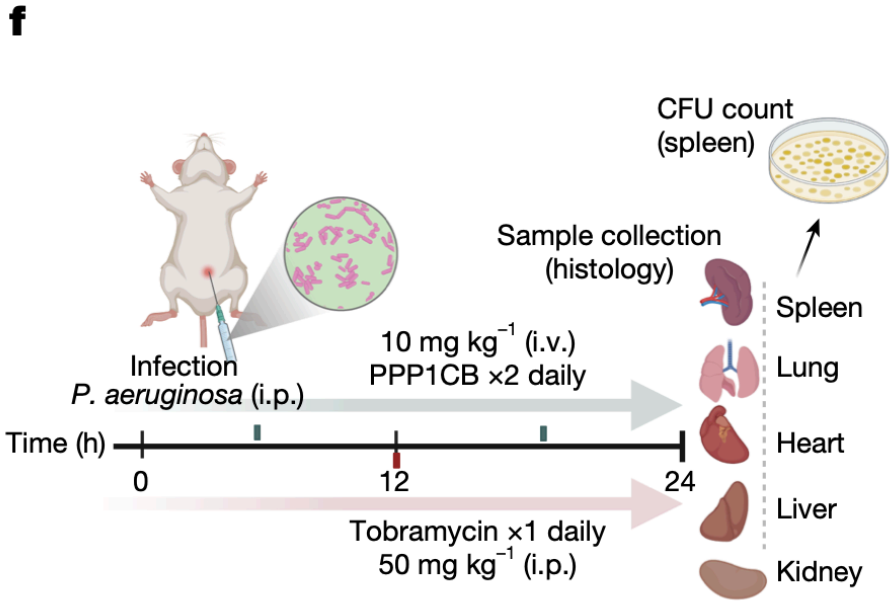


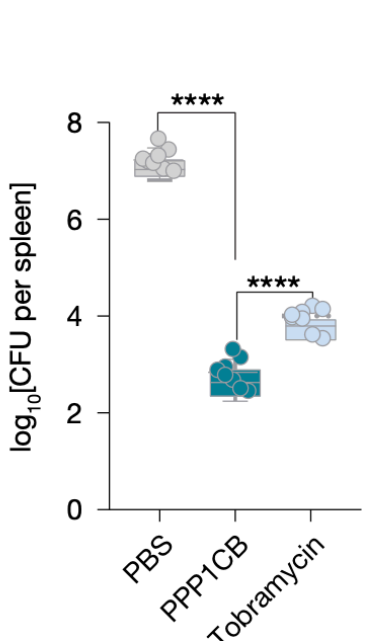
Goldberg et al, Nature 2025 https://doi.org/10.1038/s41586-025-08615-w

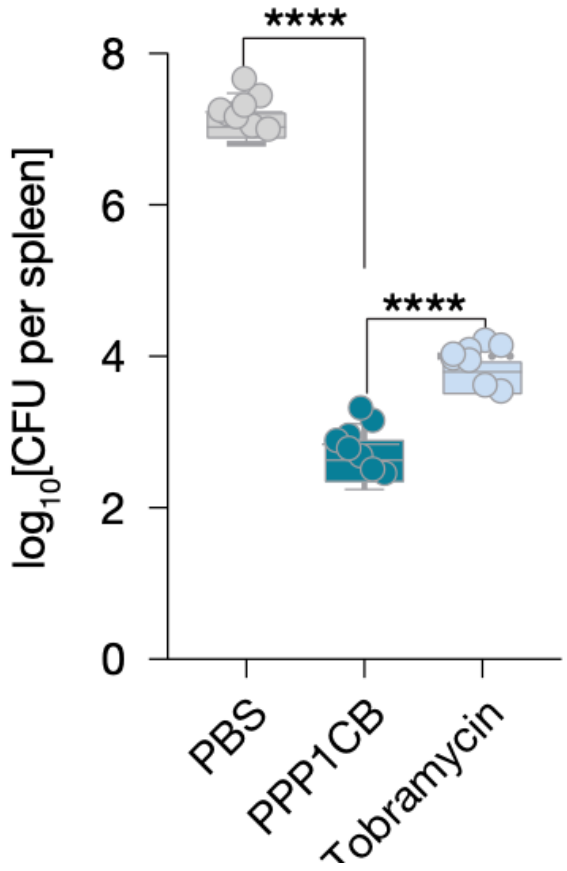
In vivo antimicrobial activity of the PPP1CB-derived peptide in models of pneumonia, bacteremia and sepsis





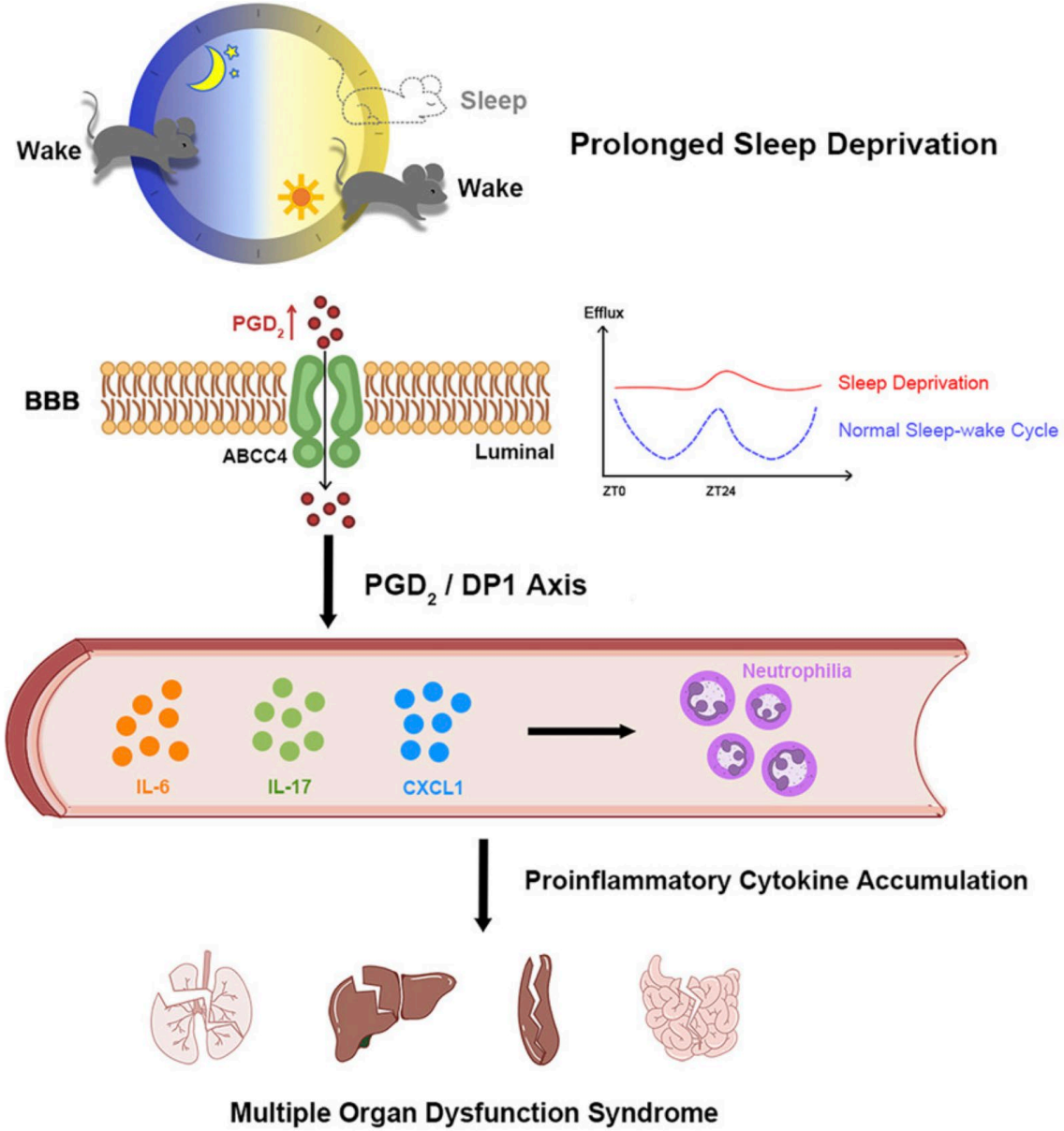






Goldberg et al, Nature 2025
https://doi.org/10.1038/s41586-025-08615-w

Prolonged sleep deprivation induces a cytokine-storm-like syndrome in mammals



Sleep deprivation increases levels of **prostaglandin D_2 (PGD_2) in the brain**, and elevated PGD_2 efflux across the blood-brain-barrier (mediated by ATP-binding cassette subfamily C4 transporter) induces both accumulation of circulating neutrophils and a **cytokine-storm-like syndrome**.

Sang et al., 2023, **Cell** 186, 5500–5516

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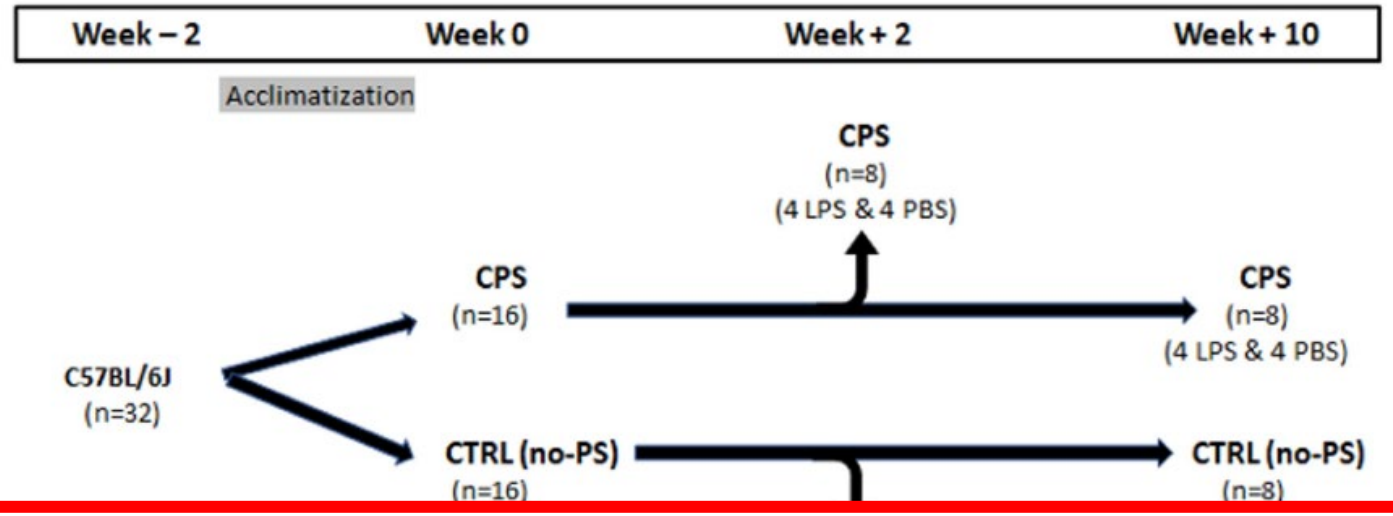
Circadian disruption dysregulates lung gene expression associated with inflammatory lung injury

A.



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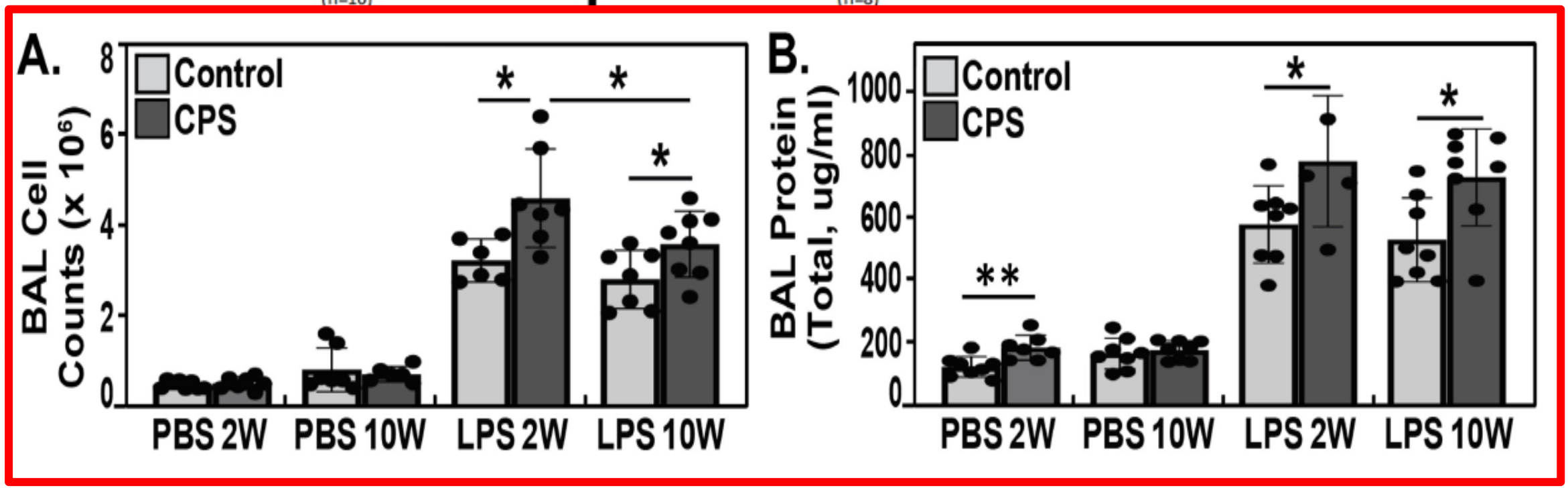

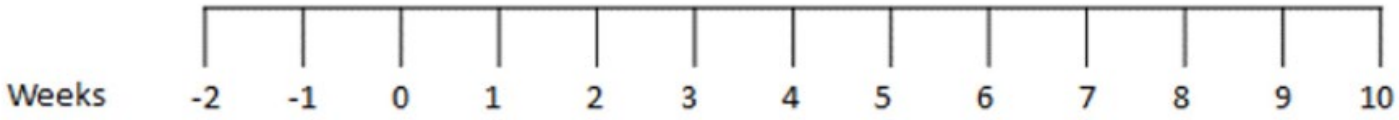

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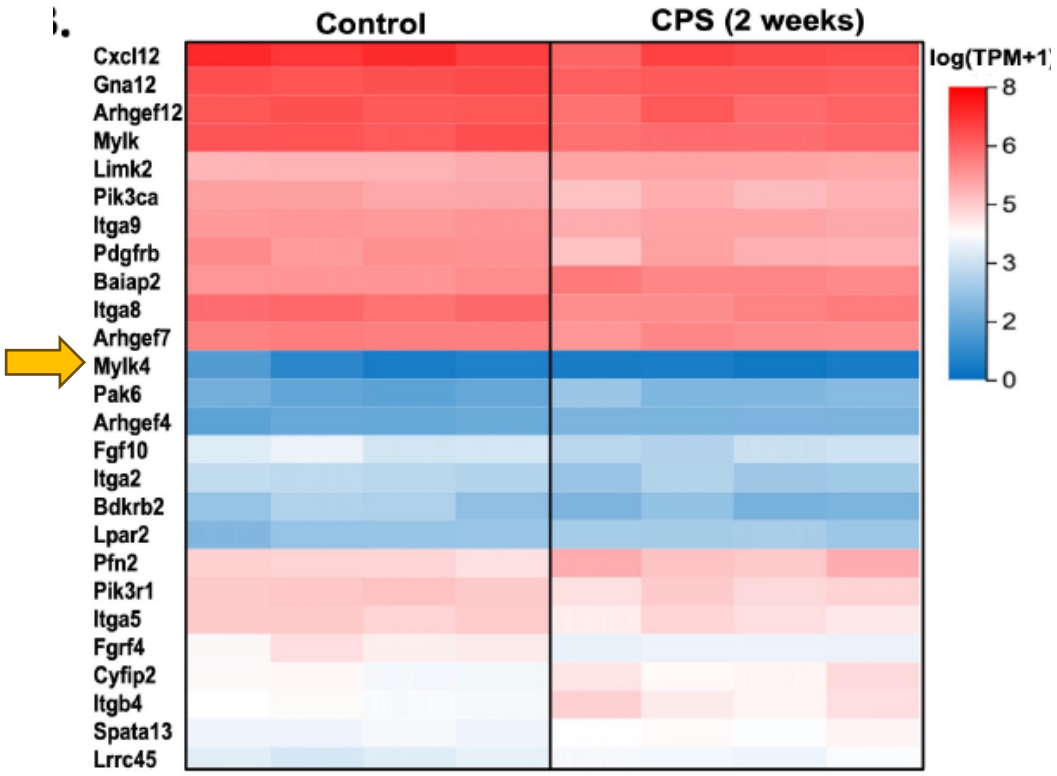
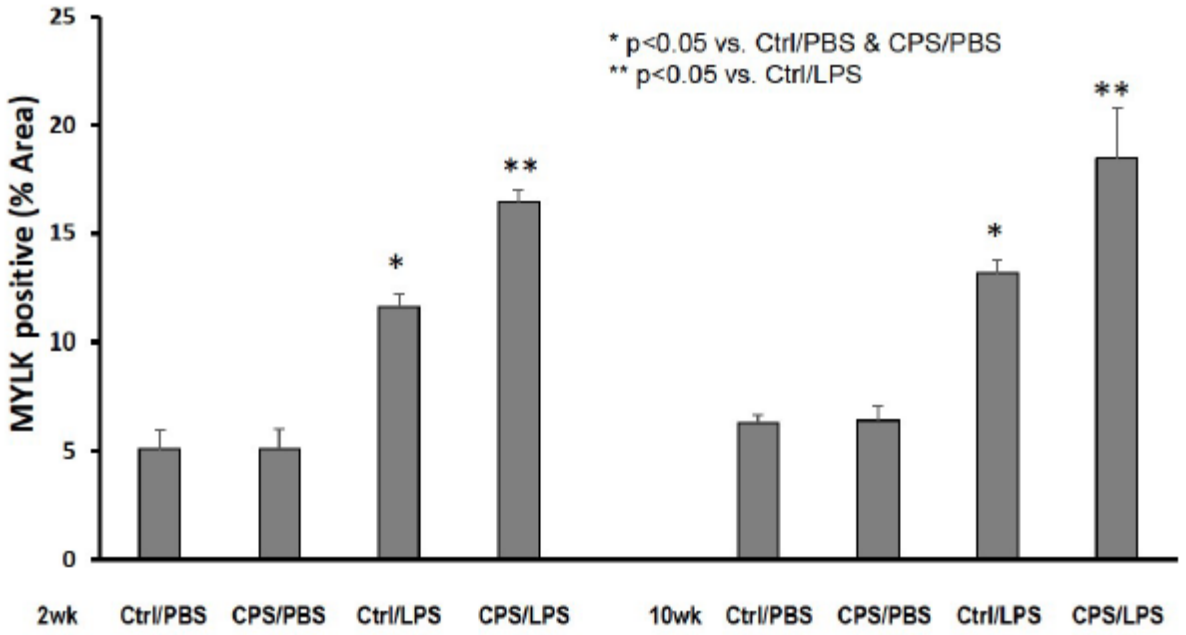
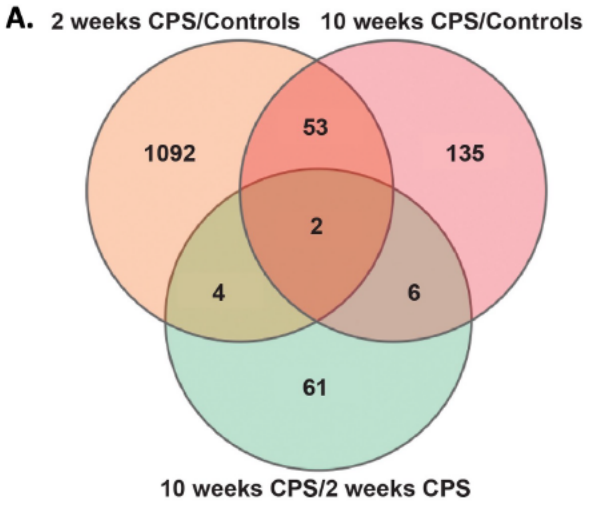
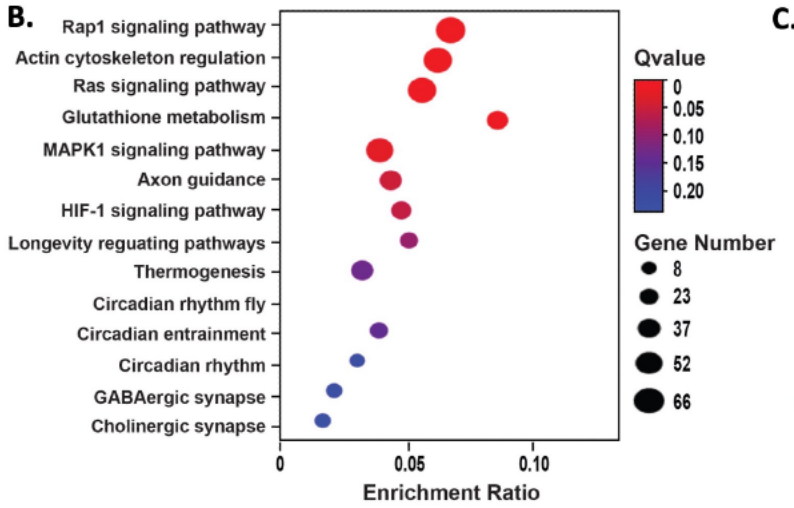
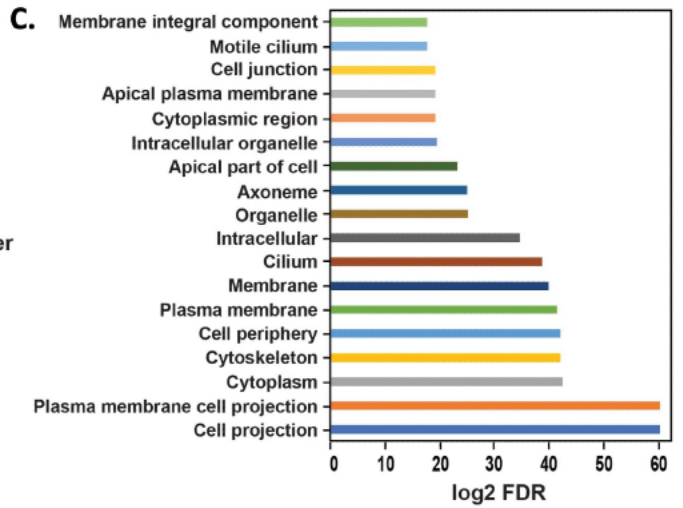
Circadian disruption induces the dysregulation of actin cytoskeleton pathway genes: Mylk4 and multiple integrin genes











Casanova et al, Front Immunol. 2024;14;15: 1348181.

California Thoracic Society

Thank you

California Thoracic Society

Update on ARDS Management Strategies and the Role of Steroids in Severe CAP and ARDS

Jeff Gotts, MD/PhD

Kaiser Permanente-San Francisco

Disclosures

- I have the following relationships with ACCME defined ineligible companies:
- **No disclosures**
- I **WILL NOT** discuss off-label use and/or investigational use of any drugs or devices.

Outline

- The (new) Global Definition of ARDS
  - History/rationale, substance
  - Critique
- Update on Management
  - ECMO
  - Steroids
  - New ATS Guidelines
  - Ongoing Trials

A Brief History of ARDS Definitions and Major Trials/Trends

1967 Adult RDS **clinical description** by Ashbaugh and Petty

1988 Murray and the Lung Injury Score (cxr, O_2, peep, compliance)

1994 **AECC Definition** "Adult"-> "**Acute**" RDS: acute onset, bilateral consolidations, p/f <= 200 ("ALI" 300<p/f<200), not due to ↑LAP

2000 ARMA trial (LPV)

Late 2009-2010s Influenza Pandemic; HFNC emerges as adult therapy

2012 **Berlin Definition**: **<1 week** with **known insult**, bilateral consolidations, p/f 200-300, 100-200, <100 **with peep >=5**

2013 PROSEVA (Proning)

2015 FLORALI (HFNC)

2020 Covid Pandemic

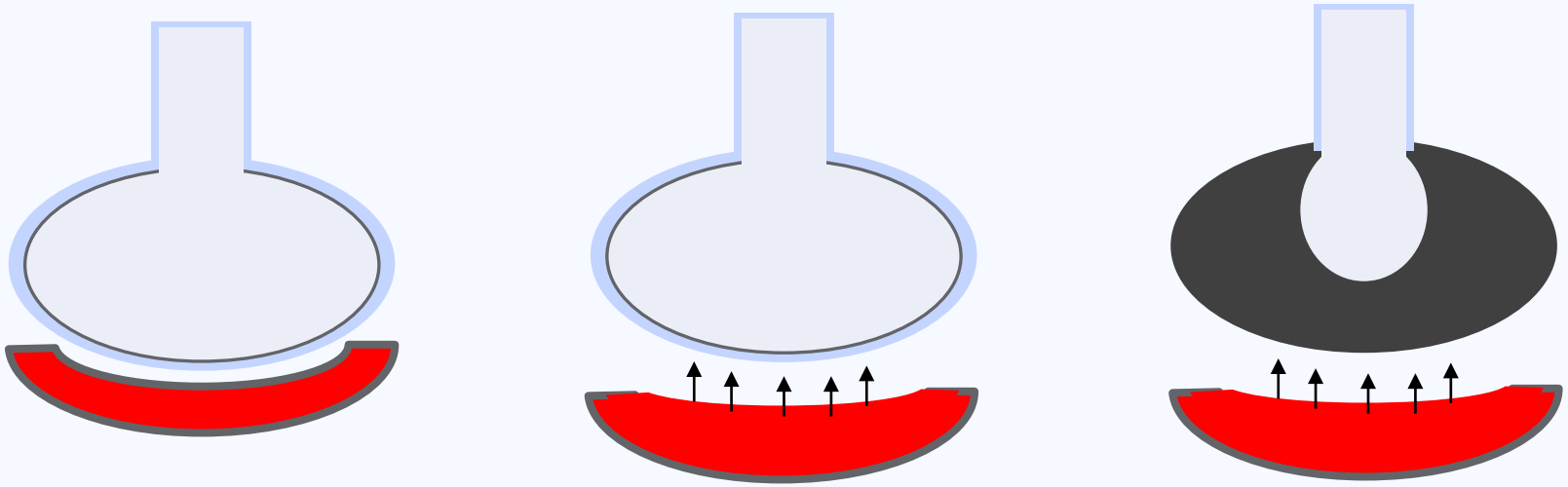
Key Limitations of the Berlin Definition

- Requirement for peep (NIPPV or Mech Vent)->excludes even very ill patients managed with HFNC
- Less use of ABG in routine clinical care
- More use of ultrasound

The Global Definition of ARDS

- June 2021 consensus conference 32 members—working groups on risk factors/timing, radiology, and oxygenation; Published in AJRCCM 1/2024
- Retained timing criterion of <1 week onset + risk factor
- Expanded Berlin Definition to allow use of s/f ratio (spo2 <97%), chest ultrasound
- Created 3 categories of ARDS
  - **Non-intubated ARDS** p/f <300 (s/f <315) on ≥ 30L HFNC or NIPPV
  - Intubated ARDS: Mild (p/f 200-300), Mod (p/f 100-200), Severe p/f <100; **or s/f**
  - **Resource-limited definition**: s/f <315, no O_2 requirement
- Elaborated on a Conceptual Model of pathogenesis

The Global Definition: Conceptual Model



Alveolar level:	↑Endothelial permeability, interstitial inflammation; Intact epithelial barrier and fluid transport	**Widespread Alveolar epithelial** injury/inflammation with high protein edema, loss of surfactant
Lung level:	Mild ↓ Compliance and ↑V_d/V_t; Oxygenation largely preserved	Gravity-dependent atelectasis, ↓↓ compliance, ↑↑V_d/V_t, Shunting

The Global Definition of ARDS– Reception/critique

- Process was not a proper Delphi process (gathering of experts was not based on predefined criteria)
- Inclusion of s/f without adequate prospective validation
- Removal of peep criterion and incorporation of ultrasound further ↑ heterogeneity of a heterogenous syndrome
- ARDS is not a single disease and the term should be abandoned

American Review of Respiratory Disease

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1975: Lumper Splitter Debate 50 years ago in AJRCCM

John Murray: "…Lumping these disorders together serves no useful purpose and has the disadvantage of detracting from important and distinctive differences in pathogenesis, therapy, and prognosis."

Tom Petty: "I believe [ARDS] is a desirable lumping of a variety of pulmonary insults. The common denominators are clinical respiratory distress…stiff lungs, poor oxygen transport, diffuse alveolar infiltrates, and heavy, airless lungs with increased extravascular lung water"

An Esoteric Debate? A Clinician's Perspective

- The application of peep and the passage of time fixes many of the patients with atelectasis-dominant physiology and/or low-protein pulmonary edema
- Low compliance, high V_d/V_t and deep hypoxemia that persist despite 24 hrs of LPV/Proning and optimal fluid mgt identify patients with prolonged high vent requirements and high mortality
- Lumping has lead to improvements in supportive care for injured lungs (mechanical force, fluid management, +/- steroids)
- Until recently diagnostic limitations have made splitting impractical for trial design
  - Exception viral PNA in 2009 and 2020-2022
  - Progress with relatively simple splits (e.g., hypo- and hyper-inflammatory based on physiology and a few biomarkers)

ARDS Mgt Update – ECMO/ECOR & Low-FIO2 Strategies

- **CESAR** (2009): Referral to ECMO center improved outcomes
- **EOLIA** (2018): 249 patients p/f <50 x 3 hrs, <80 x 6 hrs randomized to VV ECMO or continued MV; 35% vs 46% 60d mortality (ns*)
- **REST** (2021): 412 patients p/f <150 on peep 5 randomized to ECOR with TV 3 ml/kg (15-19 Fr single dual lumen cannula, heparin); 41.5% vs 39.5% 90d mortality (10 vs 2 ICH)
- **LOCO$_2$** (2020): 205 patients ARDS target PaO_2 55-70 (SpO_2 88-92%) vs 90-105 (SpO_2 >95%): 44.4% vs 30.4% 90d mortality
- **HOT-ICU** (2021): 2928 patients on ≥10L O2 target PaO_2 60 or 90: 42.9% vs 42.4% 90d mortality

40+ years of Steroids in ARDS/Severe Pneumonia

Yr	Name	Target	# pts	Steroid/duration	Result

Steroids in Severe Pneumonia/ARDS

- Timing, dose, type of steroids has varied widely
- Influenza generally excluded (2019 Cochrane review, ~30 observational & 1 RCT with 24 patients confirmed Flu)
- DEXA ARDS and CAPE COD convinced many, helped shift recent guidelines
- Most of the positive results gave steroids ***early***
  - *ESCAPe trial by Meduri 2022 586 patients CAP up to 96 hrs post-admission, no sig diff mortality vs CAPE COD rx steroids <24 hrs*
  - *Steinberg trial noted suggestion of harm if steroids started after 2 wks ARDS*

Recent Updates in ARDS Guidelines

Yr	Society	Recommendation	Strength, evidence quality

Ongoing Trials to Watch

Steroids

- DEXA-REFINE – Spain 2021-2025 acute hypoxemia + confirmed infection 980 patients: dex 6 mg x 10 days vs 20->10 over 10 days
- GuARDS Trial – UK 2024-2028 ARDS 1700 patients: dex 20->10 over days 1-10
- PRACTICAL-CORT-E2 Canada 2023-2025 acute hypoxemia 6250 patients: Early steroids, extended course for non-resolving
- ARREST – USA severe PNA 600 patients: aerosolized budesonide/formoterol vs saline bid x 5 days

Vent

- PRACTICAL- ultra low TV/ECOR; Driving pressure limited
- CAVIARDS – Multinational 2020-2026 mod-severe ARDS 760 patients: decremental peep vs peep/fio2

Drugs/Cell therapies

Sivelestat (elastase inhibitor), MSCs or vesicles, Pirfenidone, iv metoprolol, esmolol, vitamin C, trimodulin (opsonizing Ab)

REMAP-CAP – adaptive platform trial 20k enrollment >50 ICUs in 13 countries: antibiotics, hydrocortisone, anticoagulation, flu-specific, vitamin c, simvastatin, anti-platelet

Conclusions

1. The definition of ARDS remains controversial (and probably always will be)
2. Cornerstones of ARDS Mgt: LPV, Prone positioning
3. Growing consensus around:
   - ECMO for very severe ARDS
   - Steroids in early ARDS and severe CAP
   - Avoidance of low PaO_2 target
   - Use higher PEEP rather than RMs

Valley Children's HEALTHCARE

HOSPITAL | MEDICAL GROUP | HOME CARE | FOUNDATION

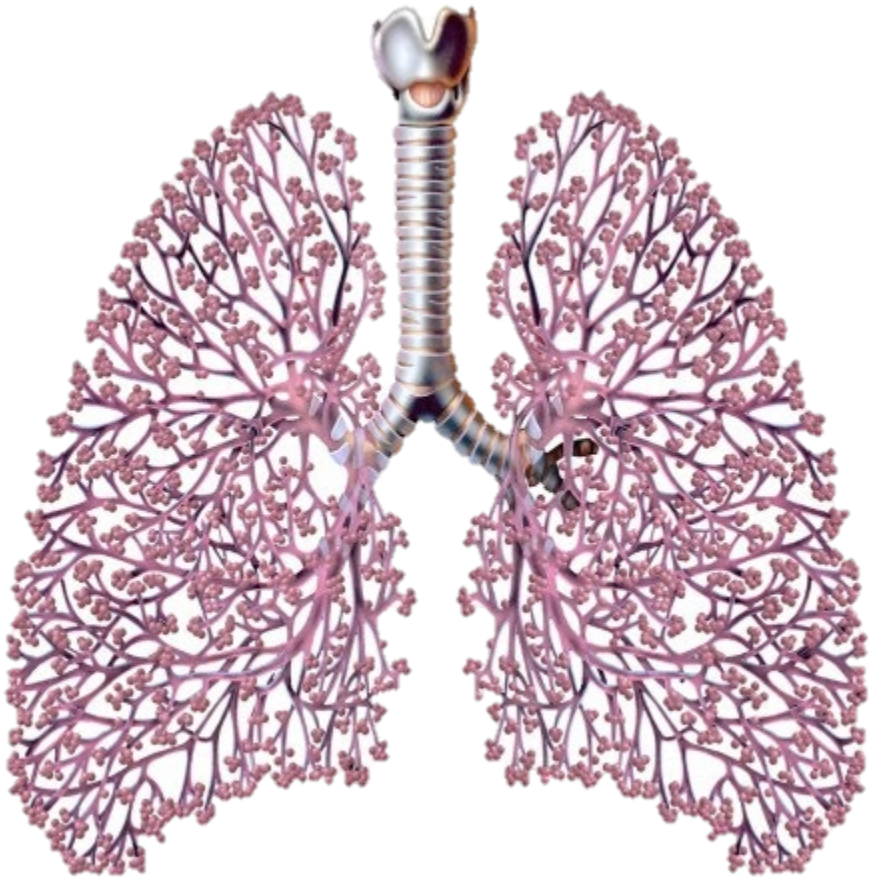
PARDS – PALICC – 2 Guidelines and Application of ECMO

Theresa Cantu, MSRC, RRT, RRT-NPS, AE-C

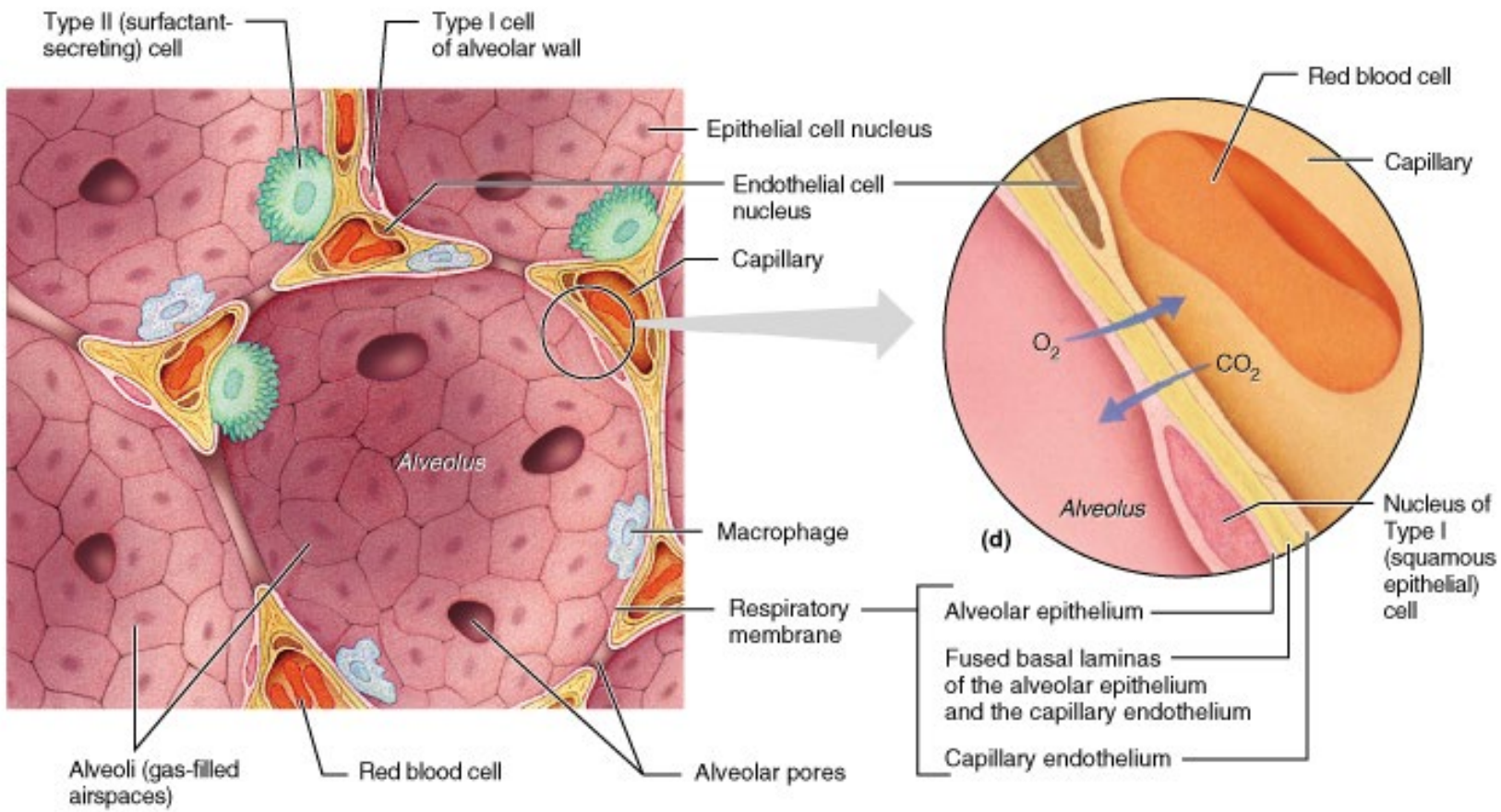
Objectives

- Describe PARDS
- Analyze definition criteria for PARDS
- Appraise recommendations for management of PARDS
- Discuss the application of ECMO in PARDS
- Describe the use of sNO in ECMO

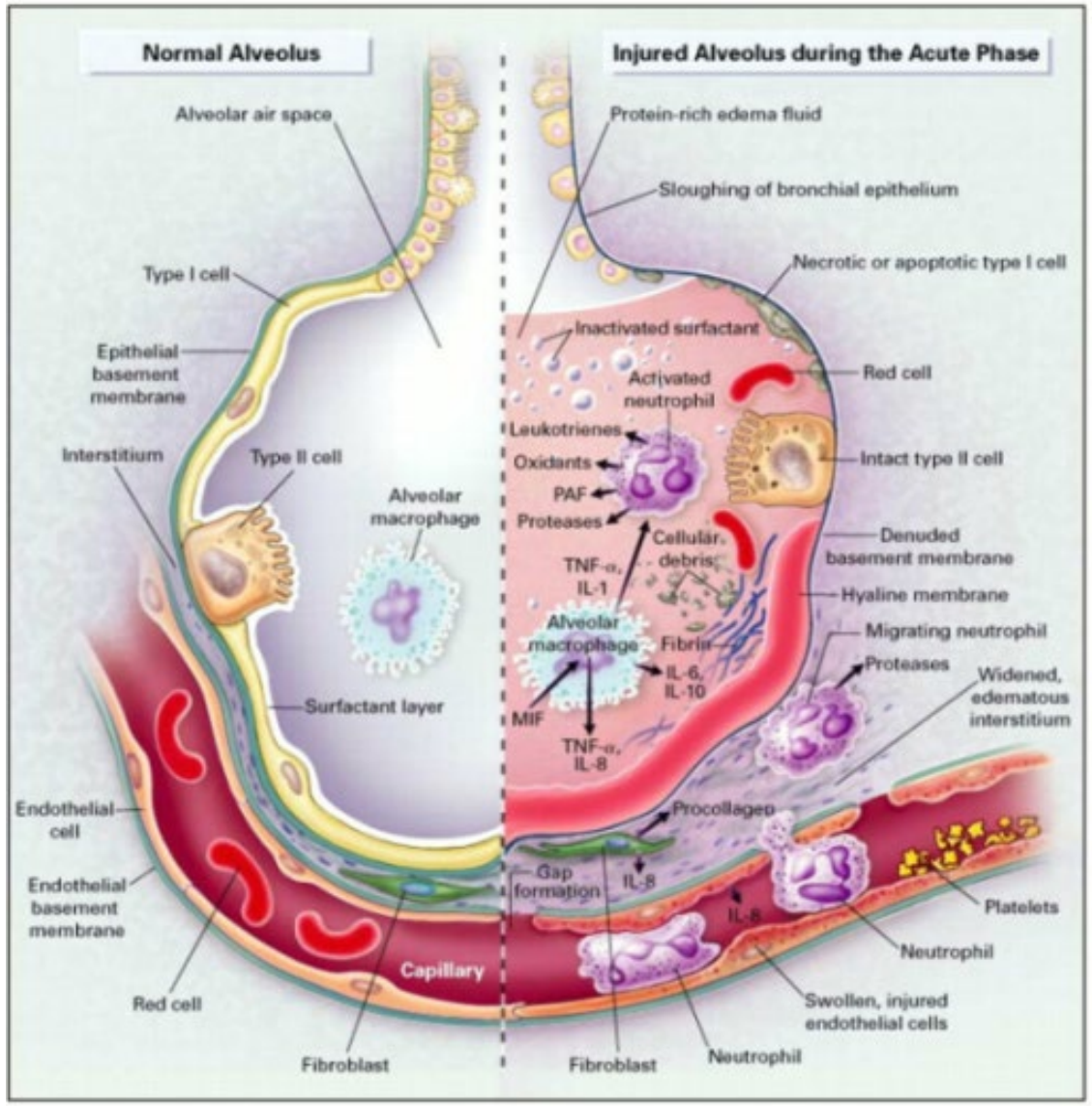
Quick Review



Alveolar Anatomy & Histology



Inflammatory Damage



PARDS

- Immune response resulting in increased alveolar permeability and subsequent flooding of alveoli
  - Severely restricts gas exchange
- Damages Type I (epithelial cells) and Type II (surfactant/healing cells) alveoli
- Treatment of ARDS with mechanical ventilation can further damage the alveoli d/t over distention (barotrauma, volutrauma, biotrauma, atelectrauma)
- Associated with pulmonary hypertension

2015 PALICC

- Pediatric Acute Lung injury Consensus Conference
  - 27 experts from 21 academic institutions in 8 countries
- Adult oriented criteria to diagnose and manage PARDS

PALICC - 2

- Second Pediatric Acute Lung injury Consensus Conference
- Guidelines for diagnosis and management of PARDS

- 52 multidisciplinary international content experts in PARDS and 4 methodology experts from 15 counties
  - 1 RCP, 1 RN, 1 PT, 1 PhD researcher
- Consensus conference methodology and implementation science

- Selection based on research in specific aspects of PARDS over 10 preceding years.

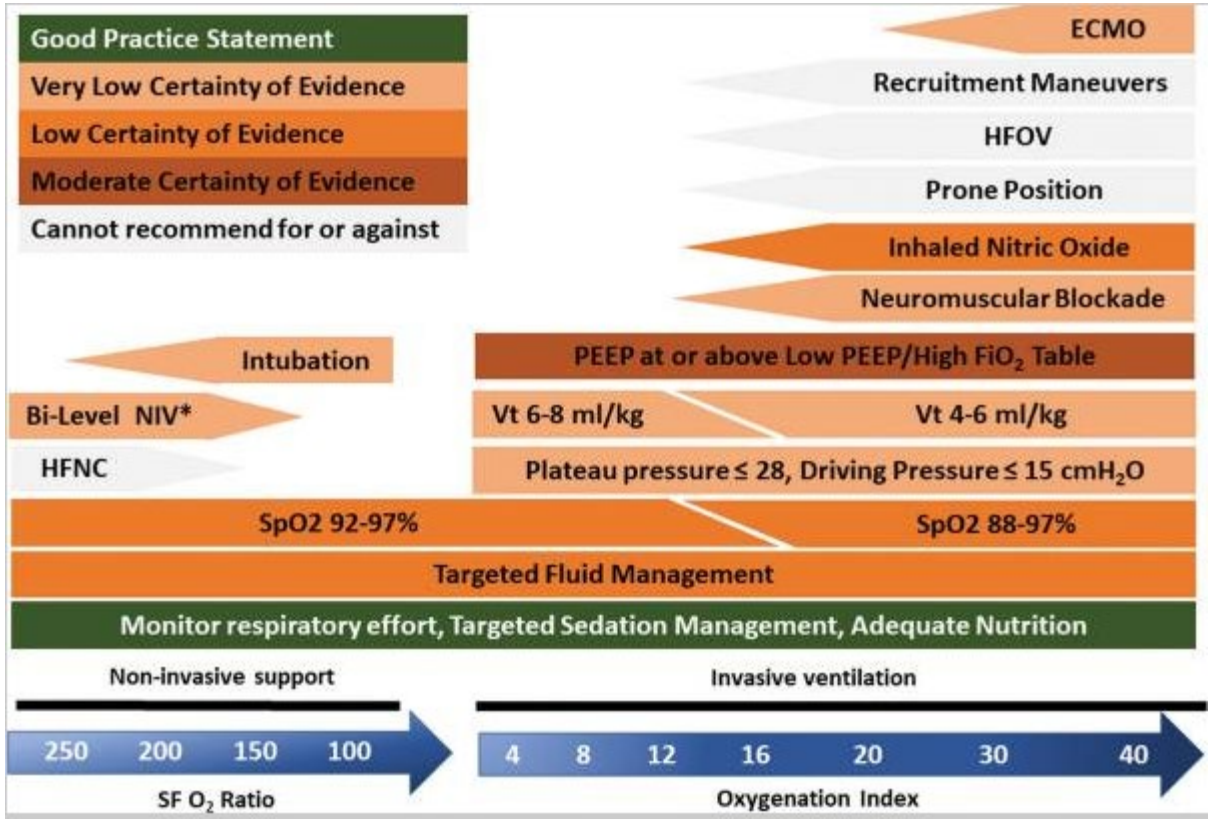
Methodology

- GRADE = Grading of Recommendations, Assessment, Development, and Evaluation,
- RAND = research and development.

- Clinical recommendations (GRADE, RAND)
- Good practice statements (GRADE, RAND)
- Research statements
- Policy statements
- Definition statements

Subgroups

- 1) definition, incidence, and epidemiology;
- 2) pathobiology, severity, and risk stratification;
- 3) ventilatory support;
- 4) pulmonary-specific ancillary treatment;
- 5) nonpulmonary treatment;
- 6) monitoring;
- 7) noninvasive respiratory support;
- 8) extracorporeal support;
- 9) morbidity and long-term outcomes;
- 10) clinical informatics and data science; and
- 11) resource-limited settings.


Good Practice Statement
Very Low Certainty of Evidence
Low Certainty of Evidence
Moderate Certainty of Evidence
Cannot recommend for or against
ECMO
Recruitment Maneuvers
HFOV
Prone Position
Inhaled Nitric Oxide
Neuromuscular Blockade
Intubation
PEEP at or above Low PEEP/High FiO2 Table
Bi-Level NIV*
Vt 6-8 ml/kg
Vt 4-6 ml/kg
HFNC
Plateau pressure ≤ 28, Driving Pressure ≤ 15 cmH2O
SpO2 92-97%
SpO2 88-97%
Targeted Fluid Management
Monitor respiratory effort, Targeted Sedation Management, Adequate Nutrition
Non-invasive support
Invasive ventilation
250 200 150 100
4 8 12 16 20 30 40
SF O2 Ratio
Oxygenation Index

Age (DS 1.1)	Exclude patients with perinatal lung disease		
Timing (DS 1.2)	Within 7 d of known clinical insult		
Origin of edema (DS 1.3)	Not fully explained by cardiac failure or fluid overload		
Chest imaging (DS 1.3)	New opacities (unilateral or bilateral) consistent with acute pulmonary parenchymal disease and which are not due primarily to atelectasis or pleural effusion[a]		
Oxygenation[b] (DS 1.4.1)	IMV: OI ≥ 4 or OSI ≥ 5		
	NIV[c]: $Pao_2/Fio_2 \leq 300$ or $Spo_2/Fio_2 \leq 250$		
	Stratification of PARDS severity: Apply ≥ 4 hr after initial diagnosis of PARDS (DS 1.4.4)		
	IMV-PARDS: (DS 1.4.1)	Mild/moderate: OI < 16 or OSI < 12 (DS 1.4.5)	Severe: OI ≥ 16 or OSI ≥ 12 (DS 1.4.5)
	NIV-PARDS[c] (DS 1.4.2; DS 1.4.3)	Mild/moderate NIV-PARDS: $Pao_2/Fio_2 > 100$ or $Spo_2/Fio_2 > 150$	Severe NIV-PARDS: $Pao_2/Fio_2 \leq 100$ or $Spo_2/Fio_2 \leq 150$
	Special populations [d]		
Cyanotic heart disease (DS 1.6.1; DS 1.6.2)	Above criteria, with acute deterioration in oxygenation not explained by cardiac disease		
Chronic lung disease (DS 1.6.3; DS 1.6.4)	Above criteria, with acute deterioration in oxygenation from baseline		

Recommendations - MV

- Cannot recommend mode (94%)
- VT 6-8ml/kg (98%)
  - <6ml/kg to stay below suggested plateau and driving pressure
- Plateau 28 cmH2O (92%)
- Driving 15 cmH2O (82%)
- PEEP at or above the lower PEEP/higher FiO2 table from ARDS Network protocol (96%)
- PEEP – oxygenation/oxygen delivery, hemodynamics, compliance measured under static conditions

Supplemental Table 1. Lower PEEP/higher FiO2 table, adapted from the ARDS Network protocol

FiO_2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
PEEP cmH_2O	5	6-8	8-10	10	10-14	14	14-18	18-24

Recruitment Maneuvers

- Cannot suggest for or against the use of recruitment maneuvers (94%)
- Careful recruitment maneuvers may be applied – slow incremental and decremental PEEP steps
- Sustained inflation maneuvers cannot be recommended

HFV

- HFOV may be considered in patients with PARDS in whom ventilatory goals cannot be met with lung protective strategies on conventional ventilation

SpO2 Targets/ pH Targets

- Mild/Moderate 92 – 97%
- Severe (after optimization if PEEP) <92%
- <88% not recommended

- Permissive hypercapnia
  - Lower limit of 7.2 (100%)
  - Exceptions
    - Intracranial hypertension, severe pulmonary hypertension, select CHD lesions, hemodynamic instability

Other considerations

- ET tube – cuffed (100%)
- iNO – no (98%)
  - Yes in documented pulmonary hypertension or severe right ventricular dysfunction, and bridge to ECMO
- Surfactant – no (100%)
- Prone – not enough data (94%)
- Suction – maintain airway (98%), routine instillation of isotonic saline should NOT be used in PARDS (94%)
- ACT – not enough data (96%)
- Routine use of steroids – no (96%)

Are you staying awake??

Non-pulmonary

- Sedation
  - Use evidence based assessment scales and protocols (100%)
  - Minimal yet effective to facilitate oxygen delivery, consumption and reduce work of breathing (96%)
- Delirium and Sleep
  - Assessed daily for delirium using validated tools (94%)
  - Multicomponent nonpharmacologic interventions as first line to prevent and treat delirium
- NMB
  - Minimal yet effective if MV cannot be achieved (98%)
  - Monitored and titrated to the goal depth established by IP team (94%)

Nonpulmonary cont….

- Nutrition
  - Early initiation of enteral nutrition
  - Facilitate recovery, maintain their growth and meet their metabolic needs
- Fluid
  - Prevent fluid overload while maintaining optimal oxygen delivery and preserving end organ function
- Transfusion
  - Hgb < 5g/dL – packed RBC
- Sleep and Rehab
  - Day/night activity and rest patterns (94%)
  - Mobility goals daily (94%) (established within 72 hours (98%)

Monitoring Parameters

- FiO2, SpO2, and or PaO2, MAP, and PEEP to assess severity and guide management
- PaCO2 and pH to adjust treatment strategy
- Continuous CO2 monitoring
- Calculate any dead space
- Cumulative fluid balance (98%)
- Arterial catheter in patients requiring frequent blood gas (92%)

Weaning

- Extubation readiness assessed daily (98%)
- SBT should be standardized (98%)

Imaging

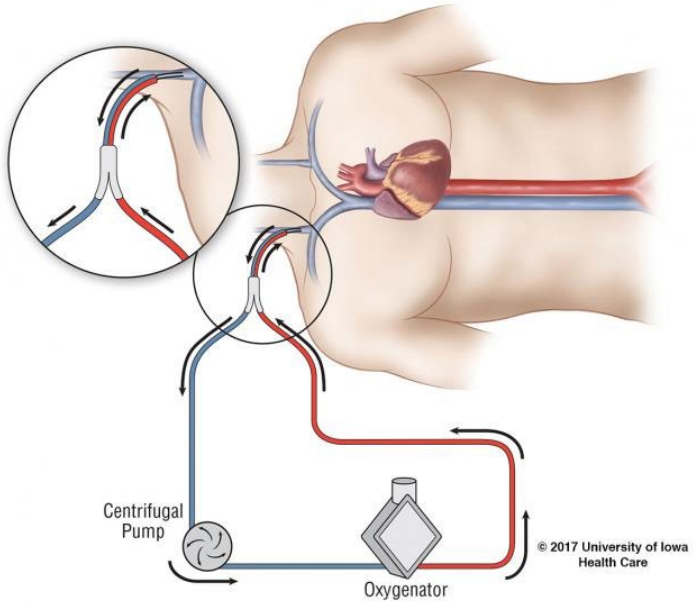
- Diagnosis (90%)
- Cannot make recommendation on routine use of x0ray, CT scan, lung ultrasound, and EIT (94%)

ECMO

- iNO as a bridge to ECMO
- Evaluation for ECMO with reversible cause of severe PARDS (96%)
- Serial evaluation compared with a single time point of assessment to guide decisions (98%)
- VV ECMO over VA ECMO (94%)
- Transfer to ECMO center should be considered in patients with PARDS who are failing to stabilize with optimal non-ECMO therapies (96%)

VV ECMO

- Venous drainage with venous return
  - Respiratory support
  - 50-75% of cardiac output captured



Pediatric Indications

Current ELSO guidelines state that there are no absolute indicators for pediatrics but consideration for ECMO is best within the first 7 days of high levels of vent support

Pediatric Contraindications

1. The “NO CHANCE” situation
    - ECMO support simply delays death but does not prevent nor relieve suffering (e.g., lethal congenital anomalies such as trisomy 13 or 18)
2. The “NO PURPOSE” situation
    - Although ECMO support may allow survival, the degree of physical or mental impairment would be unacceptable
3. The “NO ABILITY“ situation
    - ECMO support not possible d/t practical limitations (more to come)

ELSO Red Book, 2017

Practical Limitations

- Large intracranial bleed with mass effect
- Cardiac arrest without adequate CPR
- Irreversible underlying cardiac or lung pathophysiology
- Greater than two weeks of high pressure ventilation
- Pulmonary HTN with irreversible chronic lung disease
- Chronic multi-organ dysfunction
- Incurable malignancy
- Allogenic bone marrow recipients with pulmonary infiltrates

(ELSO RED BOOK, 2017)

Pediatric Respiratory Inclusion Criteria

- Children older than one month of age (>2.5kg)
  - Different pathophysiology and diagnoses than neonates
- Strict criteria not available, but generally used for lung disease that is:
  - Acute hypoxemia unresponsive to conventional/alternative therapy
  - Life threatening
  - OI > 40 for greater than 2 hours
  - Hypercarbic respiratory failure with pH < 7.2
  - Reversible
  - High risk of mortality without ECMO
  - Persistent air leak on maximal ventilator support

Anticoagulation

- During ECMO, the normal procoagulant and anticoagulant activity in the body is lost and procoagulant mechanisms are activated.
- In order to prevent this procoagulant activity in the ECMO circuit and in the patient, an exogenous anticoagulant is used: HEPARIN
  - This can result in bleeding in the systemic circulation
  - But without Heparin, the ECMO circuit would clot off
  - Bleeding complications are frequently encountered during ECMO & are the principal cause of morbidity and mortality.
- **Goal: “Don’t bleed to death but don’t clot to death”**

Labs

- The ECMO specialist will draw a series of two blood gases in combination with the patient blood gases to evaluate effectiveness of therapy
    - Patient
    - Pre-Oxygenator- Venous Blood (coming into the circuit)
    - Post-Oxygenator- Arterial Blood (coming out of the circuit)
- The bedside RN will be responsible for the patient blood gases
- Communicate with your specialist as to who/when other labs will be drawn.
- NO CAPILLARY STICKS!

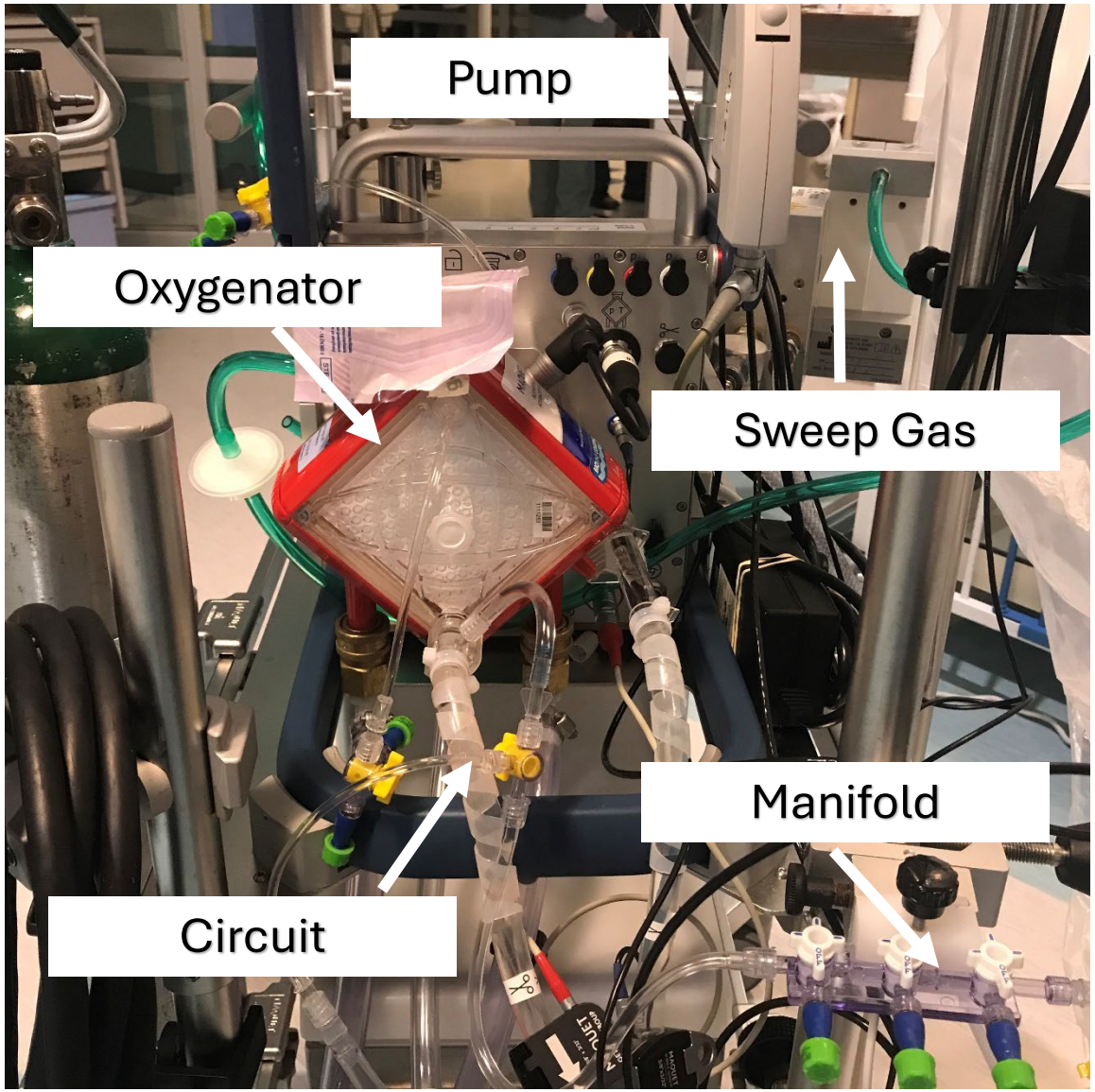
Labs

- Other lab values that are closely monitored
  - CBC with close focus on:
    - H&H and Platelet count
  - Coags: PT, PTT, INR, Fibrinogen & Hep Xa, AT III
  - D-Dimer: Indicates the presence of clot degradation
  - Plasma Free Hemoglobin: Measures free floating hemoglobin in blood serum; Indicates hemolysis
- Platelet consumption phenomenon

Respiratory Strategies During ECMO

- Ventilator Management
  - Transition to “rest” settings
  - Use Sweep gas to manage CO2 removal
  - Keep the lung open
  - Pulmonary toilet
  - Chest X-Ray
  - Bronchoscopy
  - Emergency vent settings
- Wean alternative therapies

Components of the ECMO Pump



iNO and ECMO

- iNO
- Treat pulmonary hypertension in VV ECMO

sNO

- sNO
- Potential to modulate blood-surface interaction and possibly reduce thrombosis, coagulopathy and inflammation
- Increased platelet survival
- Lower plasma beta-thromboglobulin levels
  - Marker of platelet degranulation
- Testing methemoglobin
  - Higher but no methemoglobinemia

ECMO follow-up

- Short and long term neurodevelopmental and physical functioning evaluations to assess for impairment (90%)
  - Discharge without disability
- Post ICU morbidity evaluation within 3 months of discharge (90%)

References

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Oxygen Targets in Respiratory Failure: Are We Hitting the Mark?

Brian J Smith, MSc, RRT

UC Davis Health, Dept. of Respiratory Care

Disclosures

- Fisher & Paykel
  - Paid Speaker Evidence in Action
- AARC Affiliation
  - Pediatric Aerosol Clinical Practice Guideline
  - Education Advisory Council Member
  - RT Led Research Advancement Committee

Objectives

- Summarize the evolution of complex life in the presence of oxygen and risk of supplemental oxygen therapy.
- Discuss current evidence defining optimal oxygen targets in Acute Respiratory Failure.
- Analyze known limitations in the accuracy of monitoring peripheral oxygen saturation values.

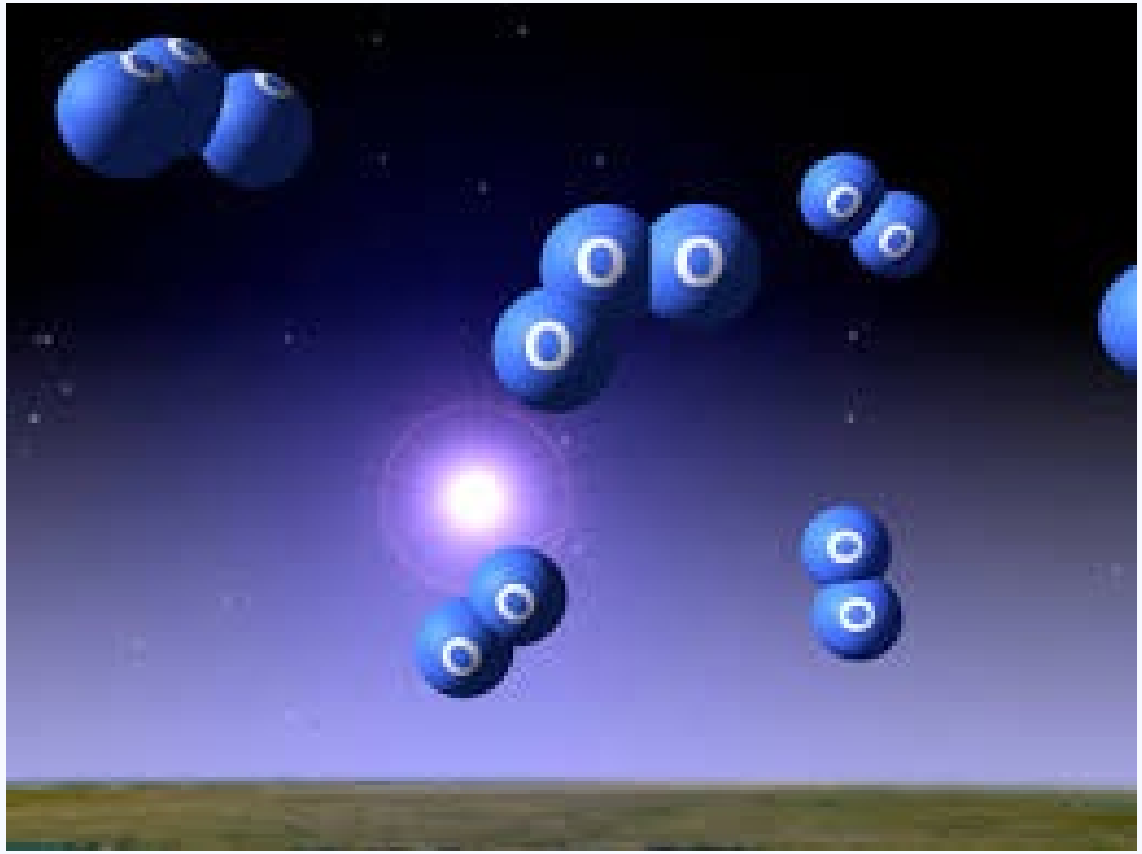
"Pre-Oxygen" Earth

- Great Oxidation Event
  - 2.45 Billion Years Ago
  - Prior to this event, environment was completely anoxic
  - That's right:
    - No oxygen bars
    - No thanks!

Bekker et al. 2004

The Oxygen Coup!

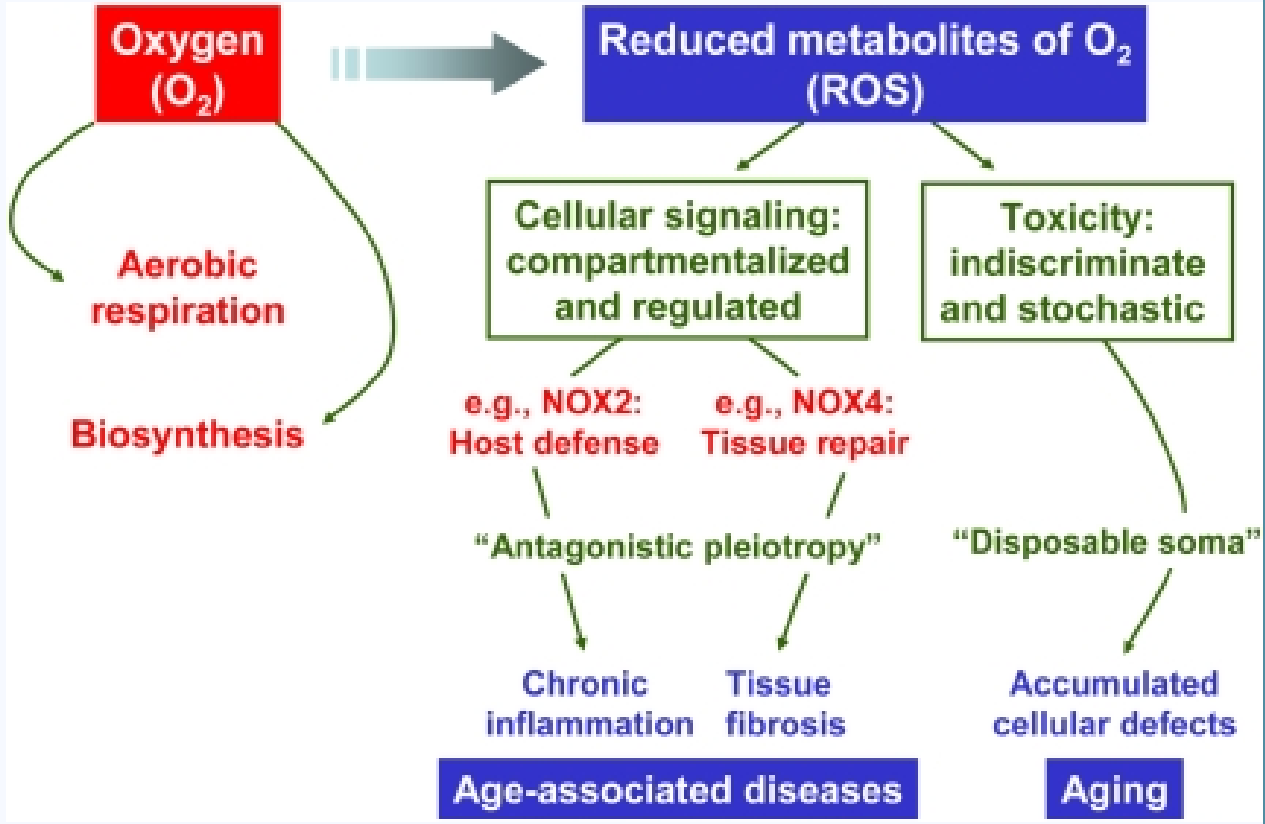
- Aerobic metabolism yields 4X's more energy per molecule of glucose ***oxidized*** than the most efficient anaerobic pathways.
- Biochemical symmetry of oxygenic photosynthesis and aerobic respiration $H_2O \rightarrow O_2 \rightarrow H_2O$ cycle
- 205 million years ago the atmospheric oxygen rose from 10% to current level of 21%
  - Corresponds with vertebrate evolution, endothermy, placentation, and proliferation of cell types



Falkowski et al. 2005

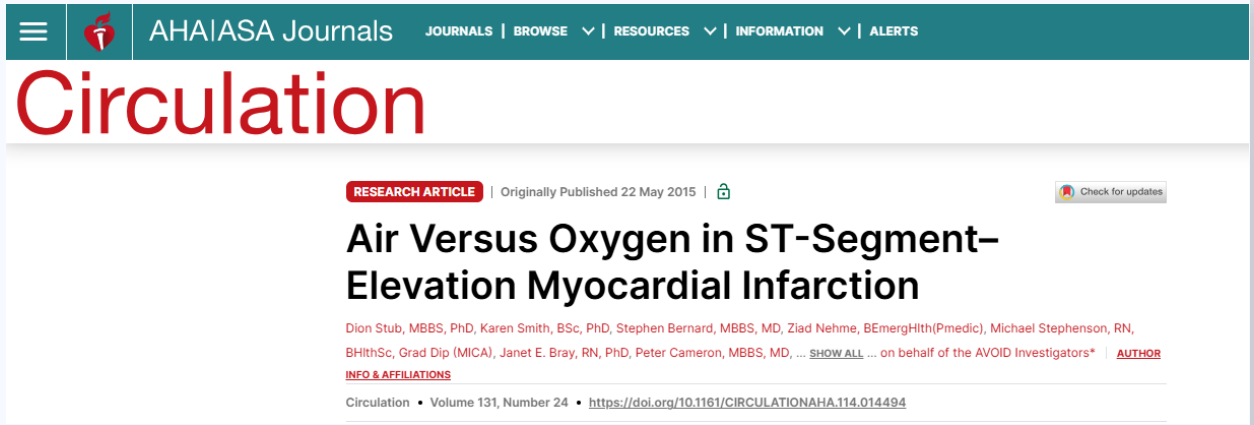
The Oxygen Double-Edged Sword

- O2 dependent biosynthesis is superior
- Aerobic respiration have significant advantages
- Oxidative stress
- Disease and aging



Thannickal 2009

Double-Edged Sword in Clinical Practice



- AVOID Study
  - Air Versus Oxygen in MI
  - Prospective, randomized, controlled trial comparing oxygen with no supplemental oxygen in patients with ST-elevation-myocardial infarction
  - (n)= 638
  - Primary end point was myocardial infarct size assessed by:
    - Cardiac enzymes, troponin 1, and creatine kinase
  - Secondary end point:
    - Recurrent MI, cardiac arrhythmia and myocardial infarct size assessed by cardiac MRI at 6 mos.
  - Outcomes:
    - Significant increase in mean peak creatine kinase (1948 vs 1543 U/L; Confidence interval 1.04-1.52; P=0.01)
    - Increase in the rate of recurrent MI and Increase in cardiac arrhythmia (40.4% vs 31.4%; P=0.05)
    - Oxygen group had increase in myocardia infarct size (n=139; 20.3 vs 13.1 g; P=0.04)

Stub et al. 2015

Enough evidence exists to be cautious

Original Research Article · Free

Effect of oxygen on breath markers of oxidative stress

M. Phillips | R.N. Cataneo | J. Greenberg Show More

European Respiratory Journal 2002 21(1): 48-51; DOI: https://doi.org/10.1183/09031936.02.00053402

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DIFFUSE LUNG DISEASE · Volume 166, Issue 4, Supplement , A3480-A3481, October 2024

IMPACT OF SUPPLEMENTAL OXYGEN THERAPY ON CLINICAL OUTCOMES IN PATIENTS WITH FIBROSING INTERSTITIAL LUNG DISEASE IN THE UNITED STATES

JOSEPH YANG · ANDREA STEFFENS · AMY OLSON · ... · BASRA GURSIMRAN · PHANI VEERANKI · JOAO ALBERTO M DE ANDRADE

American Journal of Respiratory and Critical Care Medicine

Home > American Journal of Respiratory and Critical Care Medicine > List of Issues > Volume 187, Issue 5

Clinical Risk Factors for Primary Graft Dysfunction after Lung Transplantation

Joshua M. Diamond [1], James C. Lee [1], Steven M. Kawut [1,2,3], Rupal J. Shah [1], A. Russell Localio [2], Scarlett L. Bellamy [2], David J. Lederer [4], Edward Cantu [5], Benjamin A. Kohl [6], Vibha N. Lama [7], Sangeeta M. Bhorade [8], Show All...

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RESEARCH ARTICLE | LUNG DISEASE

Oxidation increases mucin polymer cross-links to stiffen airway mucus gels

SHAOPENG YUAN, MARTIN HOLLINGER, MARRAH E. LACHOWICZ-SCROGGINS, SHEENA C. KERR, ELEANOR M. DUNICAN, BRIAN M. DANIEL, SUDAKSHINA GHOSH, SERPEL C. ERZURUM, BELINDA WILLARD, [...], AND JOHN V. FAHY +4 authors Authors Info & Affiliations

frontiers in Physiology

Front Physiol. 2019 Jan 25;10:10. doi: 10.3389/fphys.2019.00010

Pulmonary Oxygen Toxicity in Navy Divers: A Crossover Study Using Exhaled Breath Analysis After a One-Hour Air or Oxygen Dive at Nine Meters of Sea Water

Thijs T Wingelaar [1,2,*], Pieter-Jan A M van Ooij [1], Paul Brinkman [3], Rob A van Hulst [2]

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PMCID: PMC6355711 PMID: 30740057

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Journal of Intensive Care

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Guideline-based management of acute respiratory failure and acute respiratory distress syndrome

Seitaro Fujishima

Journal of Intensive Care **11**, Article number: 10 (2023) | Cite this article

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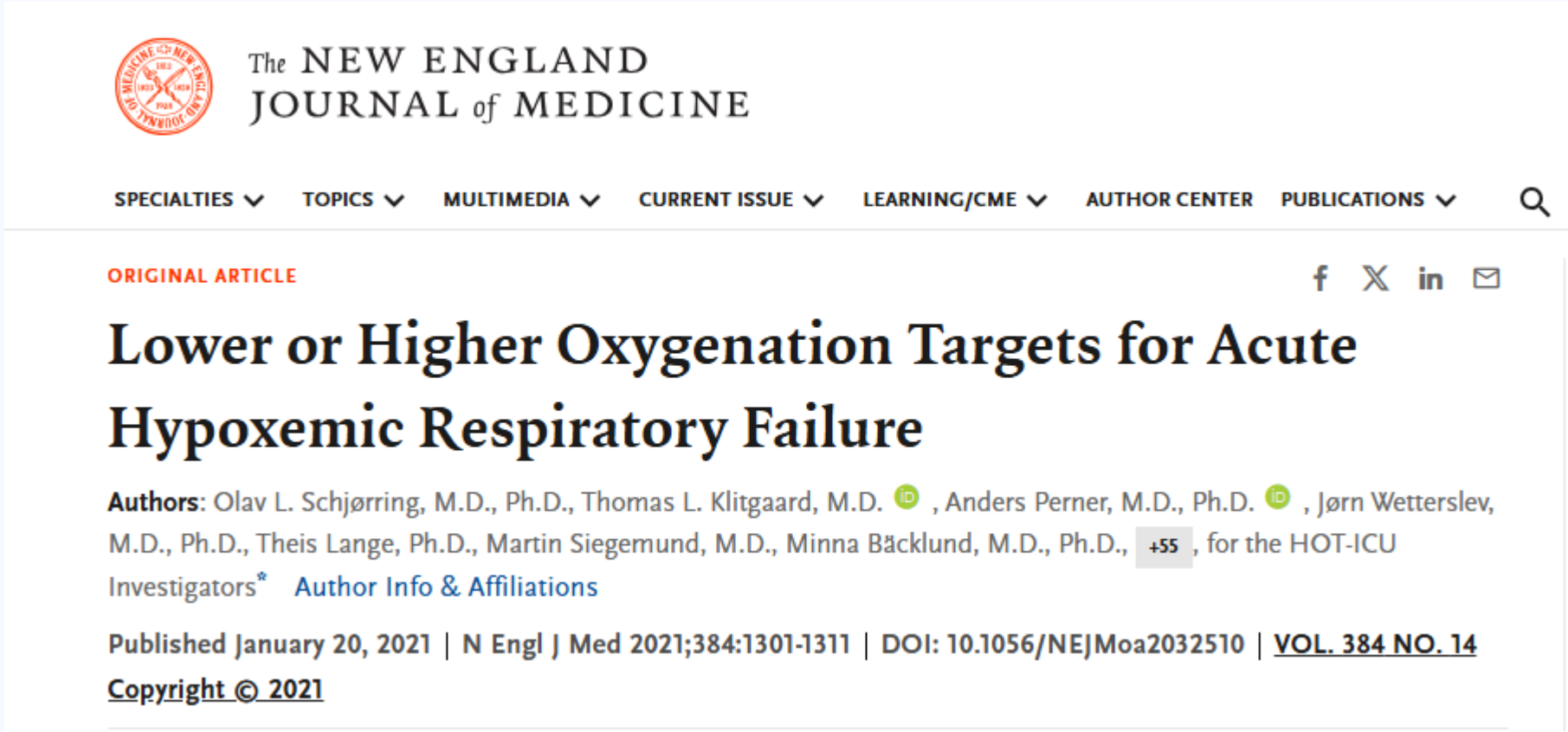
Abstract

Oxygen Targets in Acute Respiratory Failure



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ORIGINAL ARTICLE

Lower or Higher Oxygenation Targets for Acute Hypoxemic Respiratory Failure

Authors: Olav L. Schjørring, M.D., Ph.D., Thomas L. Klitgaard, M.D., Anders Perner, M.D., Ph.D., Jørn Wetterslev, M.D., Ph.D., Theis Lange, Ph.D., Martin Siegemund, M.D., Minna Bäcklund, M.D., Ph.D., +55, for the HOT-ICU Investigators* Author Info & Affiliations

Published January 20, 2021 | N Engl J Med 2021;384:1301-1311 | DOI: 10.1056/NEJMoa2032510 | VOL. 384 NO. 14

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oxygen-Saturation Targets for Critically Ill Adults Receiving Mechanical Ventilation

Authors: Matthew W. Semler, M.D., Jonathan D. Casey, M.D., Bradley D. Lloyd, R.R.T.-A.C.C.S., Pamela G. Hastings, R.R.T.-A.C.C.S., Margaret A. Hays, R.N., Joanna L. Stollings, Pharm.D., Kevin G. Buell, M.B., B.S., +11, for the PILOT Investigators and the Pragmatic Critical Care Research Group* Author Info & Affiliations

Published October 24, 2022 | N Engl J Med 2022;387:1759-1769 | DOI: 10.1056/NEJMoa2208415

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Original Investigation | Caring for the Critically Ill Patient

FREE

August 31, 2021

Effect of Low-Normal vs High-Normal Oxygenation Targets on Organ Dysfunction in Critically Ill Patients

A Randomized Clinical Trial

Harry Gelissen, MD, MBA[1]; Harm-Jan de Grooth, MD, PhD[1,2]; Yvo Smulders, MD, PhD[3]; et al

» Author Affiliations | Article Information

JAMA. 2021;326(10):940-948. doi:10.1001/jama.2021.13011

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Conservative Oxygen Therapy during Mechanical Ventilation in the ICU

Author: The ICU-ROX Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group* Author Info & Affiliations

Published October 14, 2019 | N Engl J Med 2020;382:989-998 | DOI: 10.1056/NEJMoa1903297 | VOL. 382 NO. 11

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Liberal or Conservative Oxygen Therapy for Acute Respiratory Distress Syndrome

Authors: Loic Barrot, M.D., Pierre Asfar, M.D., Ph.D., Frederic Mauny, M.D., Ph.D., Hadrien Winiszewski, M.D., Florent Montini, M.D., Julio Badie, M.D., Jean-Pierre Quenot, M.D., Ph.D., +11, for the LOCO$_2$ Investigators and REVA Research Network* Author Info & Affiliations

Published March 11, 2020 | N Engl J Med 2020;382:999-1008 | DOI: 10.1056/NEJMoa1916431 | VOL. 382 NO. 11

Pulse oximetry

Meta-Analysis > BMC Med. 2022 Aug 16;20(1):267. doi: 10.1186/s12916-022-02452-8.

The accuracy of pulse oximetry in measuring oxygen saturation by levels of skin pigmentation: a systematic review and meta-analysis

Chunhu Shi [1 2], Mark Goodall [3 4], Jo Dumville [5 6], James Hill [4 7], Gill Norman [5 6], Oliver Hamer [4 7], Andrew Clegg [4 7], Caroline Leigh Watkins [4 7], George Georgiou [4 7], Alexander Hodkinson [8 9], Catherine Elizabeth Lightbody [10], Paul Dark [11 12], Nicky Cullum [5 6]

Affiliations + expand

PMID: 35971142 PMCID: PMC9377806 DOI: 10.1186/s12916-022-02452-8

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Annals of the American Thoracic Society

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Racial Disparity in Oxygen Saturation Measurements by Pulse Oximetry: Evidence and Implications

Haya Jamali [1], Lauren T. Castillo [2], Chelsea Cosby Morgan [3], Jason Coult [4], Janice L. Muhammad [5], Oyinkansola O. Osobamiro [4], Elizabeth C. Parsons [6,7]*, and Rosemary Adamson [6,7]*

+ Author Affiliations

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Falkowski PG, Katz ME, Milligan AJ, Fennel K, Cramer BS, Aubry MP, Berner RA, Novacek MJ, Zapol WM. The rise of oxygen over the past 205 million years and the evolution of large placental mammals. Science 2005;309:2202–2204.

Stub D, Smith K, Bernard S, et al. Air Versus Oxygen in ST-Segment-Elevation Myocardial Infarction. Circulation. 2015;131(24):2143-2150. doi:10.1161/CIRCULATIONAHA.114.014494

Thannickal VJ. Oxygen in the evolution of complex life and the price we pay. *Am J Respir Cell Mol Biol*. 2009;40(5):507-510. doi:10.1165/rcmb.2008-0360PS

PRO: Early Intubation is Preferential for the Patient with ARDS on HFNC

Christiana M. Hayward, MD

Harbor-UCLA Medical Center

Disclosures

- I have no relationships with ACCME defined ineligible companies.

- I **WILL/WILL NOT** discuss off-label use and/or investigational use of any drugs or devices.

ARDS Definition

Berlin Definition of ARDS 2012			
	Classification		
	Mild	Moderate	Severe
Time to Onset	Within 7 days of insult or new/worsening symptoms		
Origin	Respiratory failure not fully explained by cardiac failure or fluid overload		
Radiographic features	Bilateral opacities on CXR or CT OR (not explained by effusions, atelectasis, nodules/masses)		
Hypoxemia PaO2/FiO2	201-300 with NIV/CPAP PEEP ≥ 5	101-200 with PEEP ≥ 5	<100 with PEEP ≥ 5

Ferguson, N.D., Fan, E., Camporota, L. *et al.* The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. *Intensive Care Med* 38, 1573–1582 (2012). https://doi.org/10.1007/s00134-012-2682-1

ARDS Definition

Berlin Definition of ARDS 2012: Kigali Modification			
	Classification		
	Mild	Moderate	Severe
Time to Onset	Within 7 days of insult or new/worsening symptoms		
Origin	Respiratory failure not fully explained by cardiac failure or fluid overload		
Radiographic features	Bilateral opacities on CXR or CT **OR U/S** (not explained by effusions, atelectasis, nodules/masses)		
~~Hypoxemia PaO2/FiO2~~	~~201-300 with NIV/CPAP PEEP ≥ 5~~	~~101-200 with PEEP ≥ 5~~	~~<100 with PEEP ≥ 5~~
Hypoxemia SpO2/FiO2	**≤ 315 with SpO2 ≤ 97%**		

Riviello ED, Kiviri W, Twagirumugabe T, et al. Hospital Incidence and Outcomes of the Acute Respiratory Distress Syndrome Using the Kigali Modification of the Berlin Definition. *Am J Respir Crit Care Med*. 2016;193(1):52-59. doi:10.1164/rccm.201503-0584OC

ARDS Definition

ARDS Global Definition 2023			
	Classification		
	Mild	Moderate	Severe
Time to Onset	Within 7 days of insult		
Origin	Respiratory failure not fully explained by cardiac failure or fluid overload		
Radiographic features	Bilateral opacities on CXR or CT OR Bilateral B-line and/or consolidations on US (not explained by effusions, atelectasis, nodules/masses)		
Intubated PaO2/FiO2	201-300 with PEEP ≥ 5	101-200 with PEEP ≥ 5	<100 with PEEP ≥ 5
Intubated SpO2/FiO2	235-315 with SpO2 ≤ 97%	148-234 with SpO2 ≤ 97%	≤ 148 with SpO2 ≤ 97%
Non-intubated PaO2/FiO2 SpO2/FiO2	**PaO2/FIO2 ≤300 OR SpO2 ≤ 315 On HFNC ≥ 30LPM or NIV/CPAP with PEEP ≥ 5**		

Matthay MA, Arabi Y, Arroliga AC, et al. A new global definition of acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine*. 2024;209(1):37-47. doi:10.1164/rccm.202303-0558ws

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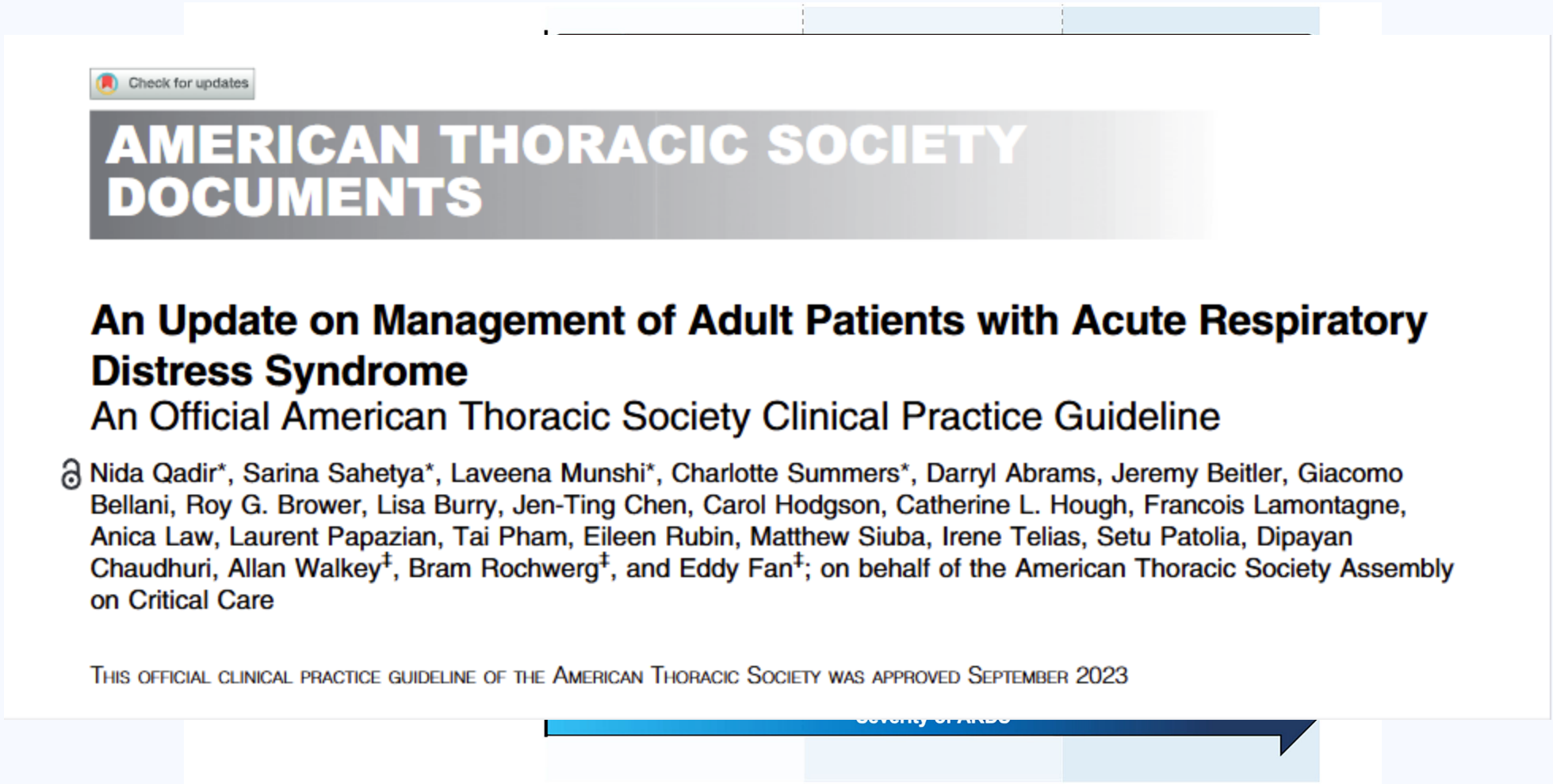
An Update to ARDS Management



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AMERICAN THORACIC SOCIETY DOCUMENTS

An Update on Management of Adult Patients with Acute Respiratory Distress Syndrome

An Official American Thoracic Society Clinical Practice Guideline

Nida Qadir*, Sarina Sahetya*, Laveena Munshi*, Charlotte Summers*, Darryl Abrams, Jeremy Beitler, Giacomo Bellani, Roy G. Brower, Lisa Burry, Jen-Ting Chen, Carol Hodgson, Catherine L. Hough, Francois Lamontagne, Anica Law, Laurent Papazian, Tai Pham, Eileen Rubin, Matthew Siuba, Irene Telias, Setu Patolia, Dipayan Chaudhuri, Allan Walkey‡, Bram Rochwerg‡, and Eddy Fan‡; on behalf of the American Thoracic Society Assembly on Critical Care

THIS OFFICIAL CLINICAL PRACTICE GUIDELINE OF THE AMERICAN THORACIC SOCIETY WAS APPROVED SEPTEMBER 2023

Qadir N, Sahetya SK, Munshi L, et al. An Update on Management of Adult Patients with Acute Respiratory Distress Syndrome: An Official American Thoracic Society Clinical Practice Guideline. *American Journal of Respiratory and Critical Care Medicine*. 2024;209(1):24-36. doi:https://doi.org/10.1164/rccm.202311-2011st

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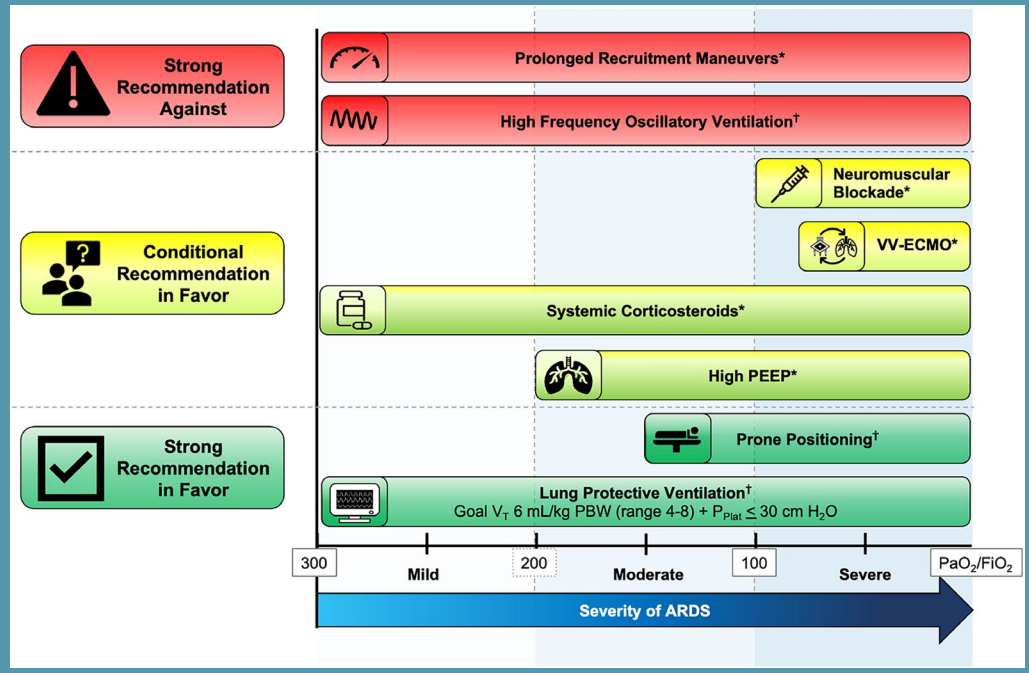
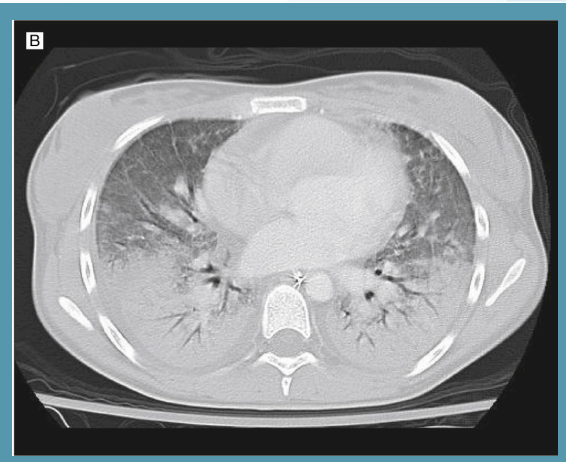
Lung Protective Ventilation: VALI Prevention

- Volutrauma
- Barotrauma
- Atelectatrauma
- Biotrauma

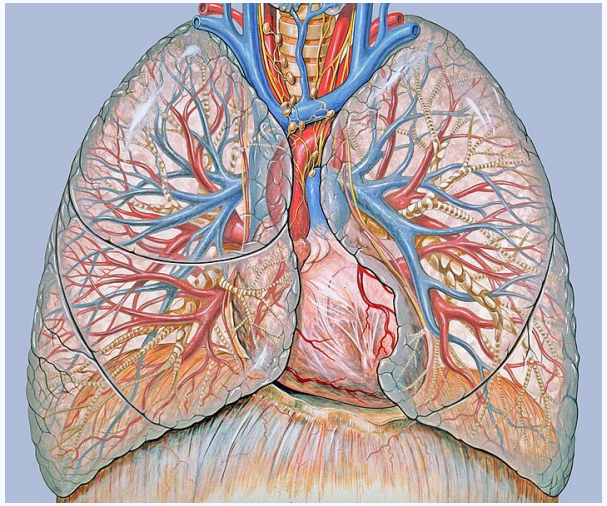




Qadir N, Sahetya S, Munshi L, et al. An Update on Management of Adult Patients with Acute Respiratory Distress Syndrome: An Official American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2024;209(1):24-36. doi:10.1164/rccm.202311-2011ST
Fan E, Needham DM, Steward TE. Ventilatory management of acute lung injury and acute respiratory distress syndrome. *JAMA*. 2005;294(22):2889. doi:10.1001/jama.294.22.2889

The Math of the Respiratory System

- $Pao(t) + Pmus(t) = PEEP + [Ers \times V(t)] + [Rrs \times Flow(t)]$
  - Pao = pressure at the airway opening
  - Pmus = pressure generated by respiratory muscles
    - Difference between the pressure generated by the relaxed chest wall and the change in pleural pressure (Ppl) at given lung volume
  - PEEP= positive end-expiratory pressure
  - Ers = respiratory system elastance
  - V = tidal volume
  - Rrs = resistance of the respiratory system
  - Flow = inspired gas flow



Mauri T, Cambiaghi B, Spinelli E, Langer T, Grasselli G. Spontaneous breathing: a double-edged sword to handle with care. *Ann Transl Med*. 2017;5(14):292. doi:10.21037/atm.2017.06.55

Patient Self Inflicted Lung Injury (PSILI)

Complex pathophysiology related to lung pathology and respiratory physiology

Physiologically driven by:

- Respiratory drive
- Respiratory effort*
- Breathing pattern

PSILI worsening pulmonary function has been studied in animal studies

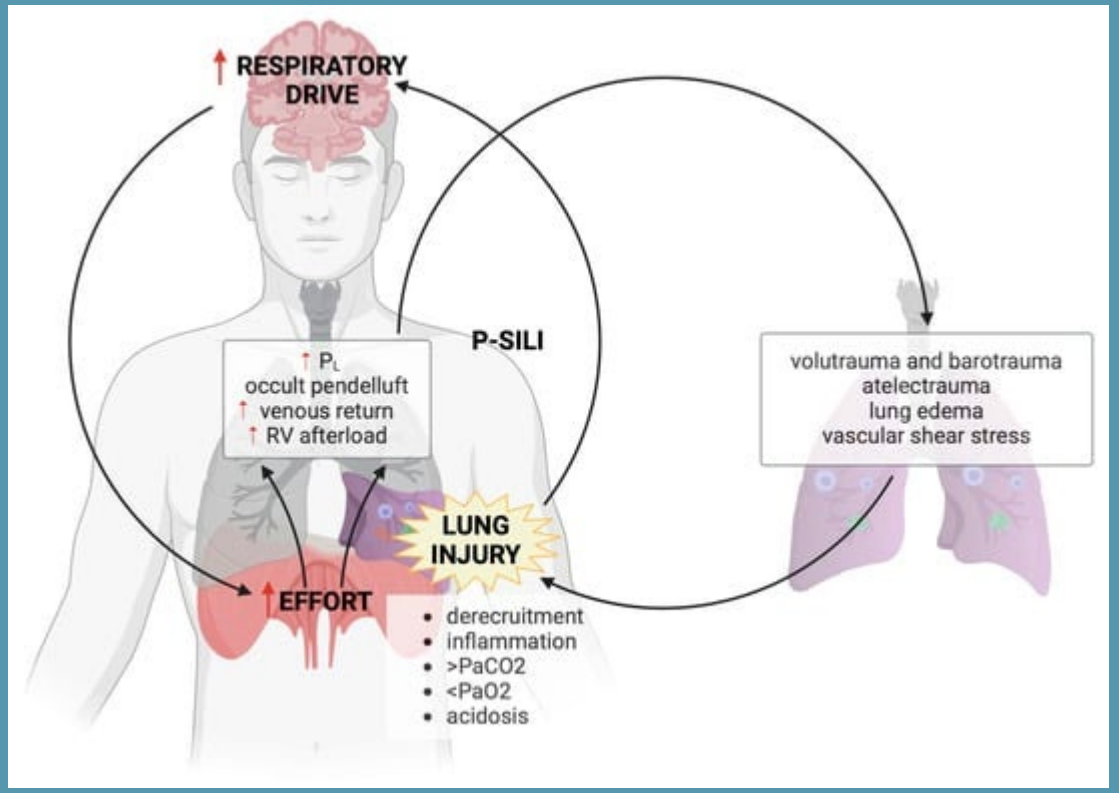


Image: Marongiu I, Slobod D, Leali M, Spinelli E, Mauri T. Clinical and Experimental Evidence for Patient Self-Inflicted Lung Injury (P-SILI) and Bedside Monitoring. *Journal of Clinical Medicine*. 2024; 13(14):4018. https://doi.org/10.3390/jcm13144018

Mauri T, Cambiaghi B, Spinelli E, Langer T, Grasselli G. Spontaneous breathing: a double-edged sword to handle with care. *Ann Transl Med*. 2017;5(14):292. doi:10.21037/atm.2017.06.55

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- Respiratory effort*
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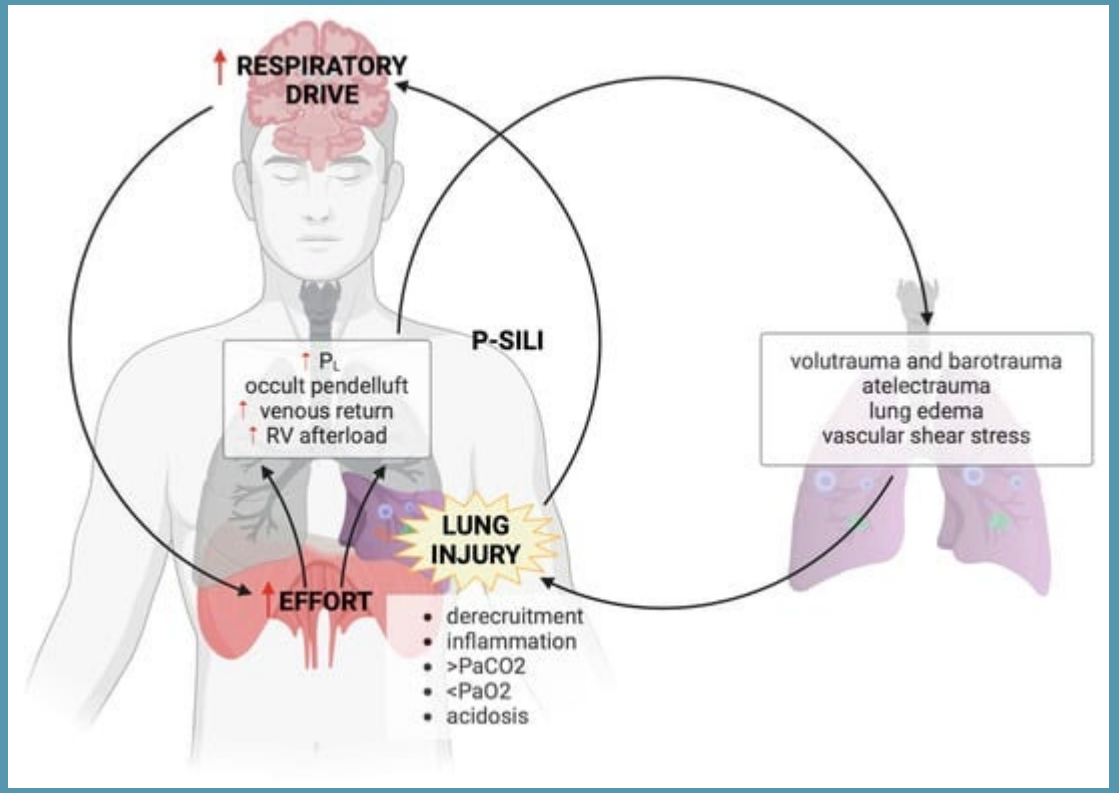
PSILI worsening pulmonary function has been studied in animal studies

- Dreyfuss et al – ventilated rats
- Mascheroni et al – ventilated vs. spontaneously breathing sheep



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Patient Self Inflicted Lung Injury (PSILI)

Intense inspiratory effort may result in PSILI leading to:

- Increased lung stress due to swings in transpulmonary pressure
- Increased vascular transmural pressure
- Pendelluft
- Diaphragm injury
- Increased lung inflammation

Strong inspiratory effort can lead to excess strain and PSILI

Image: Sklienka P, Frelich M, Burša F. Patient Self-Inflicted Lung Injury-A Narrative Review of Pathophysiology, Early Recognition, and Management Options. *J Pers Med*. 2023;13(4):593. Published 2023 Mar 28. doi:10.3390/jpm13040593

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- Increased lung inflammation

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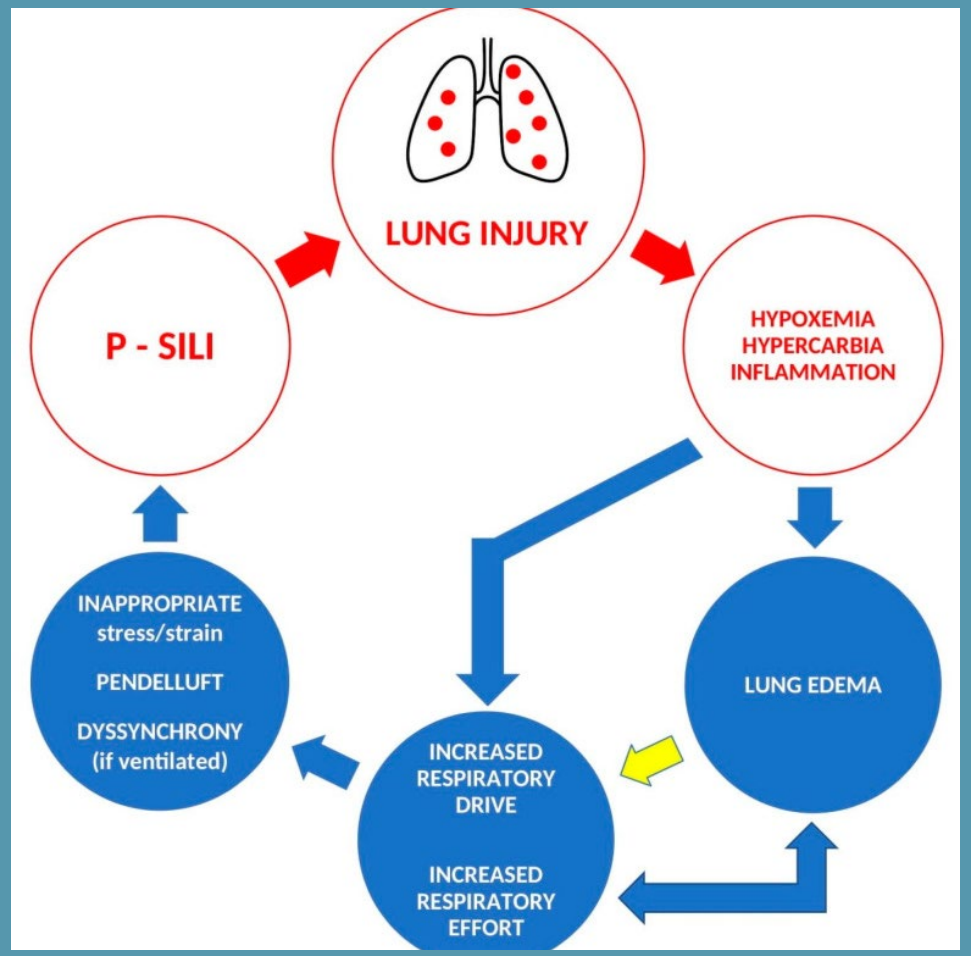

Image: Sklienka P, Frelich M, Burša F. Patient Self-Inflicted Lung Injury-A Narrative Review of Pathophysiology, Early Recognition, and Management Options. *J Pers Med*. 2023;13(4):593. Published 2023 Mar 28. doi:10.3390/jpm13040593

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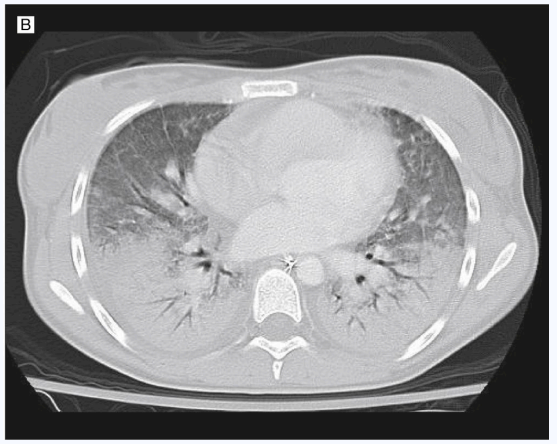
Non-intubated ARDS



- NIV in ARDS patients
  - LUNG SAFE Study
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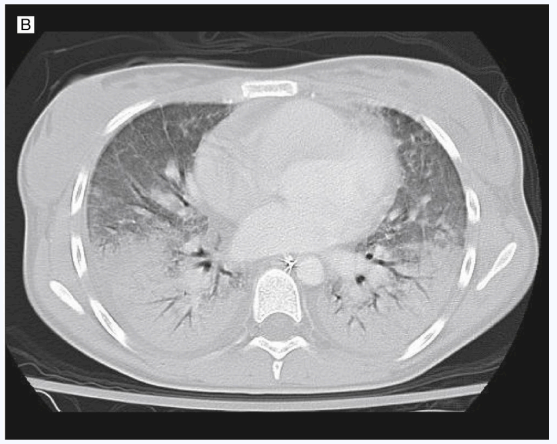

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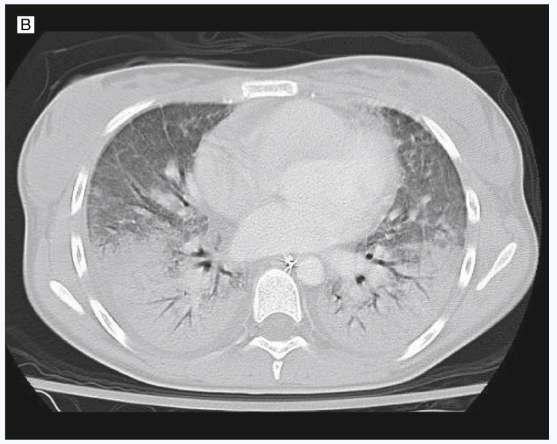
Non-intubated ARDS



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ARDS Definition

ARDS Global Definition 2023			
	Classification		
	Mild	Moderate	Severe
Time to Onset	Within 7 days of insult		
Origin	Respiratory failure not fully explained by cardiac failure or fluid overload		
Radiographic features	Bilateral opacities on CXR or CT OR Bilateral B-line and/or consolidations on US (not explained by effusions, atelectasis, nodules/masses)		
Intubated PaO2/FiO2	201-300 with PEEP ≥ 5	101-200 with PEEP ≥ 5	<100 with PEEP ≥ 5
Intubated SpO2/FiO2	235-315 with SpO2 ≤ 97%	148-234 with SpO2 ≤ 97%	≤ 148 with SpO2 ≤ 97%
Non-intubated PaO2/FiO2 SpO2/FiO2	**PaO2/FIO2 ≤300 OR SpO2 ≤ 315 On HFNC ≥ 30LPM or NIV/CPAP with PEEP ≥** 5		

Matthay MA, Arabi Y, Arroliga AC, et al. A new global definition of acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine*. 2024;209(1):37-47. doi:10.1164/rccm.202303-0558ws

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Summary

- Remember the physiology
- Mild ARDS: HFNC okay
- Moderate/severe ARDS: intubate, intubate early
- Reduce risk of PSILI

ARDS Global Definition 2023			
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California Thoracic Society Annual Conference
March 20-23, 2025
Portola Hotel and Spa - Monterey, CA

Questions?

LATE INTUBATION IS PREFERENTIAL FOR THE PATIENT WITH ARDS ON HFNC

Kathryn Bilello, M.D.

Clinical Professor of Medicine, UCSF

UCSF-Fresno

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RELEVANT FINANCIAL DISCLOSURES

- I have the no relationships with ACCME defined ineligible companies:

- I WILL NOT discuss off-label use and/or investigational use of any drugs or devices.

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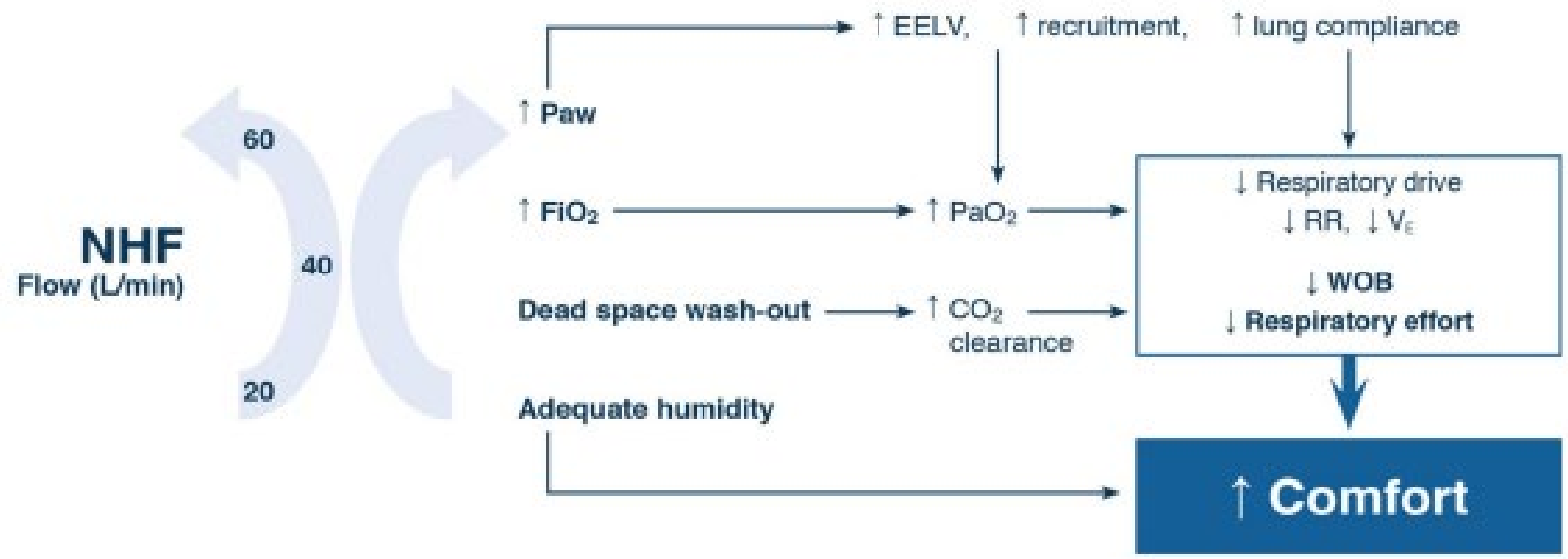
RIGHT TIMING OF INTUBATION IS PREFERENTIAL FOR THE PATIENT WITH ARDS ON HFNC

- Balance known harms of intubation and mechanical ventilation against the theoretical harms of P-SILI (patient self-induced lung injury) and known harms of delaying intubation until the patient has decompensated
- Discuss the value of HFNC in acute hypoxic respiratory failure
- Limitations of studies which support early intubation in ARDS
- Acknowledge there is a signal identifying a population that is harmed by delaying intubation in ARDS
- We need parameters that tell us when to intubate the patient with ARDS

USE OF NASAL HIGH FLOW OXYGEN DURING ACUTE RESPIRATORY FAILURE



Intensive Care Med 2020; 46:2238-2247

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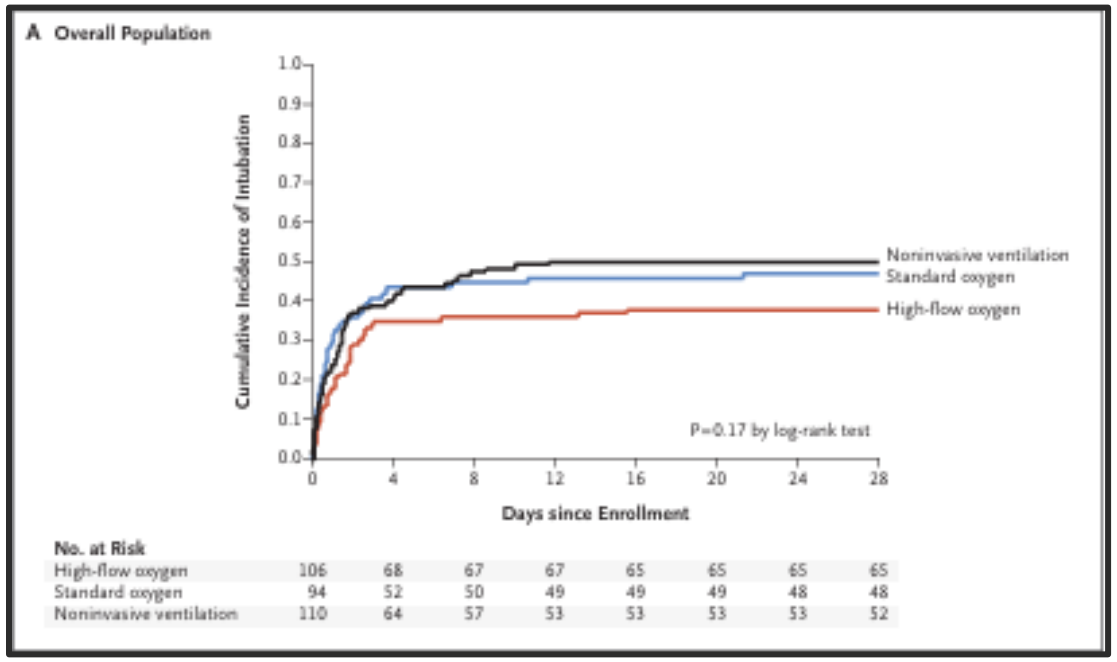
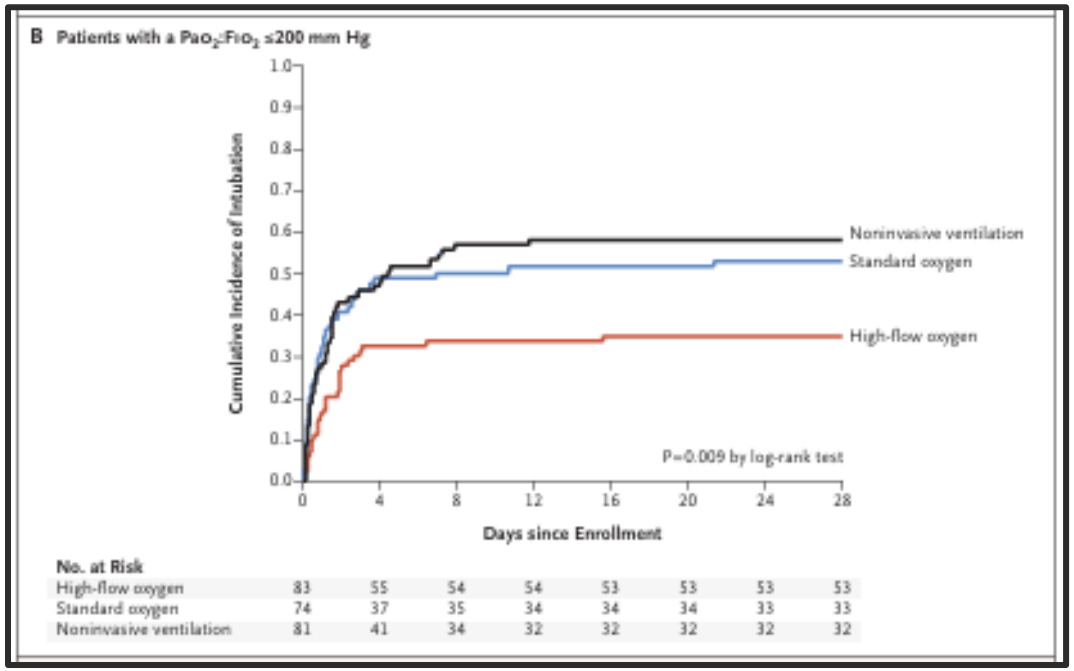
HIGH-FLOW OXYGEN THROUGH NASAL CANNULA IN ACUTE HYPOXIC RESPIRATORY FAILURE





N Engl J Med 2015; 372:2185-2195

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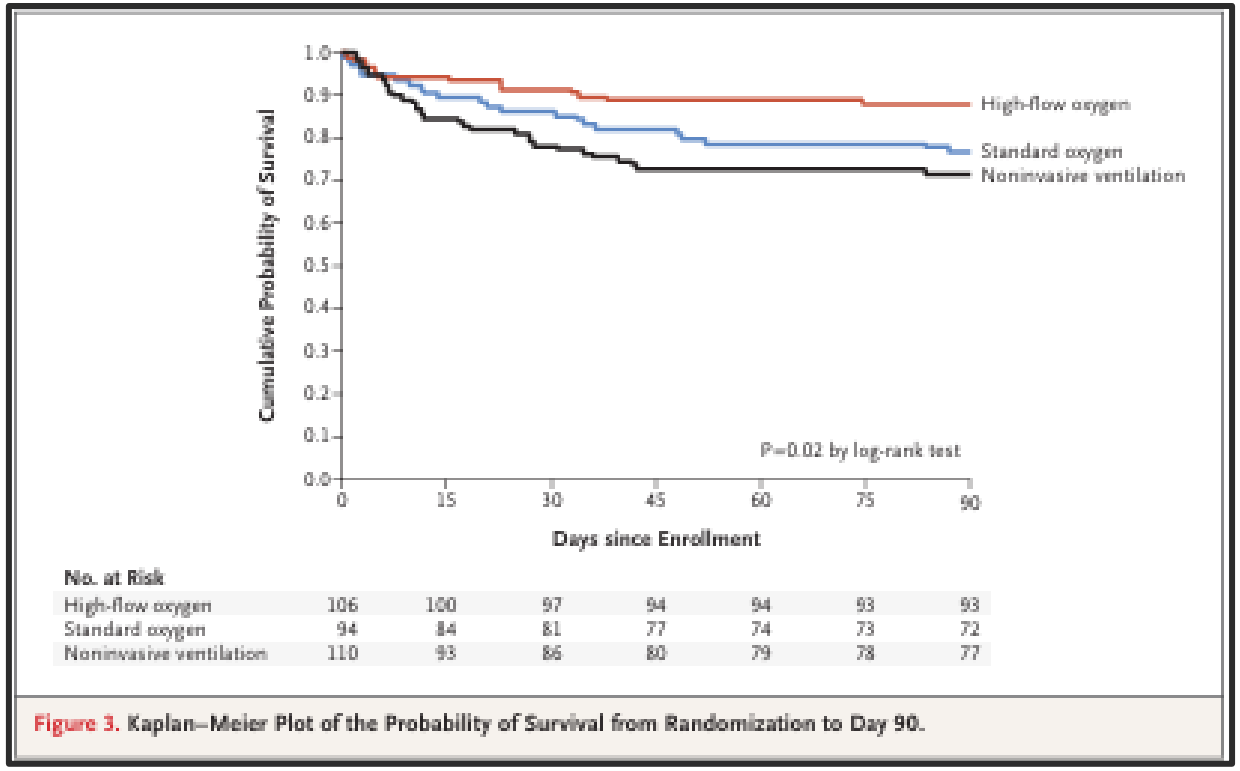
HIGH-FLOW OXYGEN THROUGH NASAL CANNULA IN ACUTE HYPOXIC RESPIRATORY FAILURE



No. at Risk

High-flow oxygen	106	100	97	94	94	93	93
Standard oxygen	94	84	81	77	74	73	72
Noninvasive ventilation	110	93	86	80	79	78	77

Figure 3. Kaplan–Meier Plot of the Probability of Survival from Randomization to Day 90.

N Engl J Med 2015; 372:2185-2196

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HFNC IN ARDS: ADVANTAGES AND DISADVANTAGES

- Potential to avoid invasive ventilation and associated complications
- Improved survival through avoidance of invasive ventilation
- Harmful effects of delaying a needed intubation (patient has decompensated)
- Theoretic potential for development of patient self-induced lung injury (P-SILI)

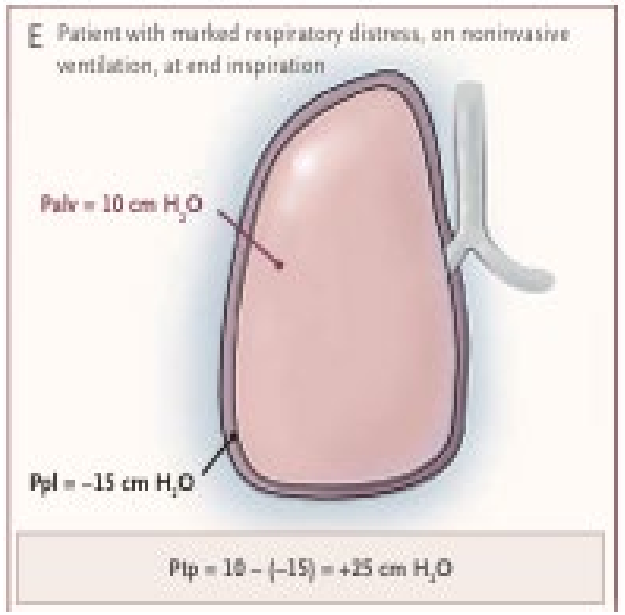
HARMS OF INVASIVE MECHANICAL VENTILATION

- Peri-intubation shock and cardiac arrest
- Ventilator-induced lung injury
- Ventilator-induced pneumonia
- Ventilator-induced diaphragm dysfunction
- ICU-acquired weakness
- Delirium
- Neurocognitive impairment
- Laryngeal/tracheal injury
- Post-traumatic stress disorder

Tobin MJ. Principles and practice of mechanical ventilation. 3rd ed. NY:McGraw Hill; 2013

PATIENT SELF-INDUCED LUNG INJURY

- High respiratory drive generates large negative swings in pleural pressure leading to high transpulmonary pressure and alveolar overdistention
- Clinical evidence for P-SILI in ARDS patients treated with HFNC is indirect
- Theoretical (or even real threat) of P-SILI is not an indication for intubation at an arbitrary time point after the onset of ARDS



N Engl J Med 2013; 369:2126-2136

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TIMING OF INTUBATION AND CLINICAL OUTCOMES IN ADULTS WITH ARDS

- Evaluated 457 patients with ARDS and compared the outcomes in pts who were intubated early (on the day they met criteria for ARDS), intubated late (after day one) and those who were never intubated

TABLE 3. Clinical Outcomes in Three Intubation Groups

	Early Intubation	Never Intubated	Late Intubation
n	351	70	36
Death at 60 d, *n* (%)	128 (36)	18 (26)	20 (56)[a,b]
Died in the hospital, *n* (%)	104 (30)	10 (14)[a]	18 (50)[a,b]
Ventilator-free days, median (IQR)	16 (0–23)	28 (23–28)[a]	7 (1–20)[b]
ICU days, median (IQR)[c]	9 (6–16)	4 (3–7)[a]	11.5 (9–17)[b]
Days of MV, median (IQR)[c]	6 (3–12)	0 (0–0)[a]	8 (4–15)[b]

Crit Care Med 2016; 44:120-129

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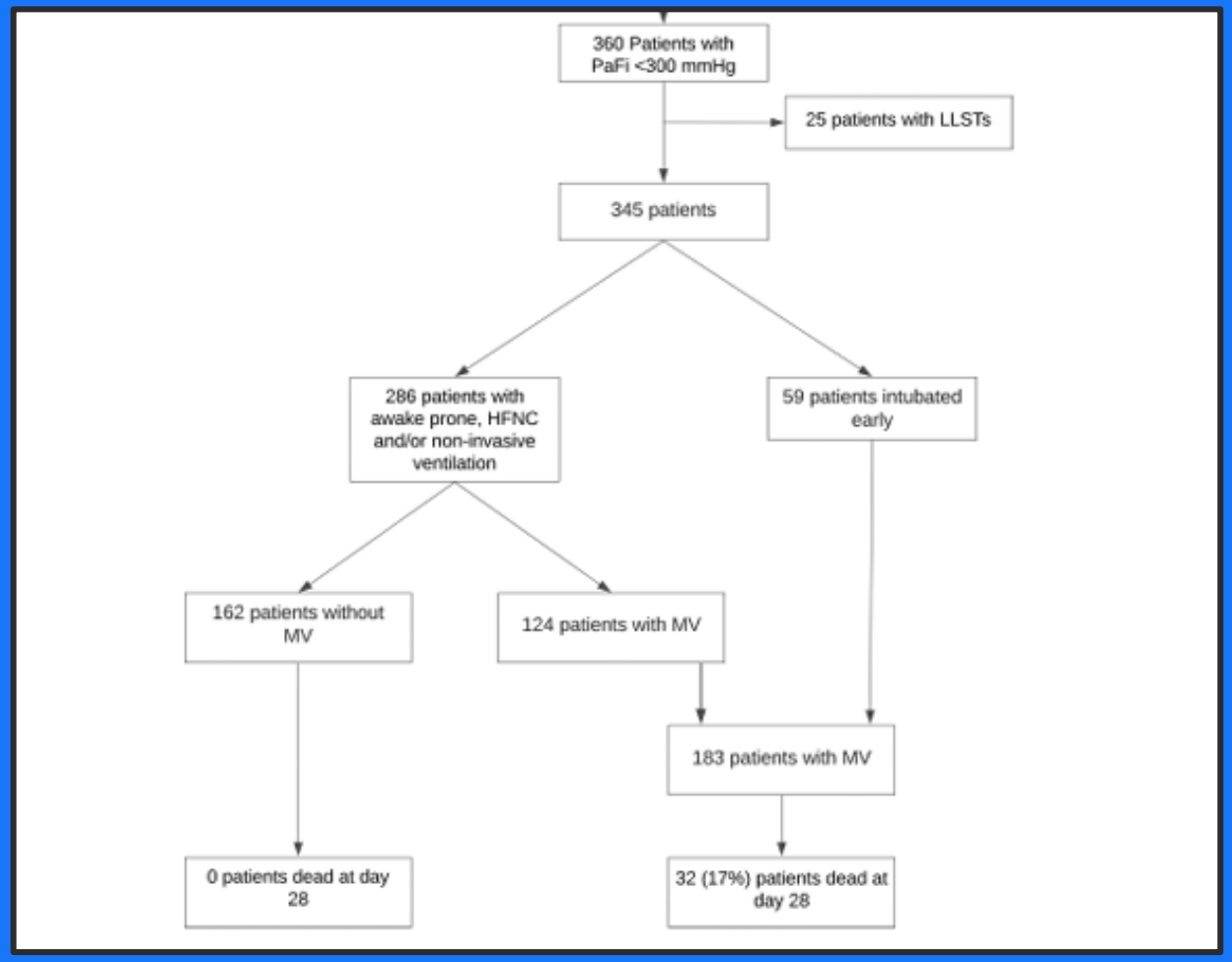
INTUBATION TIMING AND OUTCOME IN ARDS BY SARS-COV-2



J Crit Care 2021; 65:164-169

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INTUBATION TIMING AND OUTCOME IN ARDS BY SARS-COV-2

	< 48 h to OI	> 48 h to OI	P-value
Number (%)	88 (46)	95 (52)	
ICU LOS (days)	15 (9-23)	23 (12-39)	0.003
ICU mortality (%)	16 (18%)	43 (43%)	<0.001
28-d mortality (%)	11 (13%)	21 (22%)	0.087
Ventilator-free day	15 (2-20)	12 (0-19)	0.196

J Crit Care 2021; 65:164-169

TIMING OF INTUBATION AND OUTCOMES IN ARDS

- Meta-analyses and Systematic reviews have yielded conflicting outcomes
  - Papoutsi et al. Crit Care 2021; 25:121 –showed no effect in 8944 Covid pts (early intubation defined as within 24 hrs of ICU admission)
  - Manrique et al. BMC Anesthiology 2023; 23:140-favored early intubation (within 24 hrs after ICU admission) in 4198 Covid pt
- Heterogeneous populations
- Definition of early vs late intubation (defining time zero)
  - Hospital admission? ICU admission? Physiologic time zero?
- Absence of well defined trigger for intubation
  - Timing of intubation was left to clinician's judgement

TIMING OF INTUBATION AND OUTCOMES IN ARDS

- Can't know for certain that poor outcomes seen for patients in whom intubation was delayed were not due to disease virulence or patient – specific factors rather than P-SILI
- However, there is a signal suggesting some patients are harmed by delaying intubation
- The optimal timing of invasive mechanical ventilation is unclear
- Current triggers predict the *likelihood of needing* intubation but do not define *when* it should occur
  - PaO_2/FiO_2, ROX index ({SpO_2/FiO_2}/RR), dyspnea, WOB, US, P esoph, APACHE II, HACOR, combinations of criteria
- Sensitive but not specific

TIMING OF INTUBATION AND OUTCOMES IN ARDS

- Unless a patient requires immediate intubation, a trial of HFNC is reasonable
- Substantial number of patients treated with HFNC can avoid invasive mechanical ventilation
- These patients have better outcomes, in part by avoiding complications of MV
- Subjecting all ARDS patients to intubation within 24 hrs of ICU admission will impose harm on those patients who may never have required intubation
- We need validated triggers to guide the timing of intubation as some patients are likely harmed by delaying intubation
- Until that time, it behooves us to closely watch those patients at highest risk for HFNC failure and promptly intubate when indicated

CTS: Reflecting Back and Looking Forward

Tisha Wang, MD
CTS President (for 5 more minutes!)
Professor of Clinical Medicine
Senior Executive Clinical Vice Chair
UCLA Department of Medicine

California Thoracic Society – Who We Are

- The largest Chapter of the American Thoracic Society (ATS).
- A professional society committed to improving California (and Arizona!) lung health and advancing the science and practice of pulmonary, critical care, and sleep medicine through **advocacy and education**.
- "We elevate, nurture, and support the **professional development** of future clinicians, educators, scientists, and leaders."
- "We foster collaboration between **multidisciplinary professionals** essential to lung health."

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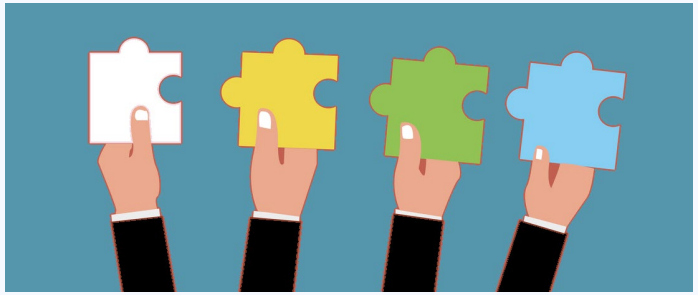
Our Committees

Newsletter – CTS Inspirations

Education

Nominating

Career Development



Healthcare Policy

Membership

Pediatrics

Representatives to the ATS Council of Chapter Representatives

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Our Recent Accomplishments

- This amazing conference you are attending today
- Frequent educational webinars targeted to multiple audiences from physicians to APPs to RTs to trainees reaching >500 people in the last 18 months
- Advocacy in collaboration with the American Lung Association and co-signing multiple letters in favor of initiatives focused on clean air efforts in California
- Renewed our 8 platinum institutional members and improved the value of membership

LOMA LINDA UNIVERSITY

Harbor-UCLA MEDICAL CENTER

UCSF
University of California
San Francisco

Stanford

UCDAVIS
UNIVERSITY OF CALIFORNIA

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The Power/Benefits of Membership

- Significant discounts to the annual CTS conference
- Access to regular educational webinars
- **The opportunity to have a community of healthcare professionals for networking and collaboration**
- Platinum/platinum plus memberships for institutions or group practice level memberships allow multiple providers to join for a deeply discounted rate
  - Institutional memberships also include benefits of posting to CTS job board (posted nationally on ATS job board) and free advertising by CTS of institutional educational conferences to our ~1000 members

Gratitude…

- To everyone of you, both for attending but also for what you do at work everyday which is to take care of the patients and our community
- To the board of directors who have become dear friends and colleagues
- To the conference planners, Nick Kolaitis and Lauren Eggert for the countless hours they have put in to ensure that every moment of this conference is high quality
- And to Jason Seidler and the CTS Executive Office – we would simply not exist without you

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Time for Awards!

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CTS Award – Clinician of Year

Gaurav Singh, MD, MPH
Treasurer

Staff Physician
VA Palo Alto Health Care System

Clinical Assistant Professor
Division of Pulmonary/Critical Care Medicine
Stanford University

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CTS Award – Woman of the Year

Angela Wang, MD

Pulmonary, Critical Care, and Sleep Medicine

Clinical Professor of Medicine
University of California, San Diego

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Handing Off The Baton

Brooks Thomas Kuhn, MD, MAS
The New CTS President!

Associate Professor
Co-Director of Comprehensive COPD Clinic +
Medical Director of the Department of
Respiratory Care

Division of Pulmonary/Critical Care Medicine
University of California, Davis

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UNDERSTANDING THE SPECTRUM OF NEUROMUSCULAR DISEASES

Chamindra Laverty, M.D.

Clinical Professor of Neurosciences

Neuromuscular Specialist

University of California, San Diego

3/21/25

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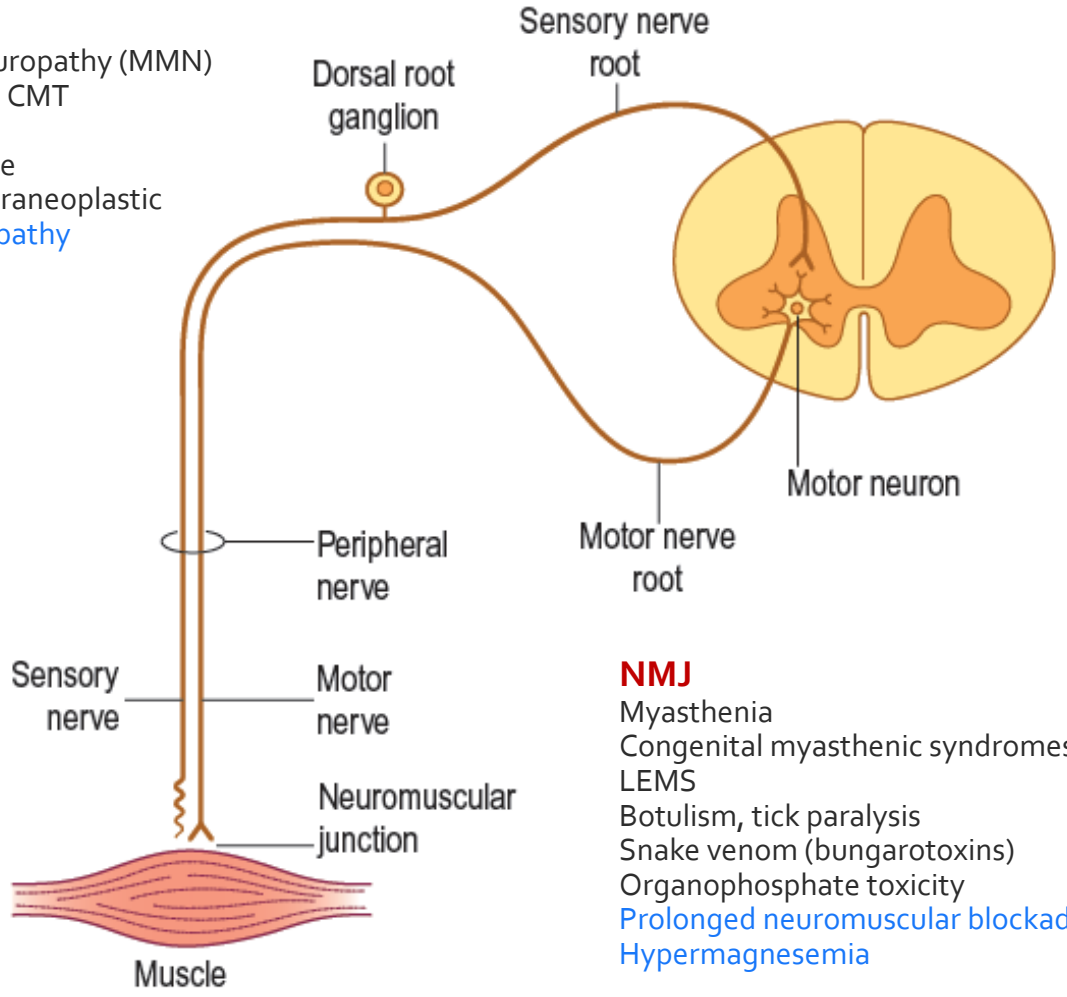
RELEVANT FINANCIAL DISCLOSURES

- I have the following relationships with ACCME defined ineligible companies:
  - Consulting: Biogen, Avidity, Sarepta, Dyne, Italfarmaco, Catalyst, Novartis.
- I WILL NOT discuss off-label use and/or investigational use of any drugs or devices.

CAUSES OF NM RESPIRATORY FAILURE

Peripheral Nerve
GBS
Multifocal motor neuropathy (MMN)
Porphyria, vasculitis, CMT
Heavy metals/toxins
HIV, diphtheria, Lyme
Paraproteinemia, paraneoplastic
Critical illness neuropathy
Phrenic nerve injury



Motor neuron
ALS
SMA type 1-3; when ill, type 4
Polio, West Nile, enteroviruses

Myopathies
Duchenne/Becker
Inflammatory/necrotic (statin)
Pompe disease
Mitochondrial myopathy
Myotonic dystrophy
Congenital myopathies
Congenital muscular dystrophies
Critical illness myopathy
Rhabdomyolysis
Electrolyte disturbances (↓PO_4, ↓K)

NMJ
Myasthenia
Congenital myasthenic syndromes
LEMS
Botulism, tick paralysis
Snake venom (bungarotoxins)
Organophosphate toxicity
Prolonged neuromuscular blockade
Hypermagnesemia

GUILLAIN BARRE SYNDROME

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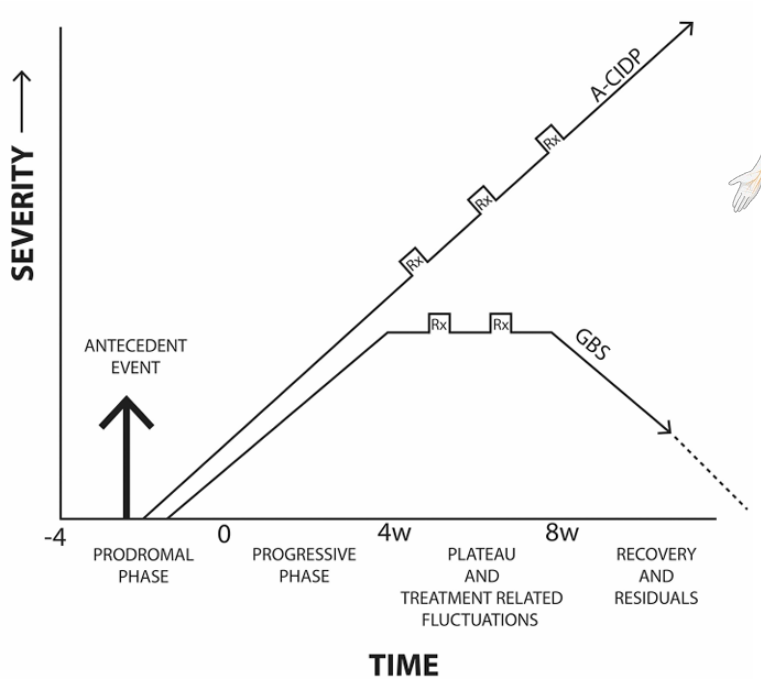
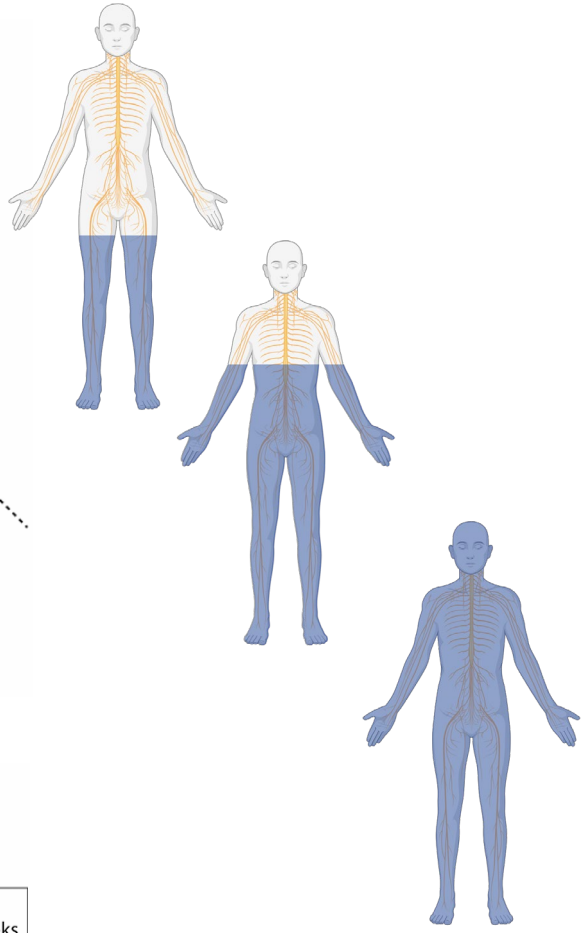
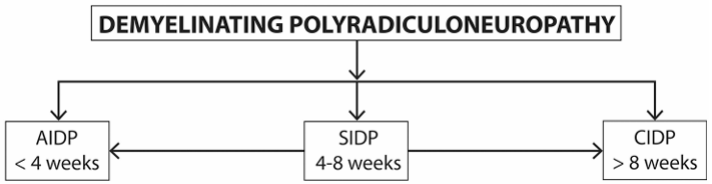
GBS – CLINICAL







Diagnostic criteria for GBS per EAN/PNS
Required:
Progressive weakness of >1 limb
Areflexia or hyporeflexia
Progression of symptoms over days to **4 weeks**
Features strongly suggestive of GBS:
Relative symmetric symptoms
Mild sensory symptoms/signs
CN involvement, especially b/l facial involvement
Autonomic dysfunction
Pain
Elevated CSF protein
Characteristic electrodiagnostic findings

Note: LP and EMG are not required.
BUT…
Might be prudent

UC San Diego Health

Continuum Neurology – Peripheral Nerve and motor Neuron diseases, GBS, Oct 2023
Van Doorn et al, EAN/PNC guideline on diagnosis and Tx of GBS, *Euro J Neurol*, 2023; *Continuum Neurology* – Peripheral Nerve and motor Neuron diseases, GBS, Oct 2023

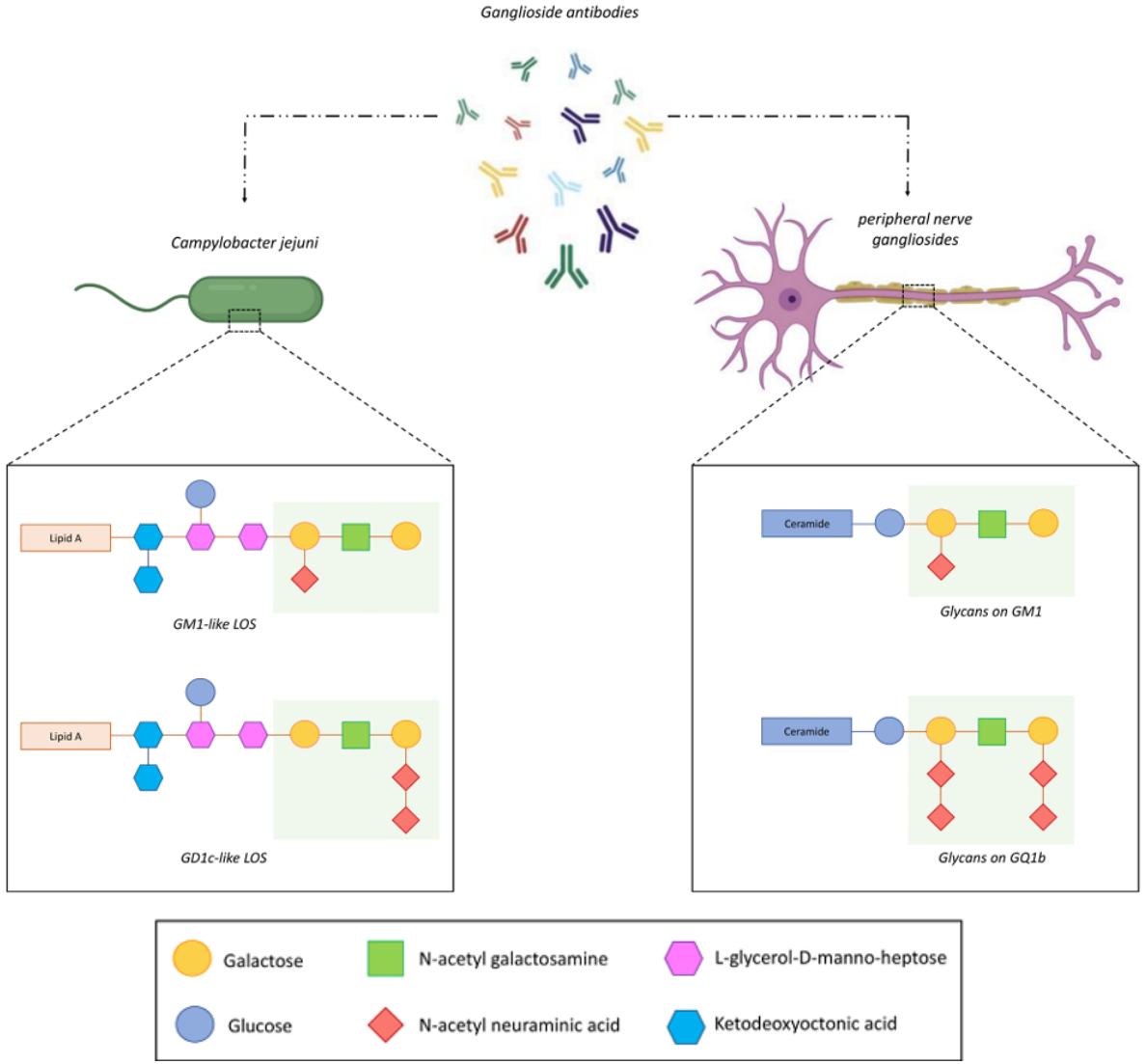
California Thoracic Society

GBS – CLINICAL

- Preceding illness
  - Median interval is 10d
  - Weakness starts on day 10-14
- Distal paresthesia
  - Excludes pure motor diseases (myasthenia, ALS, muscle)
  - Objectively mild
- LBP (nerve root inflammation)
  - 2/3rd of pts
- Motor>>sensory neuropathy
  - Symmetric
  - Ascending
  - Distal→proximal muscle weakness
  - Rapid, over days
- Areflexia/hyporeflexia
  - In weak regions
- Cranial nerve involvement:
  - Facial (50%)
  - Oropharyngeal (40%)
  - EOM (ophthalmoplegia/ptosis) (5-15%)
- Respiratory muscles/diaphragm (10-30%)
- Autonomic instability (2/3rd)
  - Autonomic nerves are less myelinated, so, less dysfunctional than motor
  - Acute phase: ↑sympathetic tone
  - Recovery phase: parasympathetic failure→Σ sympathetic
  - Tachycardia
  - Labile BP (can cause PRES) or takotsubo cardiomyopathy
  - Orthostatic hypotension
  - Abnormal sweating
  - Pupillary abnormalities
  - GI dysmotility
  - GU: paralytic ileus or urinary retention

Bellanti and Rinaldi, *Eur J Neurol*, 2024; *Continuum Neurology* – Peripheral Nerve and motor Neuron diseases, GBS, Oct 2023

GBS PATHOPHYSIOLOGY



- **2 stages of pathology**
  1. Initiation by an immunological trigger
     - Virus, bacteria, vaccine with antigenic components
  2. Immune-mediated disruption of axons and/or myelin
     - **Molecular mimicry**
- GBS = Acute inflammatory demyelinating polyradiculoneuropathy (AIDP)
- Most cases are postinfectious
  - 2/3rd report GI or respiratory antecedent illness
- Respiratory
  - Influenza A virus
  - *Mycoplasma pneumoniae*
  - *Haemophilus influenzae*
- GI
  - *Campylobacter jejuni* (GBS in 1 of 1000 cases)
- Others
  - EBV
  - CMV
  - Hepatitis E virus
  - Zika

Bellanti and Rinaldi, *Eur J Neurol*, 2024

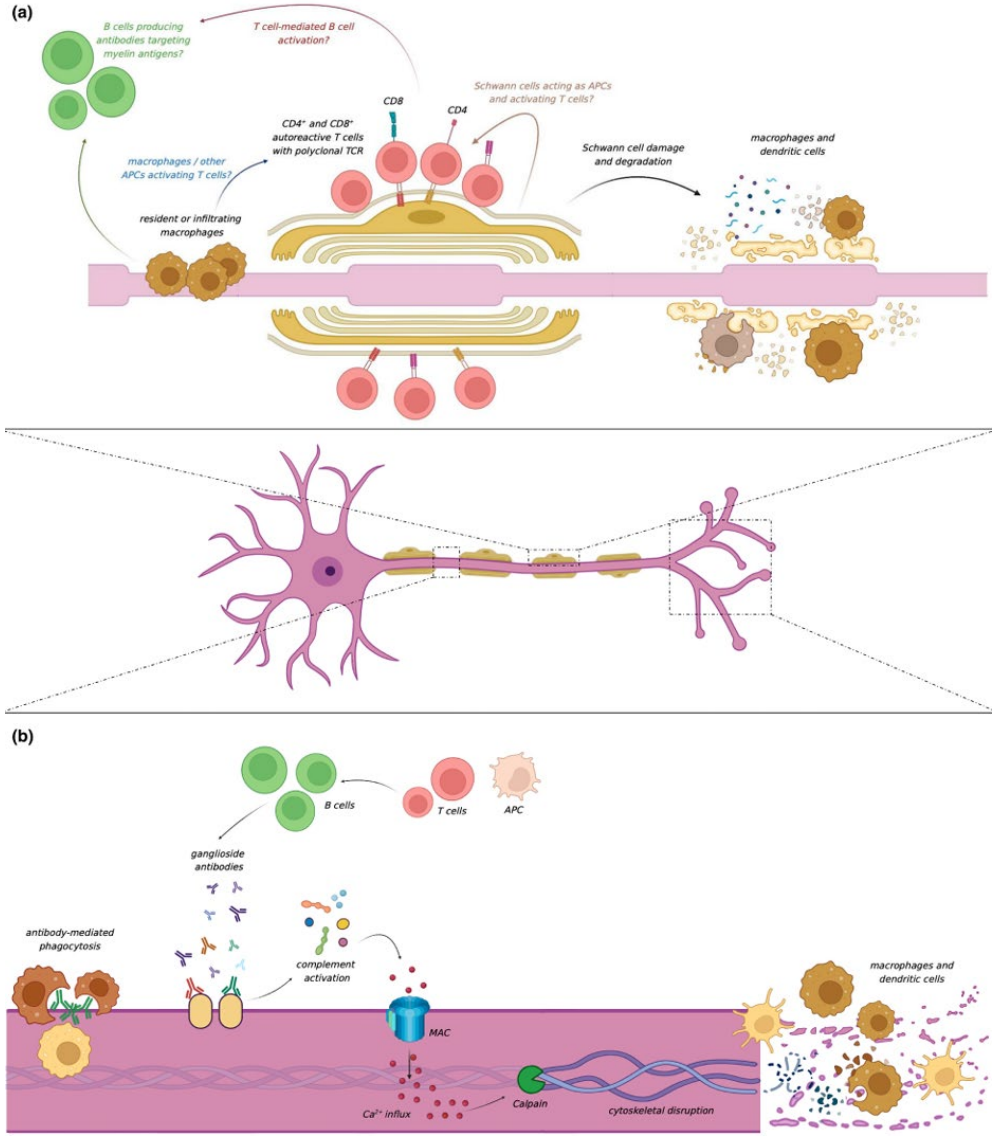
GBS PATHOPHYSIOLOGY

No antibodies for GBS/AIDP have been identified

AIDP: Complement activation on myelin

~10 days post infection, neurological symptoms develop.

Time it takes to switch from IgM to **IgG**



Bellanti and Rinaldi, *Eur J Neurol*, 2024

TREATMENT FOR AIDP/GBS

- Telemetry bed or ICU
  - ICU if dysautonomia, poor respiratory status, bulbar dysfunction
- ABC's
  - Intubate?
- Treatment minimizes endoneurial inflammation and nerve injury
- **Start immunotherapy, IVIG <2wks or PLEX <4wks**

- Both IVIG/PLEX improve time to recovery
- Neither stops progression of disease
- Treat majority of patients; even mild cases; can skip some mild MFS
- Both therapies ***EQUALLY*** effective
- PLEX shortened ventilator time; preferred agent for severe disease

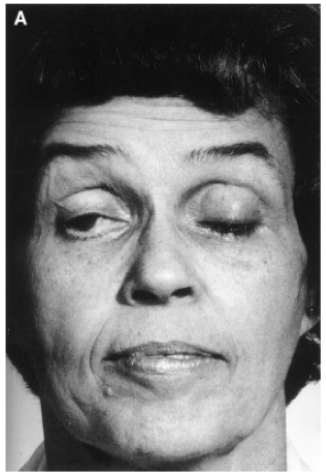
	IVIG	PLEX
Administration	Easy	Usually requires central line
Time/dose	0.4g/kg/d x 5d or 2g/kg total dose	200-250ml plasma/kg of body weight in 5 exchanges every other day
Side effects	Headaches ± meningitis Thromboembolism Anaphylaxis	Hypotension Sepsis Transfusion reactions Thrombocytopenia Poor clotting Hypocalcemia IV access issues
Response rate		**Takes 1 week to see effect**

MYASTHENIA

California Thoracic Society

MYASTHENIA - CLINICAL

- Prevalence of 10-15/ 100,000
- Bimodal incidence:
  - Young women
  - Elderly men
- 10-20% develop a life-threatening event→ respiratory failure or dysphagia
- Ocular myasthenics→ generalize within 2 years of onset
- Breath count of 1 per second after max inhalation
  - Each # equates ~100ml of FVC



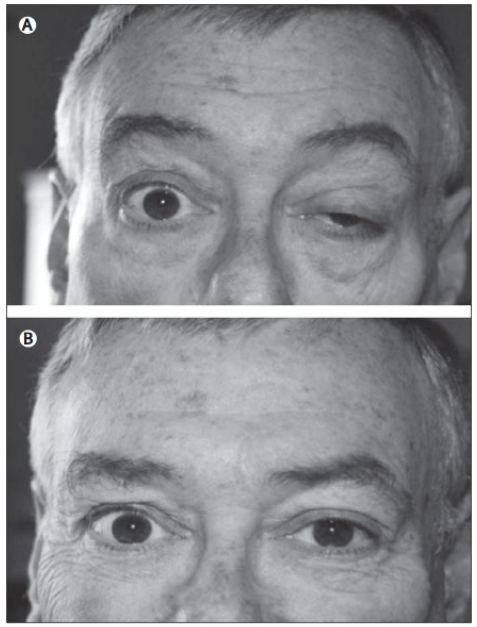
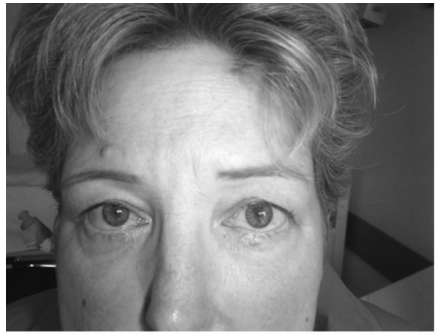
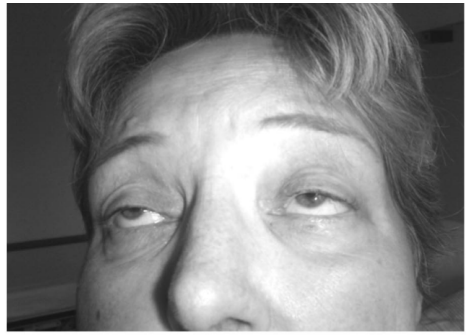


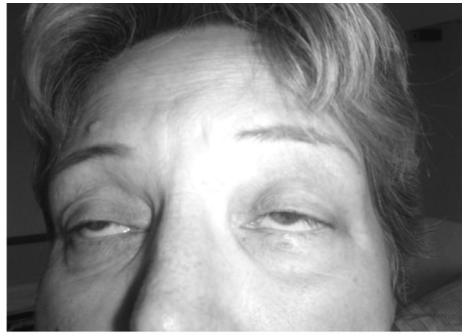
Figure 3: Response of ocular myasthenia gravis to moderate dose daily prednisone



0 sec



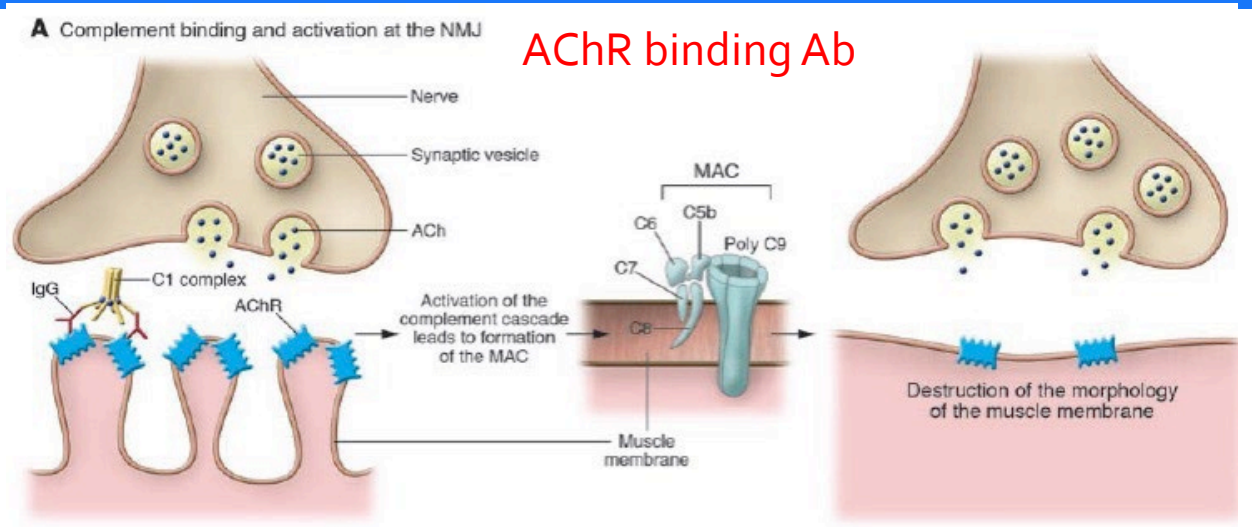
+ 10 sec upward gaze (Simpson)



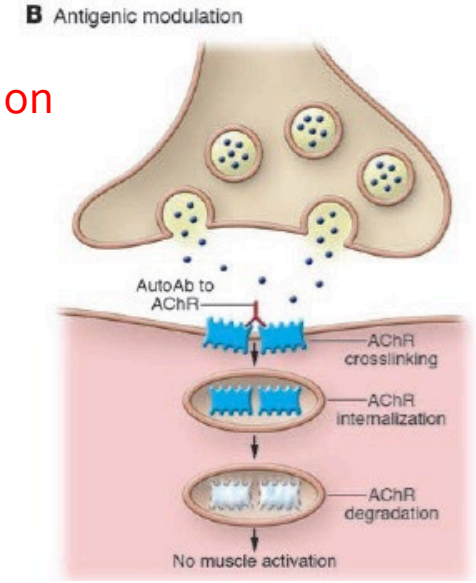
+ 30 sec upward gaze (Simpson)

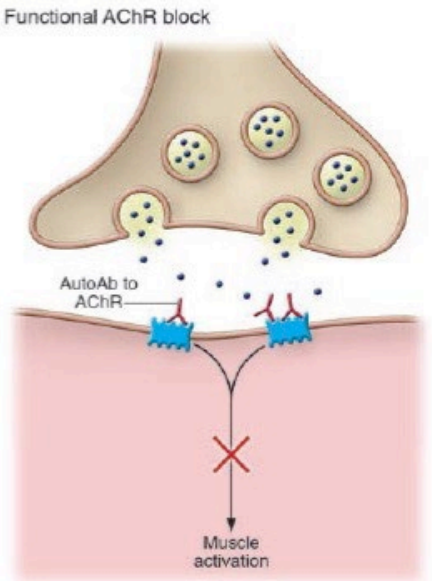
MYASTHENIA - PATHOGENESIS

AChR binding Ab



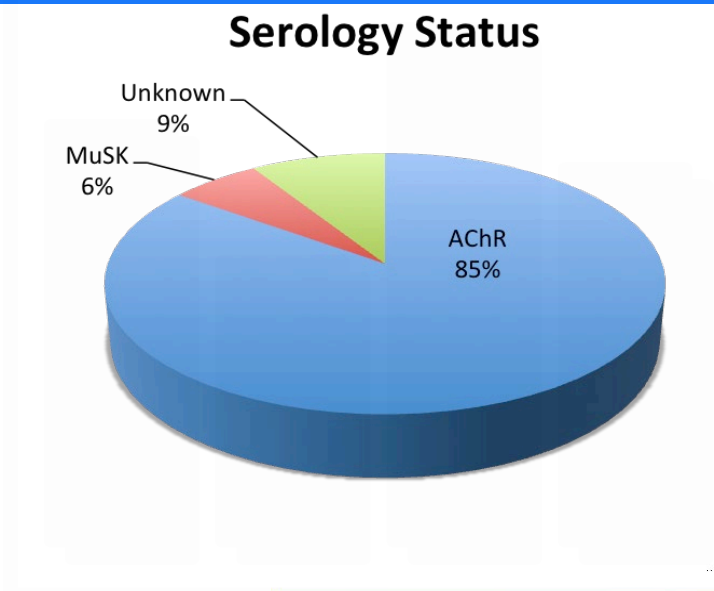
AChR modulation Ab

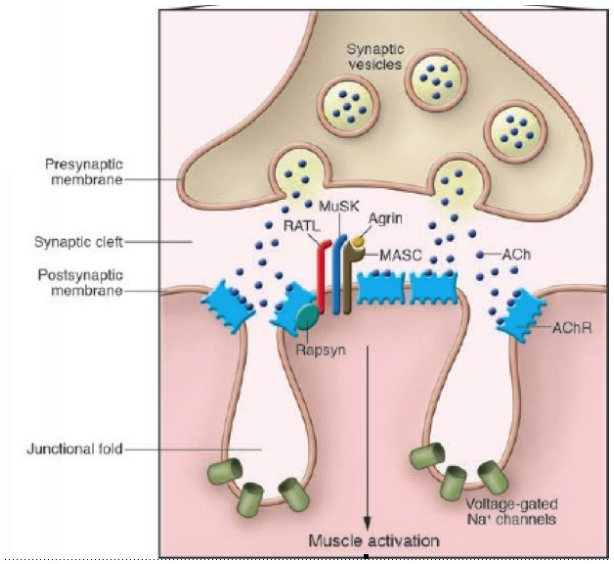


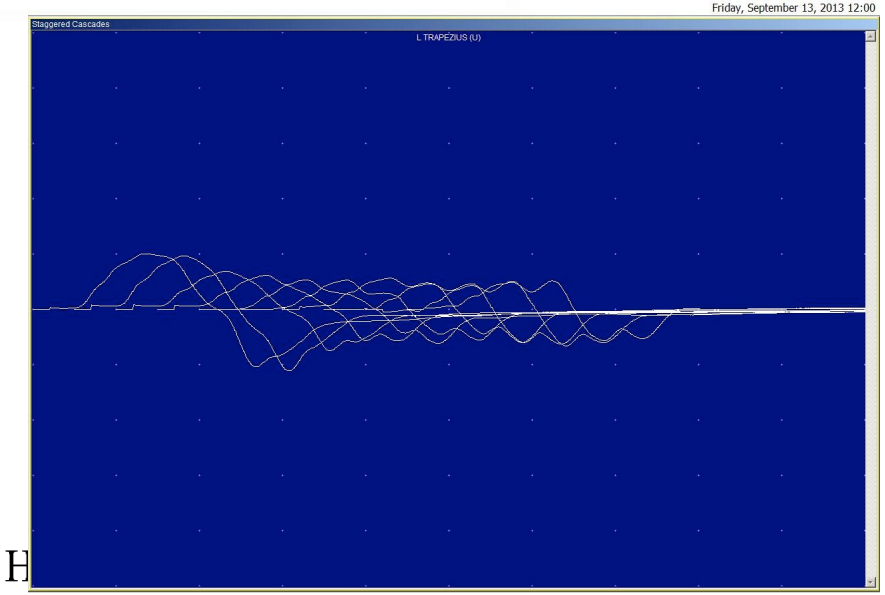


AChR blocking Ab

MYASTHENIA - DIAGNOSIS







- Positive Ab → Diagnosis!!
- 91% of all generalized myasthenics are seropositive
  - 85% AchR (Acetylcholine receptor binding) Ab
  - 6% MuSK (Muscle specific kinase)Aab
  - ~1% LRP4 (lipoprotein receptor related protein 4)
    - Clinical spectrum not fully elucidated
- 3Hz RNS
  - 80% sensitive in symptomatic generalized myasthenia
  - 50% sensitive in ocular myasthenia
  - 10% decrement

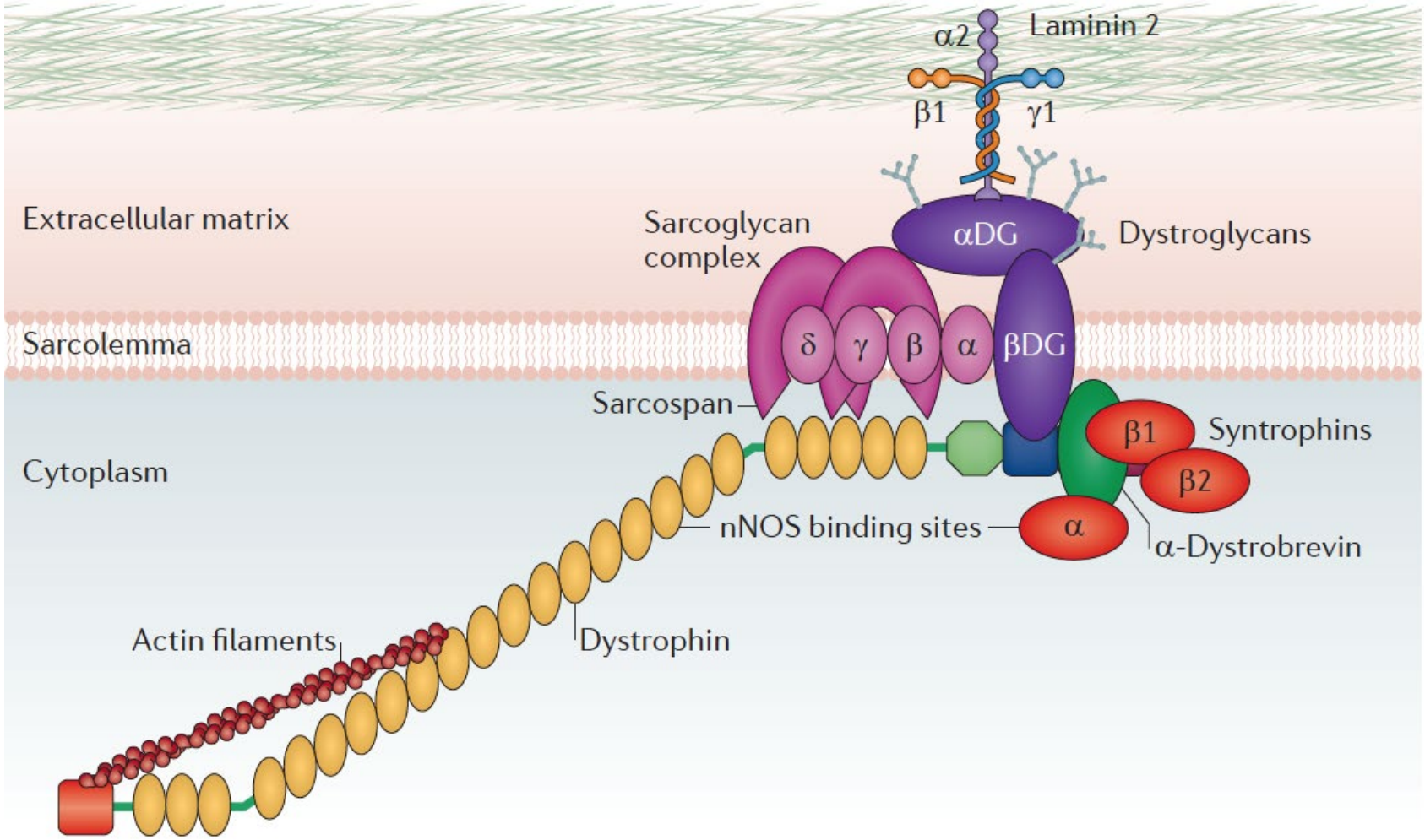
MYASTHENIC CRISIS - TREATMENT

- Hold pyridostigmine
- BiPAP if protecting airway
- Elective intubation early
- IVIG or PLEX
  - Equal efficacy
  - IVIG 2g/kg total dose, equal over 5d
  - PLEX – 5 exchanges every other day
  - Slightly higher efficacy in PLEX > IVIG in critically ill, intubated myasthenics
- Mortality decreased from 30% to <5% in 2nd half of 1900's due to better understanding, better immunotherapies, advancement in pulmonary critical care
- Should never need long-term bilevel for NMD if neurologist is doing their job

DUCHENNE/BECKER MUSCULAR DYSTROPHY

California Thoracic Society

DMD/BMD PATHOGENESIS



Fairclough RJ et al. Nature Reviews, Genetics. 2013

DUCHENNE & BECKER – CLINICAL

video placeholder

7yo M with DMD

video placeholder

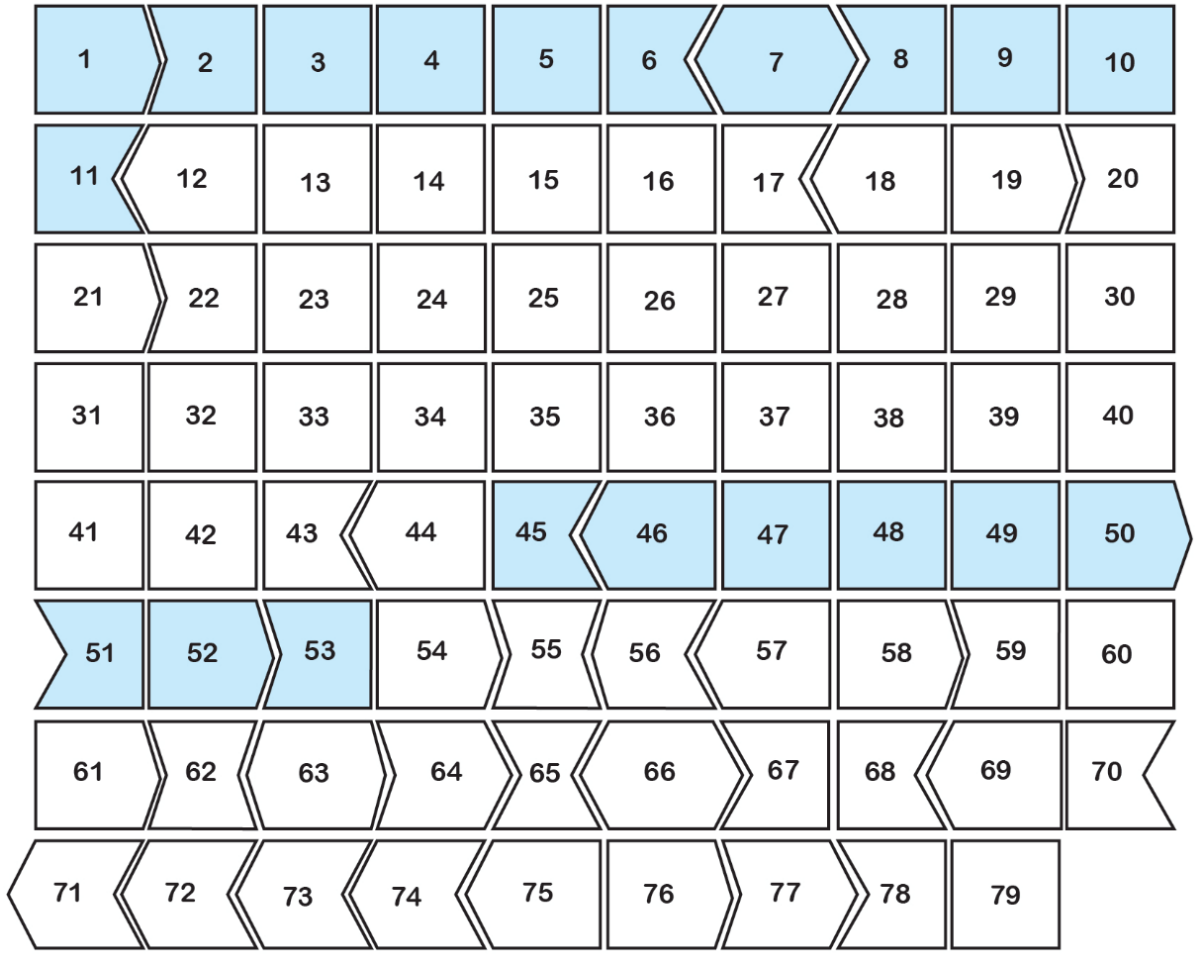
11 yo M with BMD

video placeholder

55 yo M with BMD; onset at 35y

DMD/BMD – CLINICAL

	Duchenne	Becker
Age of onset	<5yo	>5y
DNA	Out of frame deletion	In frame deletion
Protein	No functional dystrophin protein	Some functional dystrophin protein (3-10%)
Wheelchair dependent	10-14y	>15y (some exceptions)
Respiratory	Onset in late teens (bilevel)	Onset later
Survival	25-35y	60y
Disease modifying meds	Steroids Exon Skipping Gene therapy	None so far



DMD Exon Map by C. Laverty

SPINAL MUSCULAR ATROPHY (SMA)

California Thoracic Society

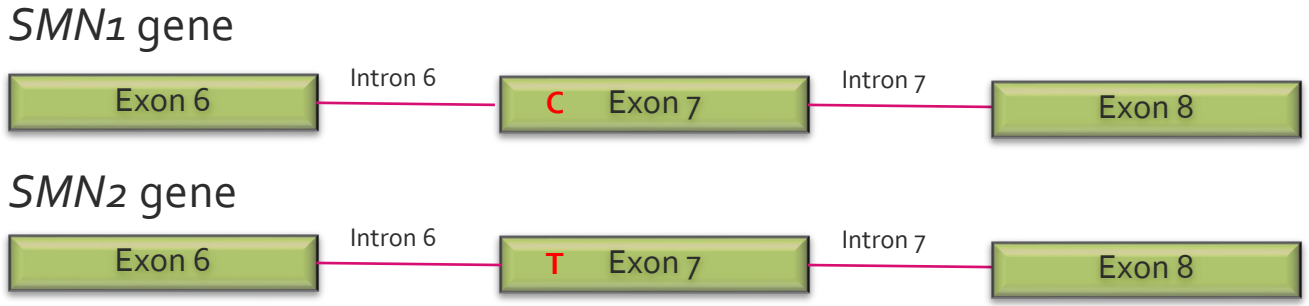
SPINAL MUSCULAR ATROPHY

- Most common genetic disorder resulting in death in infancy
  - ~1 in 10,000 births
- 2nd most common autosomal recessive disorder in the world
- Progressive neurodegenerative motor neuron disease

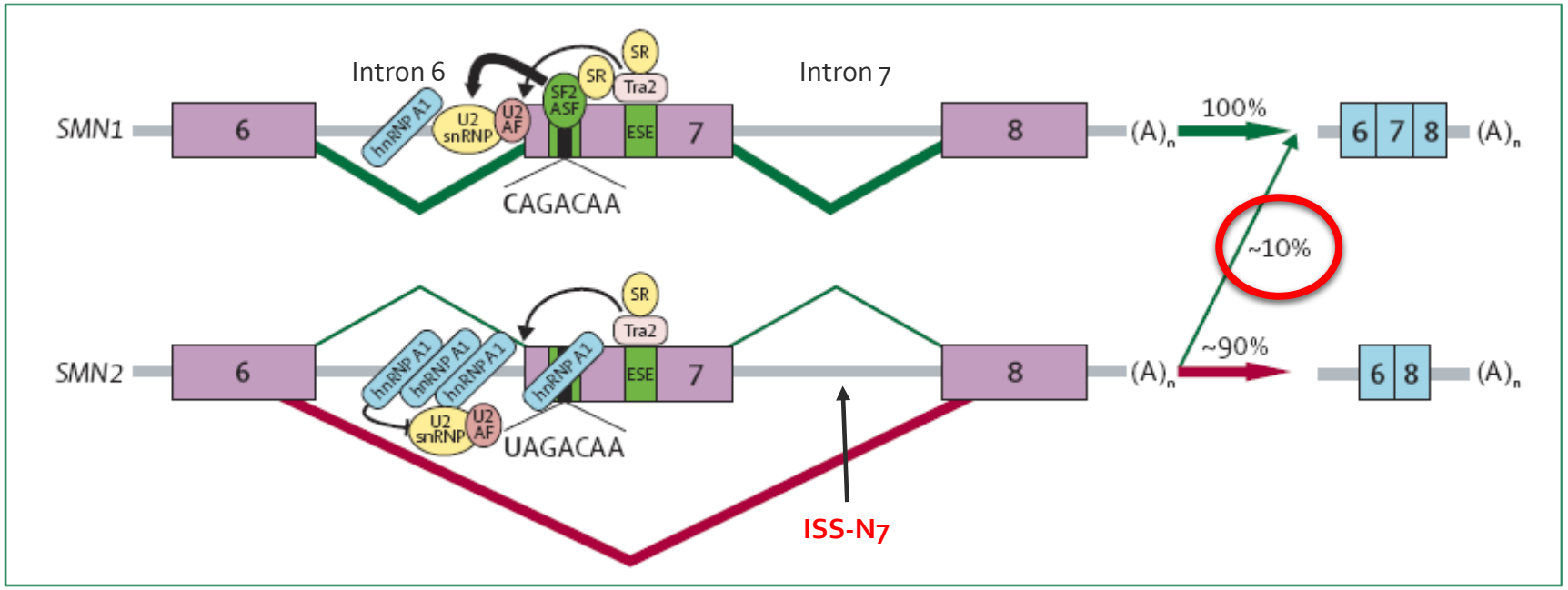
Subtype	Age at onset	Highest function achieved	SMN2 copy #	Natural age of death
Type 1	0-6 mo	Never sits	2	<2 years
Type 2	6-18 mo	Sit, never stand	3	20-40 years
Type 3	1.5-10y	Stand & walk Regresses	3-4	Near normal
Type 4	Teens-20's	Walk during adulthood Slow decline	4	Normal

Classification will become obsolete in a few years

SMA GENETICS



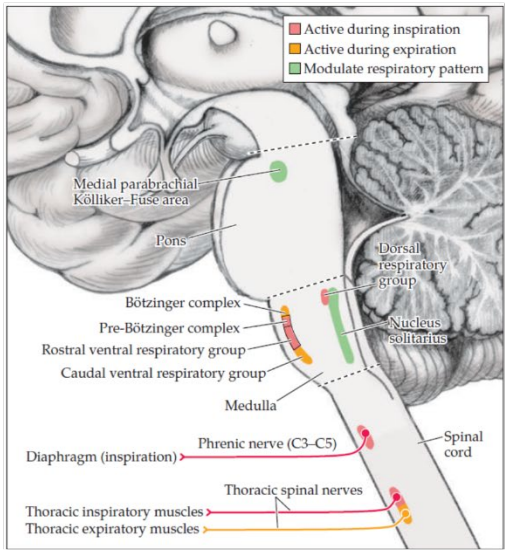
- Pre-mRNA splicing of *SMN1* and *SMN2*

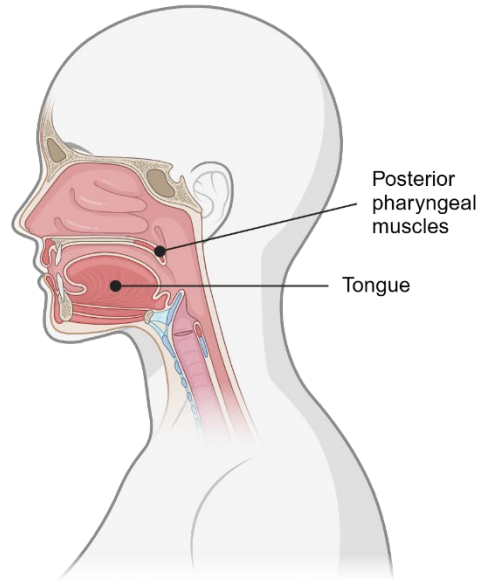


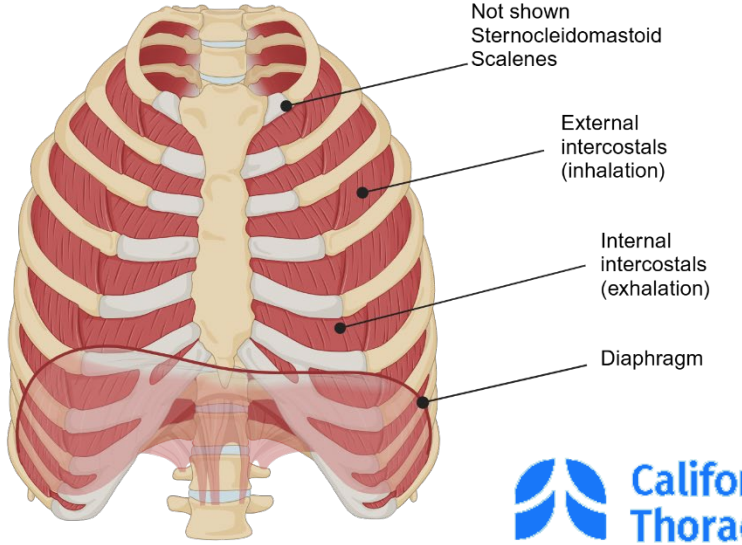
Lunn MR. Wang CH. Spinal muscular atrophy. Lancet. 2008; 371-2120-33.

BREATHING MECHANISM

1. Respiration control centers
   - Brainstem—pons, medulla
   - Ventral pools in spinal cord
     - Cord level C3-5 →diaphragm
     - Cord level T1-T12→intercostals
2. Thoracic cage
   - Shape
   - Size
3. Roots, nerves, muscles of breathing
   - Roots C3-C5→phrenic nerve→ diaphragm
   - Roots T1-T12→thoracic spinal nerves→ intercostals
   - Upper airway muscles: posterior pharyngeal
   - Accessory muscles: scalene, sternocleidomastoids, abdominal







Patel *et al*. Respiratory considerations in pts with NMD, *Muscle and Nerve,* 2023.
Blumenfeld. Neuroanatomy through Clinical Cases. Chapter 14. p647
All figures made by C. Laverty using BioRender

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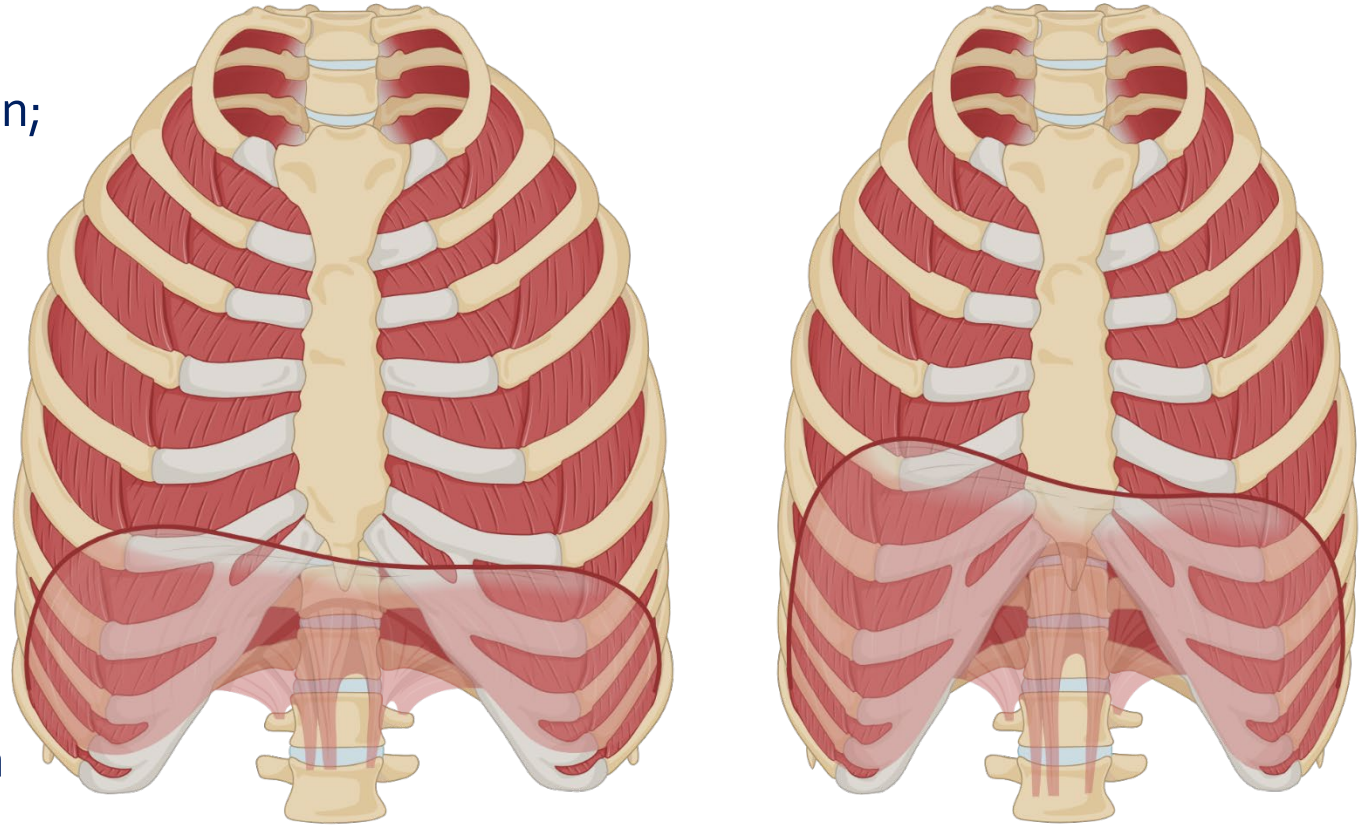
BREATHING

INSPIRATION

- Diaphragm—primary inspiratory muscles
- External intercostals—augments inspiration; moves ribs out
- Accessory muscles recruited to enhancing inspiration
  - Coughing
  - Speaking
  - Respiratory stress

EXPIRATION

- Occurs passively by lung recoil
- Internal intercostals—augments expiration
- Abdominal muscles—facilitates expiration; e.g. cough



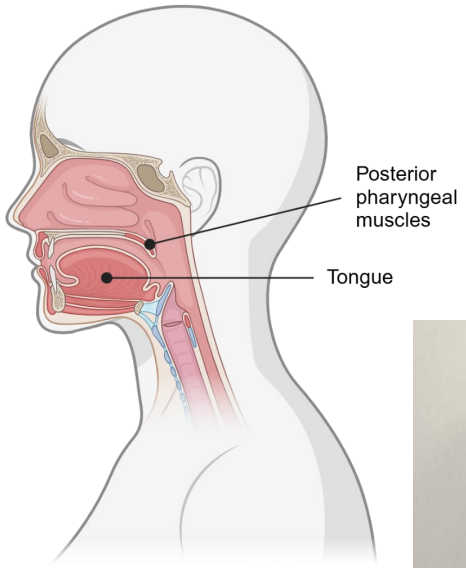
Inspiration

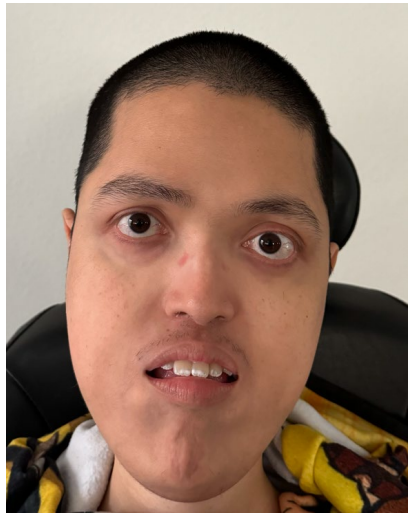
Expiration

Patel *et al*. Respiratory considerations in pts with NMD, *Muscle and Nerve*, 2023
All figures made by C. Laverty using BioRender

SYMPTOMS OF RESPIRATORY WEAKNESS

- Decreased exercise tolerance
- Sleep apnea
  - Central sleep apnea
    - Common in myotonic dystrophy 1
  - Peripheral sleep apnea
    - Upper airway skeletal muscle collapse
    - Enlarged tongue
  - Unexplained arousals from sleep
  - Morning headaches
  - Daytime hypersomnolence & fatigue
  - Non-refreshing sleep
  - Orthopnea
  - Poor concentration or mood disorders; "brain fog"
  - Restless at night or unusual movements





25yo M with merosin deficient congenital muscular dystrophy
- Tongue hypertrophy
- Elongated facies
- Abnormal jaw
- Bilevel since childhood

21 yo M with RYR1 congenital myopathy
- Elongated facies
- Abnormal jaw
- Bilevel since teens

Patel *et al*. Respiratory considerations in pts with NMD, *Muscle and Nerve*, 2023
Figure made by C. Laverty using BioRender

BREATHING IN NEUROMUSCULAR DISEASE (NMD)

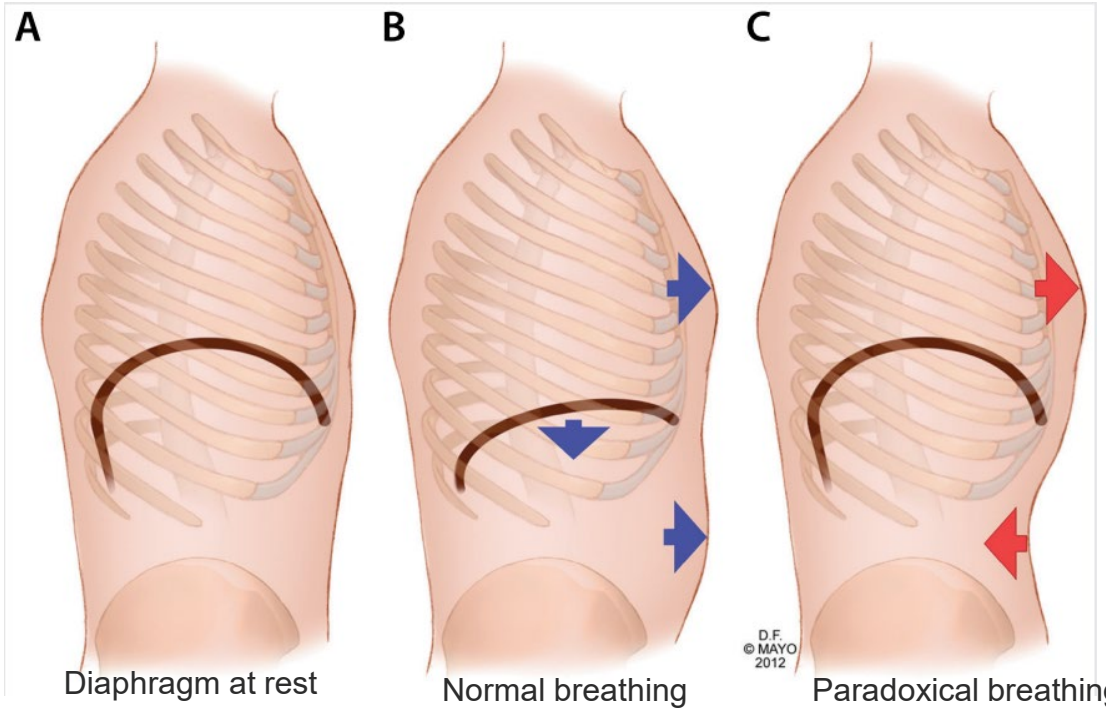
- **Acute** (over weeks) loss of breathing more typical in acquired NMD
  - ALS
  - Myasthenia
  - GBS
- **Gradual** loss of breathing in *neurodegenerative* conditions
  - ALS
  - Nearly all muscular dystrophies
  - SMA types 1, 2, and 3A
  - Nearly all congenital onset diseases:
    - Congenital myopathies
    - Congenital muscular dystrophies
    - Congenital myasthenic syndromes
  - Post-polio syndrome (if breathing affected initially)
  - Multifocal cervical radiculopathies (C_3-C_5)
  - Some genetic neuropathies (CMT)
- Breathing ***not*** affected when treated
  - Autoimmune myasthenia –if neurologist is doing their job

- Presentation
  - Acutely—with or w/o concomitant infection
  - Insidiously
  - Unilaterally or bilaterally
    - Most neurodegenerative diseases are bilateral
  - Can be presenting symptom
    - ALS
- What happens in NMD?
  - Respiratory muscle lose ability to generate force for breathing
    - Microatelectasis
    - Hypercarbia
    - Hypoxemia (late finding)

Patel *et al*. Respiratory considerations in pts with NMD, *Muscle and Nerve*, 2023

EXAM FINDINGS

- Compensation
  - Rapid, shallow breathing (tachypnea)
  - Use of accessory breathing muscles
  - Diaphragm fatigues→**paradoxical breathing**



Diaphragm at rest

Normal breathing

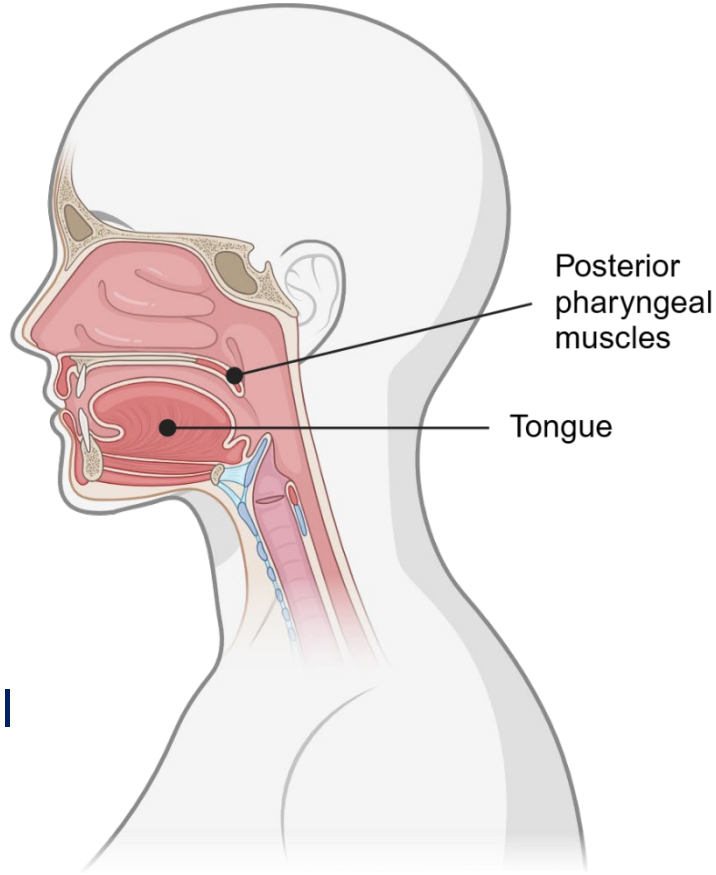
Paradoxical breathing; diaphragm weak.
Abdomen moves inward b/c ↓intrathoracic P

video placeholder

Patel *et al*. Respiratory considerations in pts with NMD, *Muscle and Nerve*, 2023
Continuum Neurology; Acute Neuromuscular Respiratory Failure, 2015; 21(5): 1324-1345
Video used with permission.

EXAM FINDINGS

- Diaphoresis
- Tachycardia
- Staccato speech
  - Needing to inhale every few words
- Nasal speech
  - Ask patient if they sound different!
  - History of nasal regurgitation
- Thoracic cage
  - Early onset NMD—SMA 1 & 2, congenital
    - Spinal deformity
    - Small chest wall

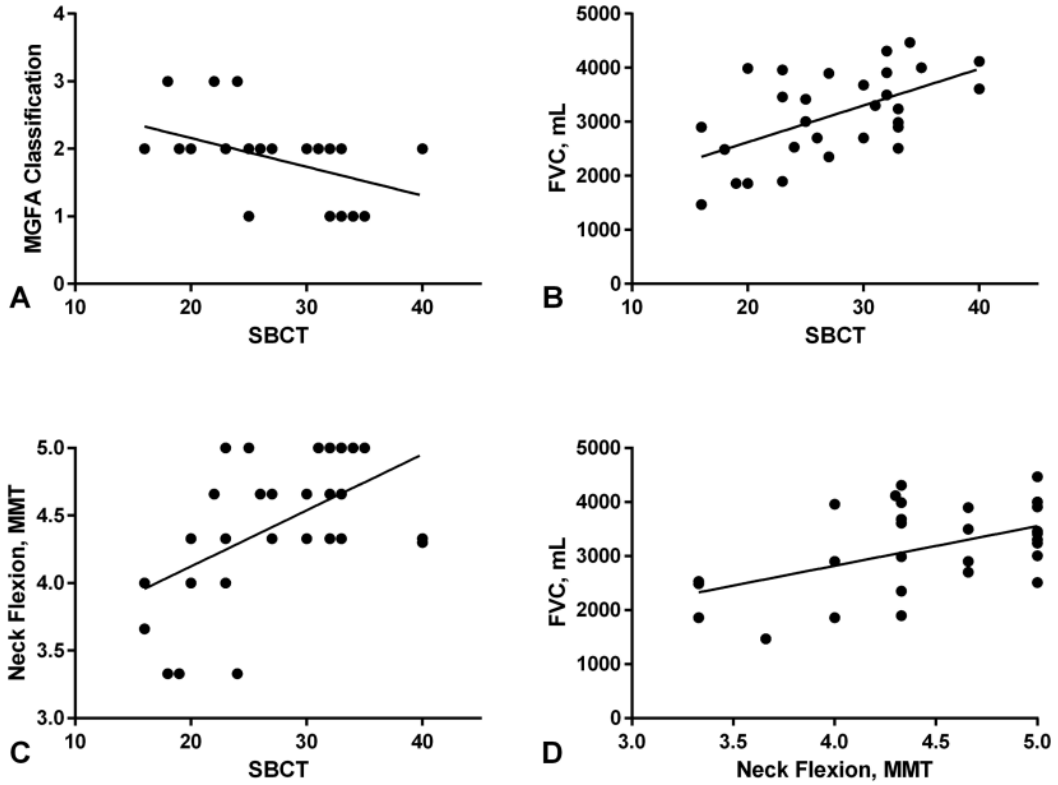


video placeholder

Patel *et al*. Respiratory considerations in pts with NMD, *Muscle and Nerve*, 2023
Video used with permission.

EXAM FINDINGS

- Neck flexion weakness
  - Count as long as possible, 1 sec/ number
  - "1001", "1002"…



NF=neck flexion; SBCT = single breath count test

video placeholder

28 yo M with MELAS, admitted for DOE requiring BIPAP, 2 months post discharge. Axial and neck flexor weakness

Elsheikh et al, *Muscle Nerve*. 2016 Jan; 53(1): 134–136.
Video used with permission.

RESPIRATORY CARE

- Pulmonary care makes all the difference

video placeholder

MANAGEMENT CONSIDERATIONS IN PATIENTS WITH NEUROMUSCULAR DISORDERS

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Assistant Professor, Division of Pulmonary, Critical Care, and Sleep Medicine

UC San Diego School of Medicine

March 2025

California Thoracic Society

RELEVANT FINANCIAL DISCLOSURES

- I have no relationships with ACCME defined ineligible companies.

- I WILL/WILL NOT discuss off-label use and/or investigational use of any drugs or devices.

California Thoracic Society

Care for Adults with Cerebral Palsy

Jacob Bailey, MD, MA
Division of Pulmonary, Critical Care, Sleep Medicine, and Physiology
UC San Diego School of Medicine

NASA, ESA, CSA, and the James Webb Space Telescope

I have 20 minutes to help you…

identify important risk factors for pulmonary complications and…

develop a management framework for individuals with cerebral palsy

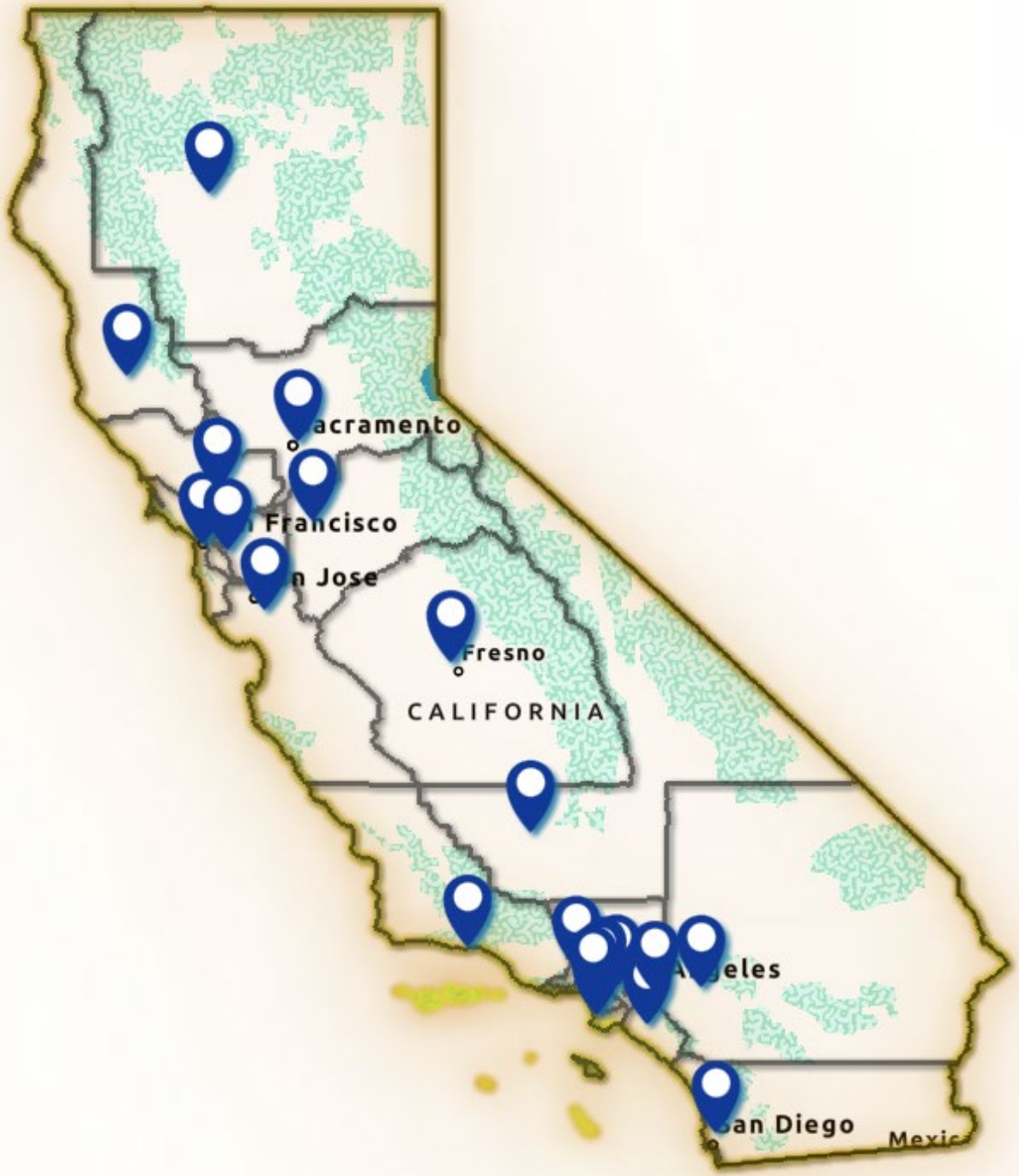

Background

It is . . .

- a motor disorder that affects movement, tone, and coordination
- due to some insult to the early developing brain

It is NOT . . .

- an intellectual disorder
- static
- just an issue of chronic aspiration
- just for pediatricians



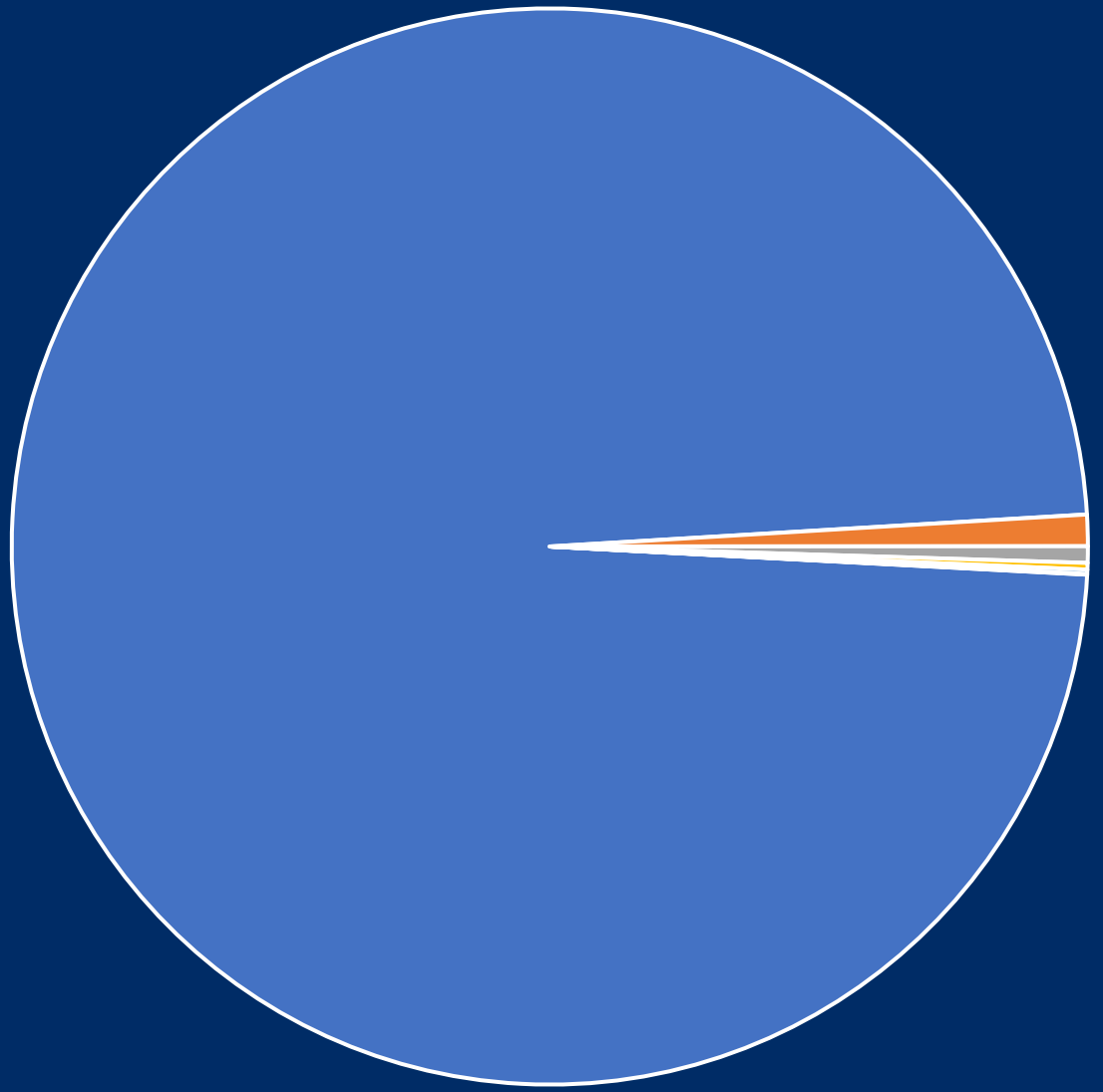
35,704 people living with CP in California

25,292 are adults

CA Department of Developmental Services

~50% die from respiratory complications

Blair E, et al. *BMC Neurol*. 2019
Stevens, J. D., et al. *Ann Phys Rehabil Med*. 2022



6060 Pubmed manuscripts on adults with CP

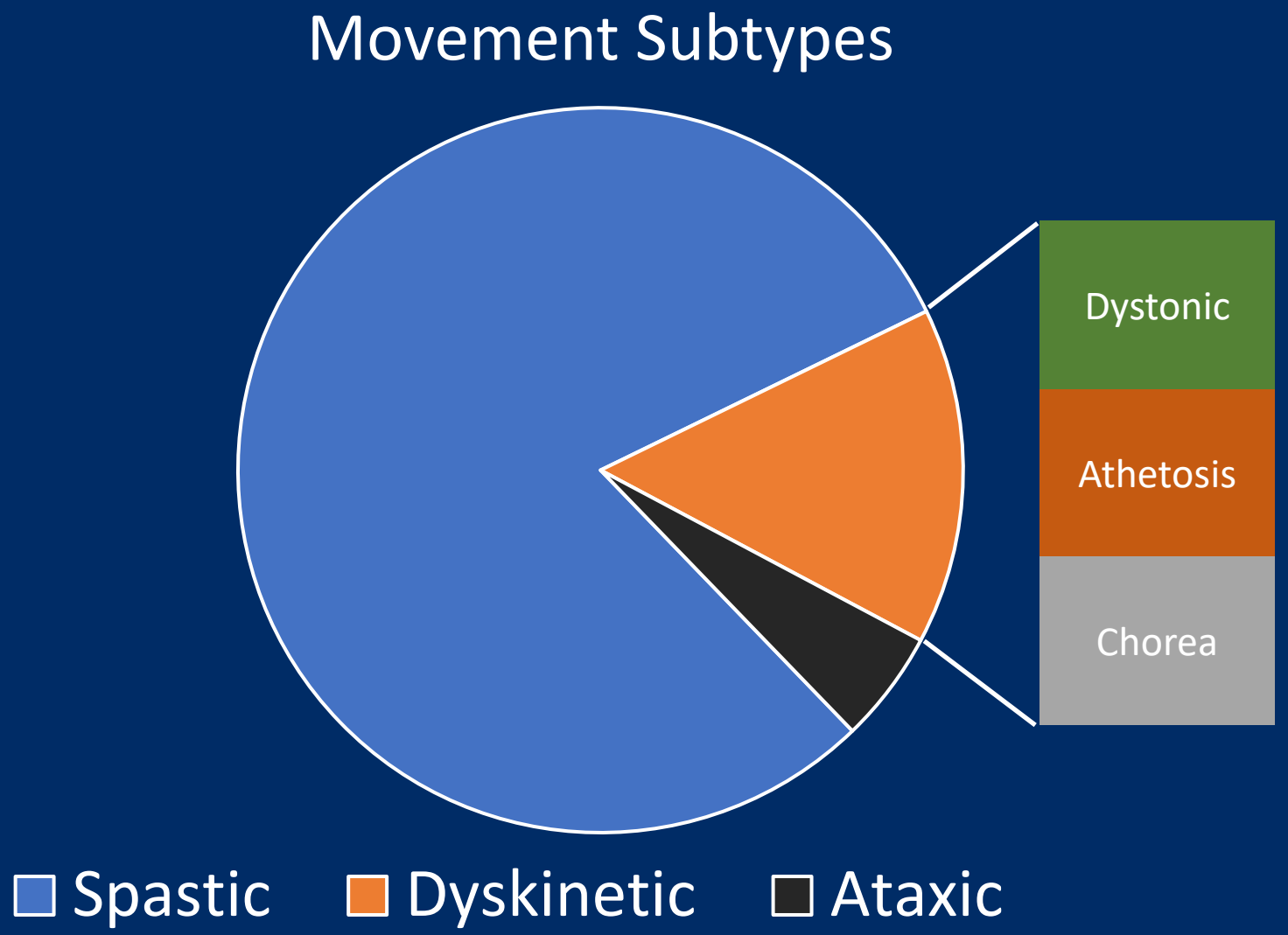
Related to lung health?
57 case reports
30 reviews
12 RCTs
1 Practice Guideline

How I approach patients with cerebral palsy

Risk assessment of pulmonary morbidity and mortality

Movement subtype
Distribution
Severity
Etiology
Associated conditions

- Movement subtype
- Distribution
- Severity
- Etiology
- Associated conditions



- Movement subtype
- Distribution
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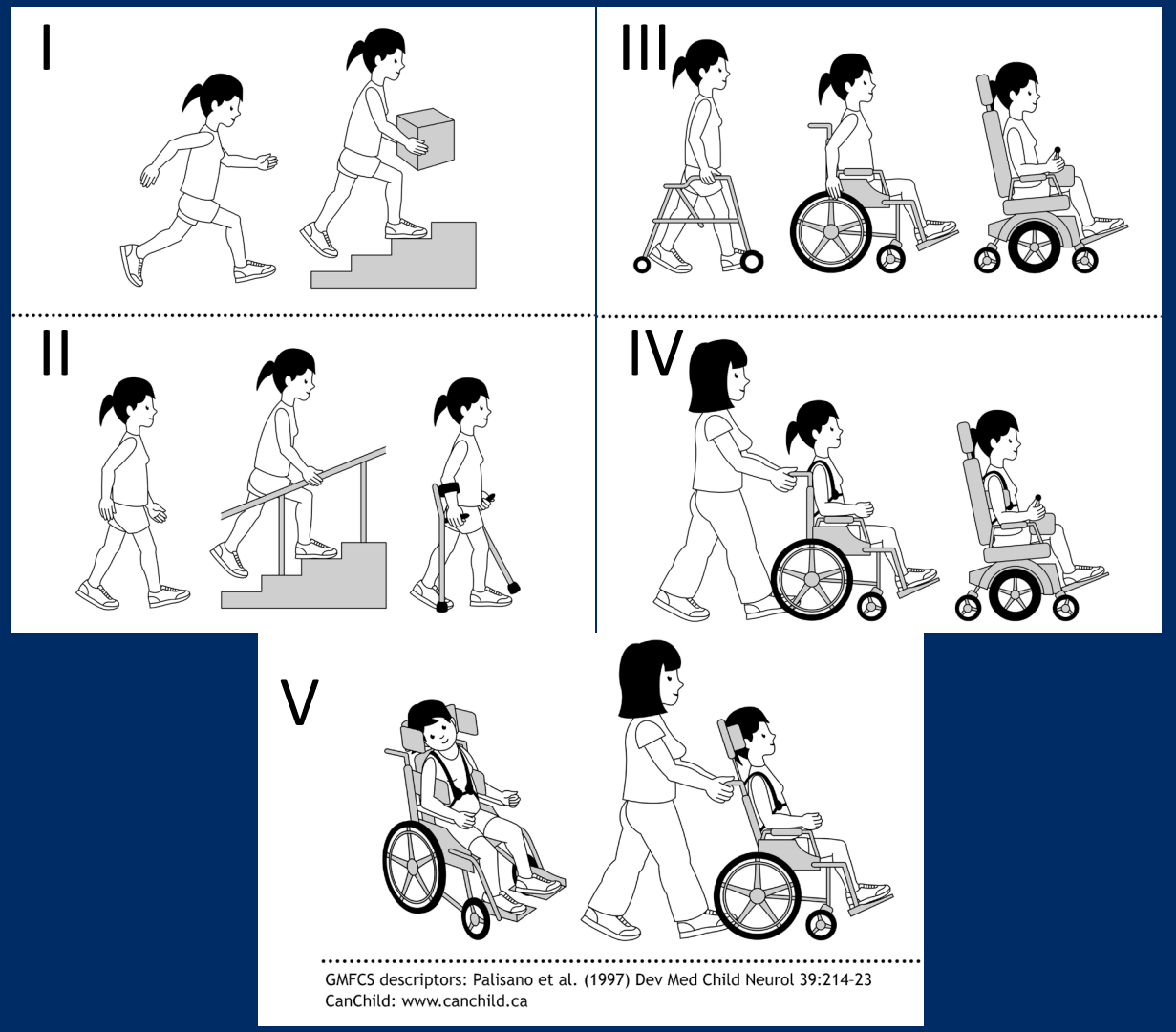
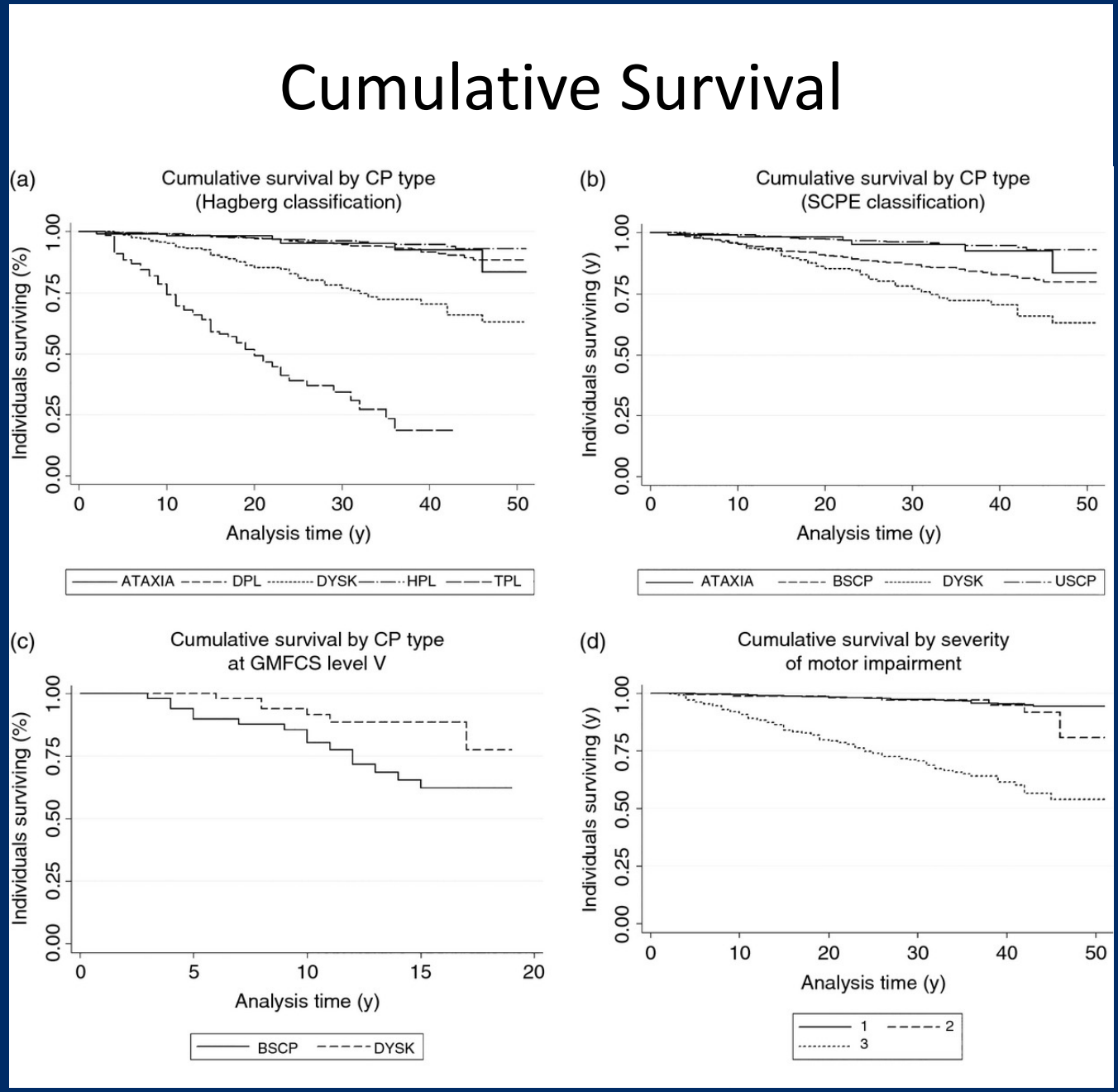
Gross Motor Functional Classification Scale

- Movement subtype
- Distribution
- Severity
- Etiology
- Associated conditions



Distribution
Movement subtype
Severity
Etiology
Associated conditions

Cumulative Survival



Himmelmann K, Sundh V. *Dev Med Child Neurol*. 2015

- Distribution
- Movement subtype
- Severity
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O'Callaghan ME, et al. *Obstetrics & Gynecology*. 2011
McMichael G, et al. *Mol Psychiatry*. 2015
Novak I, et al. *JAMA Pediatr*. 2017

- Distribution
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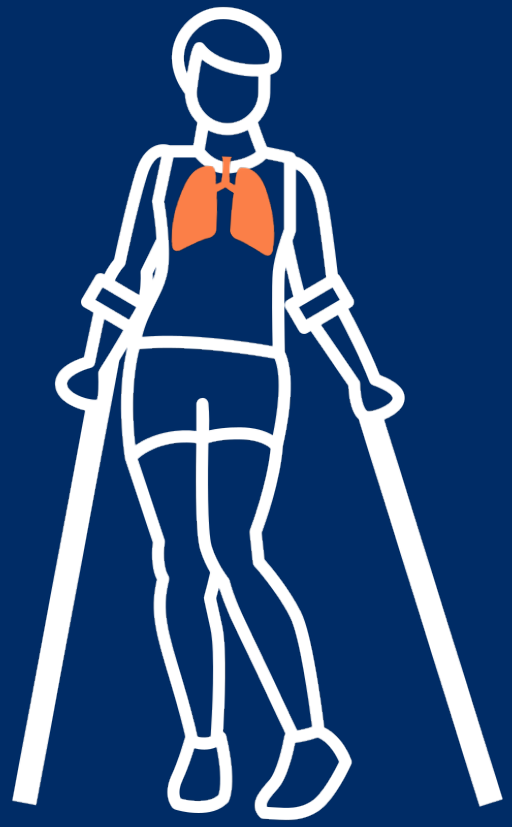

- Intellectual disabilities
- Seizure disorders
- Asthma
- Dysphagia
- Sialorrhea
- Reflux
- Gastrostomy dependence
- Scoliosis
- Bronchiectasis
- Chronic bacterial infections
- Hypoventilation
- Sleep disorders
- Oral health
- Cardiovascular health
- Osteoporosis

Vianello A, et al. *Respiratory Care*. 2015
Blackmore AM et al. *The Journal of Pediatrics*. 2016
Blackmore AM, et al. *Arch Dis Child*. 2018
Whitney D, Basu T. *Develop Med Child Neuro. 2021*

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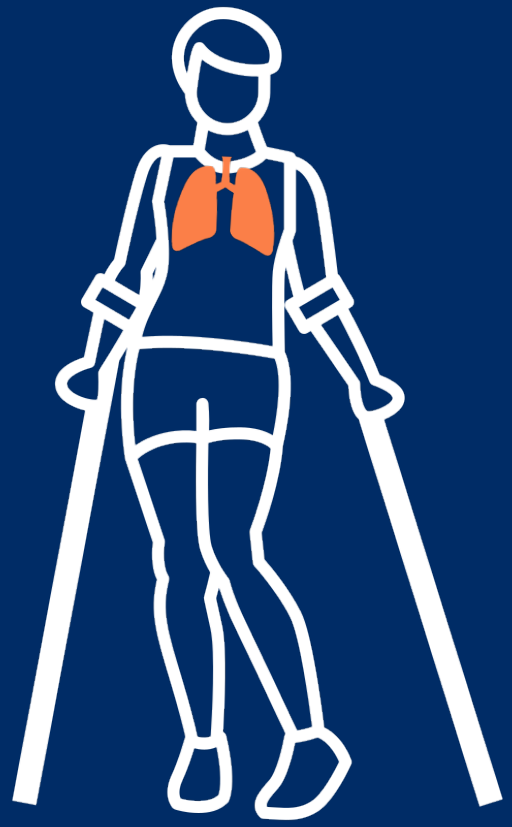

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Adjusted Odds Ratios of Respiratory Exacerbation Risk

	AOR	95% CI	*P*
Gastroesophageal reflux	23.95	1.58 - 363.86	.02
PaCO2 (Δ = 5mmHg)	12.60	1.03 – 154.33	.05
Airway mucous encumbrance	7.26	0.38 – 137.44	.18
adjusted for sex and age			

Vianello A, et al. *Respiratory Care*. 2015
Blackmore AM et al. *The Journal of Pediatrics*. 2016
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Incidence Rate Ratios for Number of Hospitalizations

	1-Yr IRR (95% CI)	2-Yr IRR (95% CI)
Oromotor dysfunction	8.8 (3.01 to 25.7)	7.1 (2.81 to 17.9)
Snoring (often/always)		2.57 (1.15 to 5.7)
Gastroesophageal reflux	1.77 (0.73 to 4.3)	3.61 (1.59 to 8.2)
Seizures	3.59 (1.35 to 9.6)	3.20 (1.38 to 7.4)
Previous hospitalization	12.9 (5.7 to 29.1)	16.2 (7.8 to 33.4)
multivariable analysis model (negative binomial model)		

Vianello A, et al. *Respiratory Care*. 2015
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Prevalence of death during 2-year follow by Whitney Comorbidity Index value

- Distribution
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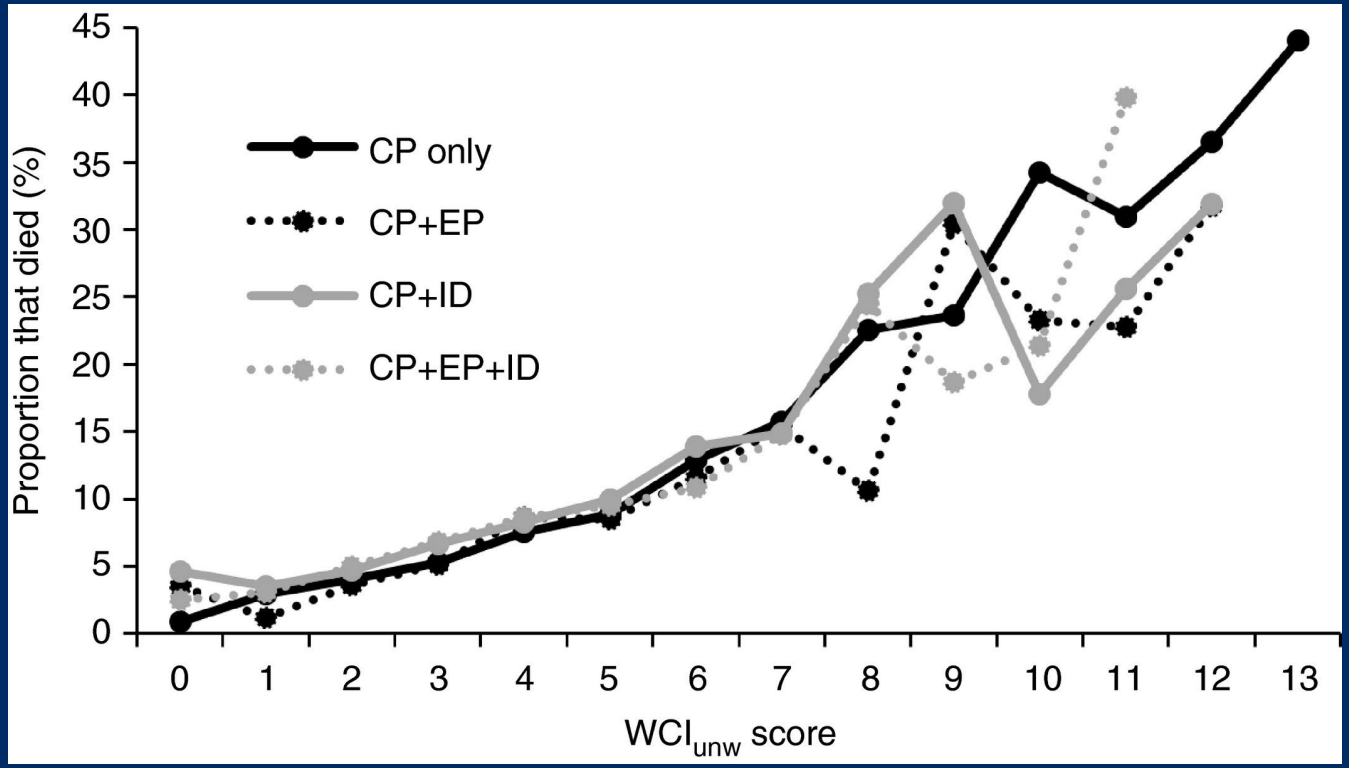
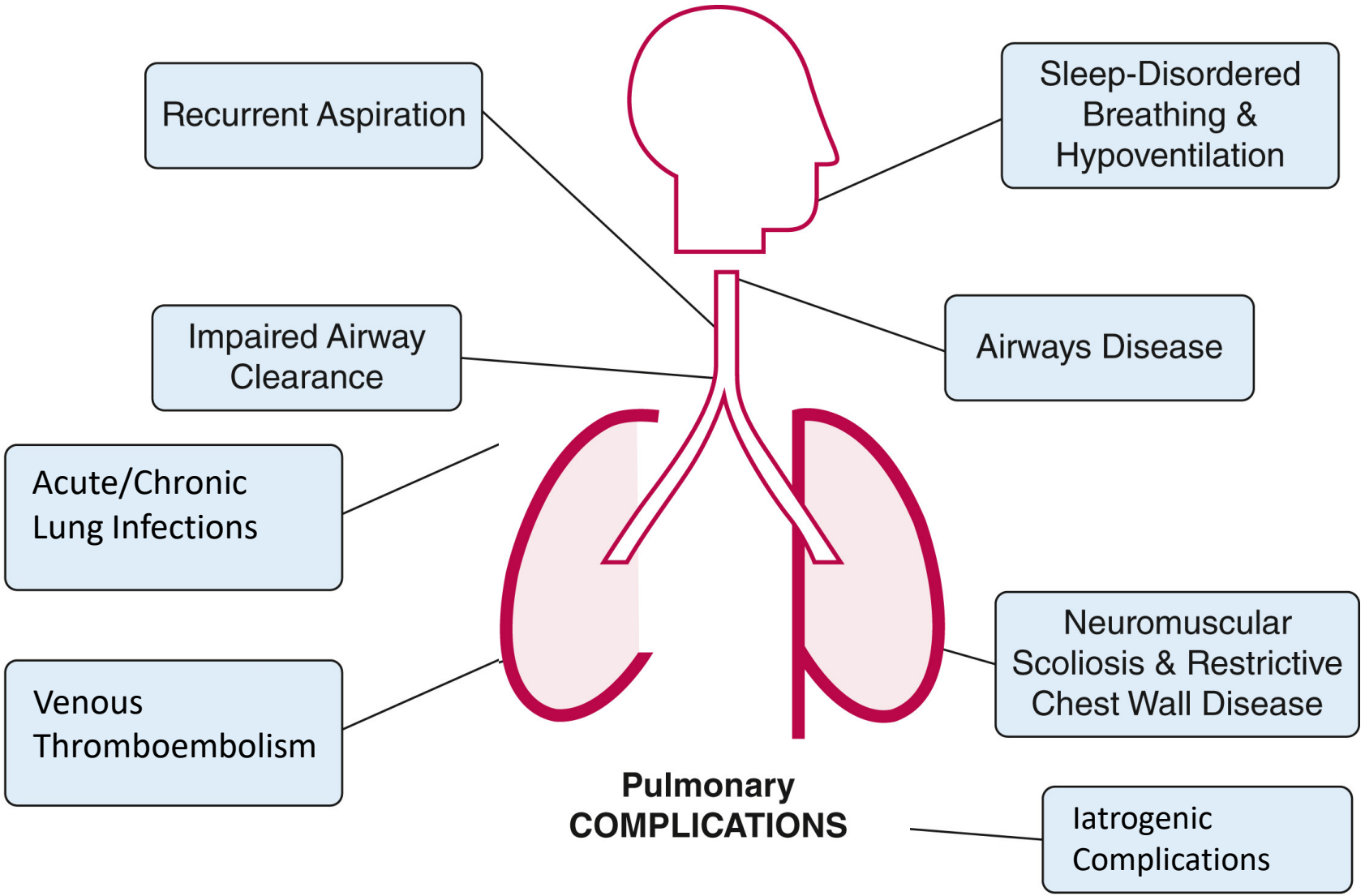


Whitney D, Basu T. *Develop Med Child Neuro. 2021*
Whitney D, Kamdar N. *Develop Med Child Neuro. 2021*



Desai B, Lesser D, Sunwoo B. *CHEST Pulmonary*. 2023

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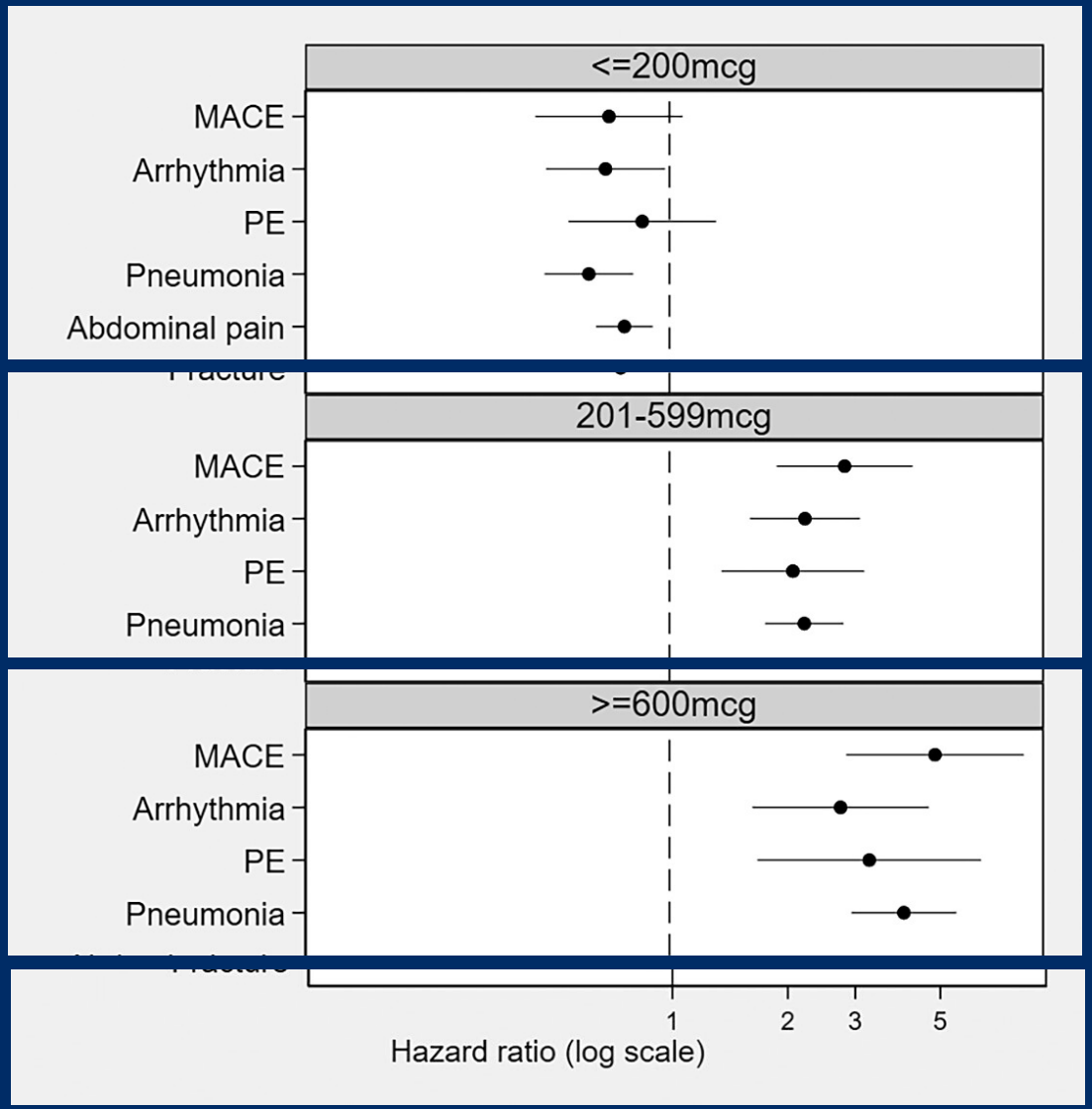
~20% are diagnosed with asthma

Cremer N, et al. *Am J Med*. 2017
Blackmore AM, et al. *Arch Dis Child*. 2018
Xie L, et al. *JAMA Netw Open*. 2020

Association Between ICS Dose and Adverse Outcomes



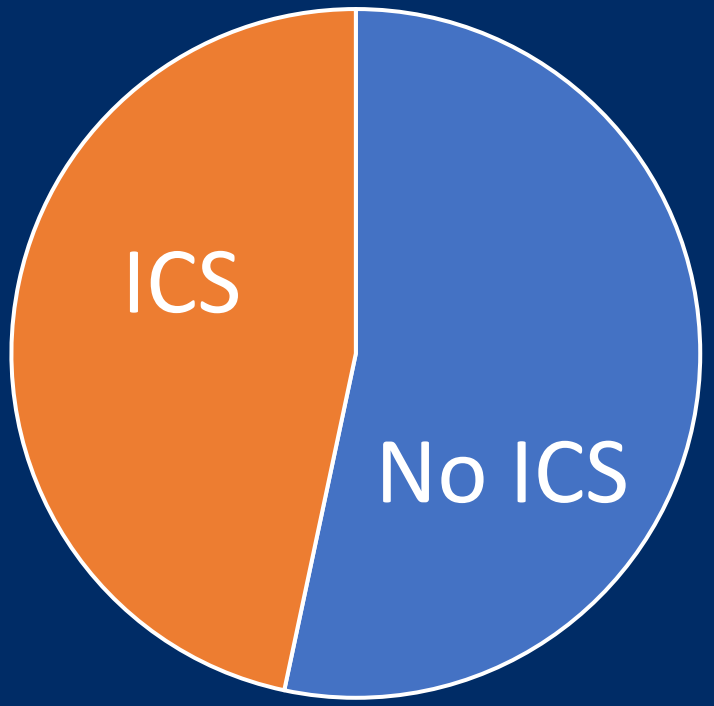
Nebulized budesonide starts at 250mcg

Bloom CI, et al. *Am J Respir Crit Care Med*. 2025

How I approach patients with cerebral palsy AND asthma

- Take a good history!
- Blood eosinophil counts
- Radioallergosorbent Test
- Quick de-escalation
- Consider alternate Dx/Rx

How I approach patients with cerebral palsy AND asthma



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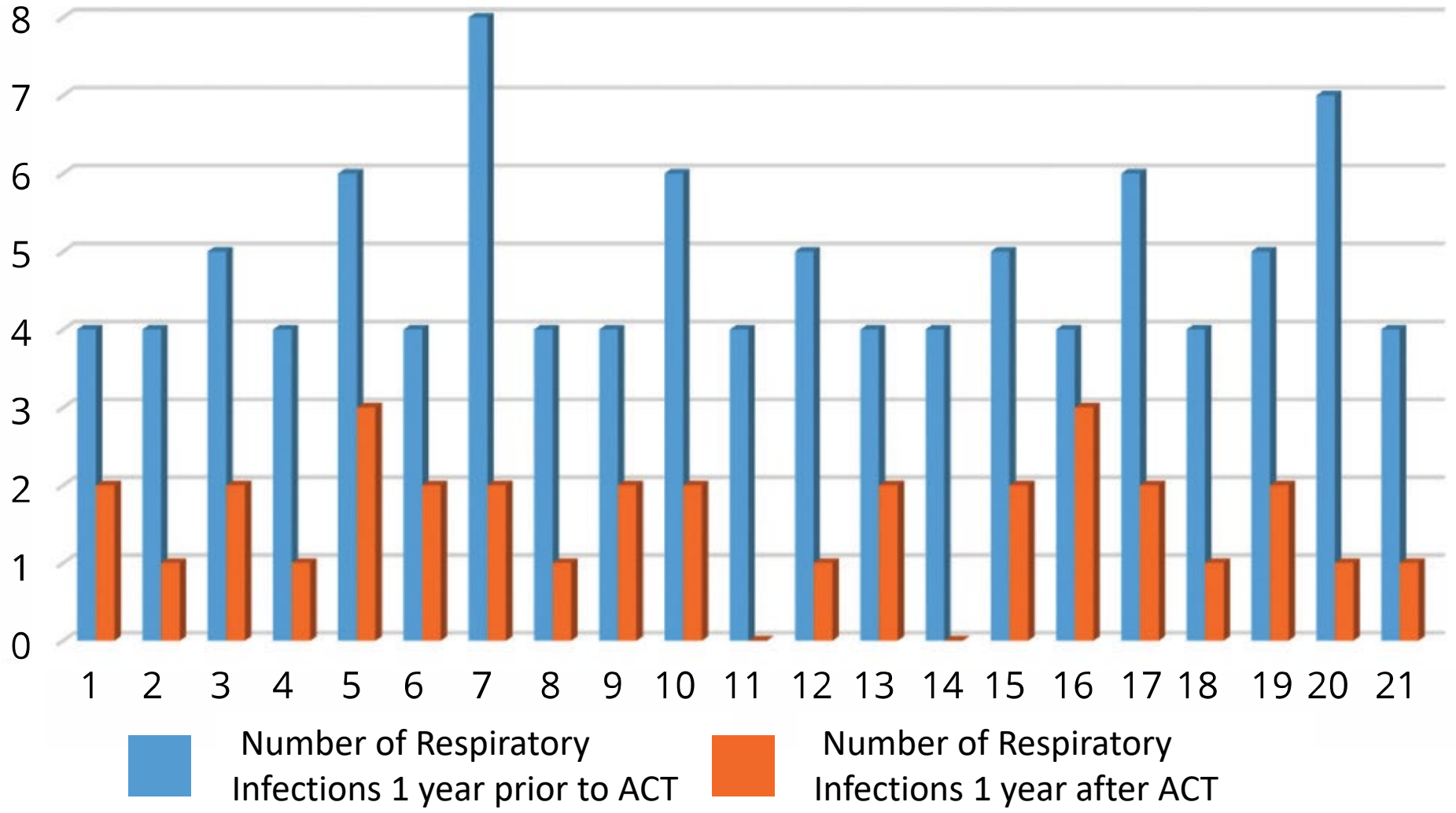
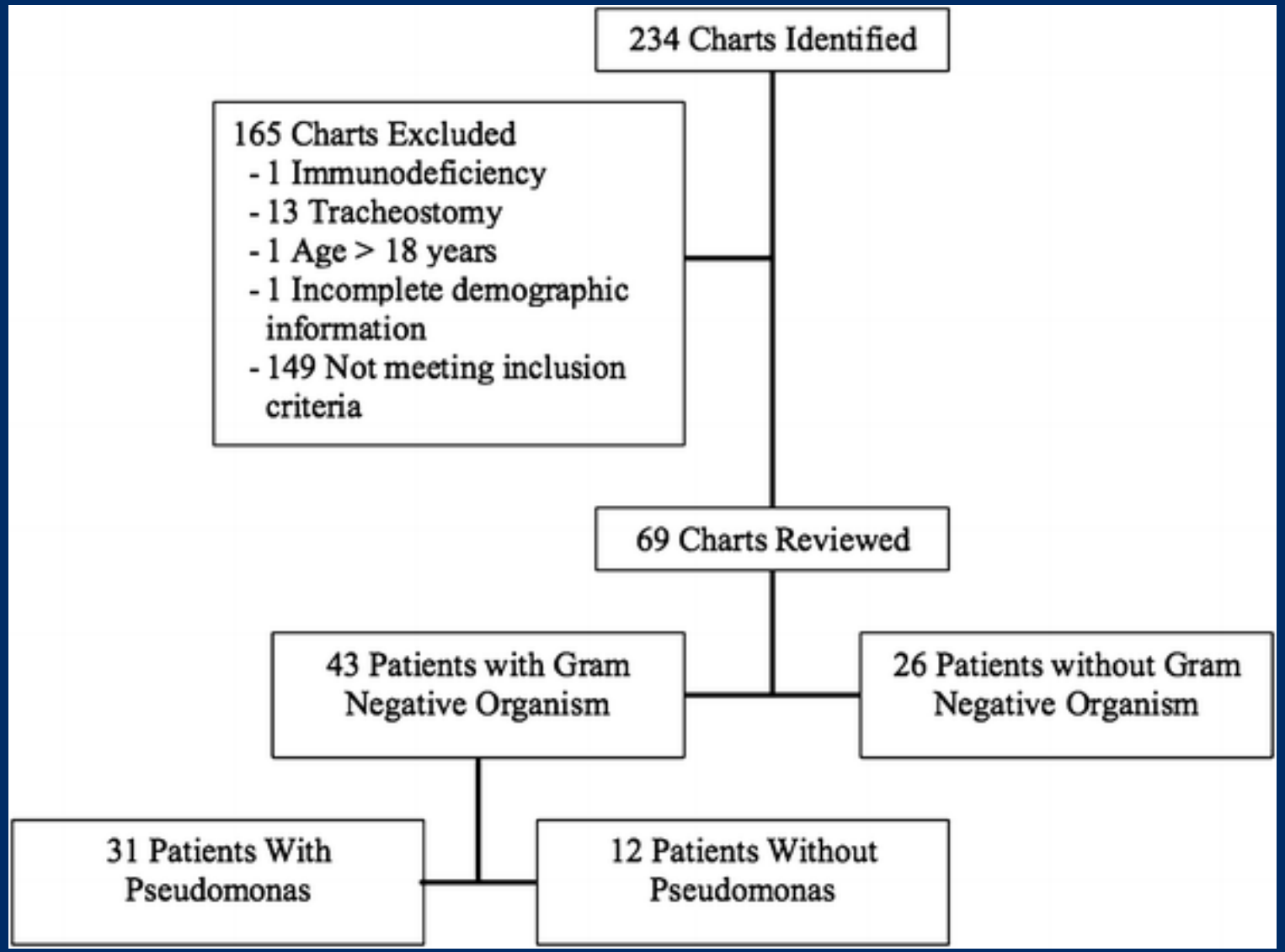
Clinical Outcomes with Daily Airway Clearance



Di Pede C, et al. *Eur J Phys Rehabil Med*. 2020

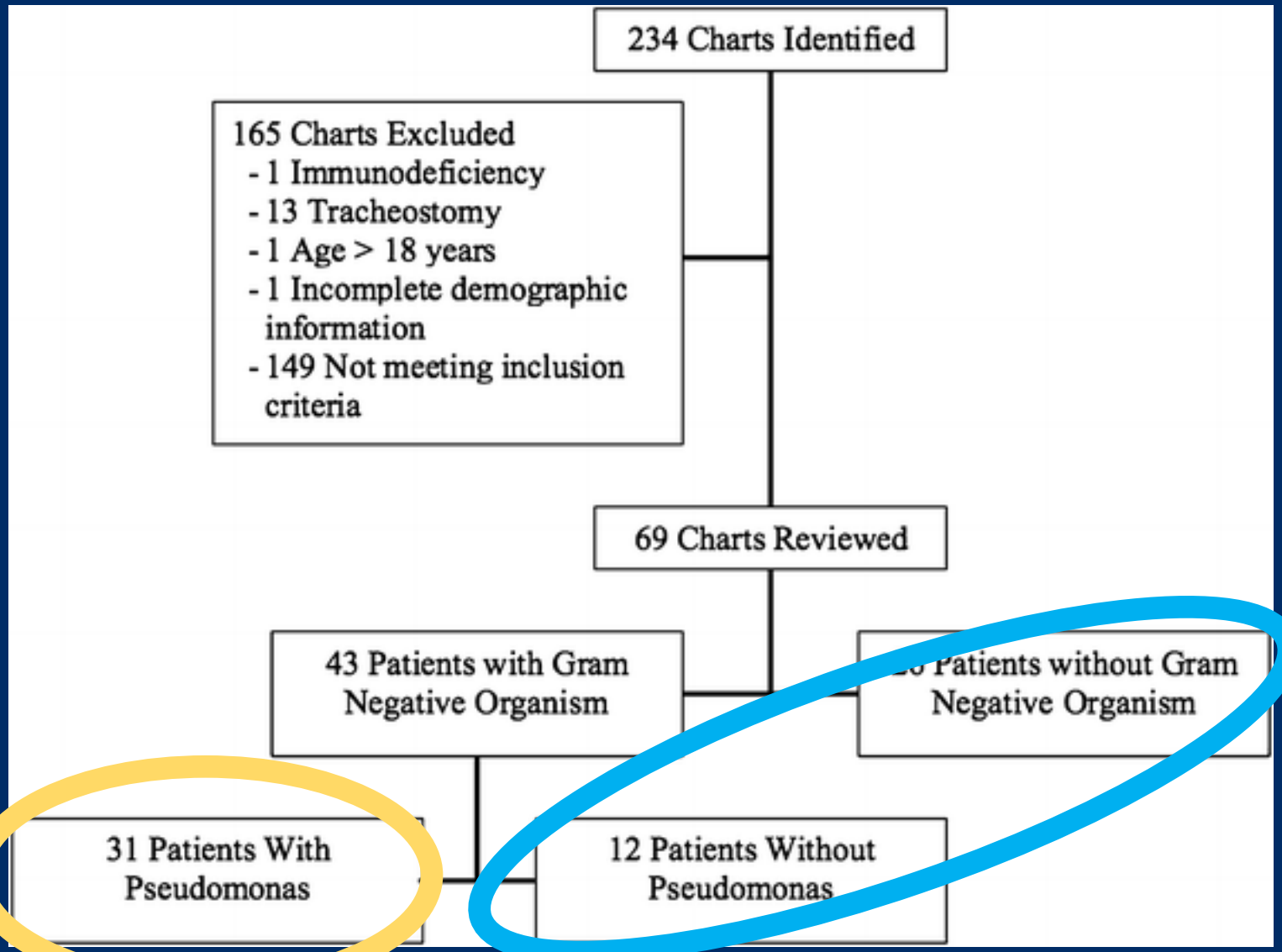
Association of Respiratory Cultures on Clinical Outcomes



- Excluded patients with tracheostomies
- No temporal association between culture and hospitalization established
- No chronicity established
- No alternative detection testing used

Gerdung CA, et al. *Lung*. 2016

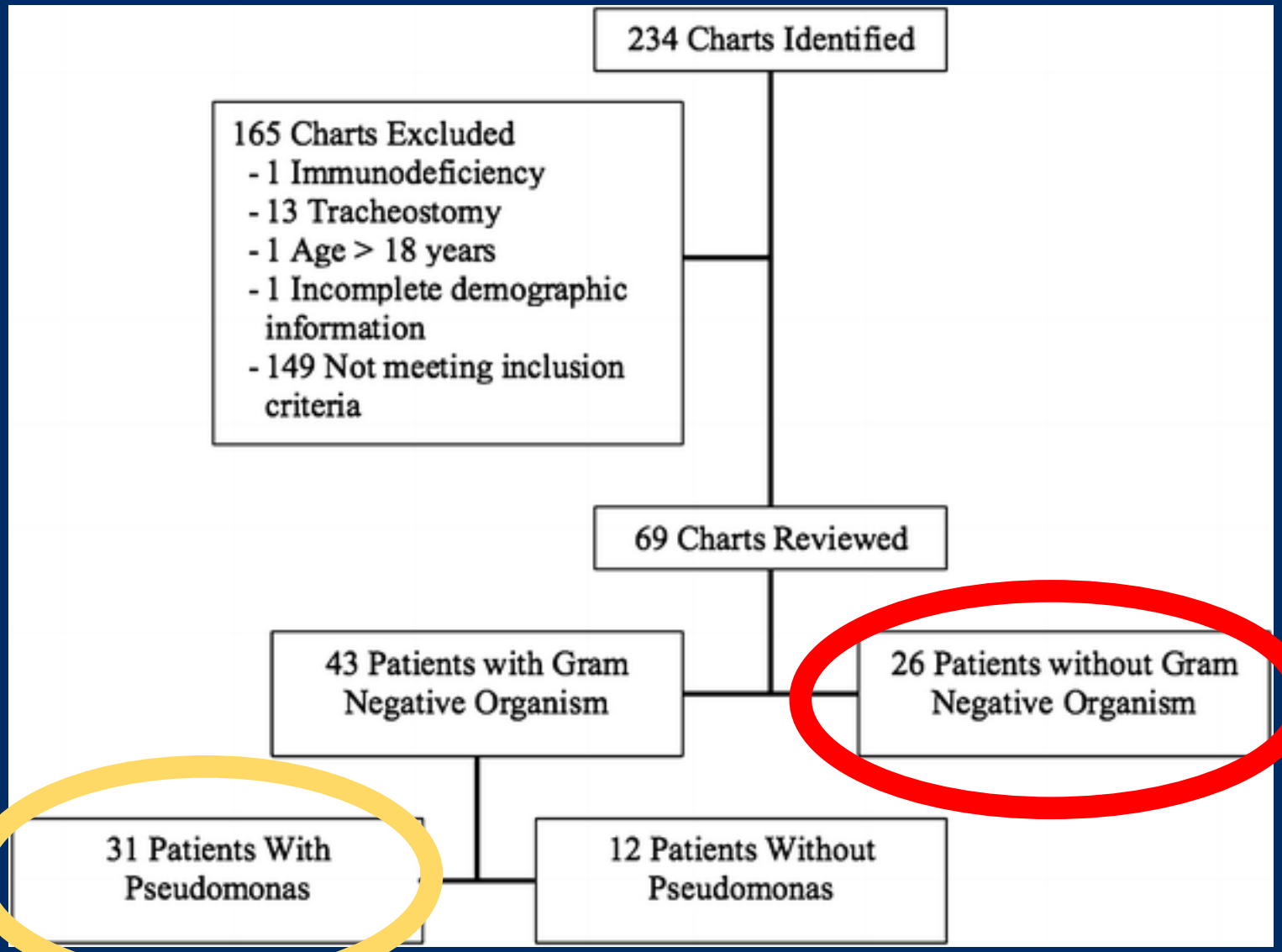
Association of Respiratory Cultures on Clinical Outcomes



Pseudomonas associated with more…
- admitted to PICU

Gerdung CA, et al. *Lung*. 2016

Association of Respiratory Cultures on Clinical Outcomes

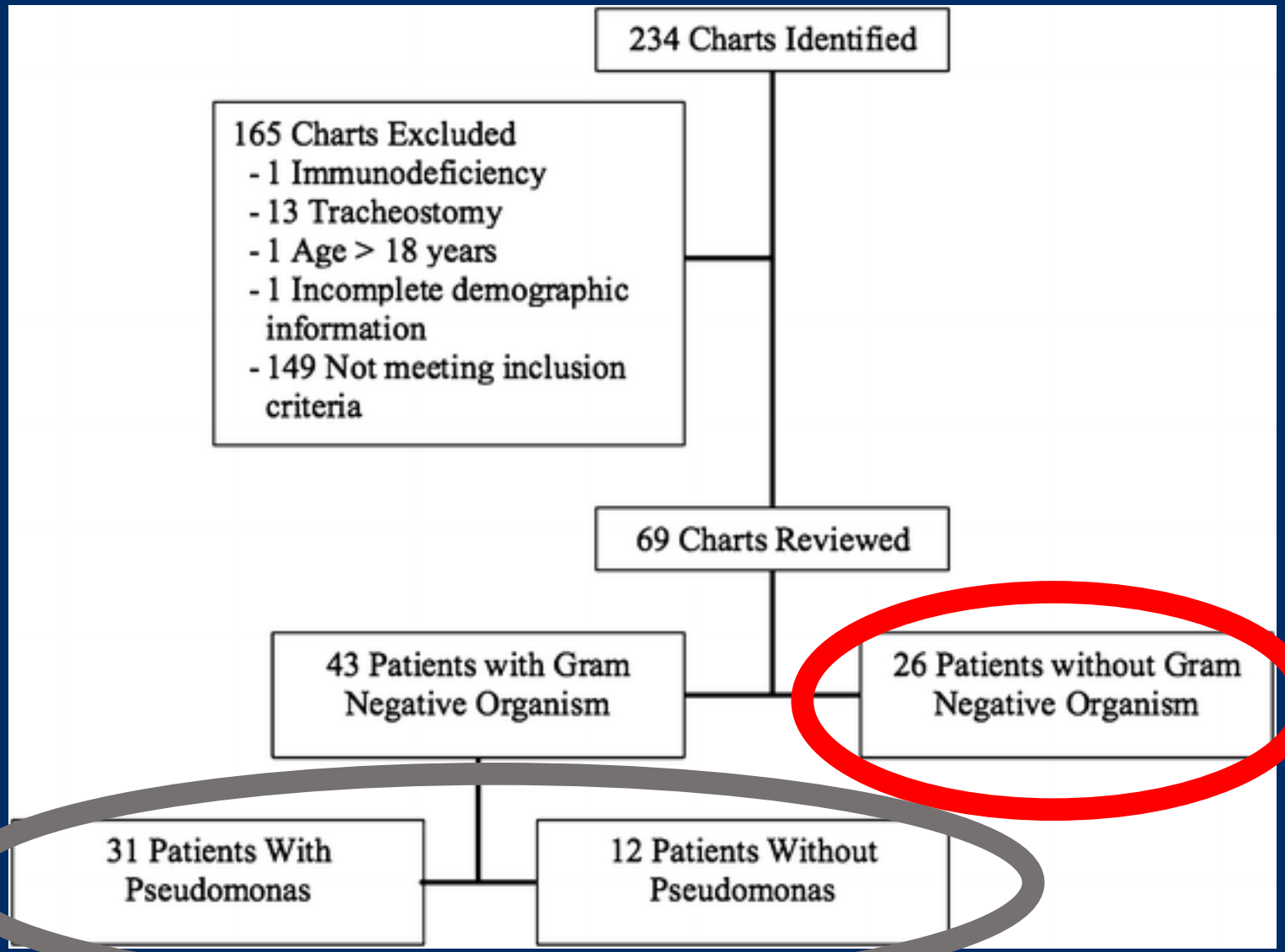


Pseudomonas associated with more…

- admitted to PICU
- lobar consolidations
- intubations

Gerdung CA, et al. *Lung*. 2016

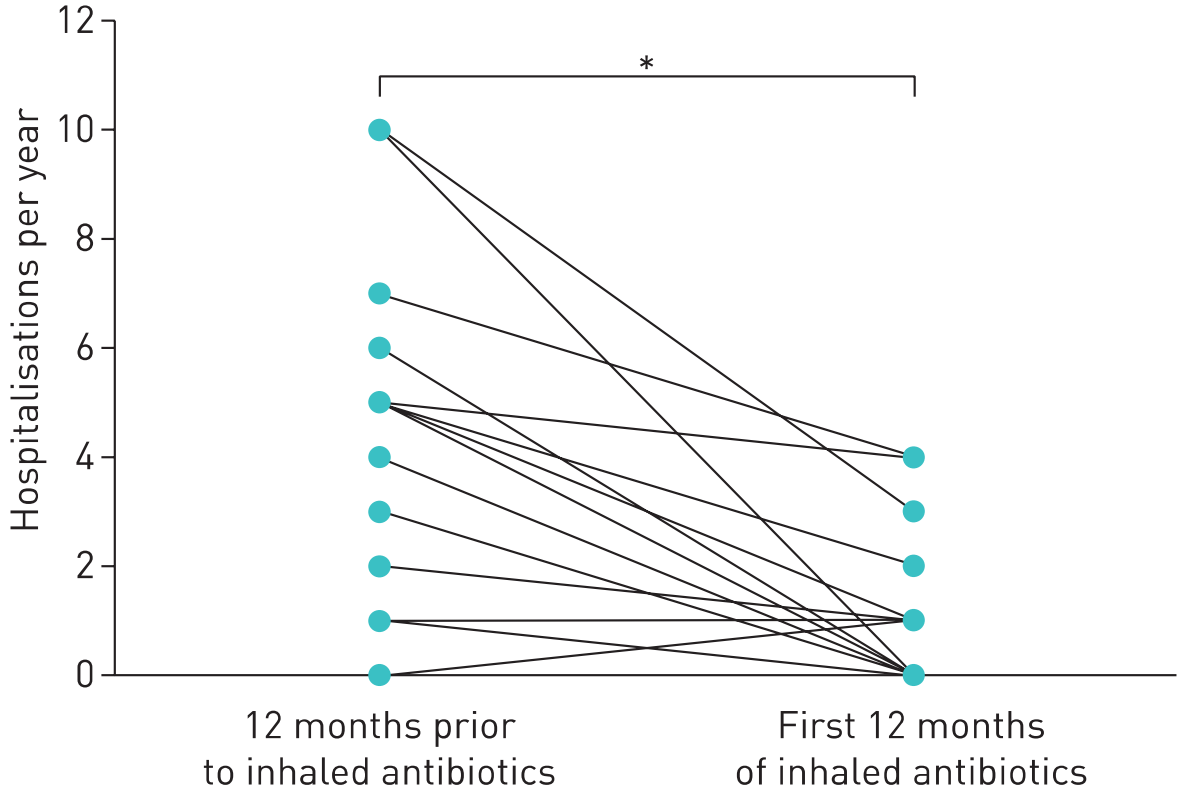
Association of Respiratory Cultures on Clinical Outcomes



Gram negative bacteria associated with more…
- admitted to PICU
- intubations

Gerdung CA, et al. *Lung*. 2016

Clinical Outcomes with Microbial Suppressive Therapy

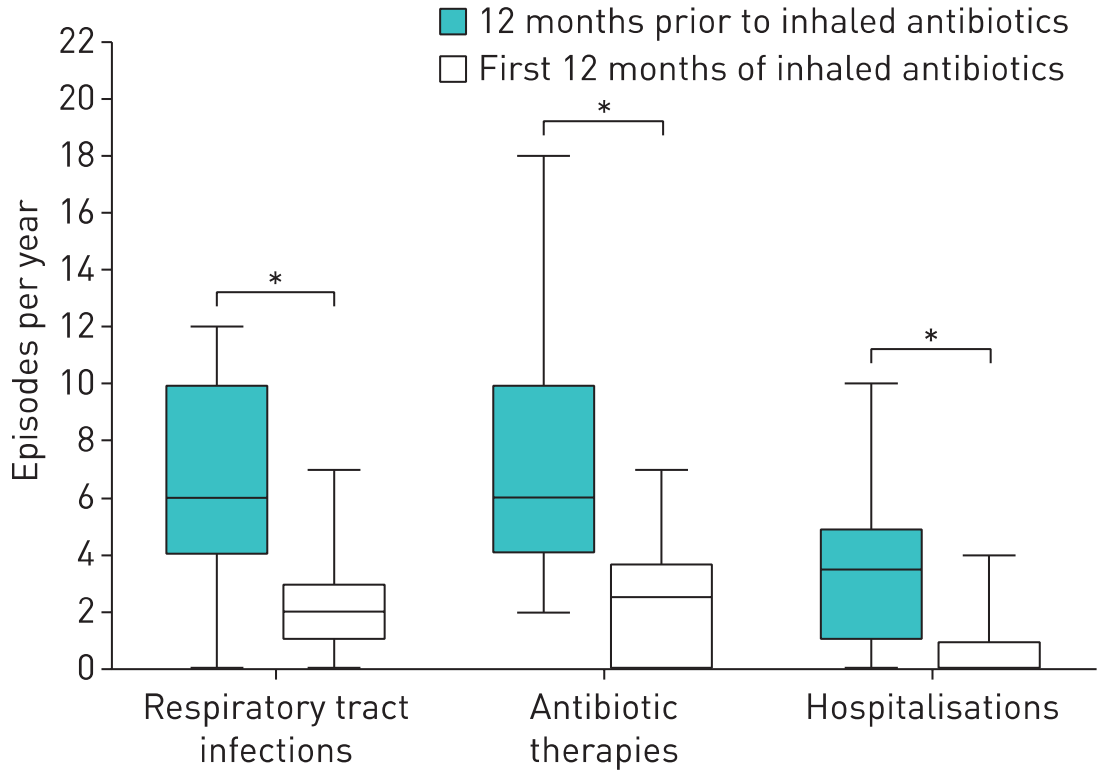


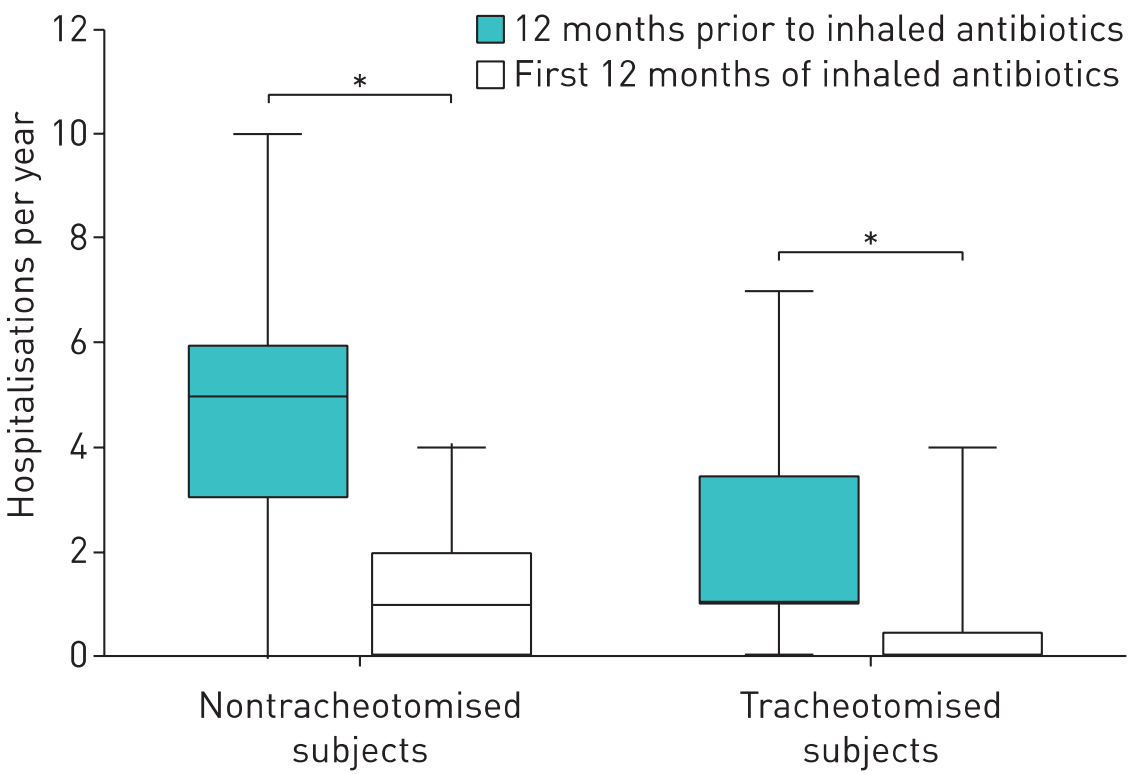
20 pediatric patients with severe neurological disorders.

8 had CP, 3 of those had tracheostomy, 2 were on NIV, 4 were receiving mechanically assisted cough therapy

Eckerland M, et al. *ERJ Open Res*. 2019

Clinical Outcomes with Microbial Suppressive Therapy



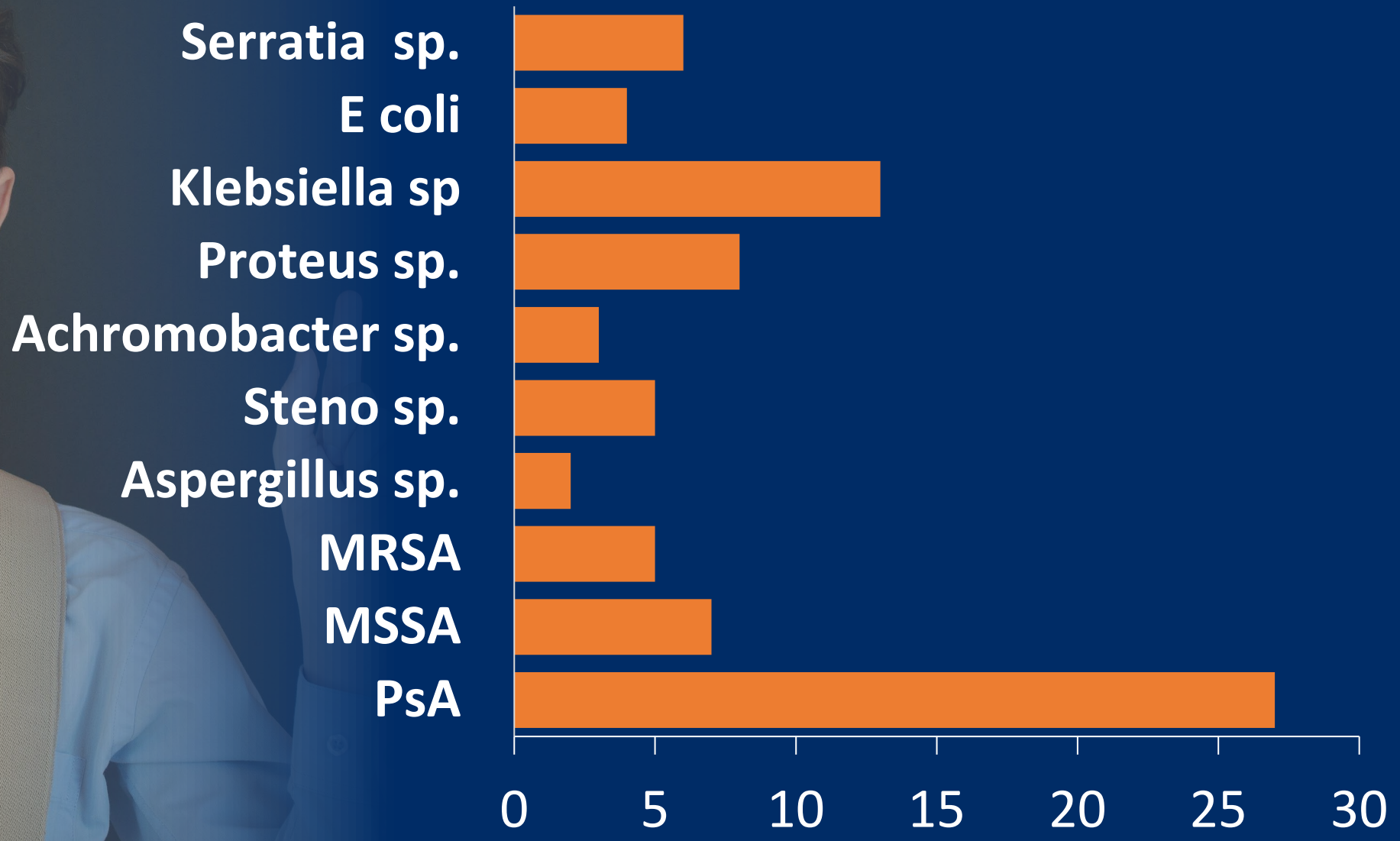


Eckerland M, et al. *ERJ Open Res*. 2019

How I approach patients with cerebral palsy AND respiratory infections

- Regular microbial surveillance
- Consider PsA eradication
- Consider PsA suppression
- Symptom driven antibiotic regimen
- Good airway clearance

Patient Counts by Organism



Intellectual disabilities
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Cardiovascular health
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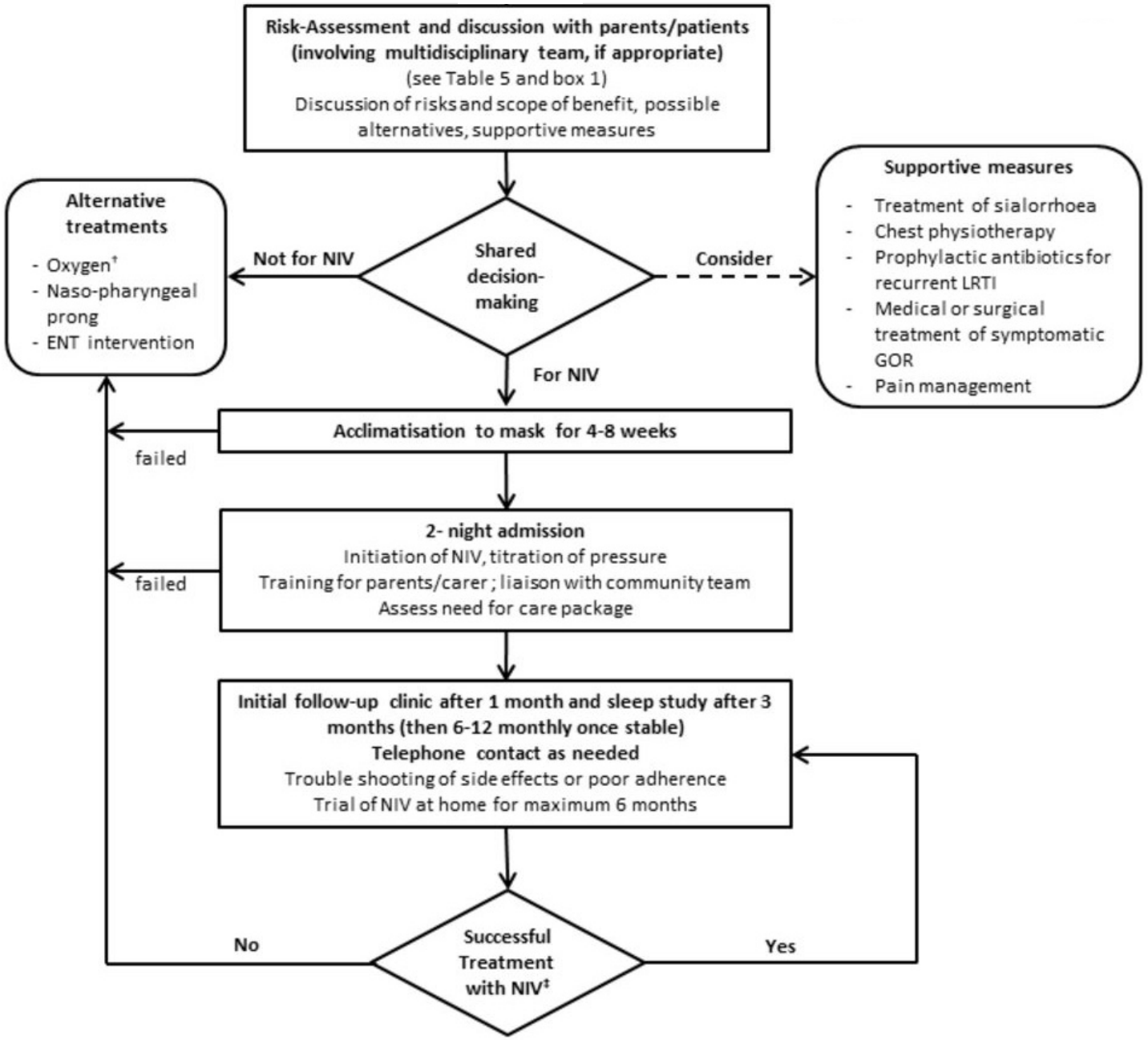
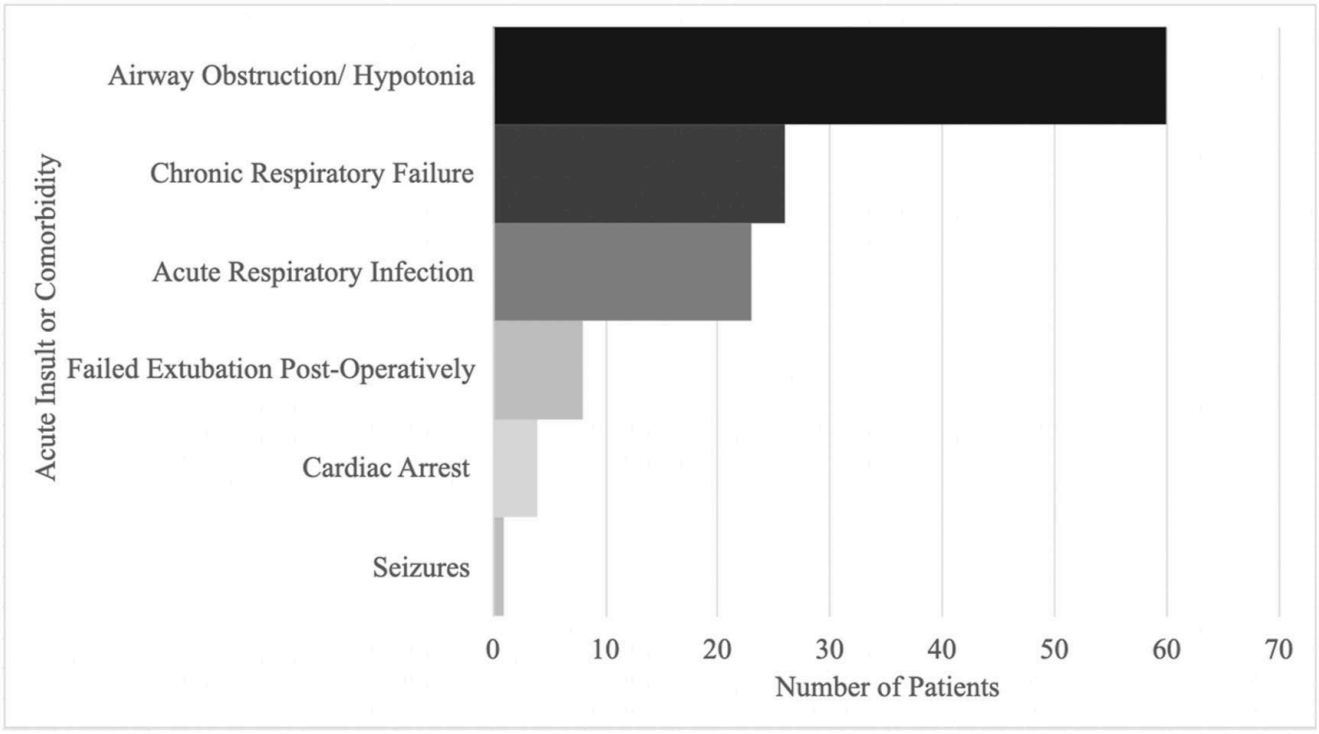
~1/3 sleep disordered breathing

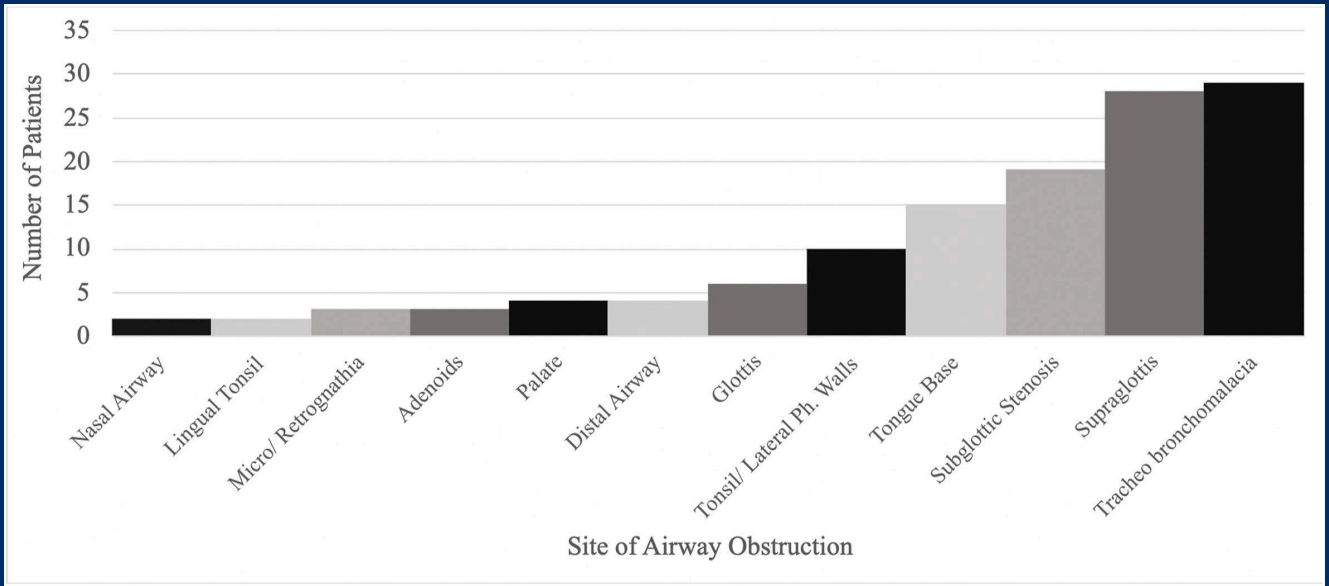
Atmawidjaja RW, et al. *Dev Med Child Neurol*. 2014
Newman CJ, et al. *Dev Med Child Neurol*. 2006
Garcia J, et al. *Dev Med Child Neurol*. 2016

A pragmatic approach?



Grychtol R, Chan EY. *Arch Dis Child*. 2018





More often due to prolonged intubation or NIV, with or without hypotonia, not recurrent infections

Median age of placement 1.7yrs

Consider site of airway obstruction

Fisher E, Valika T. *Int J Pediatr Otorhinolaryngol*. 2025

How I approach patients with cerebral palsy AND hypoventilation

- Good history and exam
- TcCO2 or blood gas surveillance
- Home sleep testing
- Echocardiogram
- Good airway clearance
- Consultant input!

Questions?

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Airway Clearance Modalities for Patients with Neuromuscular Disorders

Joseph Van Vleet, BSRC, RCP

UCLA Medical Center

Disclosures

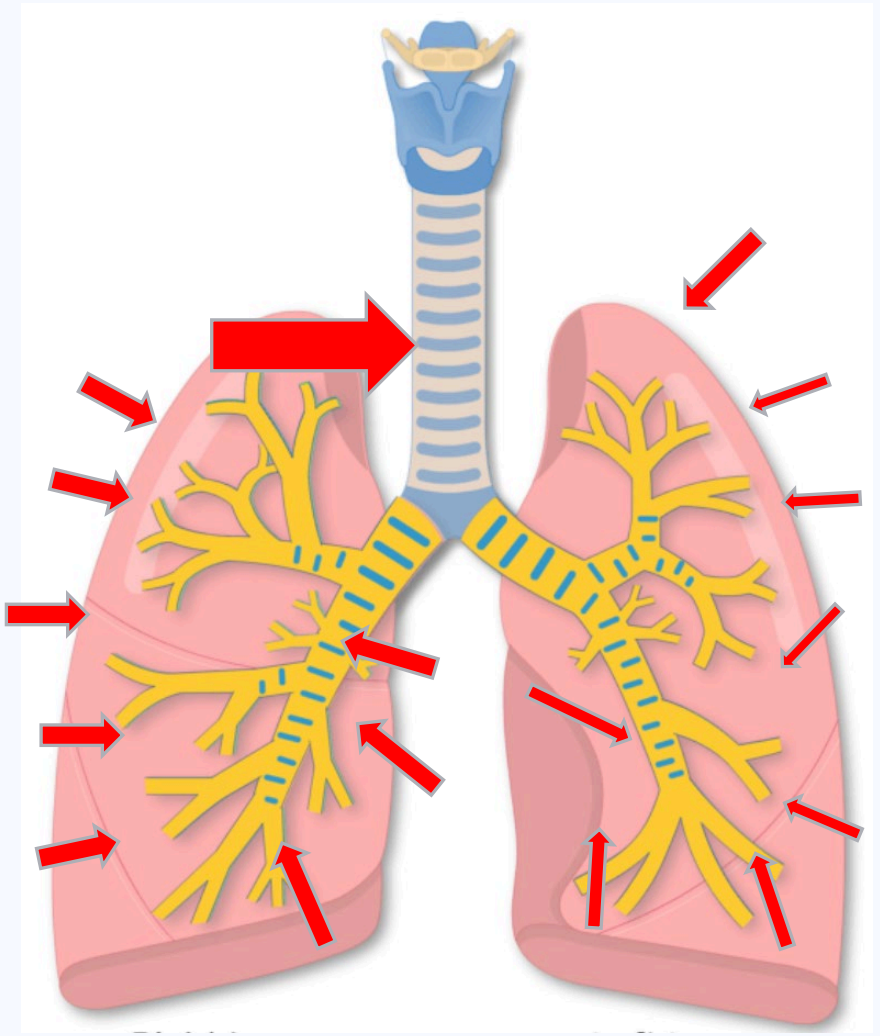
- I have no conflicts of interest to disclose
- I **WILL NOT** discuss off-label use and/or investigational use of any drugs or devices.

Objectives

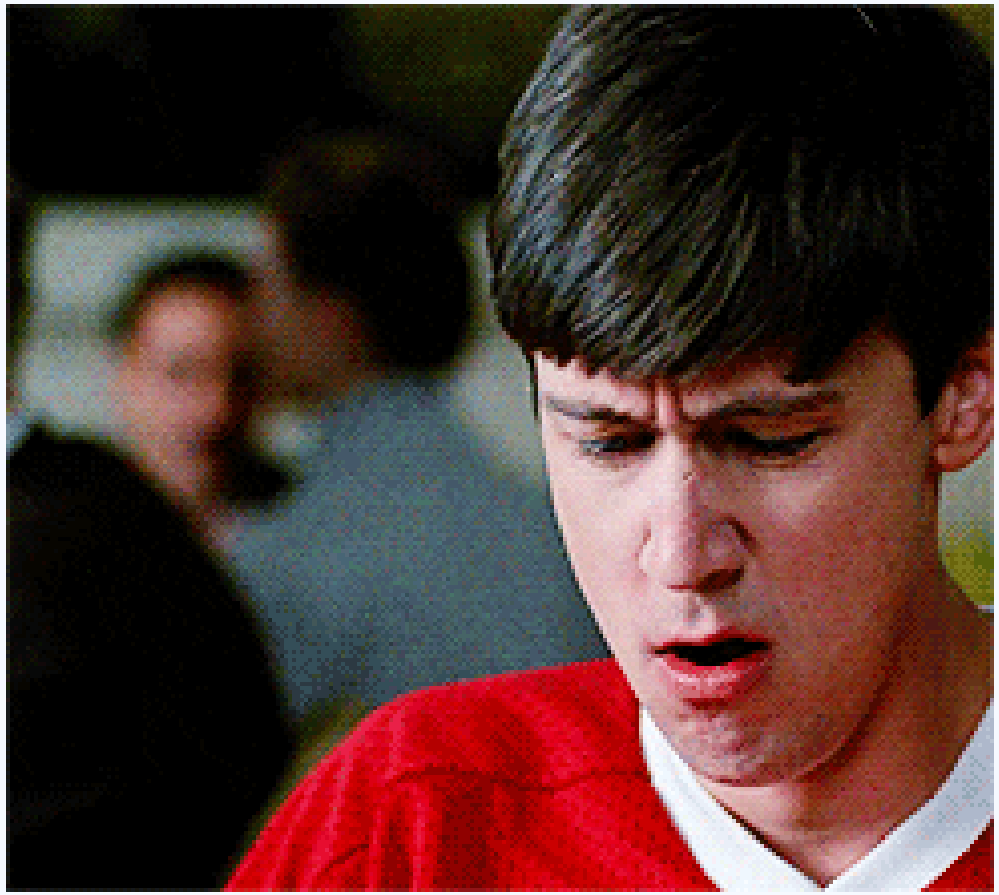
- Review normal cough and secretion clearance
- Address challenges to airway clearance with neuromuscular disease (NMD), specifically when the patient is not able to actively participate
- Review the role of airway clearance devices, medications, and humidification in the mobilization and removal of secretions
- Tailoring airway clearance therapy (ACT) regimens to the individual patient
-

Two Components of Airway Clearance

- **Proximal:** cough
- **Peripheral:** sputum mobilization



Proximal Airway Clearance: Cough, Cough, Cough



- Adapted from https://giphy.com/gifs/ferris-buellers-day-off-io3Y035fPzJKM

Cough: How it works

3 phases of a cough:

- Inspiratory
- Compression: contraction of expiratory muscles with closed glottis (increasing intrathoracic pressure)[1]
- Peak expiratory airflow phase: rapid release of air for a variable duration[1]

Result: Shearing forces of high velocity airflow dislodges secretions and debris from the airway walls

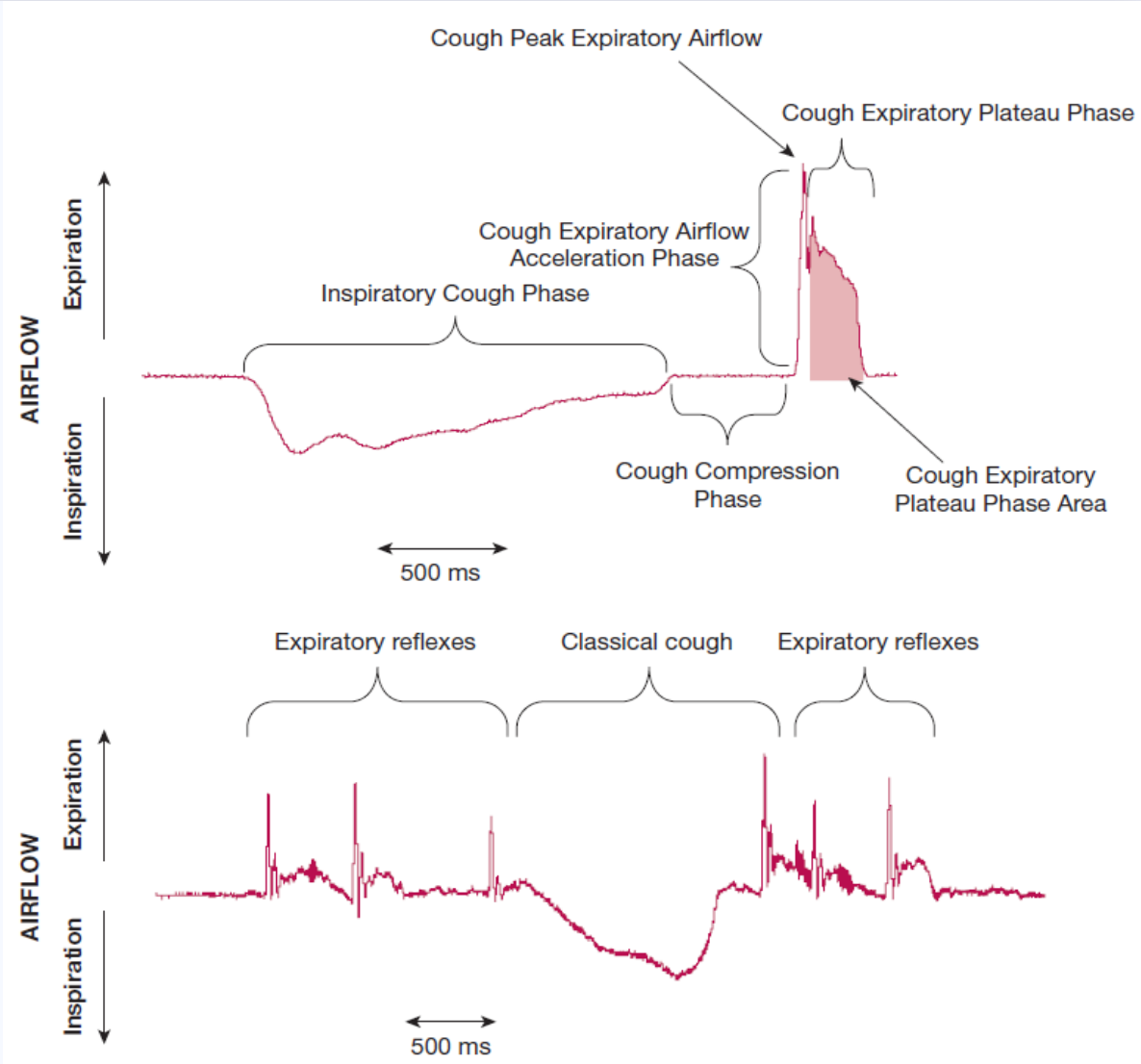


Figure 1: A three-phase flow pattern of a classical cough[2]

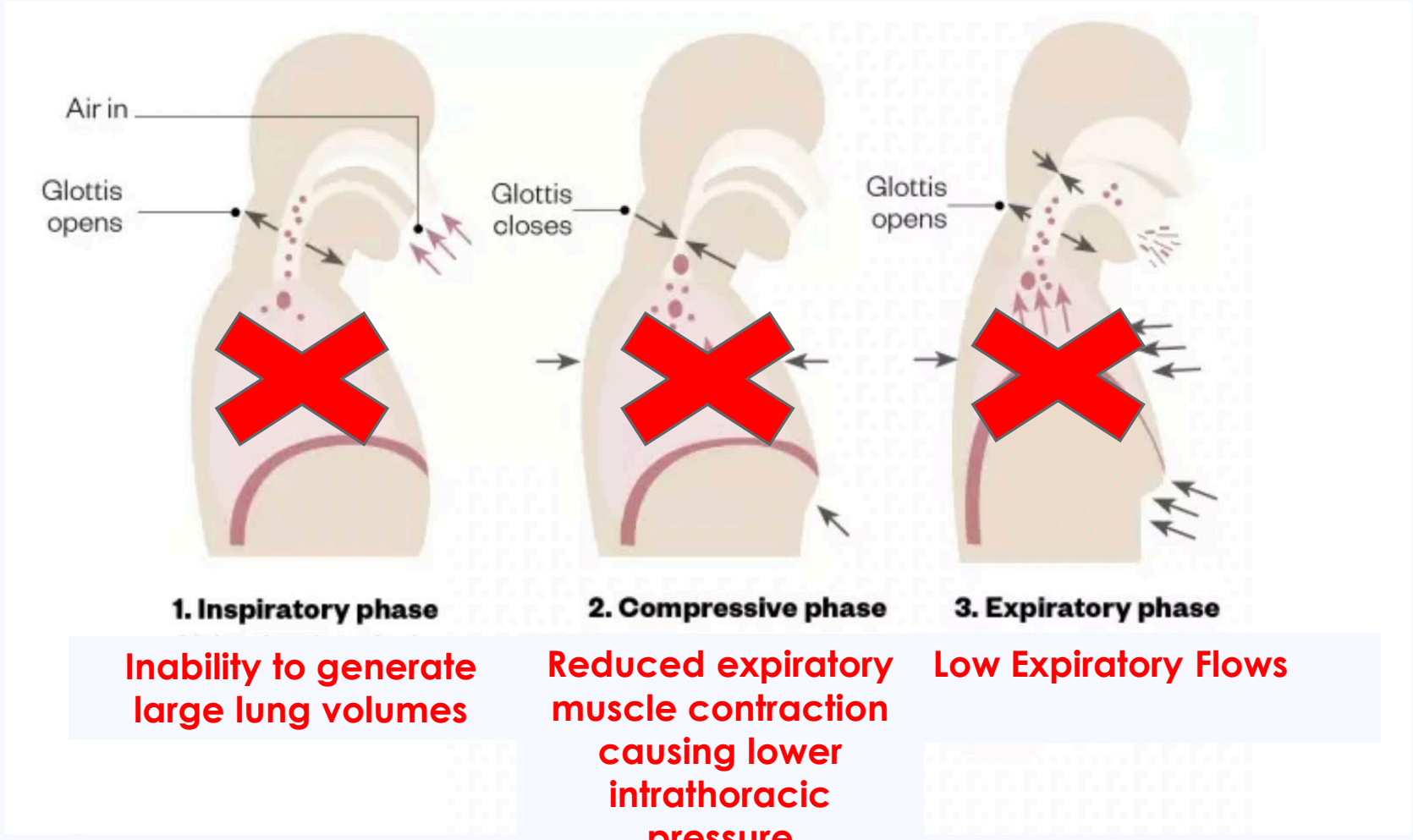
1. Lee et al., 2021, 2. Figure 1 adapted from Global Physiology and Pathophysiology of Cough Part 1, Lee et al., 2021

Cough Shaming

[1]Lee et al., 2021

California Thoracic Society
ATS Chapter Serving California and Arizona

Neuromuscular disease affect on cough: Airflow Problems



Inability to generate large lung volumes

Reduced expiratory muscle contraction causing lower intrathoracic pressure

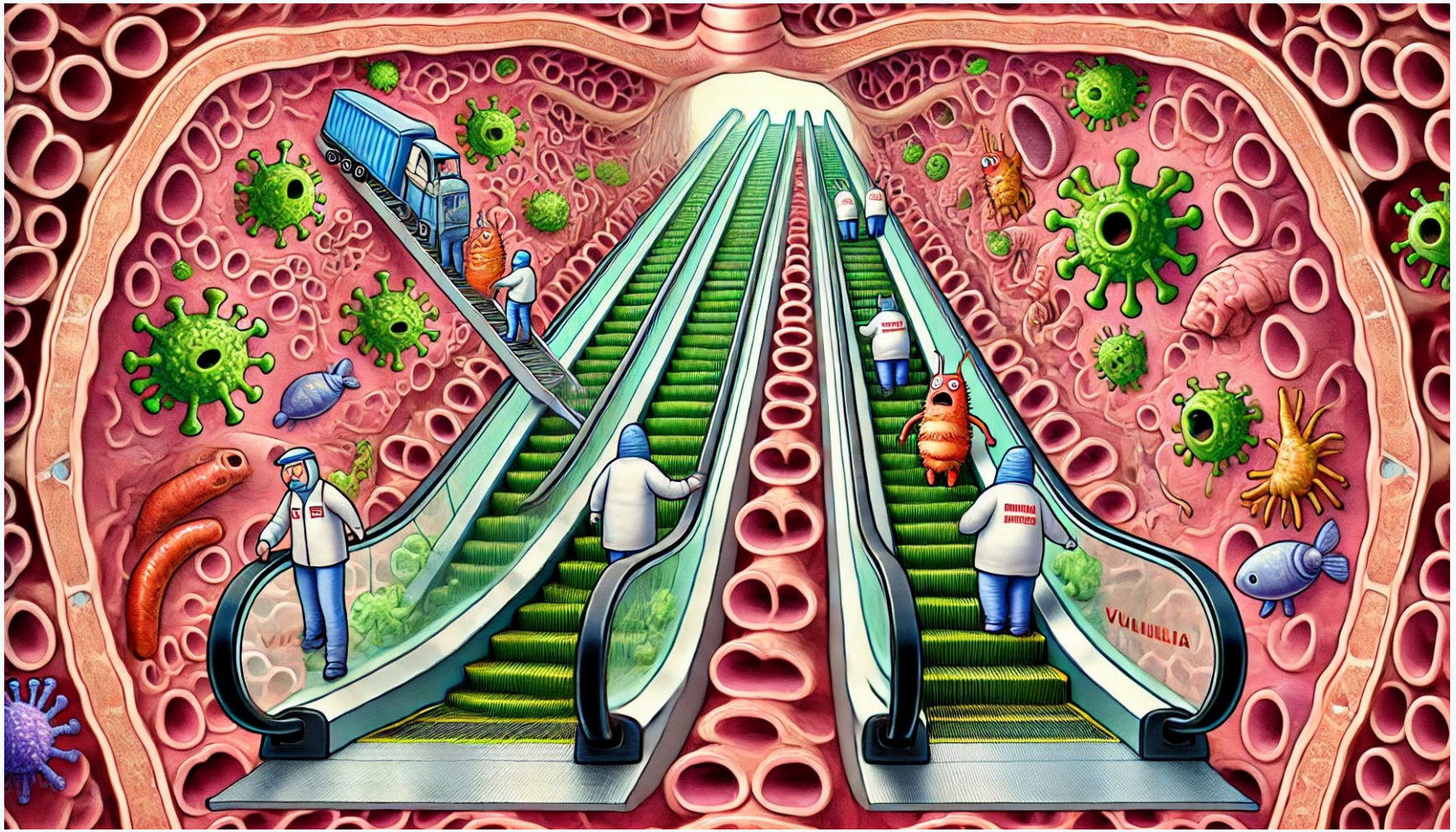
Low Expiratory Flows

• Adapted from Case-based learning: Cough. 2019

PERIPHERAL: Move the Mucus!

• Created on chatgpt.com

PERIPHERAL: Move the Mucus!



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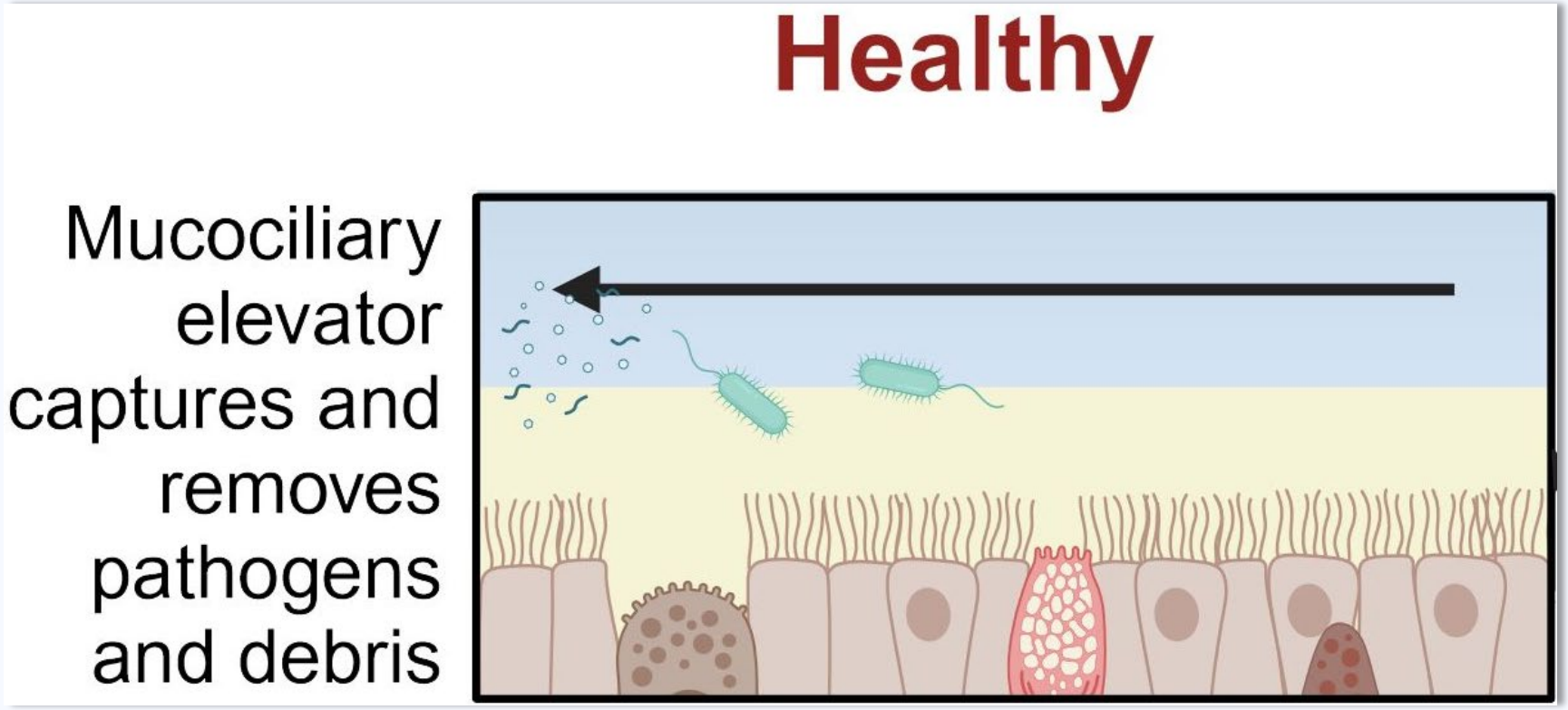
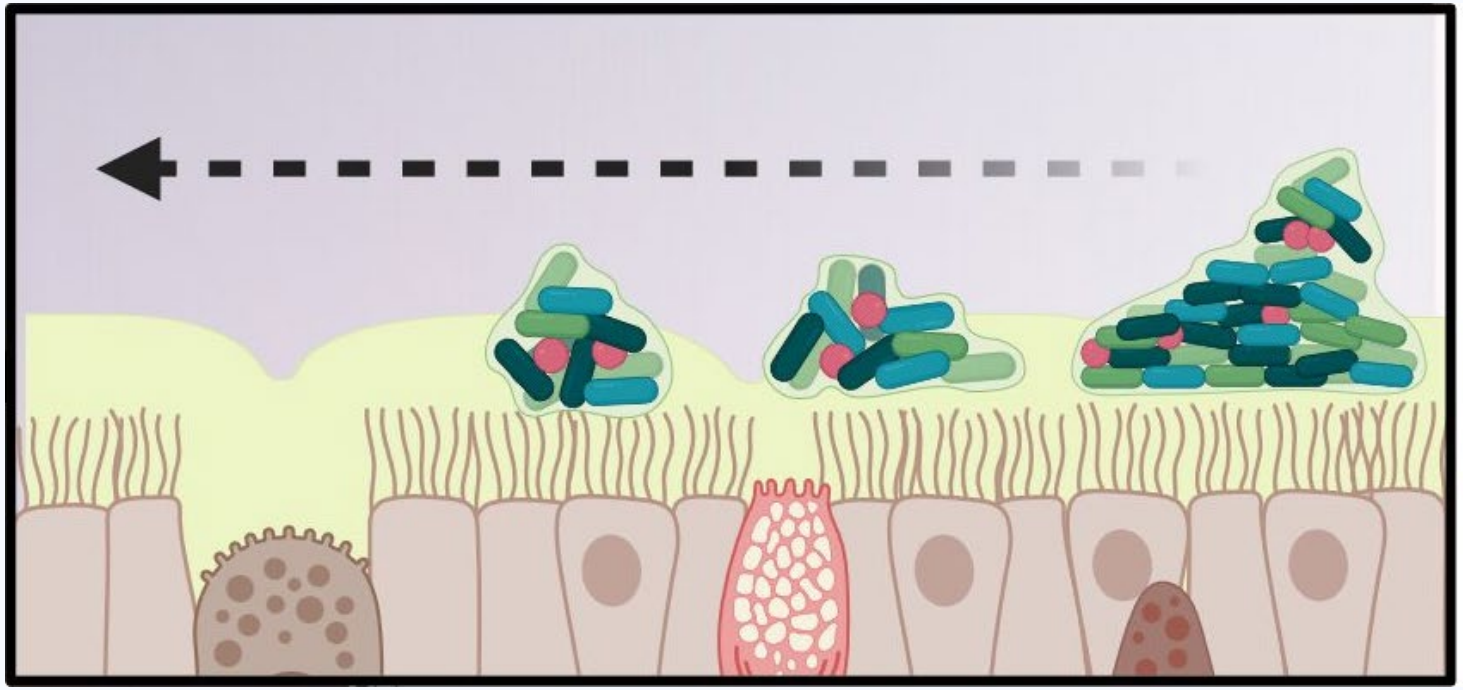
The Mucociliary Escalator



- Adapted from Team, M. (n.d.). *Journals*. Frontiers. https://www.frontiersin.org/files/Articles/1405376/fimmu-15-1405376-HTML-r1/image_m/fimmu-15-1405376-g001.jpg

Neuromuscular disease affect on cough: Dysfunctional Cilia



Mucociliary defects impair pathogen clearance

- Adapted from Team, M. (n.d.). *Journals*. Frontiers. https://www.frontiersin.org/files/Articles/1405376/fimmu-15-1405376-HTML-r1/image_m/fimmu-15-1405376-g001.jpg

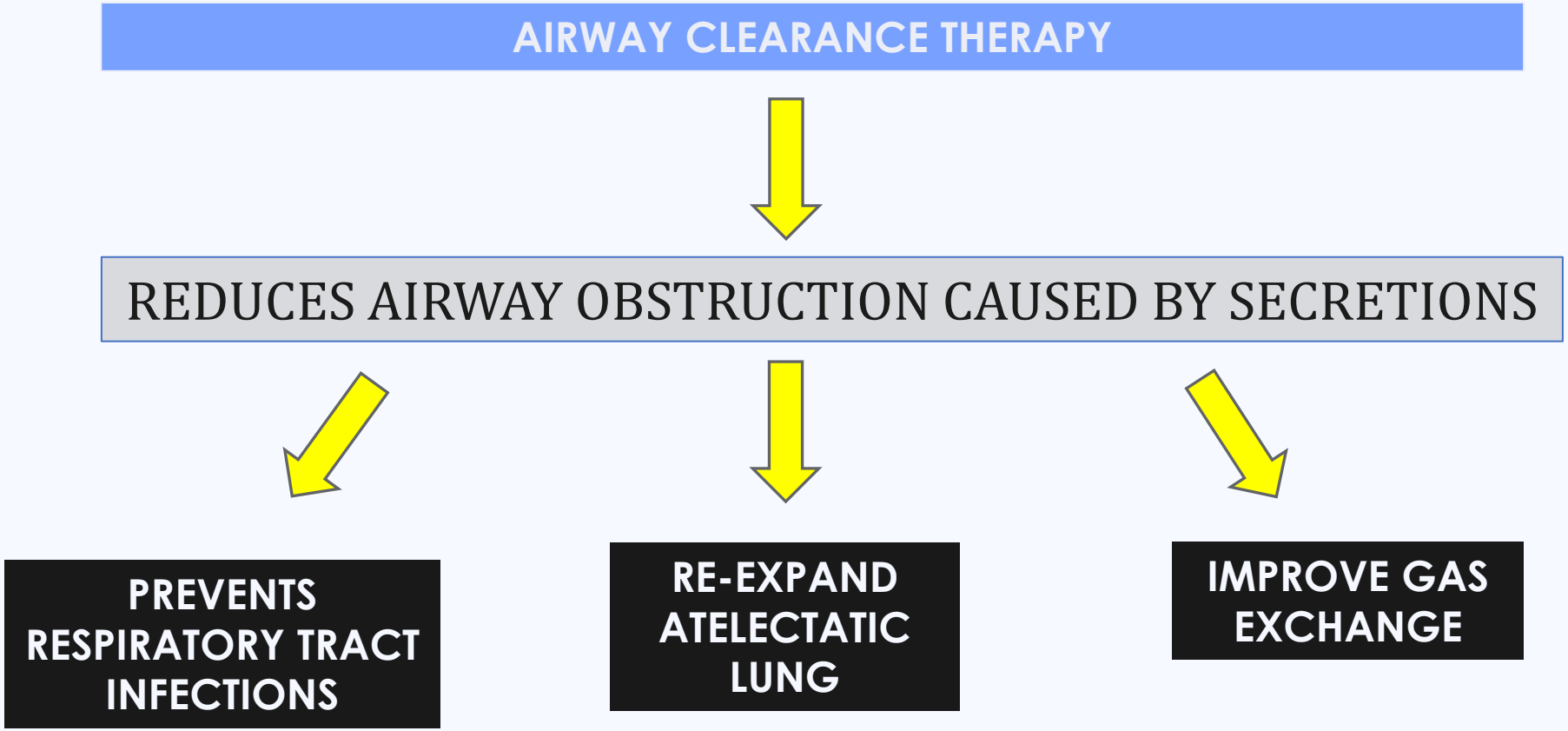
When do patients need adjunctive airway clearance?

- **Ineffective Cough**
- Inability to generate **cough transients** on expiratory flow-volume loop in cough spirometry[1]

  - A **cough peak flow (CPF)** below 270 L/min [2]
  - **Maximum expiratory pressure (MEP)** below 60 cm H2O [1]
- **Failure to Clear Secretions**
  - A video fluoroscopic swallow study demonstrating inability to clear oral secretions[1]
- **Copious Volume and/or Thickness of Secretions**
- **Tenacious and/or inspissated secretions (Peripheral)**

1. Gipsman et al., 2023, 2. Viccaro et al., 2024

Why Do I Care About Airway Clearance Therapy (ACT)?



- Belli et al., 2021

The perfect modality for each neuromuscular disease?

HTTP ERROR 404: File not found. LIMITED EVIDENCE!!!!!

We must tailor individualized airway clearance regimens

Address the patient's airway clearance deficit:

- Proximal
- Peripheral
- Both

Fine-tune device settings to the patient:

- Defer to your RTs
- Rely on the DME Supplier RTs

• Belli et al., 2021, Image adapted from Stevens, 2012

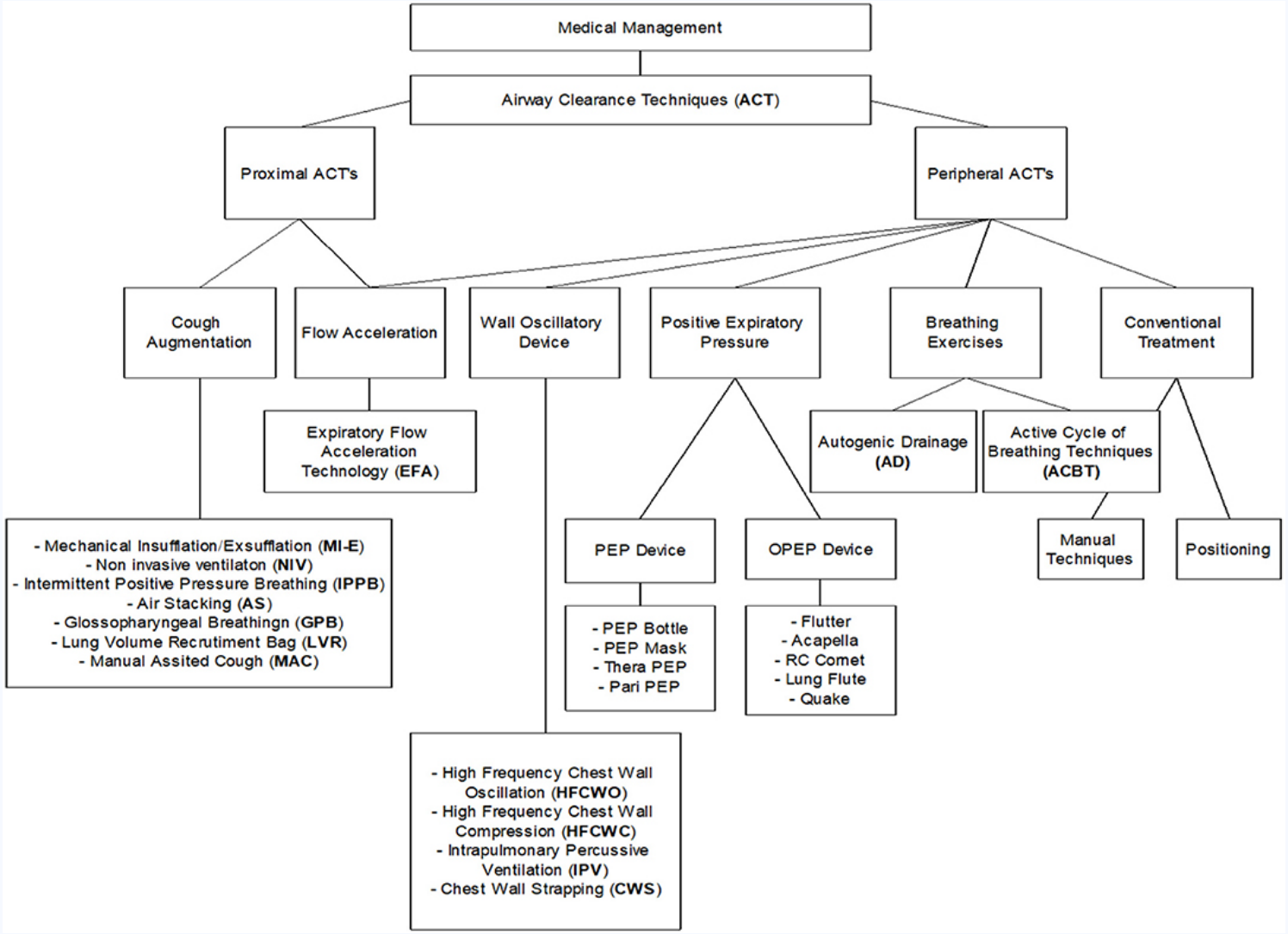
Airway Clearance Therapy

- There are three main complementary features of airway clearance devices[1]:
  - Lung expansion
  - Cough augmentation
  - Airflow oscillation

- ACT devices can focus on the peripheral and/or the proximal components of airway clearance

1. Lechtzin, 2024, 2. Belli et al., 2021

General ACT algorithm



• Image adapted from Belli et al., 2021

CASE STUDY #1

- A 23-year-old female with history of cerebral palsy is admitted and intubated for acute hypoxic respiratory failure secondary to pneumonia. At baseline, she is nonverbal and unable to follow commands. She has been hospitalized four times in the past two years with pneumonia.
- She is being treated with antibiotics and aggressive pulmonary hygiene. She has a strong cough but is unable to cough on command.
- The decision was made for tracheostomy placement due to failure to extubate due to high secretion burden. The patient has responded well to antibiotics and is close to discharge on trach collar.
- Prior to this hospitalization, the patient's home respiratory therapy routine consisted of scheduled nebulized albuterol.

CASE STUDY #1

- **What additions should be made to the patient's home airway clearance regimen?**

A. Positive Expiratory Pressure Device?

B. High Frequency Chest Wall Oscillation (HFCWO)

C. Cough Augmentation [(i.e. Mechanical Insufflation-Exsufflation (MI-E)]

D. Intrapulmonary Oscillatory Ventilation Device?

CASE STUDY #1

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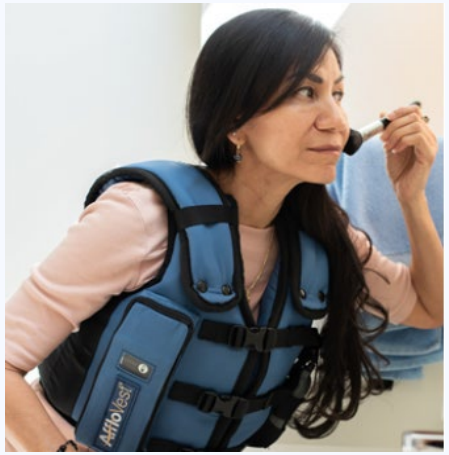
HFCWO: Proposed mechanism of action

- A pulse generator rapidly injects air into and out of hoses attached to an inflatable vest → quick chest wall compressions at preset frequencies (usually between 5 and 20 Hz)
  - Generates shear forces → mobilization of mucus
  - Produces eccentric flow patterns
  - Decreases mucus viscosity

Adapted from Incourage: RespirTech 2019

Gipsman et al., 2023

HFCWO: Device Types



Adapted from *Mobile airway clearance therapy HFCWO Vest* 2025

Adapted from *The vest airway clearance system, Model 205*

Adapted from Incourage: RespirTech 2019

Adapted from Staff, *Baxter launches Next generation of the vest system for airway clearance* 2024

HFCWO: Settings

- The initial settings for this device are a frequency starting at 5 Hz and gradually increasing to between 10 and 15 Hz.

- No studies have assessed treatment durations or number of treatments per day specifically for NMD.

- Treatments are tailored to individual patients or based on the manufacturer's preset programs.

Chatwin et al., 2018

HFCWO: The Evidence

High-frequency chest wall oscillation in ALS

An exploratory randomized, controlled trial

D.J. Lange, MD; N. Lechtzin, MD; C. Davey, MS; W. David, MD, PhD; T. Heiman-Patterson, MD; D. Gelinas, MD; B. Becker, MEd, RRT; H. Mitsumoto, MD; and the HFCWO Study Group*

- 35 patients with ALS were randomized to either High-Frequency Chest Wall Oscillation (HFCWO) treatment or standard care for a duration of 3 months.
- **Results**
  - A significant reduction in breathlessness, fatigue, and "noisy breathing" in HFCWO group compared to those in the control group.
  - In patients with baseline impaired forced vital capacity (FVC), a significantly slower decline in FVC compared to the control group

• Lange et al., 2006,

HFCWO: Evidence

Safety, tolerability, and efficacy of high-frequency chest wall oscillation in pediatric patients with cerebral palsy and neuromuscular diseases: an exploratory randomized controlled trial

Nanci Yuan [1], Peter Kane, Kristen Shelton, Julie Matel, Brian C Becker, Richard B Moss

A prospective, randomized, controlled trial of 23 children with either cerebral palsy or neuromuscular disease comparing HFCWO with standard chest physiotherapy

Results:

- Adherence was significantly better with the HFCWO group
- There was a trend towards decreased hospitalizations requiring intravenous antibiotics in the HFCWO group

• Yuan et al., 2010

HFCWO: Evidence

High-Frequency Chest Wall Compression Therapy in Neurologically Impaired Children

Kathryn Fitzgerald MSN CPNP, Jessica Dugre MSN, Sobhan Pagala, Peter Homel PhD, Michael Marcus MD, and Mikhail Kazachkov MD

Prospective study of 22 children with neurologic impairment and frequent respiratory-related hospitalizations before and after initiation of HFCWO

Results:

- The HFCWO was associated with fewer hospitalizations in the first and second years of its use

• Fitzgerald et al., 2013

HFCWO: Evidence

The Impact of High-Frequency Chest Wall Oscillation on Healthcare Use in Patients with Neuromuscular Diseases

Noah Lechtzin [1], Lisa F Wolfe [2], Kevin D Frick [3]

An analysis of a healthcare claims database that included 426 patients with neuromuscular disease who began using HFCWO

Results:

- The treatment was associated with reduced medical costs, fewer hospitalizations, and a lower incidence of pneumonia

• Lechtzin et al., 2016

HFCWO: Evidence

A RETROSPECTIVE REAL-WORLD COHORT STUDY DEMONSTRATING THE IMPACT OF HIGH FREQUENCY CHEST WALL OSCILLATION THERAPY ON HEALTHCARE COSTS IN PATIENTS WITH NEUROMUSCULAR DISORDERS

Pritesh Pandya · Gary Hansen · Derek Weycker · Charlene McEvoy

A retrospective analysis of claims data from a group of 1,080 patients with various neuromuscular conditions

Results:

- Hospitalization rates were reduced for one year after initiation of HFCWO therapy in a blended group of patients with neuromuscular conditions

• Pandya et al., 2020

HFCWO: Limitations and Disadvantages

- HFCWO does not clear secretions from central airways[1]
- Expensive[2]
- Heavy and not very portable[2]

1. Gipsman et al., 2023, 2. *High frequency chest wall oscillation,* 2024

HFCWO: Limitations and precautions

- **Precautions:**
  - port under the vest (not currently in use)
  - recent esophageal surgery
  - distended abdomen
  - bronchospasm
  - osteoporosis
  - coagulopathy

HFCWO: Contraindications

- **Contraindications:**
  - Unstable neck injury
  - port being accessed under vest
  - pulmonary embolism
  - lung contusion
  - current hemoptysis
  - hemodynamic instability
  - rib fractures
  - large pleural effusion or empyema
  - Recent spinal surgery or spinal cord injury

Case Study #1: Why HFCWO for this patient?

- **Why HFCWO?**
  - Multiple hospitalizations for pneumonia
  - No proximal ACT need:
    - Has strong cough, though not able to cough on command, able to trigger cough via deep suctioning via tracheostomy
  - Needs peripheral ACT modality
  - Unable to participate in therapy

CASE STUDY #2

A 48-year-old male with history of Amyotrophic Lateral Sclerosis (ALS) is currently hospitalized with acute hypoxic respiratory failure after one week of progressively increasing chest congestion and fever. He has been hospitalized three times in the last two years for pneumonia.

Recent PFTs show baseline CPF of 250 L/min and MEP of 50 cmH2O

The patient is being treated with antibiotics and aggressive pulmonary hygiene, including frequent nasotracheal suctioning, due to weak cough. The patient has responded well to antibiotics and is close to discharge.

Prior to this hospitalization, the patient's home respiratory therapy routine consisted of twice a day HFCWO therapy and nebulized albuterol and 3% hypertonic saline

CASE STUDY #2

- **Which of the following additions, if any, should be made to best improve the patient's home airway clearance regimen?**

A. Continue High Frequency Chest Wall Oscillation (HFCWO)

B. Add Positive Expiratory Pressure Device

C. Add Cough Augmentation Device (I.e MI-E)

D. Add Intrapulmonary Oscillatory Ventilation Device

CASE STUDY #2

- **Which of the following additions, if any, should be made to best improve the patient's home airway clearance regimen?**

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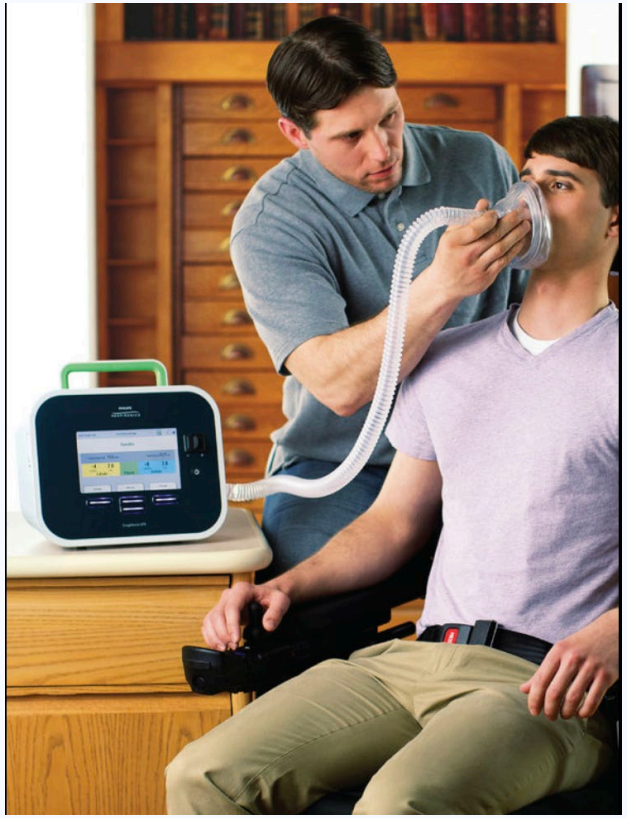
Insufflation/Exsufflation: Mechanism of Action

1. Machine deeply inflates the lung with positive pressure insufflation

2. Machine rapidly reverses the air pressure to negative exsufflation

3. High expiratory flows mobilize & expel secretions toward the mouth

4. Expectoration or suctioning of secretions from the mouth



• Gipsman et al., 2023

Insufflation/Exsufflation: Available Devices

Adapted from *Products*. CIS. 2020. https://cryois.com/product/philips-respironics-emerson-ca-3000-automatic-cough-assist/

Adapted from *Philips respironics launches CoughAssist T70 airway clearance device*, 2024

Adapted from *Synclara Cough System* 2021

Insufflation/Exsufflation: Settings Challenges

- Optimal pressure setting
  - Higher pressures (+60/-60 cm H2O) vs lower pressures (+30/-30 cm H2O) result in:[1]
    - increased CPF
    - no change in lung recruitment, neural respiratory drive, or patient-reported breathlessness
    - Increased rate of upper airway closure and patient discomfort

- The same MI-E settings do not produce the same clinical response in every patient[2]

1. Shah et al., 2024, 2. Andersen et al., 2018

MI-E Settings: General Neuromuscular Disease

Upper Airway and Translaryngeal Resistance During Mechanical Insufflation-Exsufflation

Tiina M. Andersen, PT, PhD; Anne Kristine Brekka, PT, MSc; Zoe Fretheim-Kelly, PT, PhD; Manel Lujan, MD, PhD; John-Helge Heimdal, MD; Hege H. Clemm, MD; Thomas Halvorsen, MD; Ove Fondenes, MD; Roy M. Nilsen, PhD; Ola D. Røksund, PT, PhD; and Maria Vollsæter, MD, PhD

-
- Cross-sectional study of 10 healthy adults using +20/-40 cmH2O and +40/-40 cmH2O
- **Results:**
  - Recommend using lower insufflation pressures combined with higher exsufflation pressures in clinical practice to enhance airway clearance

[1]Andersen et al., 2025

MI-E Settings: ALS

Laryngeal response patterns influence the efficacy of mechanical assisted cough in amyotrophic lateral sclerosis

Tiina Andersen [1 2 3], Astrid Sandnes [3], Anne Kristine Brekka [4], Magnus Hilland [5], Hege Clemm [3 6], Ove Fondenes [1], Ole-Bjørn Tysnes [7 8], John-Helge Heimdal [5 8], Thomas Halvorsen [3 6], Maria Vollsæter [1 3 6], Ola Drange Røksund [4 6]

Cross-sectional study observing laryngeal response to MI-E at pressures of +/- 20 to +/-50 cmH2O via transnasal fiber-optic laryngoscopy 14 patients with ALS and 6 healthy volunteers.

Results/Conclusions:

- Laryngeal adduction was seen during insufflation and exsufflation in patients with ALS and bulbar symptoms
- Recommend triggered insufflation, decreasing inspiratory flows and pressures and increase insufflation time to allow for equilibrium of pressure from the device to the lungs

• Anderson et al., 2017

MI-E Settings: ALS

Laryngeal Responses to Mechanically Assisted Cough in Progressing Amyotrophic Lateral Sclerosis

Tiina M Andersen, Astrid Sandnes, Ove Fondenes, Roy M Nilsen, Ole-Bjørn Tysnes, John-Helge Heimdal, Hege H Clemm, Thomas Halvorsen, Maria Vollsæter and Ola D Røksund

- Prospective study of 13 ALS patients assessing lung function, neurological status, and laryngeal response to MI-E using video-recorded flexible transnasal fiberoptic laryngoscopy

- **Results:**
  - Applying high insufflation pressures during mechanically assisted cough in ALS can become counterproductive as the disease progresses as well as prior to the onset of bulbar symptoms

• Andersen et al., 2018

MI-E: Recent Advancements

- Newer MI-E devices have **pressure oscillation** feature

- VC Pro Non-invasive ventilator with integrated cough assist, by ReactHealth

Needs source

MI-E: Lack of evidence supporting use in NMD

- Efficacy markers beyond peak expiratory flow (PEF) are limited.
- Use of PEF as a surrogate for cough efficiency lacks validation
- More research is needed, but ethical concerns hinder the use of less effective control modalities in studies.

• Auger et al., 2019

Case Study #2: Why Mechanical Insufflation/Exsufflation: MI-E?

- Why MI-E?
  - Multiple hospitalizations for pneumonia, despite having a home ACT regimen
  - Needs Proximal ACT
    - Weak cough: A cough peak flow (CPF) below 270 L/min and MEP less than 60 cmH2O have been linked to a higher incidence of pulmonary complications during respiratory infections in individuals with neuromuscular disorders[1]
  - The American College of Chest Physicians recommends that patients with neuromuscular disease and ineffective cough, who cannot adequately improve with alternative techniques, should consider regular mechanical insufflation-exsufflation[2]

1. Gipsman et al., 2023. 2. Khan et al., 2023

CASE STUDY #3

- A 28-year-old male with history of SMA and chronic ventilator dependence is currently hospitalized after presenting to ED for increased oxygen requirements and fevers. The patient has been hospitalized multiple times in the last year for acute on chronic respiratory failure secondary to pneumonia.
- The patient is being treated with antibiotics and aggressive pulmonary hygiene including MI-E. The patient has responded well to antibiotics, however, was intolerant of MI-E therapy. The patient is now close to discharge.
- Prior to this hospitalization, the patient's home respiratory therapy routine consisted of BID HFCWO therapy with QID duo nebs.
- **What changes, if any, should be made to the patient's home airway clearance regimen?**

CASE STUDY #3

- **What changes, if any, should be made to the patient's home airway clearance regimen?**

A. No Changes Necessary; Continue HFCWO

B. Add Positive Expiratory Pressure Device

C. Add Cough Augmentation Device

D. Add Intrapulmonary Oscillatory Ventilation Device

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Intrapulmonary Oscillatory Ventilation: Proposed Mechanism of Action

- Combines **alternating cycles** of:
  - **Continuous High Frequency Oscillation (CHFO)** -- delivers air to the lungs at frequencies ranging from 150 to 500 cycles/minute (2.5 to 8.3 Hz), higher = more distal airways (peripheral)

  - **Continuous positive expiratory pressure (CPEP)** – generating peak pressures of 10 to 40 cm H20

  - **Aerosol/Nebulizer Delivery** – to loosen secretions and bronchodilate airways
  - The high-frequency airflow helps to expand the lungs, vibrate the airways, and potentially deliver air to the distal lung units, bypassing any accumulated secretions.

2. Nickel et al., 2021

Intrapulmonary Oscillatory Ventilation Device Types

- **Intrapulmonary Percussive Ventilation (IPV) by Sentec**
  - Pneumatic, sliding venturi that enable high-velocity flow, entrainment and percussion[1]:
    - Pulse frequencies ranging from 100 – 300 cycles per minute
    - MAP: 0 – 50 cmH2O
  - Treatments consist of alternating between:
    - High-frequency, low-volume breaths (mobilizes secretions of the peripheral airways)
    - Low-frequency, high-volume breaths (mobilizes secretions of the larger, more central airways)
  - Integrates a jet nebulizer to deliver aerosol to humidify the airways
  - Can be delivered through an artificial airway, by mouthpiece, mask or cannula

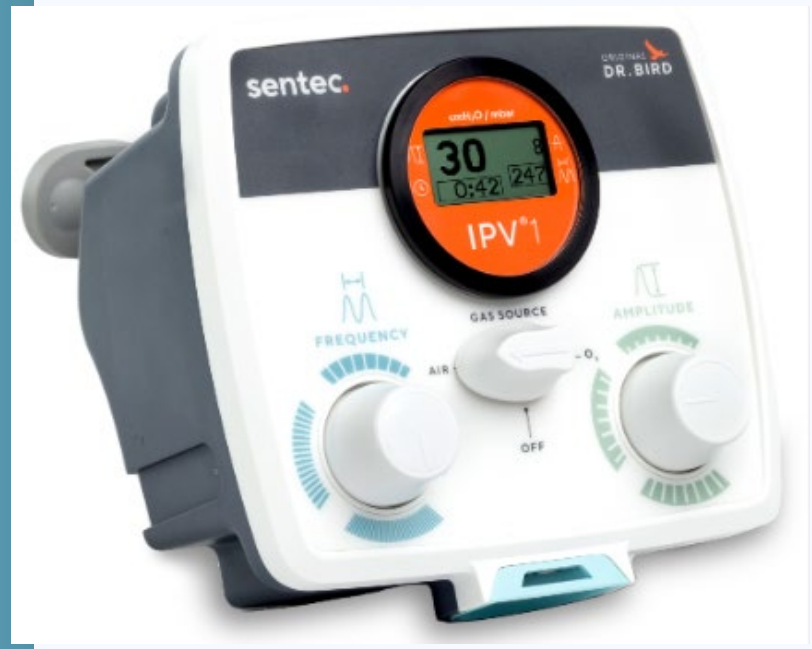
1. IPV 1, Sentec. 2023

Intrapulmonary Oscillatory Ventilation Device Types

- **Volara Oscillatory Lung Expansion (OLE) by Baxter**
  - Fixed venturi air entrainment:
    - Low, Medium and High-Frequency modes: pulse frequencies ranging from 170 – 230 cycles per minute
    - Continuous Positive Expiratory Pressure mode (CPEP): up to 25 cmH2O for lung expansion
  - Treatments consist of alternating between:
    - CPEP
    - Low frequency (central larger airways)
    - Medium frequency
    - High frequency (peripheral airways)
  - Integrates a jet nebulizer to deliver aerosol to humidify the airways
  - Can be delivered through an artificial airway, by mouthpiece or mask[1]

Nickel et al., 2021

Intrapulmonary Oscillatory Ventilation Device Types



Adapted *Intrapulmonary percussive ventilation* 2024

Adapted *Intrapulmonary percussive ventilation* 2024

Adapted from *Volara system: Ole therapy for home care 2024*

IPOV: Evidence

Intrapulmonary percussive ventilation vs incentive spirometry for children with neuromuscular disease

Christine Campbell Reardon [1], Demian Christiansen, Elizabeth D Barnett, Howard J Cabral

- Randomized, controlled trial of 18 adolescents with neuromuscular disease comparing efficacy of IPV vs incentive spirometry
- **Results:**
  - Preventive use of IPV has been suggested as useful in preventing pulmonary infections in adolescents with neuromuscular disorders who have an impaired ability to clear secretions. Antibiotic use has been lower, and hospital stays have been shorter[1]

Reardon et al., 2005

IPOV: Evidence

A comparison of high frequency chest wall oscillation and intrapulmonary percussive ventilation for airway clearance in pediatric patients with tracheostomy

Aneela Bidiwala, Linda Volpe, Claudia Halaby, Melissa Fazzari, Christina Valsamis & Melodi Pirzada

Pages 276-282 | Received 01 Apr 2016, Accepted 22 Nov 2016, Published online: 11 Dec 2016

- Single center, retrospective study comparing IPV to HFCWC in 8 complex tracheostomy patients
- **Results:**
  - Found that IPV was a superior treatment compared to HFCWO as it was associated with a significant decline in hospitalizations, decreased respiratory tract infections, decreased antibiotic, and steroid use[2]

Bidiwala et al., 2016

IPOV: Evidence

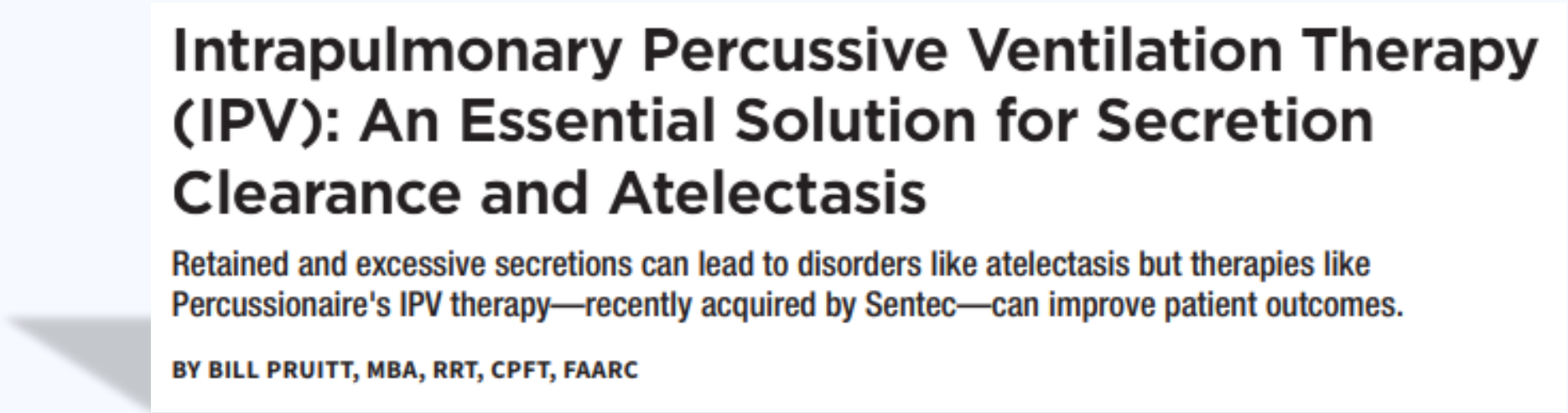
Effect of intrapulmonary percussive ventilation on intensive care unit length of stay, the incidence of pneumonia and gas exchange in critically ill patients: A systematic review

Anwar Hassan [1,2,*], William Lai [1], Jennifer Alison [2], Stephen Huang [1,2], Maree Milross [2]

- A systematic search of intrapulmonary percussive ventilation (IPV) in intensive care units was conducted across five databases, covering the years from 1979 to 2021.
- **Results:**
  - Evidence supported the role of IPV in reducing the length of stay in the ICU, improving gas exchange, and lowering respiratory rates is weak. Further investigation is needed to determine the therapeutic value of IPV in airway clearance, pneumonia prevention, and treatment of pulmonary atelectasis.

• Hassan et al., 2021

IPOV: Evidence



Intrapulmonary Percussive Ventilation Therapy (IPV): An Essential Solution for Secretion Clearance and Atelectasis

Retained and excessive secretions can lead to disorders like atelectasis but therapies like Percussionaire's IPV therapy—recently acquired by Sentec—can improve patient outcomes.

BY BILL PRUITT, MBA, RRT, CPFT, FAARC

- There are two main issues with published research on IPV:
  - the sample sizes are often too small
  - there is excessive heterogeneity in the research methods, including variations in protocols, population selection, device settings, treatment durations, and outcomes.

• Pruitt, 2023

IPOV: Contraindications

- **Contraindications:**
  - Pneumothorax
  - Radiologic evidence of blebs or bullae
  - Hemoptysis or active pulmonary hemorrhage
  - Unstable chest wall, ie. Fractures
  - Increased intracranial pressure
  - hemodynamic instability (systolic blood pressure ≤80 mm Hg, severe cardiac arrhythmia, acute myocardial infarction)
  - Pneumonectomy
  - Esophagectomy
  - gastro-intestinal bleed
  - facial injuries

Hassan et al., 2023

Case Study #3: Why IPOV for this particular patient?

- Has been using HFCWO therapy at home without a reduction in hospitalizations
- Needs peripheral airway clearance
- Tried MI-E during hospitalization but didn't tolerate

- **TEST DRIVE IN THE HOSPITAL!!!!**

ACTs for patients on mechanical ventilation

- **Ventilator hyperinflation** is a method of airway clearance for patients on invasive mechanical ventilation which uses the delivery of increased tidal volumes aimed at assisting with secretion removal[1]
- Studies on ventilator hyperinflation have utilized various criteria to determine the inspiratory volume, including: 50% above the current tidal volume, 130% of the set tidal volume, 15 mL/kg, and the volume corresponding to a peak inspiratory pressure of 40 cm H2O.
- Regardless of the specific criteria used, the peak inspiratory pressure was consistently limited to 40 cm H2O.
- The primary modes employed for ventilator hyperinflation were volume control Continuous Mandatory Ventilation (CMV) and pressure support ventilation.

Volpe et al., 2020

Ventilator Hyperventilation

- Although different settings have been used to deliver ventilator hyperinflation, the studies cited have reported benefits in secretion removal and improvement in physiological parameters. However, it is reasonable to suggest that there is a combination of settings that may achieve the best outcomes.
- Limited research was found on the safety and cost savings of performing ventilator hyperventilation at the home as opposed to adding a secondary device such as MI-E or IPV.

Volpe et al., 2020

Heated Humidification: “Secretions become Concretions”

- Insufficient humidification may be associated with mucosal drying, increased mucus viscosity, and retention of secretion.

- Life-threatening complications, including the obstruction of the upper airway by inspissated secretions were reported in cases of prolonged NIV without humidification[1]

Esquinas, 2023

Heated Humidification: Evidence

Heated air humidification versus cold air nebulization in newly tracheostomized patients

Richard Birk MD ✉, Alexander Händel, Angela Wenzel MD, Benedikt Kramer MD, Christoph Aderhold MD, Karl Hörmann MD, PhD, Boris A. Stuck MD, J. Ulrich Sommer MD, PhD

- Twenty newly tracheostomized patients were treated with either cold-air nebulization or heated humidification. The study assessed the number of tracheal suctioning procedures needed to clear the trachea, as well as tracheal ciliary beat frequency (CBF).

- The results indicate that heated humidification improved mucociliary transport, which led to a reduced number of suctioning procedures required for the trachea. This finding may enhance postoperative patient care.

Birk et al., 2017

Nebulized Hypertonic Saline

- Review/search of the Cochrane Cystic Fibrosis and Genetic Disorders Group's Cystic Fibrosis Trials Register
- **Results:**
  - In patients with cystic fibrosis, nebulized 7% hypertonic saline reduces exacerbations and enhances quality of life

Wark & McDonald, 2009

Nebulized Hypertonic Saline

Use of Nebulized Hypertonic Saline in Patients With Neuromuscular Diseases or Cerebral Palsy in the United Kingdom

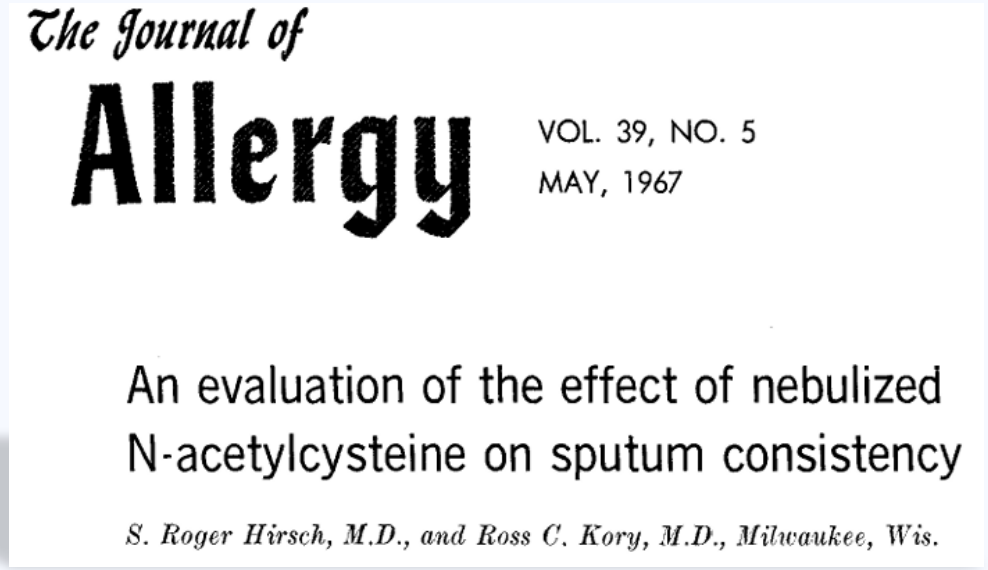
Natalia Galaz-Souza [1,2,✉], Hui-Leng Tan [1,3], Matthew Hurley [2,4], Andrew Bush [1,3]

- Survey conducted to audit current prescription practices for nebulized HS in NMDs and CP patients in the UK

- **Results:**
  - Despite limited evidence, many clinicians prescribe HS during acute exacerbations and as an ongoing treatment. Practices vary significantly across the UK, underscoring the need for clinical trials to develop evidence-based guidelines.

Galaz-Souza et al., 2024

Nebulized Acetylcysteine



The Journal of
Allergy

VOL. 39, NO. 5
MAY, 1967

An evaluation of the effect of nebulized N-acetylcysteine on sputum consistency

S. Roger Hirsch, M.D., and Ross C. Kory, M.D., Milwaukee, Wis.

- WHAT KIND OF A STUDY IS THIS? LOL!!!

- **Results:**
  - Demonstrated that nebulized NAC, administered at 10–20% concentrations, can significantly reduce sputum consistency.

• Hirsch et al., 1967

Nebulized Acetylcysteine

RESEARCH Open Access

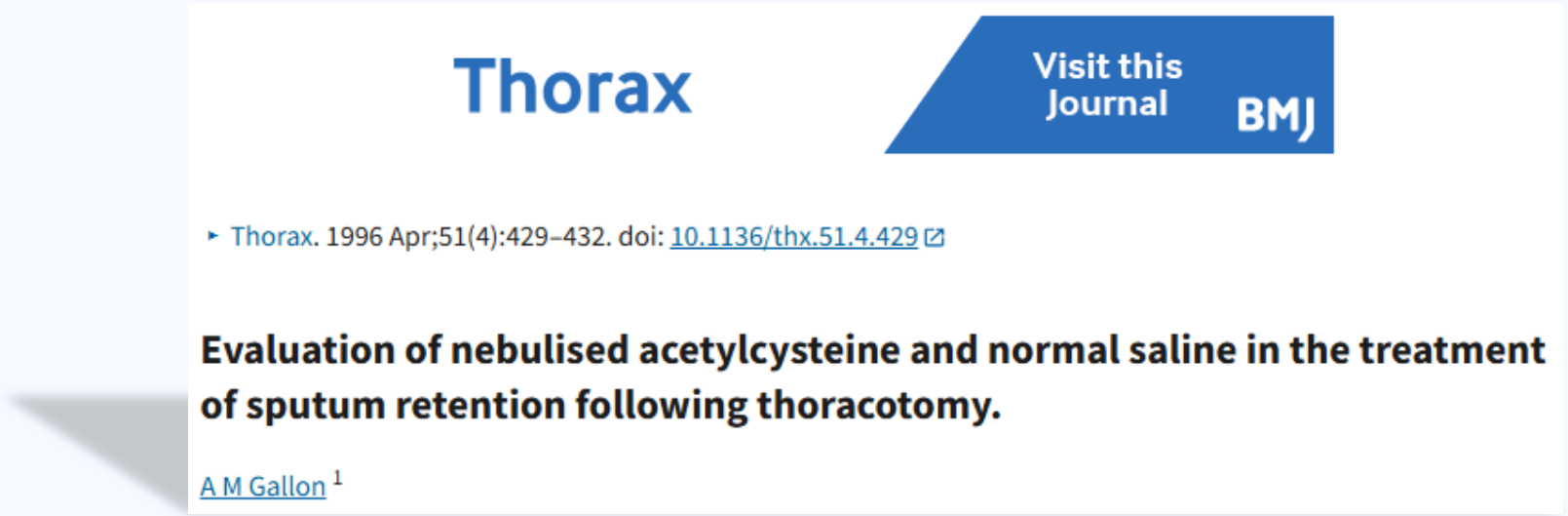
The effect of nebulized N-acetylcysteine on the phlegm of chronic obstructive pulmonary disease: the NEWEST study

Chin Kook Rhee[1], Seong Yong Lim[2], Won-Yeon Lee[3], Ji Ye Jung[4], Yong Bum Park[5], Chang Youl Lee[6], Yong Il Hwang[7], Jin Woo Song[8], Won-Il Choi[9], Kwang Ha Yoo[10*], Ki Uk Kim[11], Yu-Il Kim[12], Tae-Hyung Kim[13], Seong Ju Park[14], Kyeong-Cheol Shin[15], Soo-Jung Um[16], Hyoung Kyu Yoon[17], Ho Sung Lee[18], Deog Kyeom Kim[19], Ah Young Leem[4] and on Behalf of the Korean Pulmonary Rehabilitation Study Group[20]

- 12 week, prospective, single-arm, open-label phase IV multi-center trial with COPD patients
- **Results:**
  - The CAT phlegm score at baseline was 3.47 ± 1.06, whereas after 12 weeks of nebulized NAC it significantly decreased to 2.62 ± 1.30 ($p < 0.01$). More than half (53.5%) of the patients expressed satisfaction with the effects of nebulized NAC therapy. Adverse events occurred in 8 (8.0%) patients. Notably, no serious adverse drug reactions were reported.

• Rhee et al., 2024

Nebulized Acetylcysteine



- Single blind, two-way crossover design. Measurements taken before and after each treatment included sputum viscosity and weight, difficulty of expectoration, and oxygen saturations
- **Results:**
  - Observed that nebulized NAC effectively reduces sputum viscosity and facilitates expectoration while increasing the weight of expectorated sputum.

• Gallon, 1996

Artificial Airway Suctioning

AARC Clinical Practice Guidelines: Artificial Airway Suctioning

Thomas C Blakeman, J Brady Scott, Mark A Yoder, Emily Capellari and Shawna L Strickland

Respiratory Care February 2022, 67 (2) 258-271; DOI: https://doi.org/10.4187/respcare.09548

- Either closed or open suction system can be used safely and effectively
- Use sterile procedure for open suctioning events to protect the patient from potential cross-contamination
- Suction catheters should occlude < 70% of the artificial airway
- Suction pressures should be kept below -200 mmHg in adults and below -120 mm Hg in neonates and peds. Use lowest effective pressure
- The clinician should keep the suctioning procedure as brief as possible and no longer than 15 seconds

Blakeman et al., 2022

We must tailor individualized airway clearance regimens

Address the patient's airway clearance deficit:

- Proximal
- Peripheral
- Both

Fine-tune device settings

The overall effectiveness of an ACT regimen is dependent on adherence.

Adherence is dependent on a patient's:

- Satisfaction
- Motivation
- Perceived effectiveness

• Belli et al., 2021, Image adapted from Stevens, 2012

What is the best airway clearance device for your patient?

The best airway clearance device for a specific patient is the one that they **want** to use on a daily basis!

• Belli et al., 2021, Image adapted from Stevens, 2012

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Insufflation/Exsufflation: Setting

- Setting:
  - Inhalation time: 0 - 3 seconds
  - Inhalation pressure: 10 - 50 cmH2O
  - Pause time: 0 - 3 seconds
  - Exhalation time: 0 - 3 seconds
  - Exhalation pressure: 10 - 50 cmH2O
  - Coughs: 1-10 coughs per set for 1- 10 sets

Noninvasive Ventilation (NIV) in Neuromuscular Disease (NMD)

Hugo Paz y Mar, MD

Pulmonary, Critical Care and Sleep Medicine

University of California Irvine

Disclosures

- I have the following relationships with ACCME defined ineligible companies:
- **None**
- I **WILL/WILL NOT** discuss off-label use and/or investigational use of any drugs or devices.

Overview

- Recognize the symptoms of respiratory failure in NMD
- Discuss the objective assessment of respiratory muscle weakness in NMD
- Describe guidelines for the initiation of NIV in NMD
- Identify the different modalities of NIV in NMD
- Discuss the practical aspects of NIV initiation in NMD

The Genesis of the Iron Lung

Philip Drinker, Charles F. McKhann, James L. Wilson, and Early Attempts at Administering Artificial Respiration to Patients with Poliomyelitis

Howard Markel, MD, PhD

Incidentally, I don't know the origin of the horrible name "iron lung"—I think some reporter first used it.
James L. Wilson, MD[1]

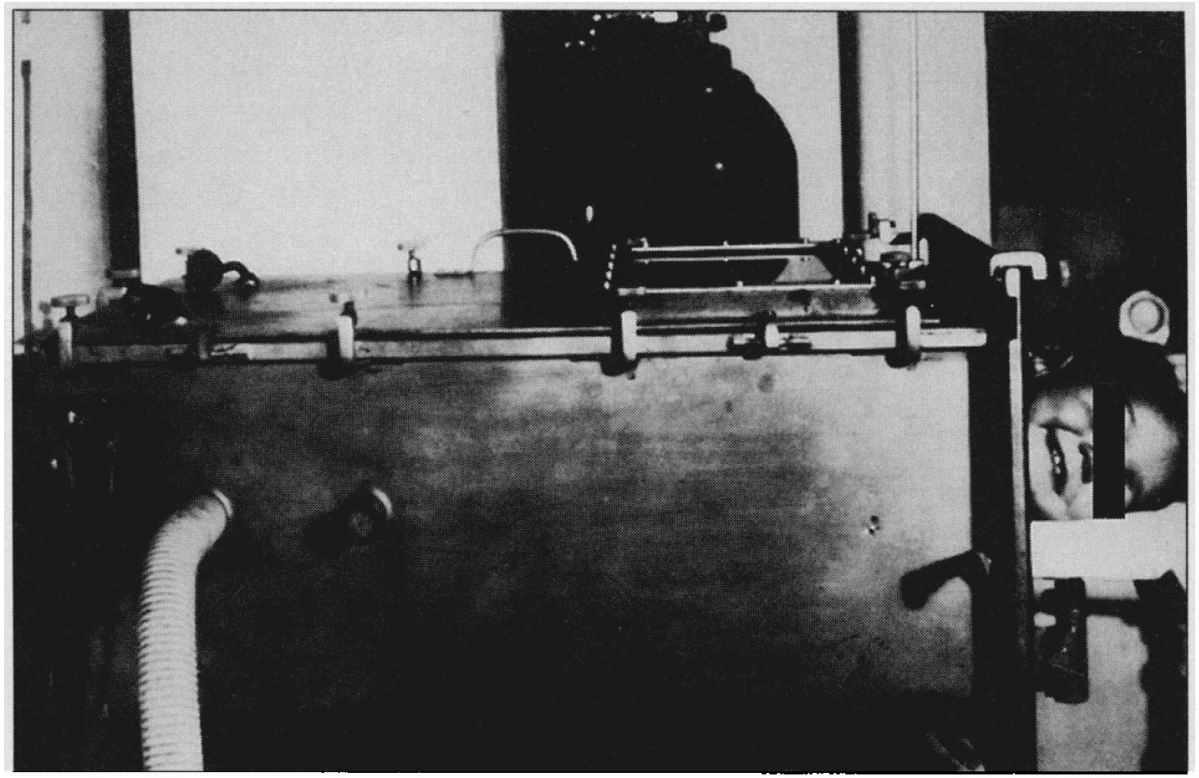
One of the most dreaded and reproduced images of a disease now largely forgotten by medical professionals and the lay public alike, poliomyelitis, was that of a child trapped in a cumbersome "iron lung" responsible for her every breath.[2,3] Despite the cultural icon of 20th-century illness it represents, however, the development of the artificial respirator or iron lung for children and adults stricken with poliomyelitis and respiratory paralysis remains an overlooked yet pivotal chapter in the history of medicine and technology (**Figure 1**).

Howard, M. Arch Pediatr Adolesc Med. 1994;148(11):1174-1180

The iron lung

function was disrupted. James L. Wilson, MD, eloquently described in 1932 the frustration and tragedy of a physician witnessing suffocation in these patients:

Of all the experiences that the physician must undergo, none can be more distressing than to watch respiratory paralysis in a child ill with poliomyelitis—to watch him as he becomes more and more dyspneic, using with increasing vigor every available accessory muscle of neck, shoulder and chin, silent wasting no breath for speech, wide-eyed and frightened, conscious almost to the last breath.[5]



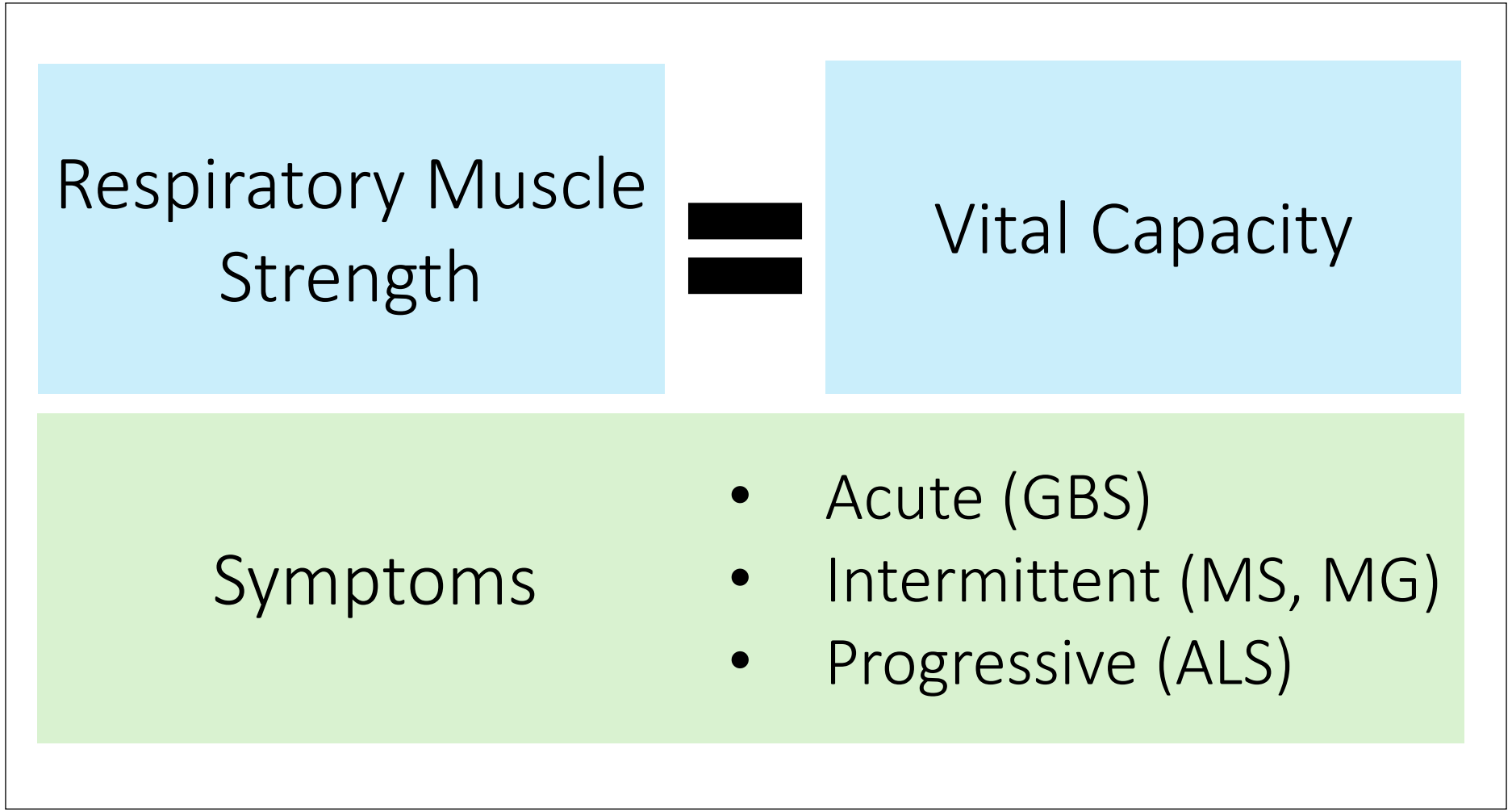
Howard, M. Arch Pediatr Adolesc Med. 1994;148(11):1174-1180

In neuromuscular disease (NMD), respiratory muscle weakness (RMW) is common and death often results from respiratory failure

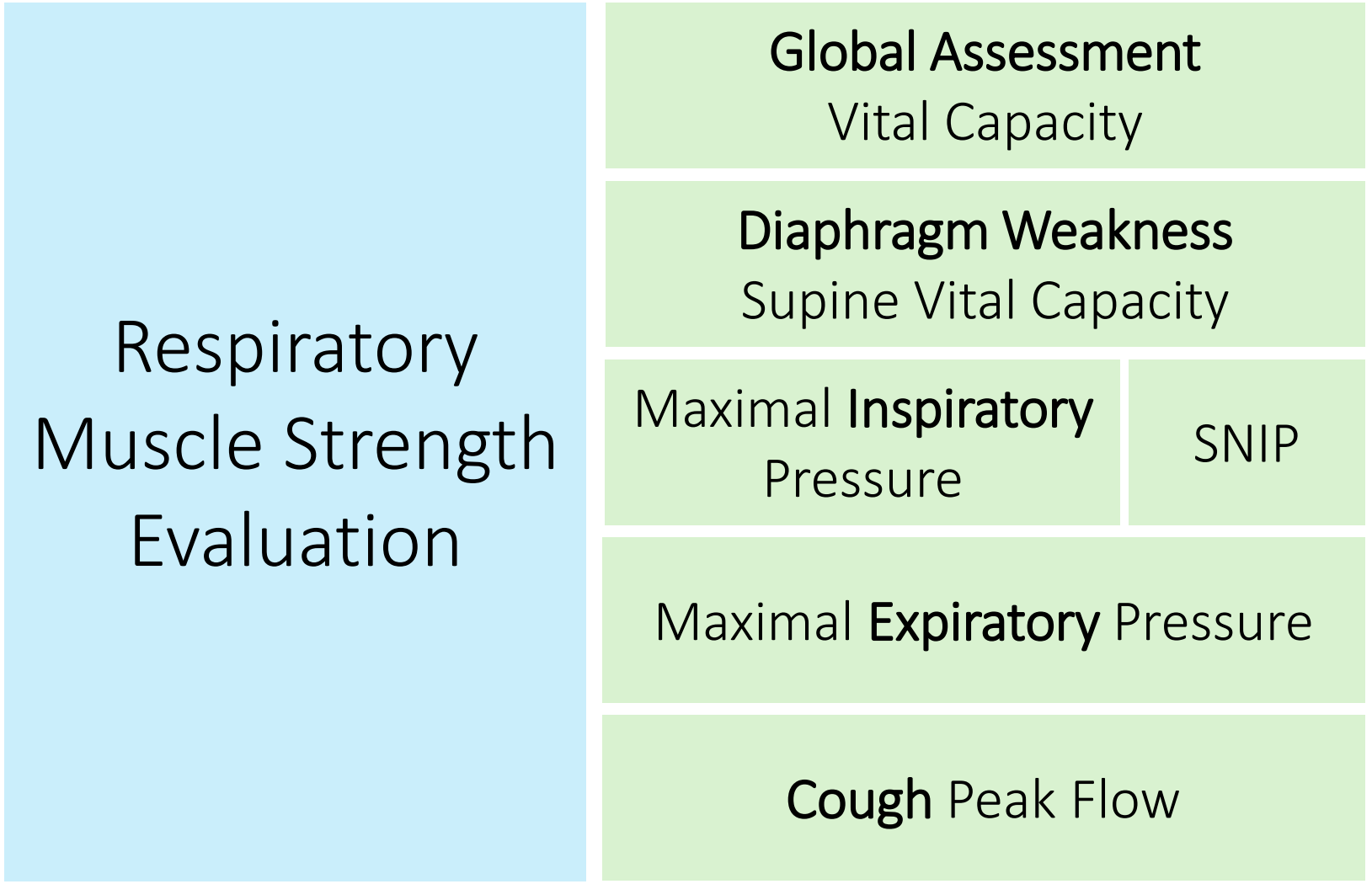
Respiratory muscle weakness in NMD

- Shortness of breath often presents late
- Diaphragmatic weakness causes orthopnea (paradox)
- Symptoms include restless and unrefreshing sleep
- Diurnal hypercapnia does not usually develop until RMW is severe

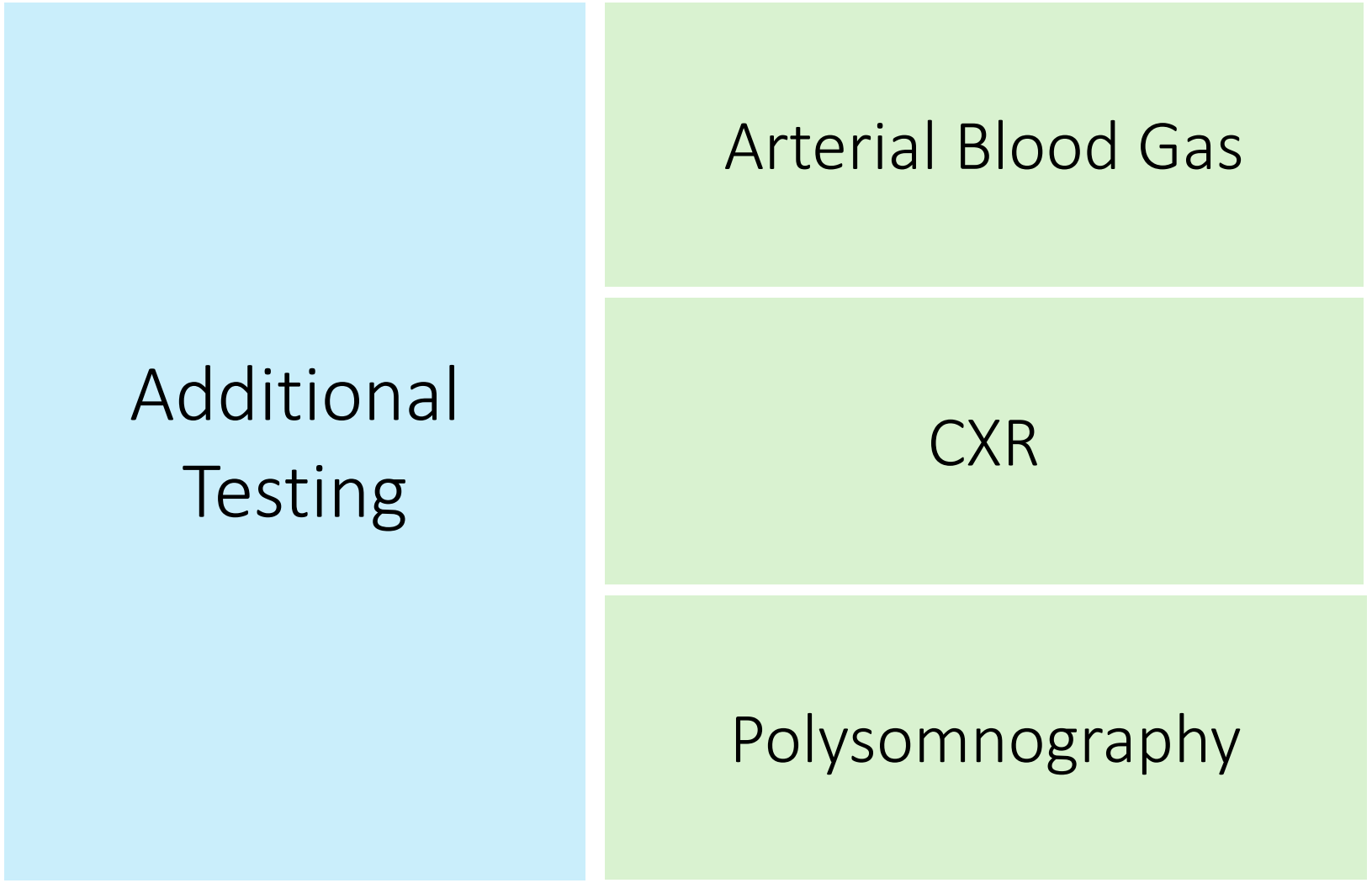
Respiratory muscle weakness in NMD



Respiratory muscle weakness in NMD

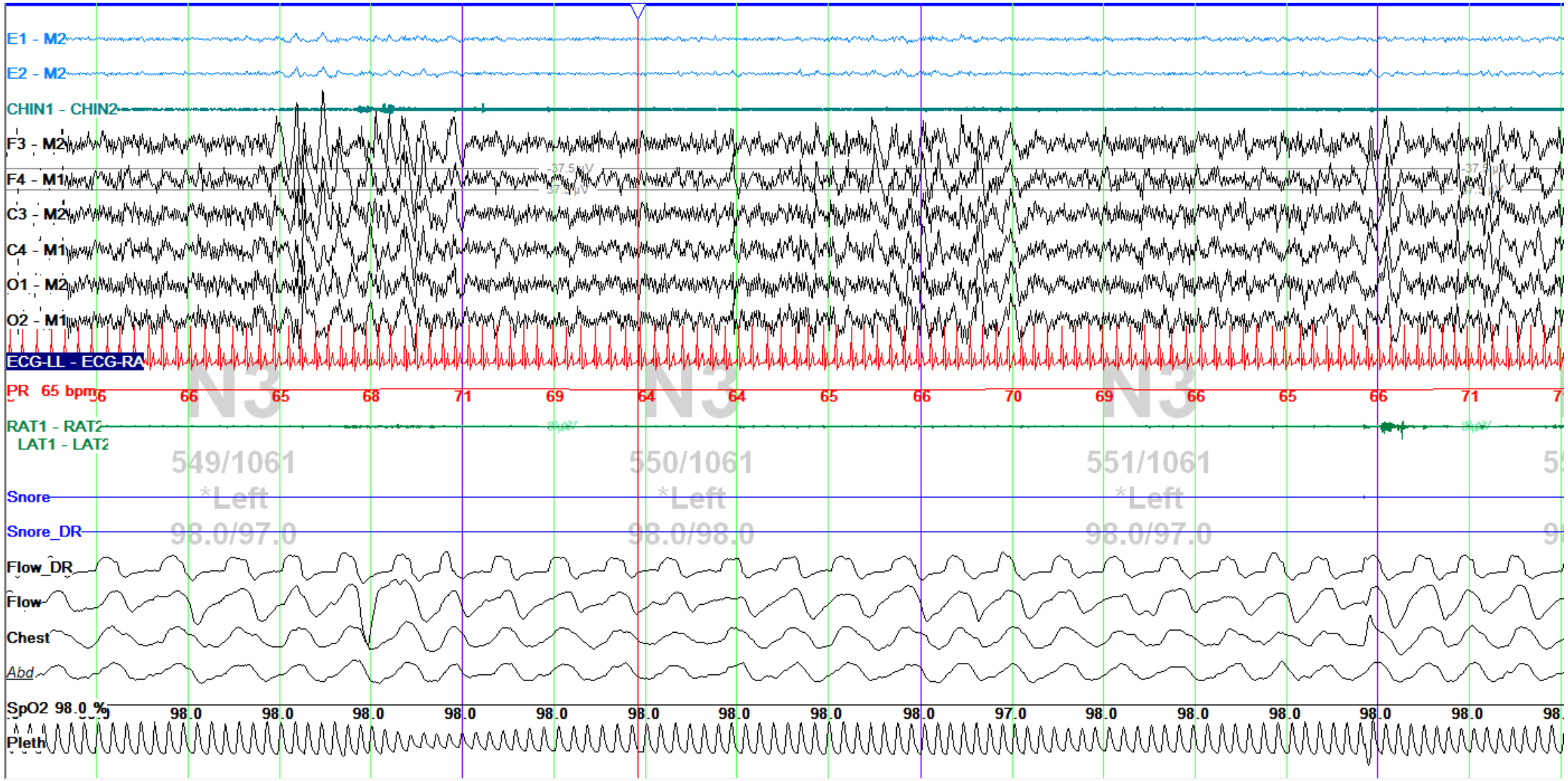


Respiratory muscle weakness in NMD

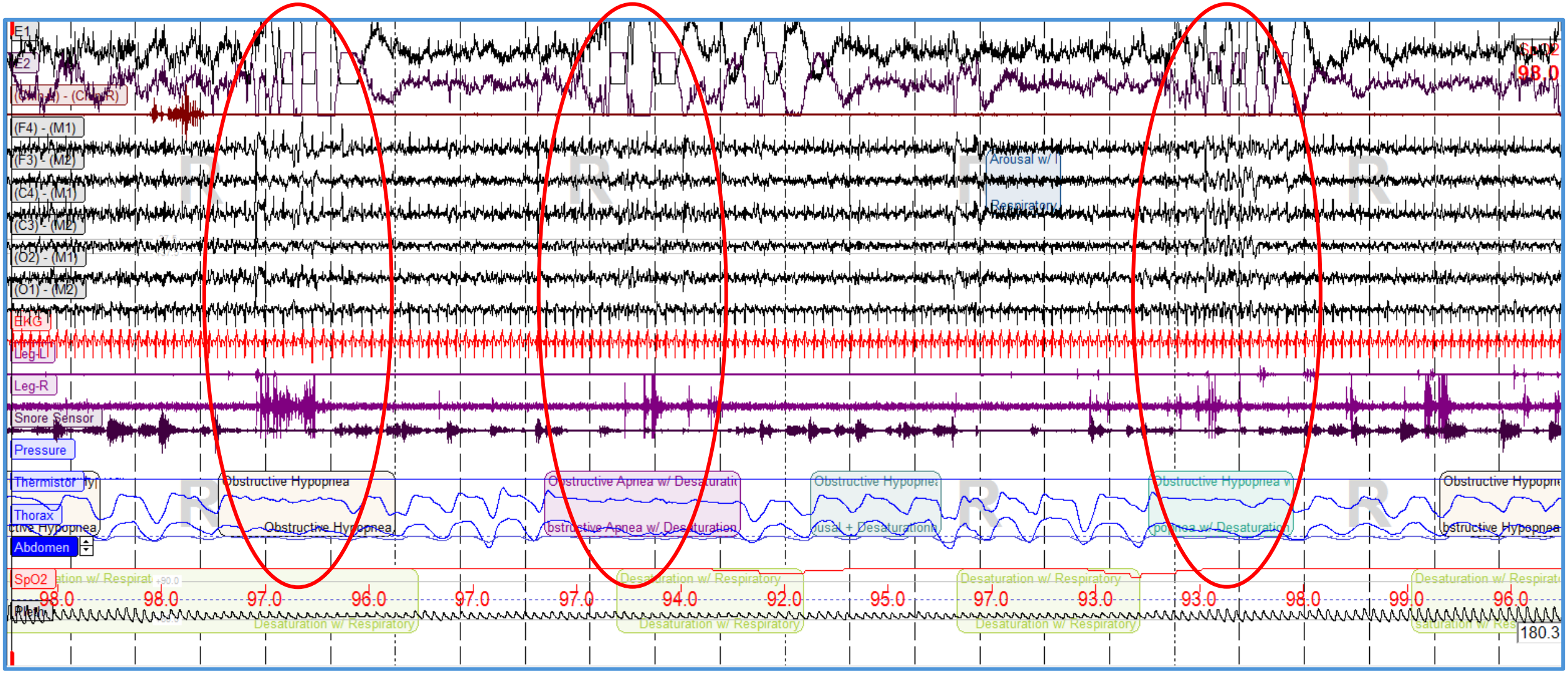


1984

N3 sleep


E1 - M2
E2 - M2
CHIN1 - CHIN2
F3 - M2
F4 - M1
C3 - M2
C4 - M1
O1 - M2
O2 - M1
ECG-LL - ECG-RA
PR 65 bpm
RAT1 - RAT2
LAT1 - LAT2
Snore
Snore_DR
Flow_DR
Flow
Chest
Abd
SpO2 98.0 %
Pleth
N3
549/1061
550/1061
551/1061
*Left
98.0/97.0
98.0/98.0

REM sleep hypoventilation



Decision to initiate NIV in NMD

1. Symptoms of respiratory failure and muscle weakness
2. Objective physiologic testing
3. Nocturnal/diurnal hypoventilation (late)

[Critical Care Guidelines and Consensus Statements]

CHEST

Respiratory Management of Patients With Neuromuscular Weakness

An American College of Chest Physicians Clinical Practice Guideline and Expert Panel Report

Akram Khan, MD; Lindsy Frazer-Green, PhD; Reshma Amin, MD; Lisa Wolfe, MD; Garner Faulkner, RRT; Kenneth Casey, MD; Girish Sharma, MD; Bernardo Selim, MD; David Zielinski, MD; Loutfi S. Aboussouan, MD; Douglas McKim, MD; and Peter Gay, MD

Khan, A, et al CHEST 2023; 164(2):394-413

CHEST

Respiratory Management of Patients With Neuromuscular Weakness

An American College of Chest Physicians Clinical Practice Guideline and Expert Panel Report

4. For patients with NMD and chronic respiratory failure, we recommend using NIV for treatment (Strong Recommendation, Very Low Certainty of Evidence)

The clinical indications for NIV can vary depending on NMD, patient age, and rate of disease progression

PFT Criteria for NIV in NMD

- FVC < 80% predicted with symptoms
- FVC < 50% predicted without symptoms
- MIP < 60 cm H2O
- MEP < 40 cm H2O
- PCF < 270 L/min
- SNIP < 70 cm H2O (males) SNIP < 60 cm H2O (females)

Nocturnal oximetry/ABG criteria

- SpO_2 ≤ 90% for ≥ 2% of sleep time
- $PaCO_2$ on ABG > 45 mm Hg

NICE National Institute for Health and Care Excellence July 2010

Motor neurone disease: assessment and management

Criteria for non-invasive ventilation in NMD

- FVC <50% of predicted
- FVC <80% of predicted plus symptoms/signs of respiratory impairment
- SNIP or MIP <40 cmH2O
- SNIP or MIP <65 cmH2O (men) or 55 cmH2O (women) plus symptoms/signs of respiratory impairment
- Decrease of SNIP or MIP > 10 cmH2O per 3 months
- Nocturnal hypoventilation
- SpO2 < 90% for >5% of the night
- $TCCO_2$ > 48.8 mmHg
- Daytime hypercapnia

EUROPEAN JOURNAL OF NEUROLOGY
THE OFFICIAL JOURNAL OF THE EUROPEAN FEDERATION OF NEUROLOGICAL SOCIETIES

EFNS guidelines on the Clinical Management of Amyotrophic Lateral Sclerosis (MALS) – revised report of an EFNS task force

The EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis: Peter M. Andersen[a], Sharon Abrahams[b], Gian D. Borasio[c], Mamede de Carvalho[d], Adriano Chio[e], Philip Van Damme[f], Orla Hardiman[g], Katja Kollewe[h], Karen E. Morrison[i], Susanne Petri[h], Pierre-Francois Pradat[j], Vincenzo Silani[k], Barbara Tomik[l], Maria Wasner[m] and Markus Weber[n]

Indications to start NIV in ALS

- FVC < 80% associated with symptoms such as tachypnea, and use of accessory muscles, tachypnea, excessive fatigue, EDS
- SNIP < 40 mmHg
- MIP < 60 mmHg
- Daytime hypercapnia PCO_2 > 45 mmHg
- Nocturnal saturation < 88% for 5 consecutive minutes

Symptoms of Respiratory Failure in NMD

Non-Pulmonary Symptoms
• Fatigue • Headaches (morning) • Concentration difficulties • School/work performance difficulties • Memory changes • Snoring/poor sleep quality

A rapid decline in respiratory function associated with respiratory symptoms, is more useful in clinical practice than absolute values

Modified from: Khan, A, et al CHEST 2023; 164(2):394-413

Initiation of NIV

How to initiate NIV	• Education • Expectations • Discuss goals • Family involvement • Close follow up • Inpatient vs outpatient
Goals	• Treat hypoventilation • Comfort (NIV settings, interface) • Improve QOL/symptoms

Initiation of NIV

Location	• Home • Sleep lab (PSG) • Inpatient
Interface	• Nasal • Pillows • Oronasal (FFM) • Mouthpiece
Timing	• Nocturnal • Nocturnal and daytime (progressive disease)

Interfaces

Nasal Pillows

Under the Nose FFM

Nasal Mask

Full Face Mask

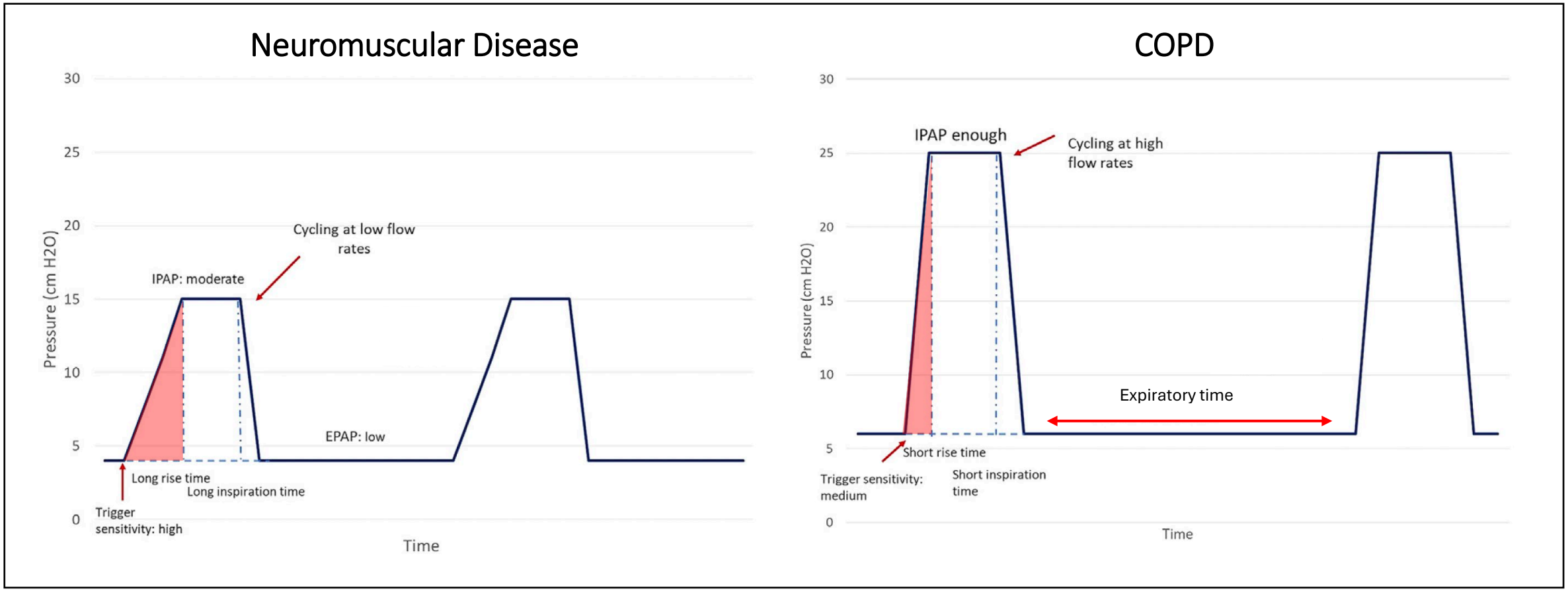
Images from: ResMed

Bilevel Ventilation

Mode	Bilevel S/T	
IPAP	10-12 cm H2O	Titrate by 1-2 cm H2O to improve dyspnea and hypoventilation
EPAP	4-5 cm H2O	Minimum unless obstructive events
Vt	6-8 → 10 mL/kg	Increase gradually to improve gas exchange
BUR	2 bpm < baseline RR	
Trigger Sensitivity	High	Prevents ineffective triggering and supports muscle weakness
Rise Time	Slow 300 ms	Ensures adequate distribution of ventilation (↓ chest wall compliance)
Ti	Long 1:2	Ensures sufficient Vt
Cycle Sensitivity	Low	

Adapted from: Duiverman, ML, et al Sleep Med Clin 19 (2024) 419–430

NIV settings in NMD vs Obstructive Lung Disease



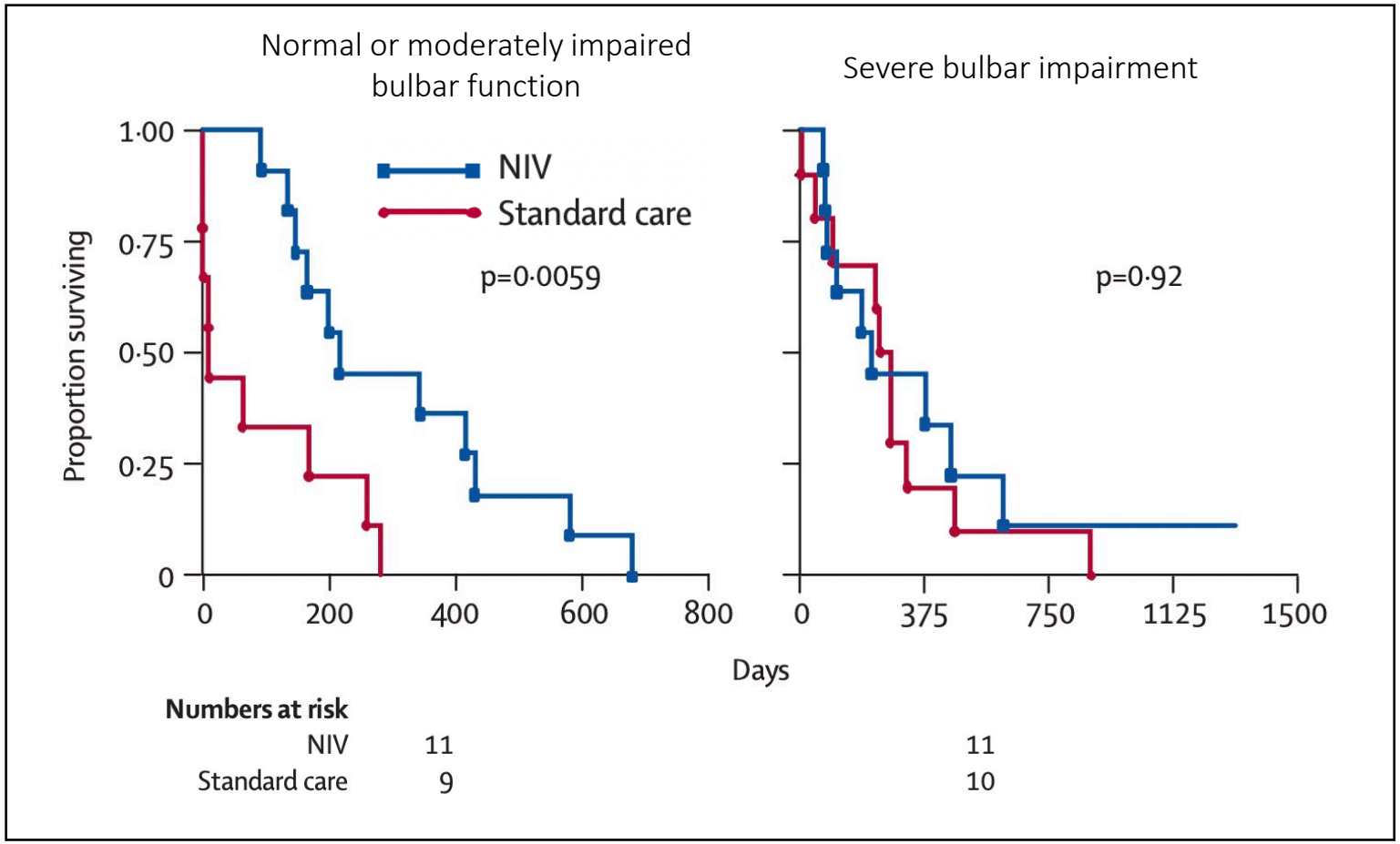
NIV and survival in NMD

- The effect of nocturnal NIV in survival in the NMD population has been evaluated mostly in the context of ALS

- NIV is effective in prolonging survival with improvement in quality of life in patients with ALS

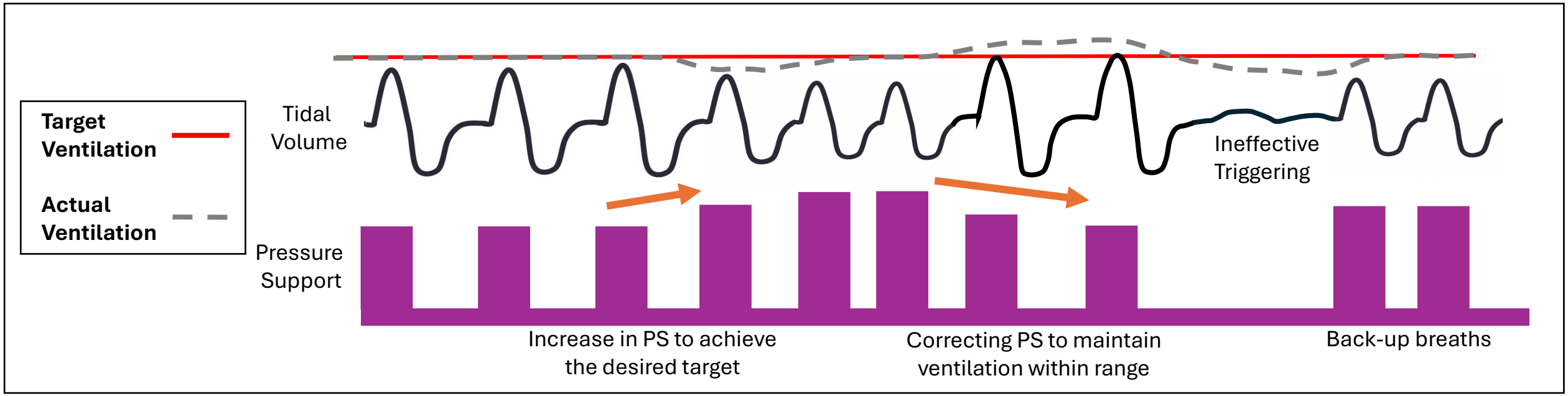
NIV and survival in ALS

Median survival for patients treated with NIV was 216 days versus only 11



Volume Assured Pressure Support (VAPS)

- VAPS devices sense changes in the patient's respiratory flow over several breaths
- Proportionally **adjust** the inspiratory pressure to reach a respiratory target
- Respiratory targets could be either **Vte** (AVAPS (average)), or **alveolar ventilation** (iVPAS (intelligent))



Volume Assured Pressure Support (VAPS)

Mode	iVAPS	
Target $\dot{V}a$	6-8 → 10 mL/kg	Titrate to improve gas exchange
MinPS	5 cm H2O	
MaxPS	20 cm H2O	Increase gradually to improve gas exchange
EPAP	4-5 cm H2O	Fixed vs minEPAP 5 cm H2O, maxEPAP 20 H2O ↑ EPAP if OSA
BUR	2 bpm < baseline RR vs Auto	
Trigger Sensitivity	High	Prevents ineffective triggering
Rise Time	Slow 300-600 ms	Adequate distribution of ventilation, adjust for comfort, dyspnea
Ti	Long 1:2	Ensures sufficient Vt, adjust for comfort
Cycle Sensitivity	Low	Longer Ti, Vt and gas exchange

VAPS vs Bilevel in NMD

Study	Condition	Comparison	Design/n	Result
Nicholson T et al. 2017	ALS	VAPS vs. Bilevel ST	Retrospective (271)	VAPS: ↑ PS and Vt, ↓ rapid shallow breathing No difference in adherence
Sunkonkit K et al. 2021	**Pediatric** DMD	VAPS vs. Bilevel ST	Prospective (20)	VAPS: better adherence No difference in RR, Vt, $\dot{V}E$
Saddi V et al. 2021	**Pediatric** NMD, other*	VAPS vs. Bilevel ST	Retrospective (19)	VAPS: ↑ Vt, ↓ sleep $TcCO_2$ No difference in sleep efficiency, adherence, obstructive apnea index

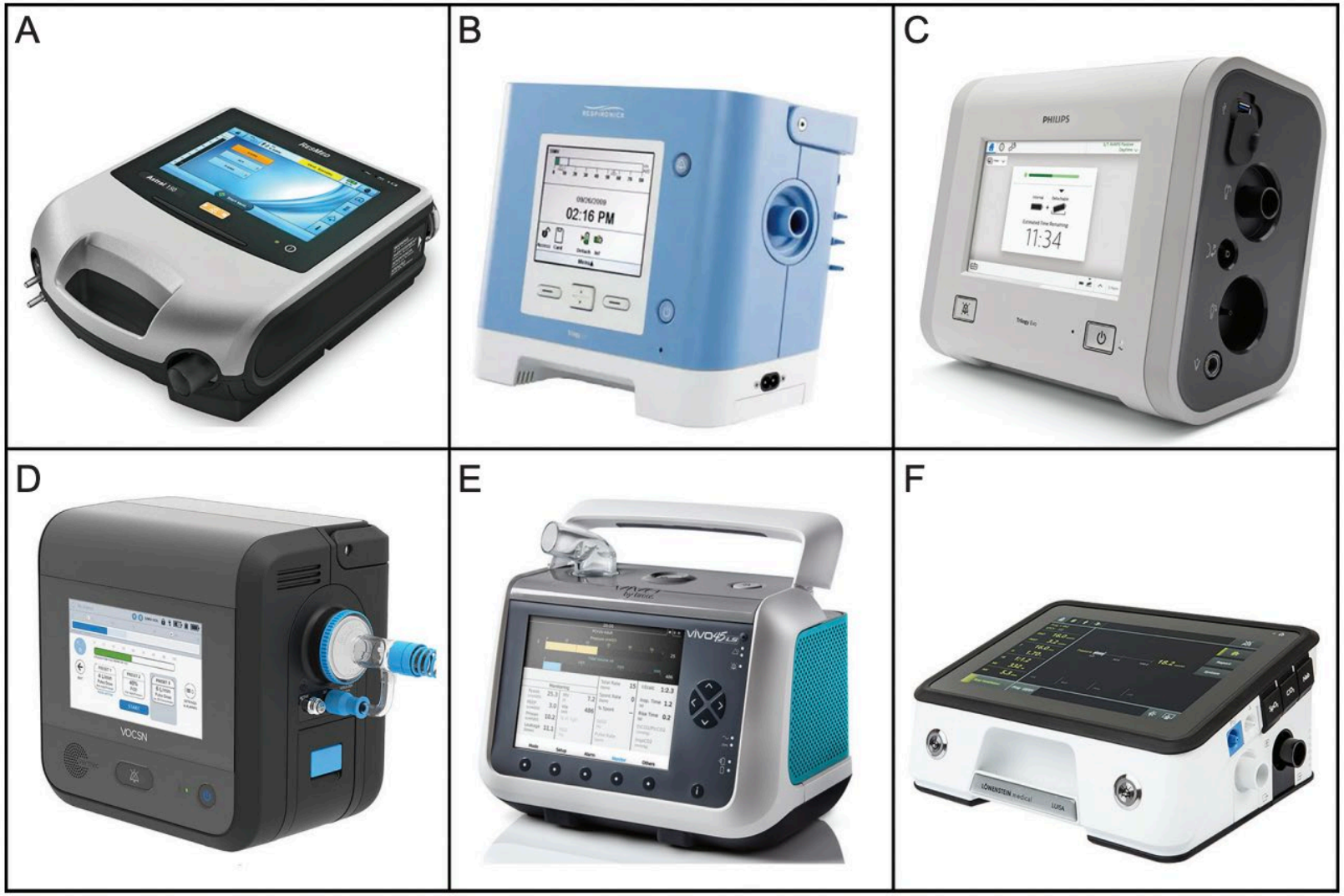
* Obstructive hypoventilation, parenchymal lung disease, congenital central hypoventilation syndrome

1. Nicholson T, et al Ann Am Thorac Soc. 2017 Jul;14(7):1139-1146
2. Sunkonkit K et al. Sleep Breath. 2021 Jan 19;25(4):1843–1850
3. Saddi V et al. J Clin Sleep Med. 2021 May 1;17(5):925-930

Volume-Cycle Ventilation

Mode	Volume Control	
Vt:	6-10 mL/kg	Gradually titrate Vt by 25-50 mL s tolerated to achieve target Vt/$\dot{V}E$
EPAP	4-5 cm H2O	Minimum unless obstructive events
BUR	2 bpm < baseline RR	

Portable Ventilators



A. ResMed Astral

B. Philips Trilogy Legacy

C. Philips Trilogy Evo

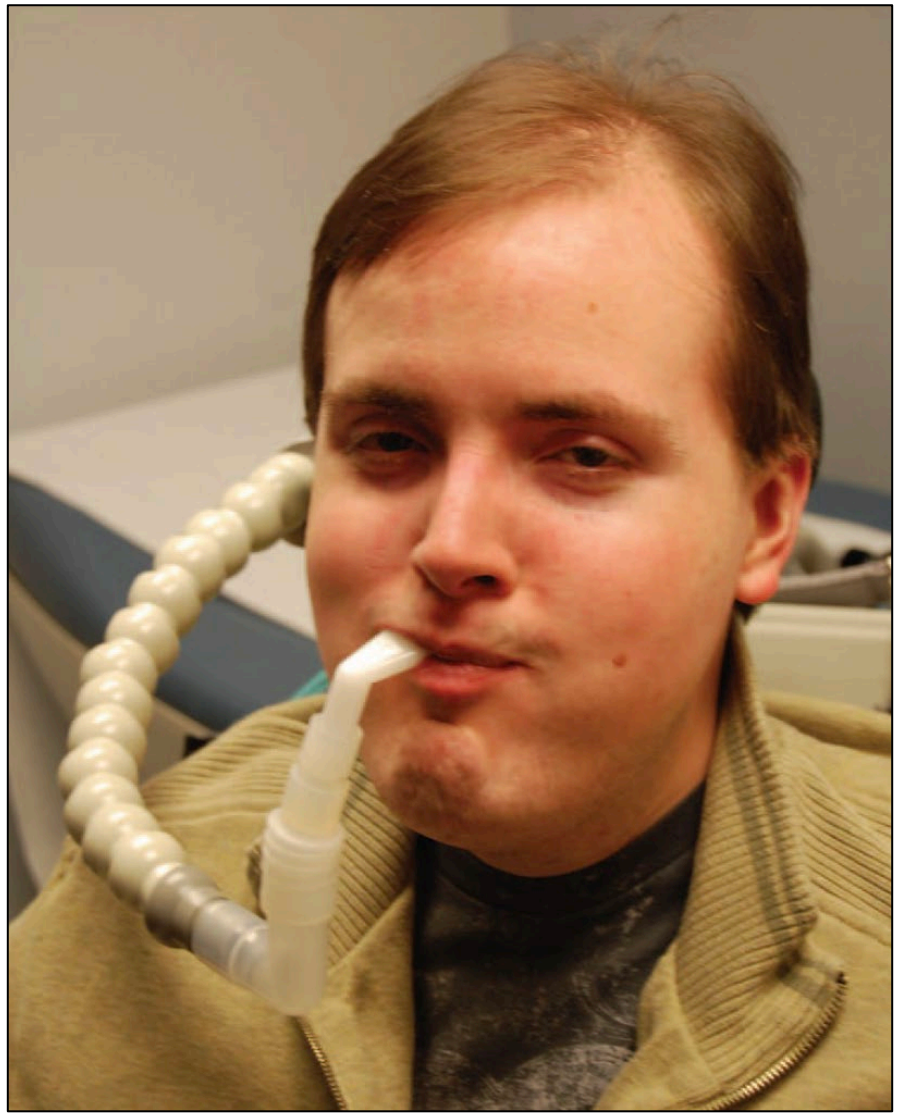
D. Ventec V+Pro

E. Breas Vivo 45 LS

F. Lowenstein LUISA

Image from: Hansen-Flaschen J et al. Respir Care. 2023 Aug;68(8):1123–1157

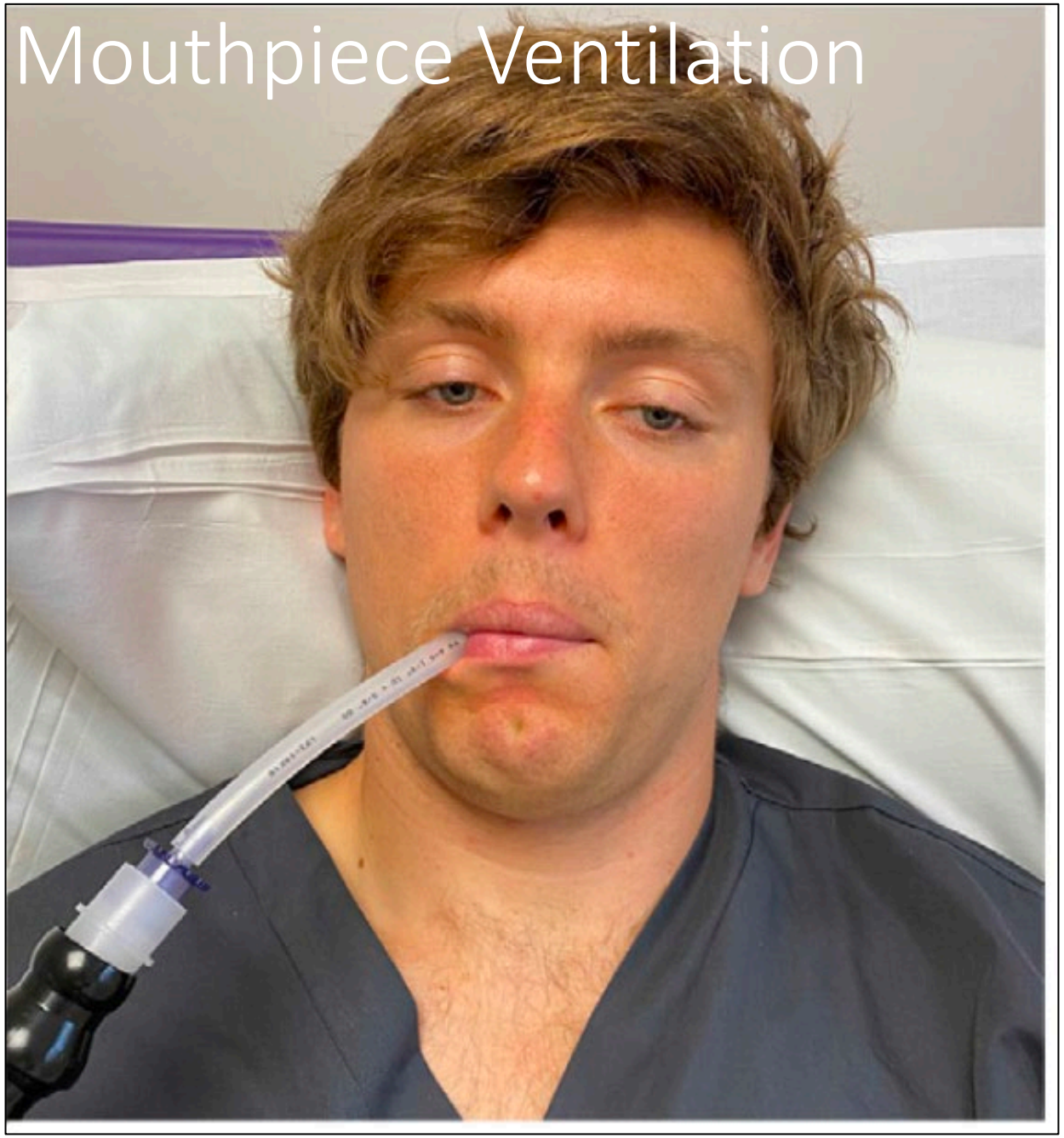
Mouthpiece Ventilation

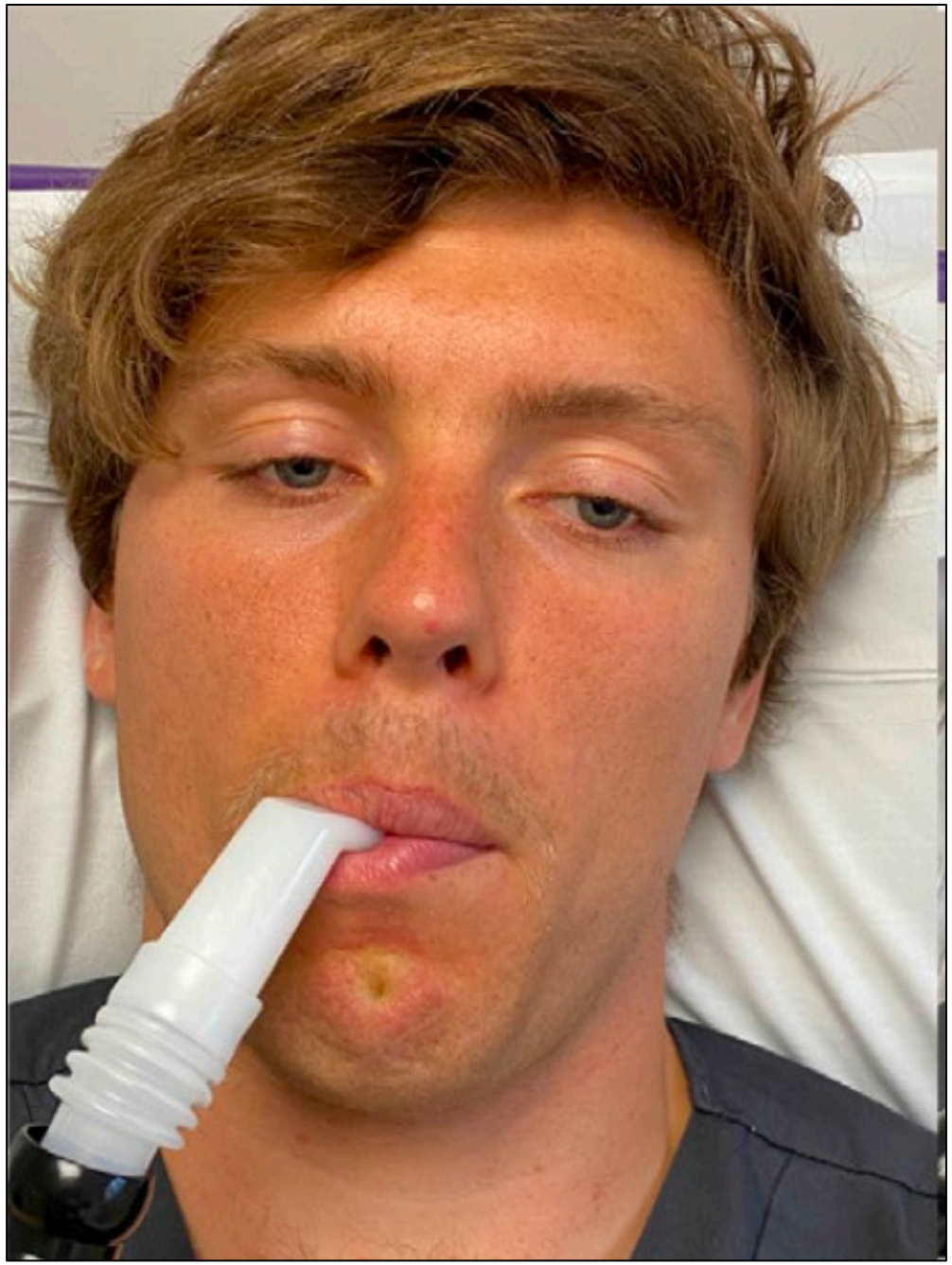


- The use of the mouthpiece was first described in 1953 in patients with polio
- The technology is still not commonly used
- Used with single, non-vented circuit ventilators frequently, in volume-controlled mode
- **Requires a preserved cognitive and bulbar muscle function**
- Effective alternative to tracheostomy or intolerance to NIV with mask

Image from: Benditt JO, Respir Care 2019;64(6):679–688

Mouthpiece Ventilation





Images from: Chatwin M, et al. Neuromuscul Disord. 2020 Sep;30(9):772-781

Support System/Arm for MPV

Pictures from: CANVent Ottawa,
https://www.youtube.com/watch?v=km_P7yq69Bk

Mouthpiece Ventilation

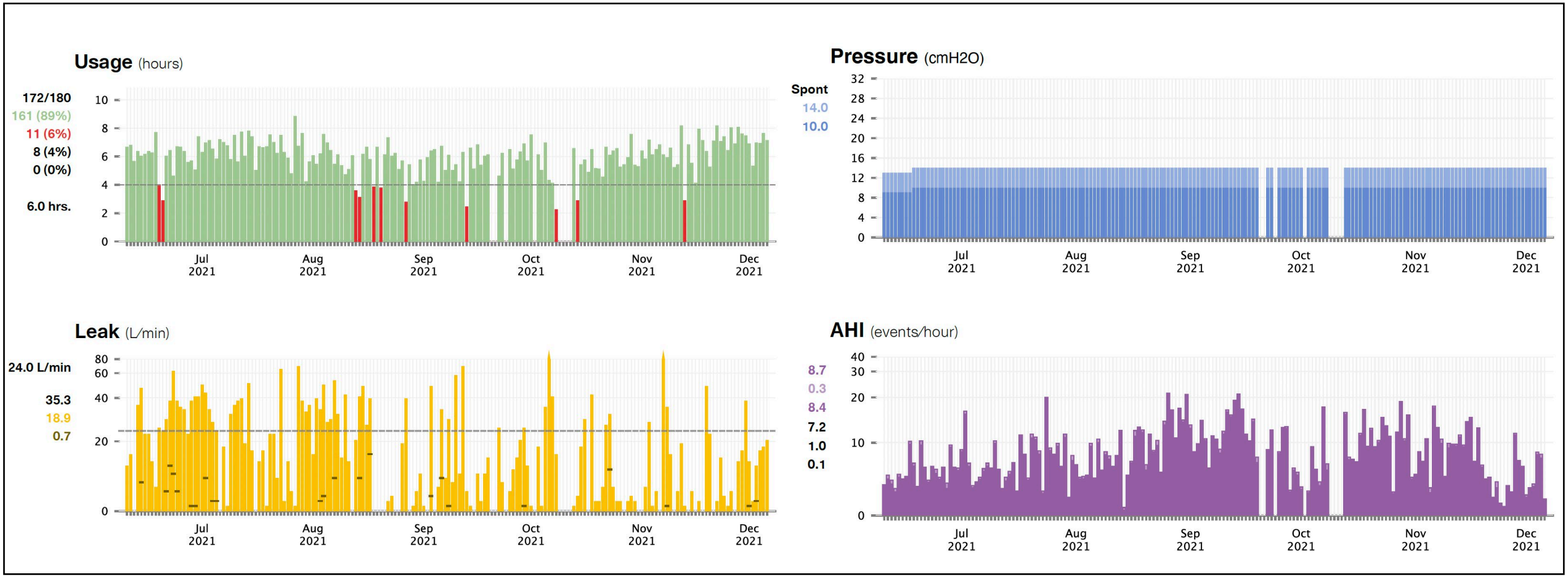
Mode	**Volume Control**	
Vt:	8-10 mL/kg (700-1500 ml)	Allows breath stacking
EPAP	0	
BUR	As needed	
Ti	0.8-1.3 sec	
“MPV mode”	Allows intermittent or “on demand” ventilation	Apnea, disconnection, low pressure alarms turned off
Trigger Sensitivity	“Kiss” trigger	

252nd ENMC international workshop: Developing best practice guidelines for management of mouthpiece ventilation in neuromuscular disorders. March 6th to 8th 2020, Amsterdam, the Netherlands

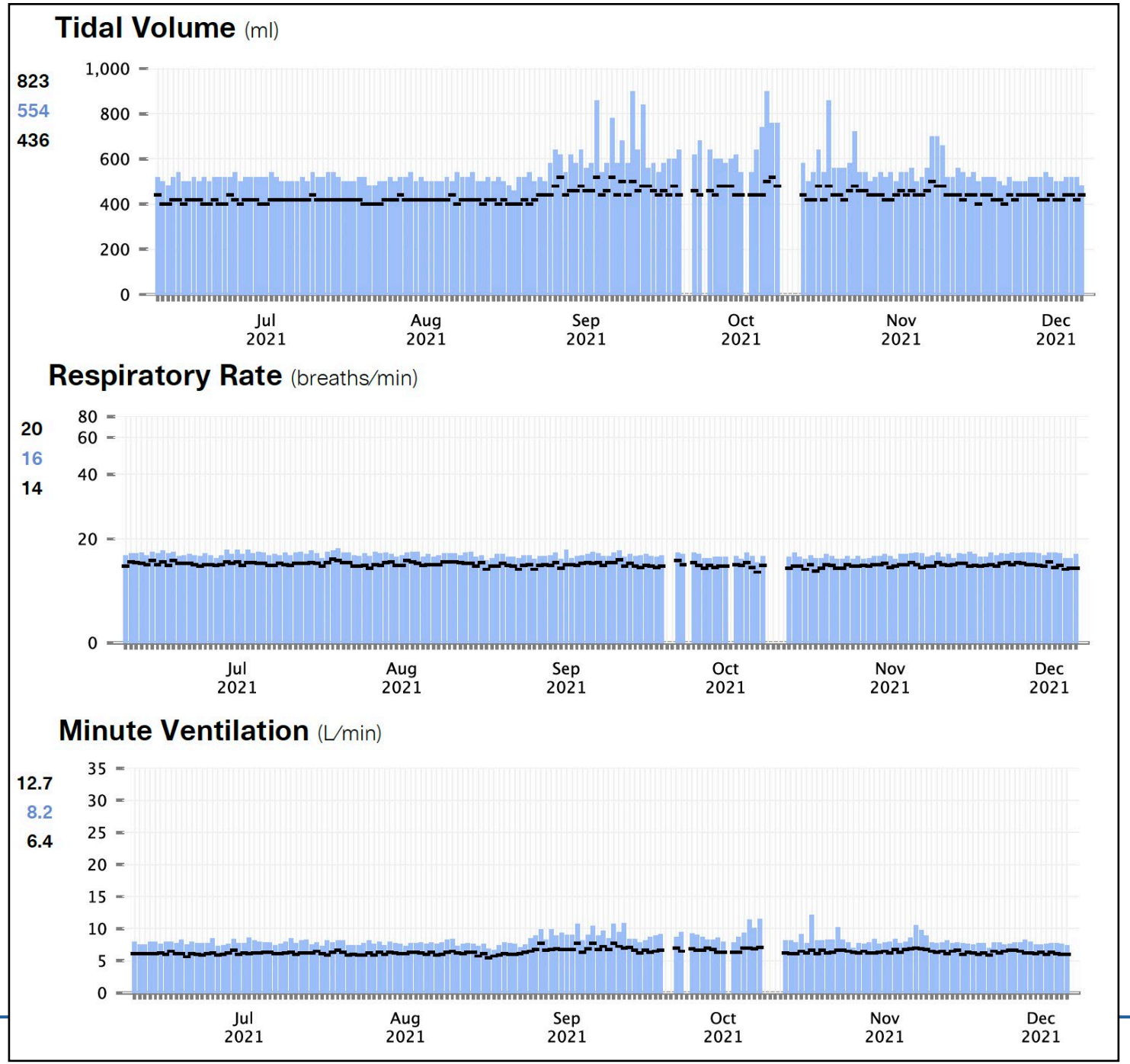
Michelle Chatwin[a,*], Miguel Gonçalves[b], Jesus Gonzalez-Bermejo[c], Michel Toussaint[d], on behalf of the ENMC Respiratory Therapy Consortium

"MPV should be introduced in those that wish to peruse noninvasive daytime ventilatory support and can maintain a lip seal when ventilatory support is **greater than 12 h per day** with or without daytime hypercapnia"

NIV Adherence Report



NIV Adherence Report



Ventilator Settings

Active Preset	Mode	Patient Type	Humidification	Circuit Type
NIGHT	Vol. Targeted-PS	Adult	Humidifier	Valveless

Breath Rate	Inspiratory Time	Tidal Volume	Pressure Adj. Rate	Pressure Minimum
12 BPM	1.0 secs	450 mL	Slow	6 cmH_2O

PEEP / EPAP	Flow Trigger	Rise Time	Apnea Rate
5 cmH_2O	3.0	3	10 BPM

Flow Cycle	Time Cycle
65%	1.0 secs

Therapy Dashboard

Avg PIP	Avg PEEP	Avg minute ventilation	Avg Vte	Avg breaths per minute
16.7 cmH_2O	4.0 cmH_2O	10.6 L/min	467.7 mL	23.2 BPM

# Pt. Triggered Breaths	I:E Ratio	Avg total leak	% days used < 4 hours	Days not used
98.6 %	1:3.1	38.1 L/min	1.0	0

Max usage	Min usage	Cumulative usage	Avg used (days used)
11.0 hours	1.0 hours	79.0 hours	5.6 hours

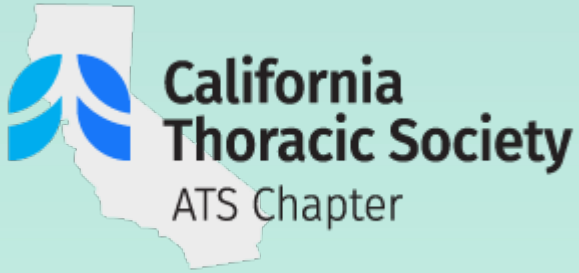
Summary

Respiratory Muscle Strength		Hypoventilation		
Vital Capacity		Nocturnal Oximetry	ABG	Symptoms
MIP	SNIP			
MEP	CPF			

NIV Initiation

Ventilation Mode		Nighttime	Daytime			Monitoring
VAPS	PS	Mask NIV				1, 3, 6 months • Nocturnal Oximetry • ABG/VBG • $TcCO_2$ • Ventilator report
VAPS	PS	Mask NIV				
PS/VAPS	VC	Mask NIV	MVP	MPV	MPV	
PC(IMV)/PS/VC/VAPS		Trach + invasive ventilation				

Women in Medicine: Tackling the Gender Burnout Gap



Tisha Wang, MD, ATSF (UCLA)
Jessica Goggin, PhD, MAS, RN (UCSD)

UCLA Health | Department of Medicine

The Problem Statement

- The healthcare workforce has a very high rate of burnout, and it is disproportionately impacting women
- Early and mid-career providers appear to be particularly vulnerable
- In academics, women take on average 1-3.5 years longer than men to move beyond the associate professor rank, and many women stagnate in the middle of their careers or leave academia entirely

The Data

- It has been known since 2000 that women physicians have a 60% higher rate of burnout compared to their male colleagues
- Nationwide physician burnout is now above 50% and still ~50% higher in women
- RT burnout was reported to be as high as 79% in 2023
- Burnout in women nurses/APPs was 86% in a survey from 2024

Consequences of Burnout

- Lower patient care quality, safety, and experience
- Increased malpractice claims
- Increased risk of substance use disorder, depression, and suicide – physicians and in particular female physicians at higher risk for suicide than general population
- Lower physician and care team morale and productivity
- Higher turnover + staff shortages that affect workload and patient access to care

Multiple Contributing Factors

- Work-life balance with childcare, elder care, household duties, spouses that work (8-14 hours/week of extra work at home), parental leave
- Gendered expectations in clinical care:
  - 2 min more time per patient
  - More likely to discuss psychosocial/emotional topics
  - More likely to have a practice with predominantly female patients (who make more contact in EMR)
- Presence of gender inequality – salaries, resources, opportunities, unconscious/ conscious bias

Multiple Contributing Factors

- Presence of microaggressions and/or sexual harassment, bullying, or other disruptive workplace behaviors
- Minority tax of needing to represent (even more marked in underrepresented women)
- Lack of professional development, mentoring, or role models
- Difficulty with promotion/tenure
- No sense of purpose, belonging, or fair access
- Lack of autonomy or control
- Impostor syndrome or lack of self-esteem

Multiple Contributing Factors

- Specific to RTs:
  - Poor/ineffective leadership
  - Inadequate staffing
  - High workload
  - Working in non-leadership position
  - Work environment

Protective Factors Across All Healthcare Professions

- Supportive and flexible working environment
- Access to professional development
- Supportive relationships
- Intentional mindfulness practices
- Sense of respect from their leadership

Open Discussion

- What would support you the most as a woman healthcare professional? Are there ways in which the CTS community could provide support?
- What tangible things have you seen done at your institution that could potentially start to close the gender burnout gap?
- How can we work together interprofessionally to optimize well-being of the multidisciplinary teams that provide care for our pulmonary, critical care, and sleep medicine patients?