# Keynote - Implementation of a High-Quality Lung Cancer Screening Program

**David Tom Cooke, MD**
**Professor**
**UC Davis**

Dr. David Tom Cooke is a Professor at the University of California, Davis School of Medicine. He is the founding Chief of the Division of General Thoracic Surgery, Director of the General Thoracic Surgery Robotics Program, the Vice Chair for Faculty Development and Wellness for the Department of Surgery, the Associate Director for the Office of Inclusivity, Diversity, Equity and Accessibility (IDEAL) and the Interim Physician-in-Chief, UC Davis NCI designated Comprehensive Cancer Center. Dr. Cooke specializes in the surgical treatment of malignant and benign lung and esophageal disease and is a national leader in robotic thoracic surgery. Dr. Cooke's research includes oncologic trials, surgical outcomes/health services research, patient-centered outcomes research, surgical education, medical social media, and public medical communication. He has authored over 100 peer-reviewed publications. He is president of the Thoracic Surgery Directors Association, a director of the American Board of Thoracic Surgery, a director of the Accreditation Council for Graduate Medical Education (ACGME), member of the American Surgical Association and an associate member of the American College of Surgeons Academy of Master Surgeon Educators. Dr. Cooke currently serves on the American Lung Association National Lung Cancer Expert Medical Advisory Panel. Dr. Cooke completed his cardiothoracic surgery training at the University of Michigan in Ann Arbor, general surgery residency at the Massachusetts General Hospital in Boston, medical school at Harvard Medical School and undergraduate at UC Berkeley.

# Implementation of a High-Quality Lung Cancer Screening Program

**California Thoracic Society Annual Educational Conference**
**March 8th, 2024**

David Tom Cooke, MD, FACS
Professor and Chief, Division of General Thoracic Surgery
Interim Physician-In-Chief, Comprehensive Cancer Center

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# Disclosures

- **Bristol Meyers Squibb**
  - Speakers Honoraria
- **AMGEN and AstraZeneca**
  - Support for the UCLCC Screening & Prevention Taskforce

## Lung cancer kills more Men AND Women…

**Lung Cancer > Breast Cancer + Prostate Cancer + Colon Cancer**

American Lung Association
State of Lung Cancer
2023

•Close to **238,000** people will be diagnosed with lung cancer this year, with the rate of new cases varying by state.
•Lung cancer has one of the lowest five-year survival rates because cases are often diagnosed at later stages, when the disease is less likely to be curable. The national average of people alive five years after a lung cancer diagnosis is **26.6%**
•Nationally, only **26.6%** of cases are diagnosed at an early stage.


## Menthol Cigarette Smokers

Race and Ethnicity

| | |
|---|---|
| African American | 82.6% |
| Hispanic | 32.0% |
| White | 23.8% |

among smokers 12 years of age and older, 2004 to 2008

*Source: NSDUH, 2009.*

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# Lung cancer is a leading cause of cancer mortality among AA populations

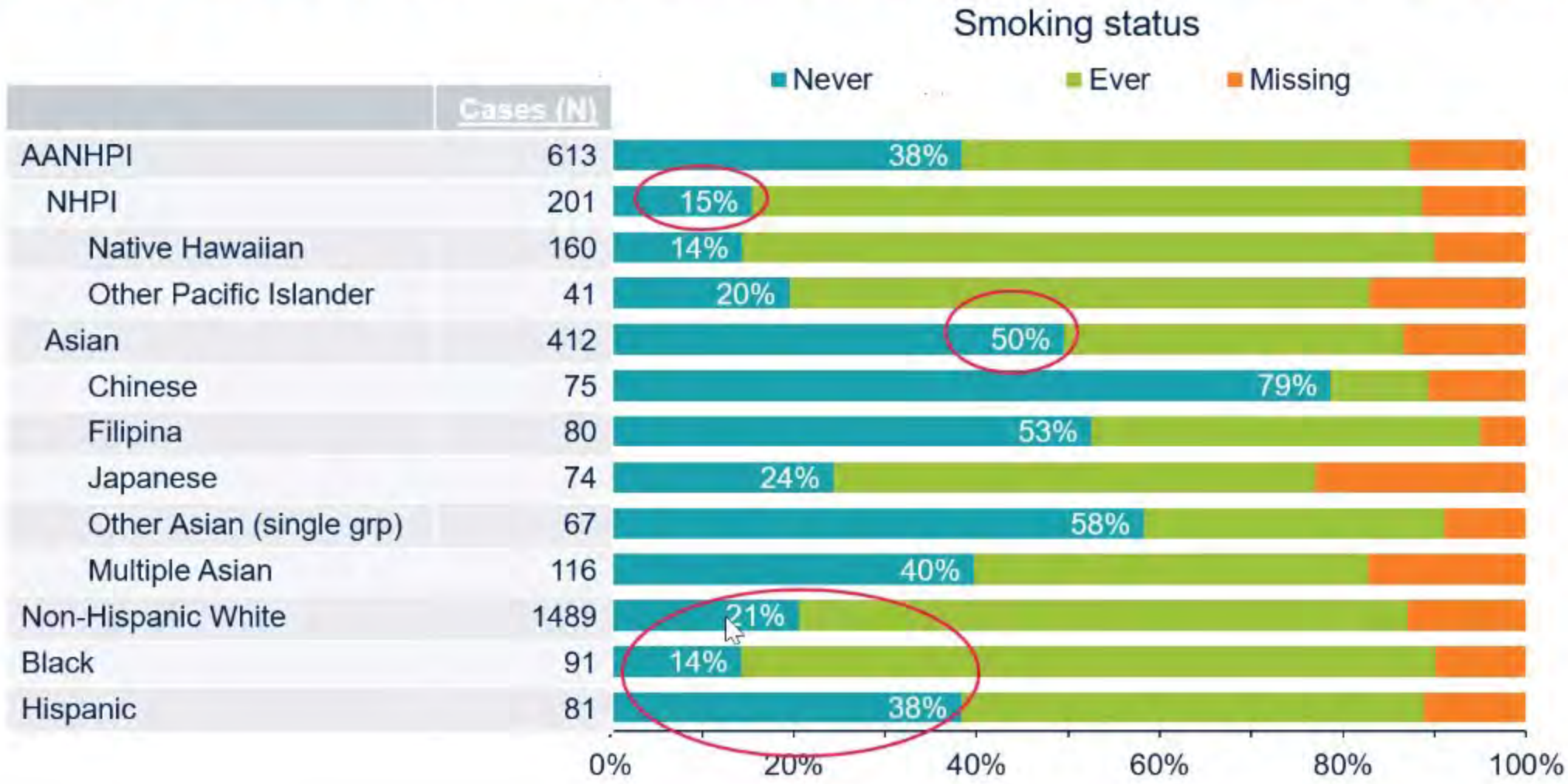
## Rank (based on age-adj mortality rate) & % (of all cancer deaths) of top 5 cancer sites, 1990-2008

| Male (rank) | Asian Indian | Chinese | Filipino | Japanese | Korean | Vietnamese |
|---|---|---|---|---|---|---|
| 1 | Lung 19.0% | Lung 28.13% | Lung 30.7% | Lung 23.9% | Lung 22.8% | Lung 28.1% |
| 2 | Colorectal 8.3% | Liver 11.7% | Colorectal 10.8% | Colorectal 13.1% | Stomach 14.6% | Liver 22.3% |
| 3 | Prostate 8.1% | Colorectal 10.4% | Prostate 8.9% | Prostate 8.9% | Liver 12.9% | Colorectal 7.9% |
| 4 | Pancreas 7.0% | Stomach 6.5% | Liver 7.6% | Stomach 8.8% | Colorectal 11.0% | Stomach 6.5% |
| 5 | Leukemia 6.3% | Pancreas 5.9% | Pancreas 5.7% | Pancreas 8.4% | Pancreas 7.4% | Pancreas 4.4% |
| **Female (rank)** | **Asian Indian** | **Chinese** | **Filipino** | **Japanese** | **Korean** | **Vietnamese** |
| 1 | Breast 19.8% | Lung 22.2% | Breast 19.5% | Lung 21.4% | Lung 18.5% | Lung 21.7% |
| 2 | Ovary 9.7% | Breast 11.8% | Lung 18.1% | Colorectal 12.9% | Stomach 11.6% | Breast 10.3% |
| 3 | Lung 9.3% | Colorectal 11.9% | Colorectal 9.0% | Breast 10.7% | Colorectal 11.4% | Colorectal 9.6% |
| 4 | Colorectal 6.8% | Pancreas 7.2% | Pancreas 6.7% | Pancreas 9.6% | Pancreas 8.2% | Liver 9.3% |
| 5 | Pancreas 5.9% | Stomach 5.4% | Ovary 6.0% | Stomach 6.5% | Liver 7.2% | Stomach 6.3% |

Thompson CA, et al. The burden of cancer among Asian Americans: a report of national mortality trends by Asian ethnicity CEBP 2016

# Cohort description – Female lung cancer cases (n=3867)

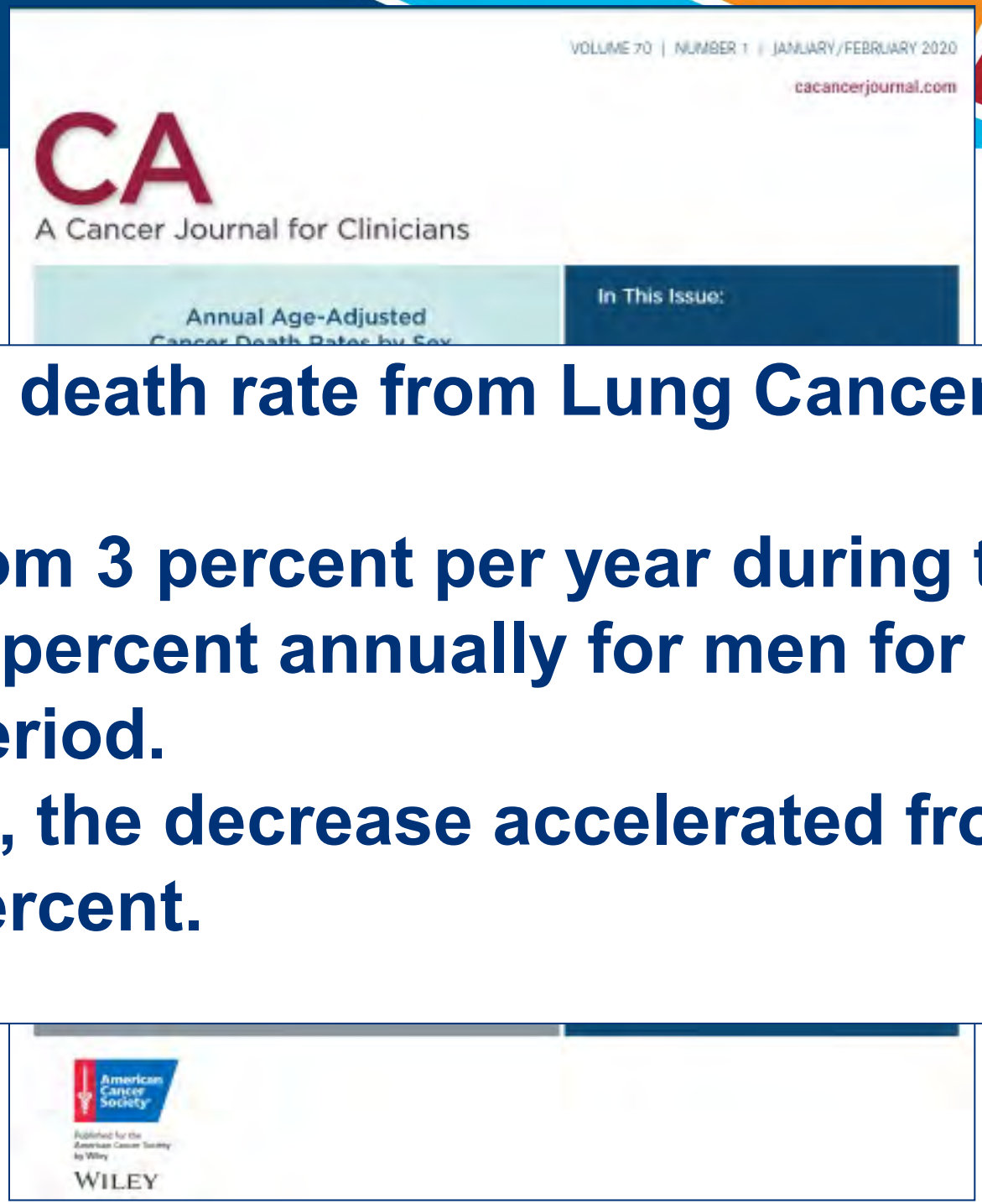
| | Cases (N) |
|---|---|
| AANHPI | 613 |
| NHPI | 201 |
| Native Hawaiian | 160 |
| Other Pacific Islander | 41 |
| Asian | 412 |
| Chinese | 75 |
| Filipina | 80 |
| Japanese | 74 |
| Other Asian (single grp) | 67 |
| Multiple Asian | 116 |
| Non-Hispanic White | 1489 |
| Black | 91 |
| Hispanic | 81 |




DeRouen, et al. CEBP, 2021


Morris CR, Movsisyan A, Hofer BM, Parikh-Patel A, Keegan THM, Cooke DT, Wun T.

- **Compared with White patients, Black/African American patients were more likely to be diagnosed at late-stage disease.**
- **Late stage at diagnosis was examined for six screen-detectable cancers: female breast, cervical, colorectal, prostate, lung, and oropharyngeal cancers. A significantly higher percentage of Black/African American (vs. White) patients with lung (78.4 vs. 72.9 percent), and other cancers were diagnosed at late stage.**




# Decline in the death rate from Lung Cancer:

- Sped up from 3 percent per year during the 2008-2013 period to 5 percent annually for men for the following five-year period.
- For women, the decrease accelerated from 2 to almost 4 percent.

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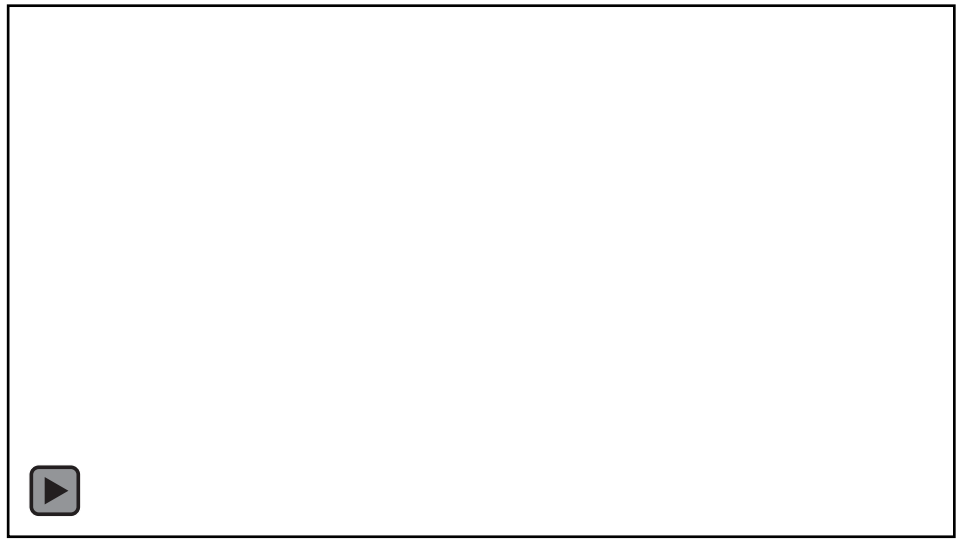
# Cancer Disparities

- Cancer mortality rates among Black/African American men declined by 2.3 percent per year for all cancers combined.
- Among Black/African American women, cancer mortality rates for all cancers combined declined as well, by 2.1 percent per year.


Why?

# Why?

- **Population Health**
  - Prevention
    - Radon awareness
    - Tobacco Recovery and Prevention
  - Screening
- **Treatments**
  - Advances in Surgery
  - Stereotactic Body Radiotherapy
  - Precision Medicine
  - Immunotherapy
- **Patient Activation**



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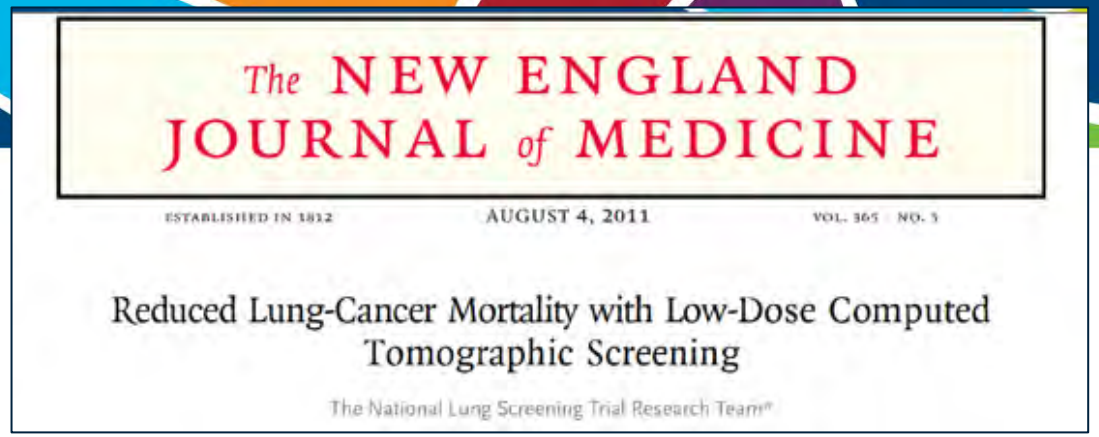


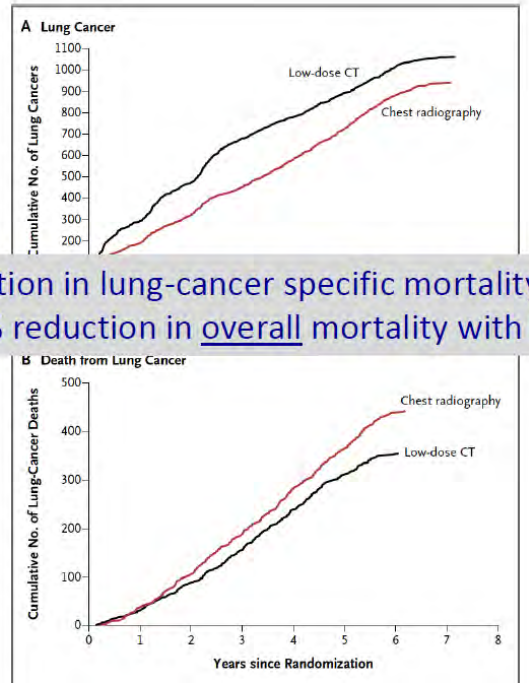


20% reduction in lung-cancer specific mortality with LDCT
6.7% reduction in overall mortality with LDCT

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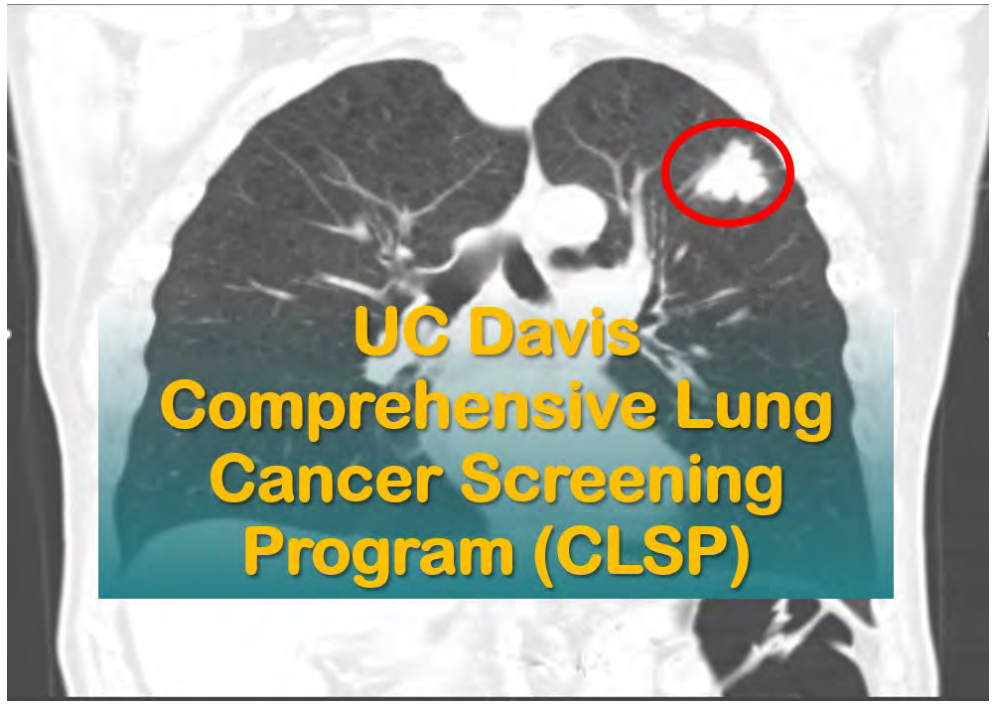
# Lung Cancer Screening

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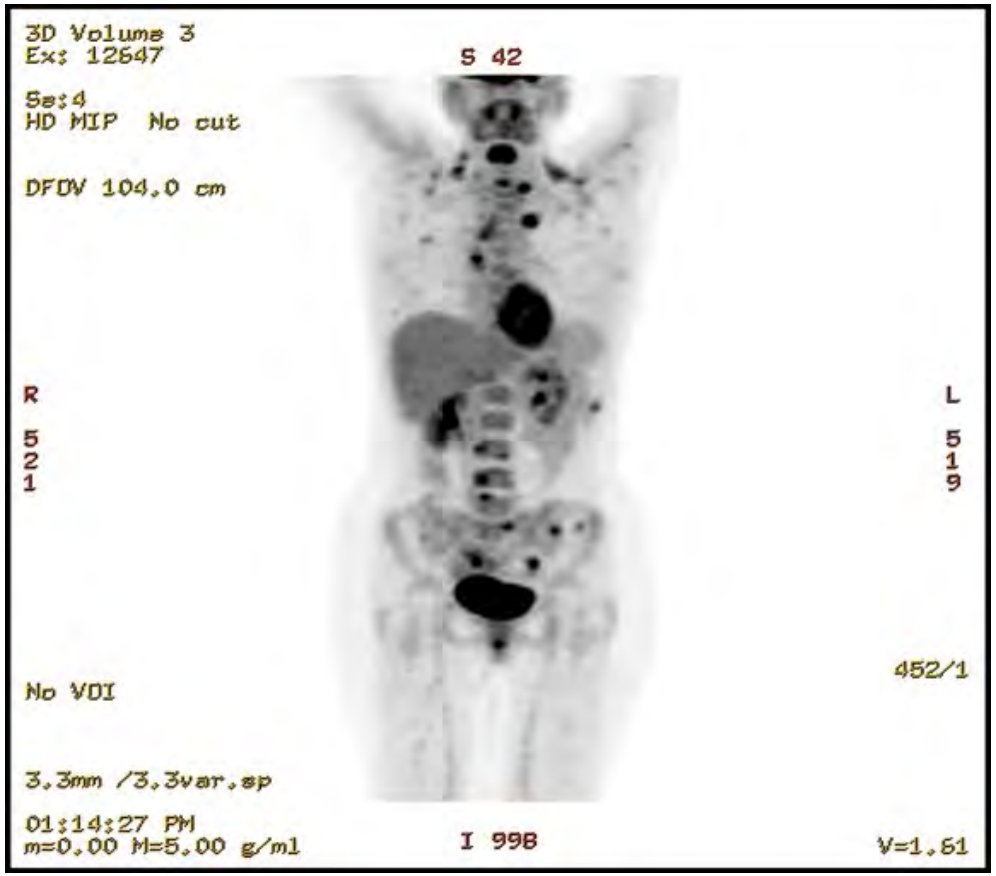
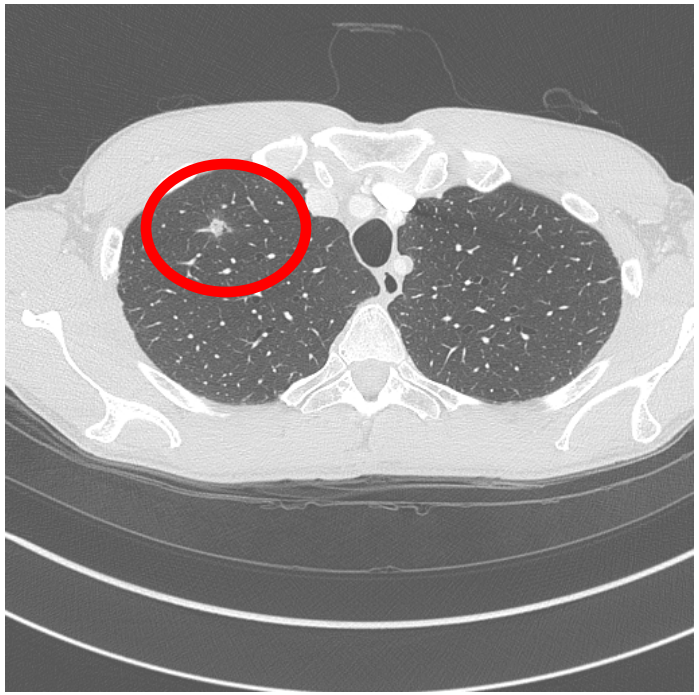
# Stage IV NSCLC




**<5%**

**5 year Survival with Best Medical Management**

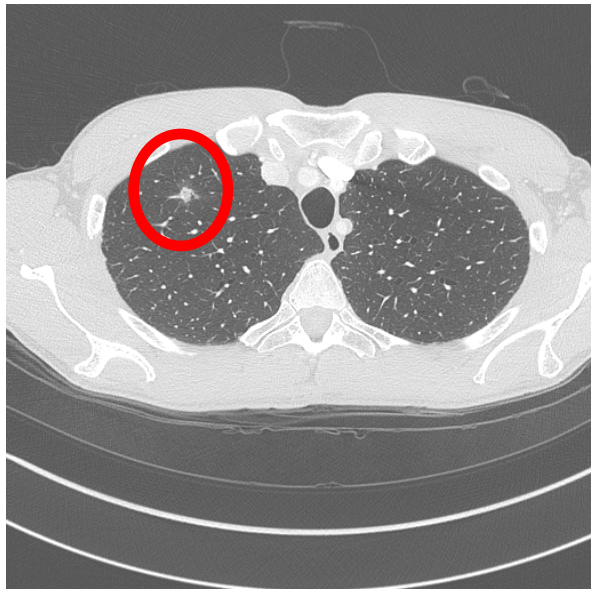
# Stage I NSCLC



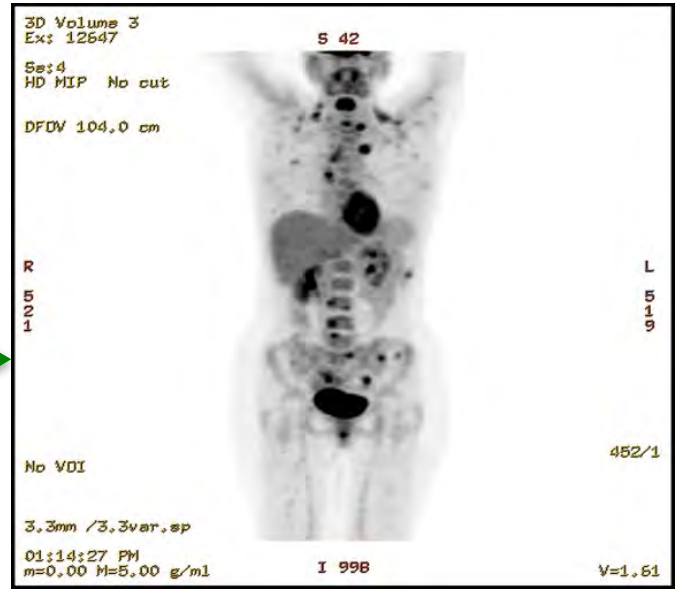
>80%
5 year Survival After Surgery

# Goal of Lung Cancer Screening

No Symptoms



Symptoms




Screening

**Stage I**
**>80% 5 year Survival**

**Stage IV**
**<5% 5 year Survival**

The NEW ENGLAND JOURNAL of MEDICINE

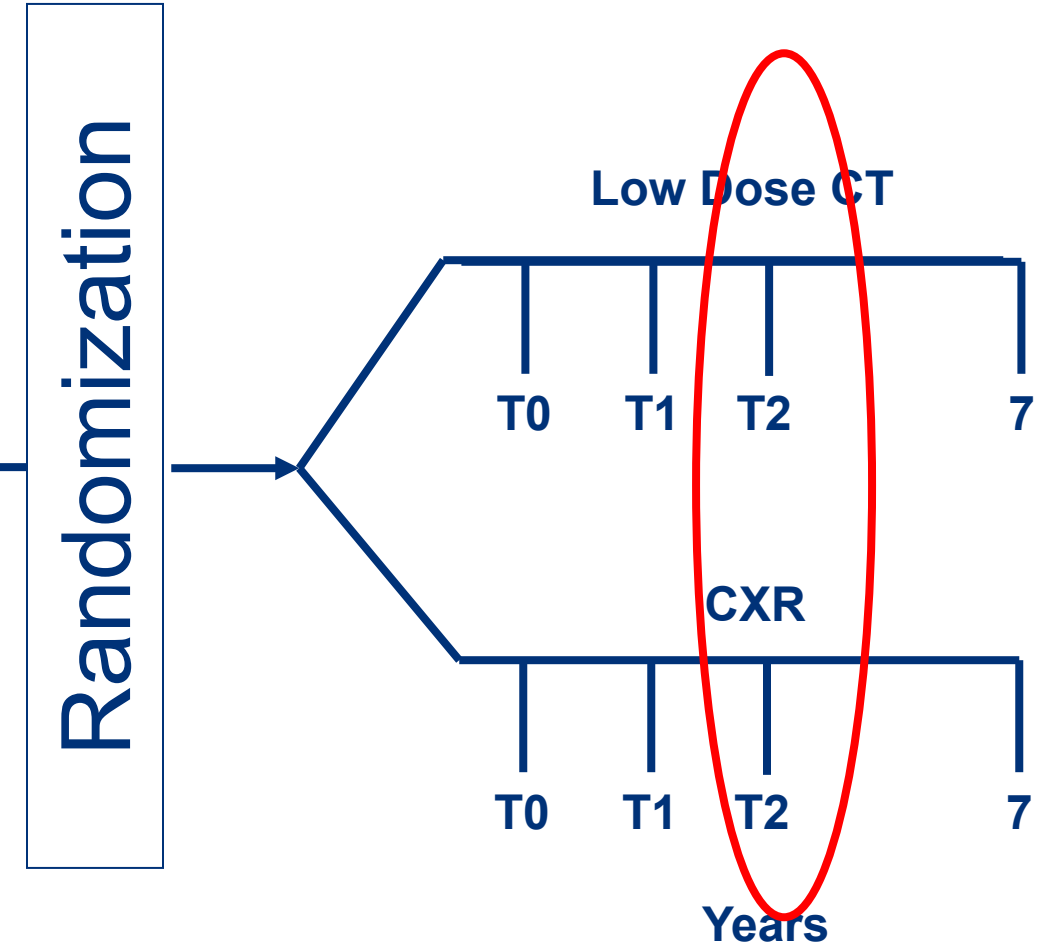
ESTABLISHED IN 1812 AUGUST 4, 2011 VOL. 365 NO. 5

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

- **To determine whether screening with low-dose computed tomography (LDCT), as compared with chest radiography (CXR), reduces mortality from lung cancer among high-risk persons**
  - **Eligible participants**
    - 55-74 years old
    - History of cigarette smoking of at least 30 pack-years
      - If former smoker, had quit within the previous 15 years

# National Lung Screening Trial: NLST

≥ 30 Pack years
Active Smoker or
Quit > 15 years
Aged 55-74
+50,000

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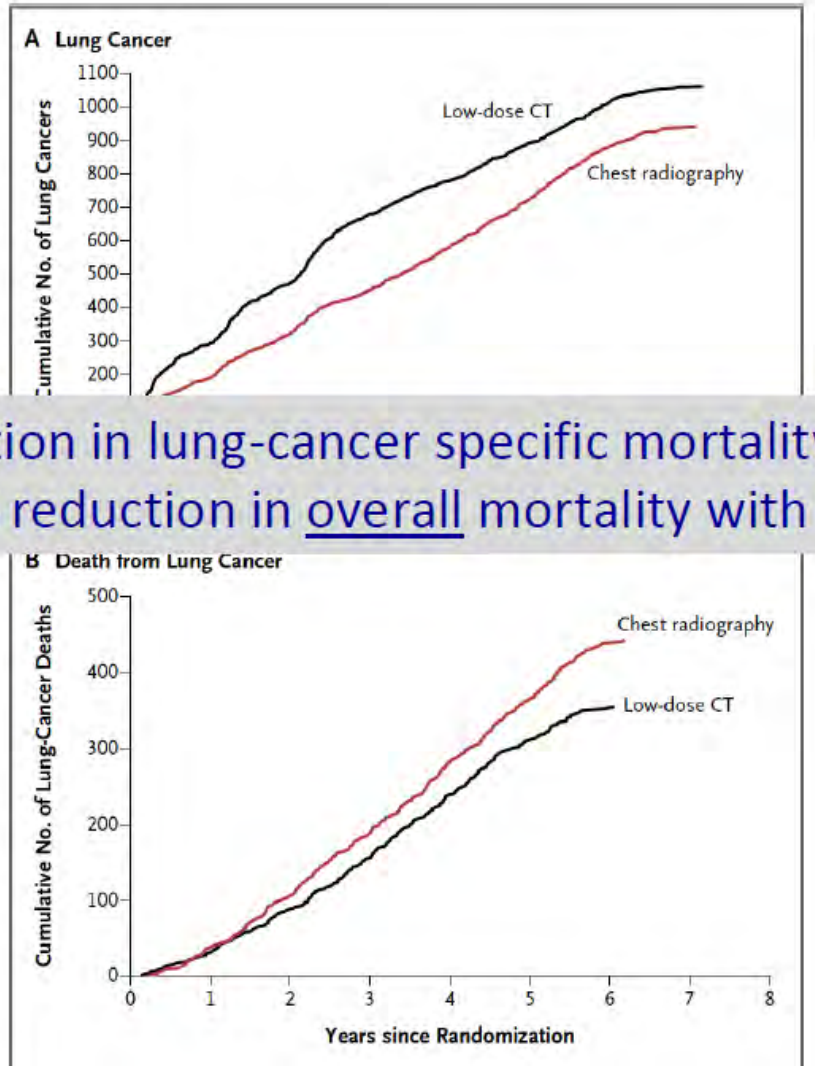
# National Lung Screening Trial Results: Stage Shift

| Stage | Positive Screen | AJCC - NSCLC |
|---|---|---|
| I | 63% | 24% |
| II | 7% | 6% |
| IIIA | 9% | 23% |
| IIIB | 8% | |
| IV | 13% | 44% |
| Early (Stages I – II) | 70% * | 30% |
| Late (Stages III- IV) | 30% | 70% |

* = for years T0-T3

# Background: NLST




20% reduction in lung-cancer specific mortality with LDCT

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# NELSON - trial ISRCTN 63545820


- Randomized Controlled Trial
- Recruitment through population-based registries
- CT screening vs. no screening
- Different screening intervals
- Volume & Volume Doubling Time of nodules
- Central reading of CT images
- Expert causes of death committee &
- Follow up through national registries

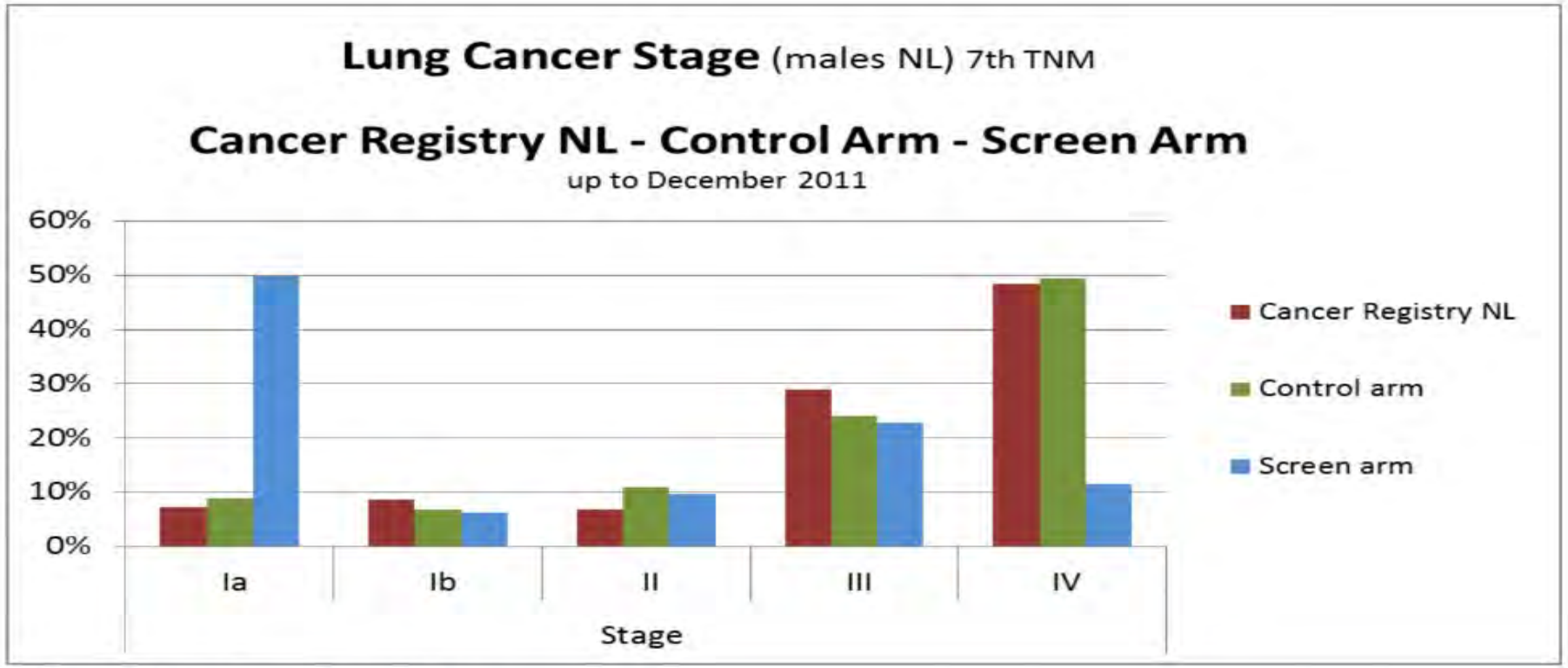
Trial, initially powered (80%) for high risk **males**, to detect a lung cancer mortality reduction of ≥ 25% at 10 years after randomization (individual FU)

And includes a small subgroup of women (16%)

Harry J. de Koning, Erasmus MC, Public Health Rotterdam

Presented at the 2018 WCLC

# NELSON




Yousaf-Khan et al., in preparation

NELSON

# NLST & NELSON: Lung cancer CT screening Mortality data

| Male v Female ratio | |
|---|---|
| NLST+ | 41/59 |
| NELSON | 16/84 |

| Percent LC Mortality Decrease | | | |
|---|---|---|---|
| Trial | Men | Women | 50:50 M/F |
| NLST* | 8% | 27% | 18% |
| | | | |
| NELSON** | 26% | 39-61% | 33 – 44% |
| | | | |

Pinsky et al. The National Lung Screening Trial:. *Cancer* 2013; **119**(22): 3976-83. +Aberle, et al. The National Lung Screening Trial: overview and study design. *Radiology* 2011; **258**(1): 243-53.
**Effects of Volume CT Lung Cancer Screening: Mortality Results of the NELSON Randomised-Controlled Population Based Trial De Koning et al 2018

## New Data

- **Black/AA smokers have a higher risk of lung cancer and at lower levels of smoking intensity than White smokers[1]**
- **Latino/Hispanics who smoke accumulate fewer pack-years than White smokers[2,3]**
- **Women accumulate fewer pack-years than men[4]**


1. N Engl J Med. 2006;354(4):333-342.
2. Am J Prev Med. 2014;46(5):496-506.
3. Tob Induc Dis. 2016;14:23
4. N Engl J Med. 2013;368(8):728-736.

## New Data

- **Southern Community Cohort Study participants found that 17% of Black/AAs who smoke were eligible for lung cancer screening based on the 2013 USPSTF eligibility criteria compared with 31% of White smokers.**
- **Among those diagnosed with lung cancer, only 32% of Black/AA persons who smoke were eligible for screening compared to 56% of White smokers.**

JAMA Oncol. 2019;5(9):1318-1324.

# Disparities in Access

- African-Americans are more likely to die from Lung Cancer than White Americans.  But African-Americans are screened less.
- However, African-Americans may have a higher incidence of positive screening exams.
- **When detected by screening, AA exhibit the same survival advantage and lower stage detection as their white counterparts.**

Pasquinelli MM, et al. JAMA Oncol. 2018;4(9):1291-1293.

# USPSTF New Recommendations

| | |
|---|---|
| What does the USPSTF recommend? | Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years:<br>• Screen for lung cancer with low-dose computed tomography (CT) every year.<br>• Stop screening once a person has not smoked for 15 years or has a health problem that limits life expectancy or the ability to have lung surgery.<br>Grade: B |
| How often? | • Screen every year with low-dose CT.<br>• Stop screening once a person has not smoked for 15 years or has a health problem that limits life expectancy or the ability to have lung surgery. |

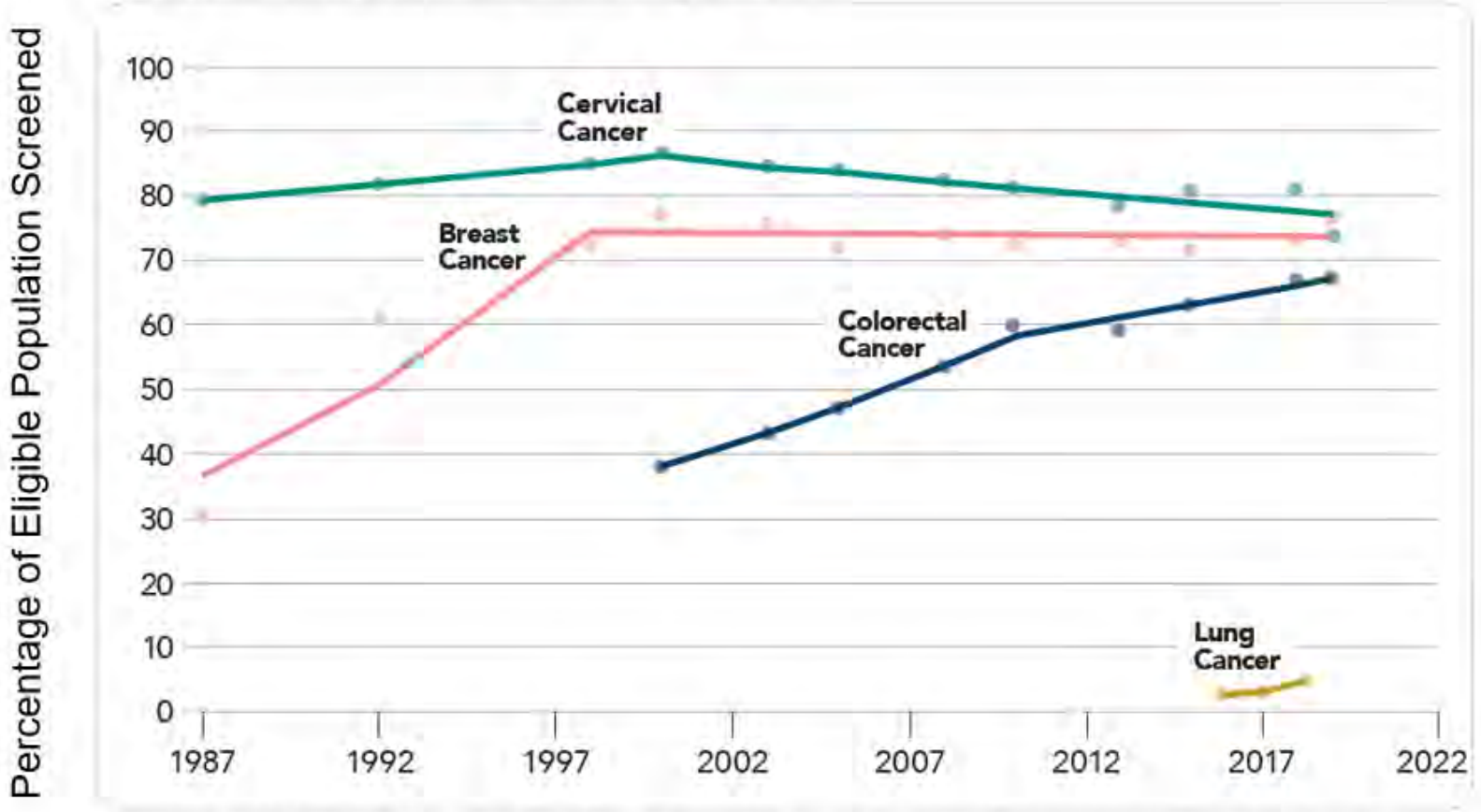
## USPSTF New Recommendations

- **New criteria would increase the relative percentage of persons eligible for screening by 87% overall**
  - 78% in White adults, 107% Black adults, and 112% in Hispanic adults compared with 2013 USPSTF criteria.
- **Increase the relative percentage of persons eligible for screening by 80% in men and by 96% in women.**

Agency for Healthcare Research and Quality; 2021.
AHRQ publication 20-05266-EF-2.

# Lung Cancer Screening

**Figure 1.** U.S. Cancer Screening Rates




Sources: National Cancer Institute. Available from http://progressreport.cancer.gov.
& Fedewa SA et al. J Natl Cancer Inst. 2021;113(8):1044-52. Figure by Chen M.

# National Failure

- **ALA survey of over 1,000 people eligible for LCS, only 15% aware that LCS is an essential health benefit and covered by most healthcare plans with no or minimal costs.**
- **The top reason why not screened their doctor never recommended it.**
- **3% of women cited lung cancer as a relevant health issue.**

https://www.lung.org/our-initiatives/lung-force/lung-health-barometer

## National Failure: Patient Communication

- Rates of Physician-Patient Discussions About Lung Cancer Screening **Very Low and Declining** (American Association for Cancer Research)
  - Prevalence of physician-patient discussions about lung cancer screening

**In 2012**

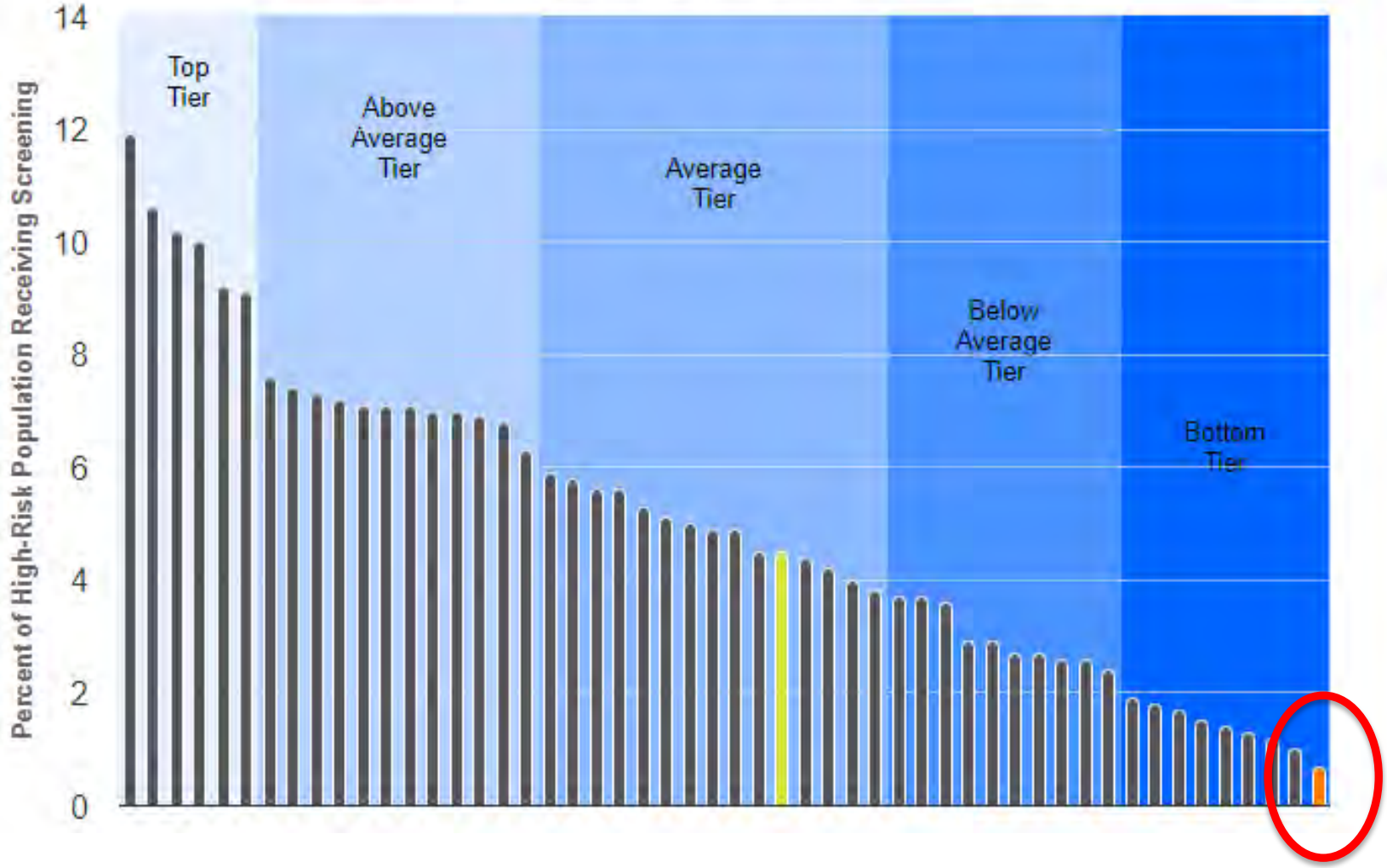
- 6.7% in the general population
- 12% among current smokers

**In 2017**

- 4.3% in the general population
- 8.7% among current smokers

American Lung Association
State of Lung Cancer
2023

## State Ranking by High-Risk Screening Rate




### Screening for High Risk:

- In California, **0.7%** of those at high risk were screened, which was **significantly lower** than the national rate of 4.5%.
- It ranks **51st** among all states, placing it in the **bottom tier**.
- Actual screening rates may be higher in states with large, regional managed care providers that did not share screening data.

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GOLDEN S
30
KINGS
5


CHASE CENTER
GOLDEN STATE WARRIORS Playoffs Watch Party
PRESENTED BY CHASE
65 66
PLAYOFFS
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HEDIS

# New Measure Coming for Lung Cancer Screening

November 15, 2022 · Andy Reynolds

**Description:** The Healthcare Effectiveness Data and Information Set (HEDIS) is a tool used by more than 90 percent of U.S. health plans to measure performance on important dimensions of care and service. More than 190 million people are enrolled in health plans that report quality results using HEDIS. Since 2008, HEDIS has also been available for use by medical providers and practices. Because so many health plans use HEDIS and because the measures are so specifically defined, HEDIS can be used to make comparisons among plans. To ensure that HEDIS stays current, the National Committee for Quality Assurance (NCQA) has established a process to evolve the measurement set each year through its Committee on Performance Measurement.

HEDIS

# New Measure Coming for Lung Cancer Screening

November 15, 2022 · Andy Reynolds

## Targeted Approach with Quality Goals

NCQA will look at how routine information shared in health encounters can help identify individuals who should get a lung cancer screening. Once implemented, this measure will help payers and providers steer a greater number of high-risk patents to lung cancer screenings, facilitate early detection, and ultimately reduce the number of deaths attributed to lung cancer.

We expect to develop the measure by the end of 2024.

- **Population Health**
  - Prevention
    - Radon awareness
    - Tobacco Recovery and Prevent
  - Screening
- **Treatments**
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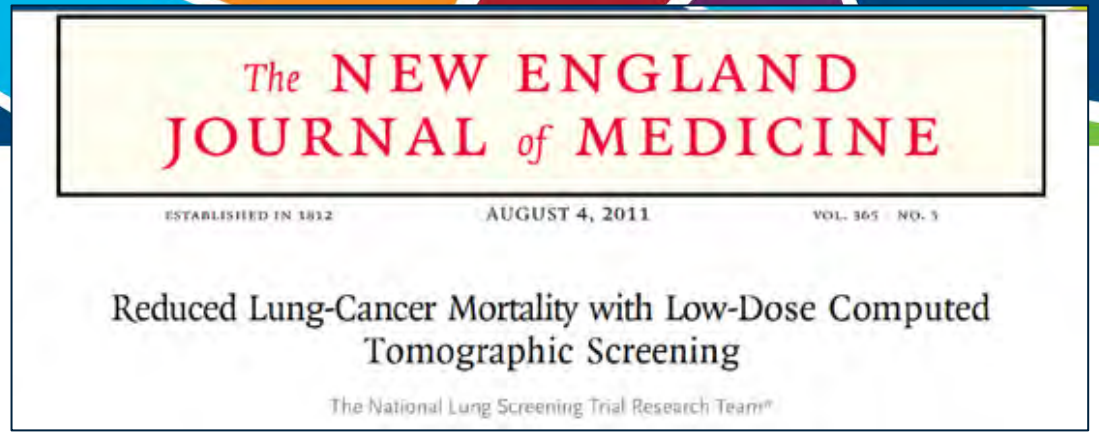


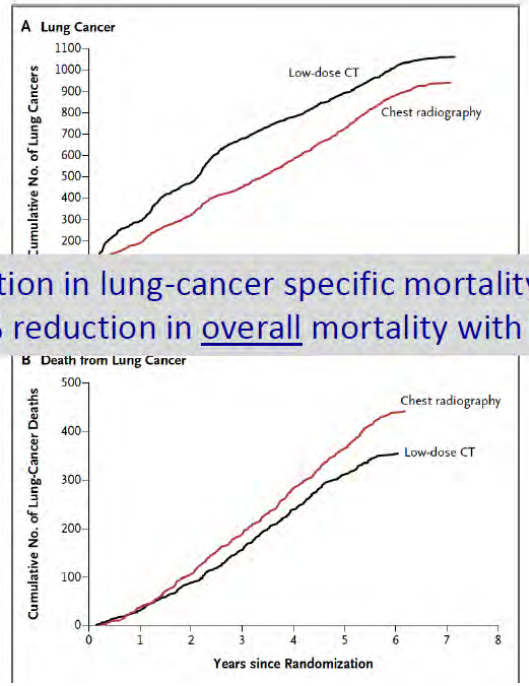


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# Outreach

UC DAVIS HEALTH UC Davis Health Lung Cancer Initiative

## HELP US BETTER UNDERSTAND, PREVENT, AND TREAT LUNG CANCER IN AFRICAN AMERICANS

David Tom Cooke, M.D., F.A.C.S.

David Cooke is the head of General Thoracic Surgery and an educator on lung cancer at UC Davis Health.

*"African Americans are diagnosed with and die from lung cancer more than any other demographic group in the United States. But that does not have to be the case. We have resources to eliminate those disparities!"*

UC DAVIS HEALTH Clinical and Translational Science Center

The CTSC at UC Davis has teamed up with the Lung Cancer Initiative to support lung cancer awareness and highlight research study oppoprtunities.

To see more information about Lung Cancer clinical research studies at UC Davis, visit https://studypages.com/ucdavis and search for "lung cancer".

## RISK


African Americans are more likely to get lung cancer, and more likely to die from it. African American men especially have an increased risk, and are 37 percent more likely to develop lung cancer despite a low overall exposure to cigarette smoke, the primary risk factor for lung cancer. But research tells us that if African Americans get screened and their disease is detected early, they have an equal chance at survival as other patients.

## LUNG CANCER SCREENING

Lung cancer screening with low-dose CT scanning for people at high risk was proven to be effective in 2011, and saves lives. Yet, of the more than 7.6 million Americans eligible for screening, only 2 percent have been screened. Most Americans don't know that lung cancer screening is covered by most health care plans, Medicare and Medi-Cal with minimal or zero costs.

The problem is that most doctors aren't recommending it. And like mammography for breast cancer, the eligibility criteria for lung cancer screening is well established. Any adult 55 to 80 who has a 30 pack-year history of smoking (equal to the number of packs smoked per day multiplied by the number of years smoked) and either smokes currently or has quit within the past 15 years is eligible.

Lung cancer screening is a game changer. Most lung cancers detected by the scan are stages I or II with the highest rate of cure, especially today with advanced treatments like minimally invasive surgery and targeted and immunotherapies.

Screening is easy, too. Low-dose CT is a special X-ray. A patient's doctor will order the scan after discussing the risks and benefits of the exam. It takes no more than 10 minutes. There are no needles involved. A radiologist reviews the scan and sends the results back to the doctor who ordered it. The patient typically learns the results within a few days. Lung cancer screening is accessible at UC Davis Health as part of our Comprehensive Lung Cancer Screening Program.

To see more information about lung cancer screening visit https://health.ucdavis.edu/surgery/specialties/cardio/lung_cancer_screen.html

## ALL YOU NEED TO GET LUNG CANCER ARE LUNGS

Although 80% of lung cancers are caused by tobacco exposures, 20% is not. Researchers have examined smoking behavior, workplace exposures, genetics, acce to health care, discrimination and social stress, as well as other possible contributors. The answer appears to be that lung cancer is also caused by a mix of biological, environmental, sociodemographic factors, including asbestos and radon exposure, poor air quality and unmeasured genetic factors.

## LUNG CANCER RESEARCH AT UC DAVIS

UC Davis has several clinical trials for lung cancer patients available at any given time. Clinical trials, also known as "clinical research studies", or "clinical studies", are studies in human volunteers that try to answer specific health questions. Some clinical trials measure the safety and effectiveness of potential new treatments. Other clinical trials observe health issues and behaviors in large groups of people.

The importance of enrollment in clinical trials is not to be underestimated. Studies have found that patients who have participated in lung cancer clinical trials exhibited a cancer specific survival benefit. However, people of color, especially African Americans are less likely to participate in lung cancer clinical trials.

References:


- https://www.lung.org/assets/documents/research/ala-lung-cancer-in-african.pdf
- https://health.ucdavis.edu/ctsc/area/clinicaltrials/documents/African-Americans-and-Clinical-Research.pdf
- C.J. Chow, E.B. Habermann, A. Abraham, et al. **Does enrollment in cancer trials improve survival?** J Am Coll Surg, 216 (2013), pp. 774-780 discussion 780-1
- N. Duma, J. Vera Aguilera, J. Paludo, et al. **Representation of minorities and women in oncology clinical trials: review of the past 14 years** J Oncol Pract, 14 (2018), pp. e1-e10


**Have questions about lung cancer screening and prevention?**

Call the UC Davis Comprehensive Lung Cancer Screening Program (CLSP) at (916) 734-0655. Monday-Friday 9 am to 5pm.

**Visit the CLSP Website**

To see more information about lung cancer screening https://health.ucdavis.edu/surgery/specialties/cardio/lung_cancer_screen.html

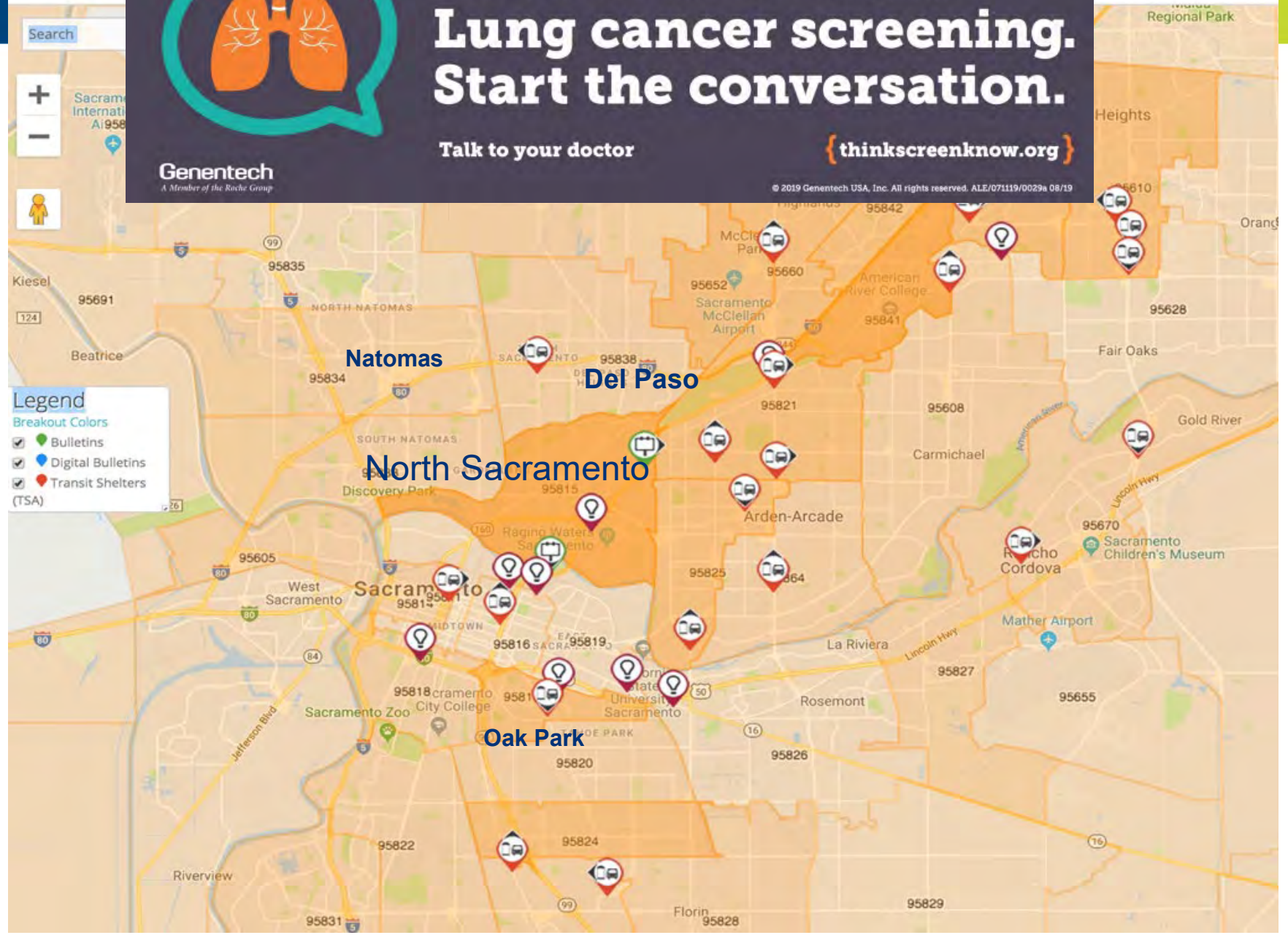
UC DAVIS HEALTH Clinical and Translational Science Center

UC DAVIS HEALTH

# Outreach


GOOD FIXINS ARE LIKE GOOD SONGS THEY SOOTHE
AND WARM THE SOUL
I'LL TAKE YOU THERE
AIN'T TO PROUD TO BEG
SOON AND VERY SOON
RN

# Outreach


If you are 55-80 years old and a current or former heavy smoker
Lung cancer screening.
Start the conversation.
Talk to your doctor
thinkscreenknow.org
Genentech
A Member of the Roche Group
© 2019 Genentech USA, Inc. All rights reserved. ALE/071119/0029a 08/19
Search
Legend
Breakout Colors
Bulletins
Digital Bulletins
Transit Shelters
(TSA)
Natomas
Del Paso
North Sacramento
Oak Park
Regional Park
Heights
Kiesel
95691
Beatrice
95835
NORTH NATOMAS
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SOUTH NATOMAS
Discovery Park
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95652
Sacramento McClellan Airport
American River College
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Sacramento City College
Sacramento Zoo
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Rosemont
La Riviera
Mather Airport
95827
95655
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95670
Sacramento Children's Museum
Rancho Cordova
Lincoln Hwy
Jefferson Blvd
95822
95824
Riverview
95831
Florin
95828
95829

# Outreach


IF YOU SMOKED:
This new lung cancer screening could save your life
SavedByTheScan.org
Ad Council
AMERICAN LUNG ASSOCIATION.
LUNG FORCE
TANNING
NAIL

# Outreach

Understanding Disparities in Lung Cancer - Episode 4

## Addressing Disparities in Lung Cancer Screening

November 24, 2020
Kristie L. Kahl

# Outreach Works!

**From:** [redacted]
**Sent:** Thursday, December 17, 2020 7:52 AM
**To:** Thoracic Surgery <thoracic@UCDAVIS.EDU>
**Subject:** Dr Cooke's article in Cure Magazine..

Hi Dr. Cooke,
As an African American female lung cancer survivor, I wanted to thank you for your article in Cure. I found it really informative and wish I had seen it before I was diagnosed. I'm actually one of the lucky ones. I saw the American Lung Association billboard on the side of Highway 880 as I drove home to Fremont from my job in San Jose. I'll always say that billboard saved my life because it made me aware of such a thing as a low dose CT scan. Being stuck in traffic, I read that early detection is important.

I won't go into how my PCP refused to order the test at first because she concluded that I "didn't meet the criteria". Suffice it to say " I persisted" and it saved my life. Although your interview was good, as a patient, I wish more doctors would mention that fear and stigma are just as much a barrier to getting screened and treated as a compromised health care system. I think we have to get people to realize and understand that early detection is key. Thank you for everything that you do.
—
[redacted]

UCDAVIS HEALTH | COMPREHENSIVE CANCER CENTER

# Educating the Next Generation

# Educating the Next Generation

AMERICAN LUNG CANCER SCREENING INITIATIVE

UC BERKELEY

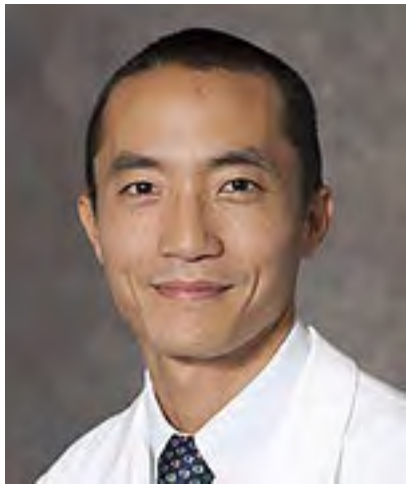
UC DAVIS

UC IRVINE

UC LOS ANGELES

# Patient Centered Outcomes Research

# Direct Patient Contact



Eric Wai Chak, M.D., M.P.H.

ADVANCING HIGH VALUE HEALTH CARE

THE AMERICAN JOURNAL of MEDICINE®

## Electronic Population Health Tools Enhance Preventive Care for Older Adults

Eric W. Chak, MD, MPH,[a] Elizabeth Cortez-Toledo, MA,[a] Randy Luna, BS,[b] Scott MacDonald, MD,[b] Susan L. Stewart, PhD,[c] David T. Cooke, MD,[d] Moon S. Chen Jr., PhD, MPH[e]

Title: Enhancing Electronic Health Systems to Decrease the Burden of Colon Cancer, Lung Cancer, Obesity, Vaccine-Preventable Illness, and Liver Cancer (CLOVER)
Project: GRANT12965631 (Chak)
Agency: National Institutes of Health

| CLOVER Parameter | Outcome Measure | #At-Risk | Baseline Adherence (Prior to August 2020) | CLOVER Adherence (August 2020-May 2021) | Relative Change |
|---|---|---|---|---|---|
| Lung Cancer | CT Lung Completion | 280 | 6% | 18.9% | 315% |

# Direct Patient Contact

**Dr. Chak's CLOVER Lung Screening component**

- Scott MacDonald's team (Randy Luna) created custom Epic Workbench report
- Report contains all Smokers at Carmichael, for example, with upcoming appointments
- Staff member (Pre-visit planner-PVP) reaches out to patients with upcoming appointments with PCP (1-2 weeks in advance) to discuss and verify smoking History prior to upcoming appointment and updates smoking Hx in Epic
- Report is not granular enough to meet all the specific requirements to identify if the patient meets screening criteria and reason for staff needing to call pt to identify missing information.
- Once the staff member speaks to patient and verifies correct history and they meet criteria they are scheduled to either have a phone call by Dr. Chak or sent to the Cancer center Lung Ca screening staff for counselling/informational session
- If patient agrees to screening Dr. Chak places CT order. The PVP follows up to make sure the CT is completed, acts as a patient navigator.
- Results go to PCP and ordering provider
- Results are followed up—PCP always involved—

**Eric W Chak**
I'll add here that it is the smoking history in the EHR that is usually inaccurate. It is not regularly updated so we are trying to update/correct it to ensure that are truly LCS candidates.

**Eric W Chak**
The results go to the ordering provider (may not be PCP), but we always forward result to PCP to keep them in the loop.

# Strategic pillars

- Develop a Regional System of Care
- Deliver Exceptional Patient and Care Team Experiences
- Advance Health Equity and Address Disparities
- **Develop and Grow Integrated, Patient-Centric Service Lines**

# What is an Integrated Service Line?

- An Integrated Service Line (ISL) is the organization of **multidisciplinary clinical programs** into an integrated **care continuum around a population or disease state**.

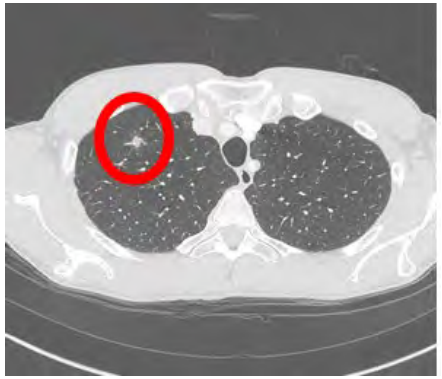
- Service lines reach beyond the traditional departmental structure in that the **accountability and responsibility for optimizing clinical services**, non-clinical operations, and capital and operational budgets reside with service line leadership (may be matrixed with clinical departments and operations).

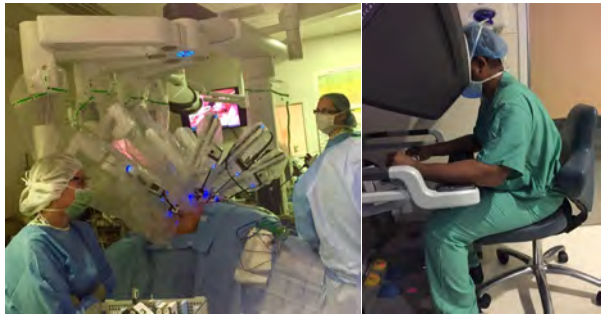
# Why Build a Patient-Centered Service Line?

- A service line structure is intended to provide a more **integrated and focused patient experience** while contributing to clinical efficiencies, clinical research, performance improvement, and expansion and integration of clinical areas with high market demand.

# UC Davis Health &
# Lung Cancer Integrated Service Line
## Trust – Simple - Peace of Mind

James gets a lung cancer screening CT and finds an early staged lung cancer.





Charles' incidental lung cancer is diagnosed at an early stage and cured.

Linda and her family are happy with the speed of her diagnosis & ease of her care. They want to give back to UC Davis.

Sarah's doctor is amazed how fast her referrals get into UC Davis.

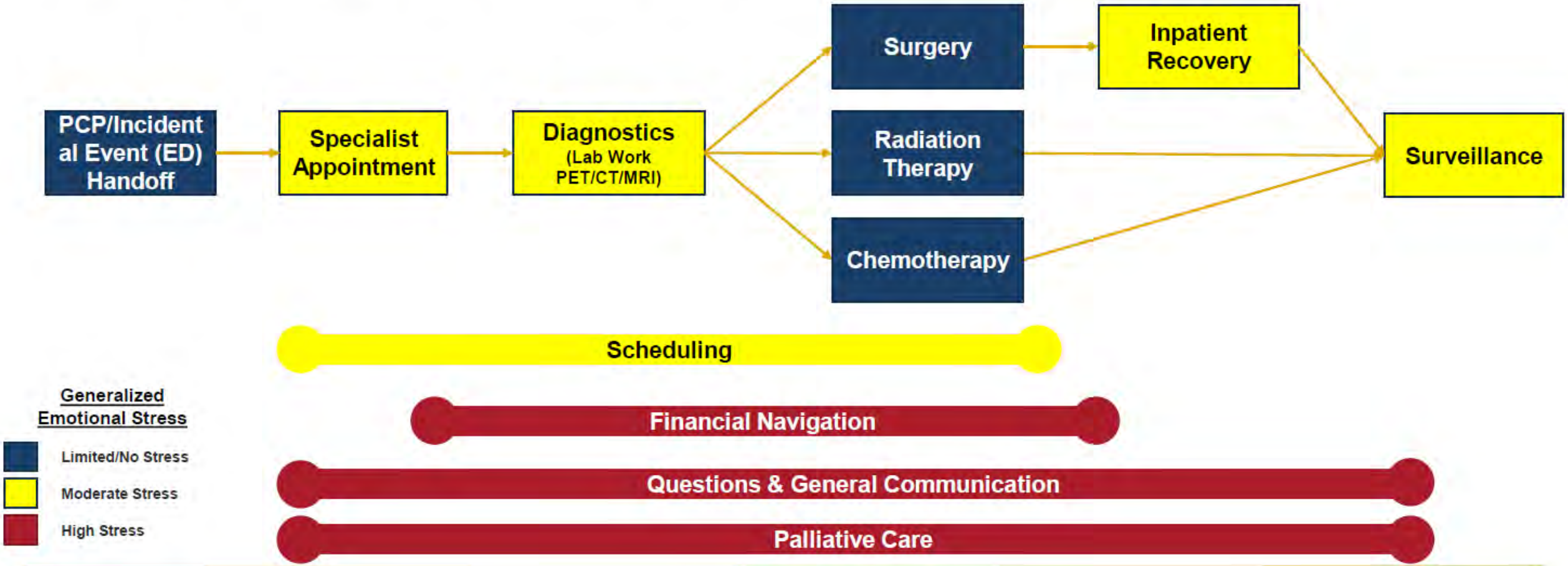
David Tom Cooke, MD
Assoc. Physician Lead

Jonathan Riess, MD
Physician Lead

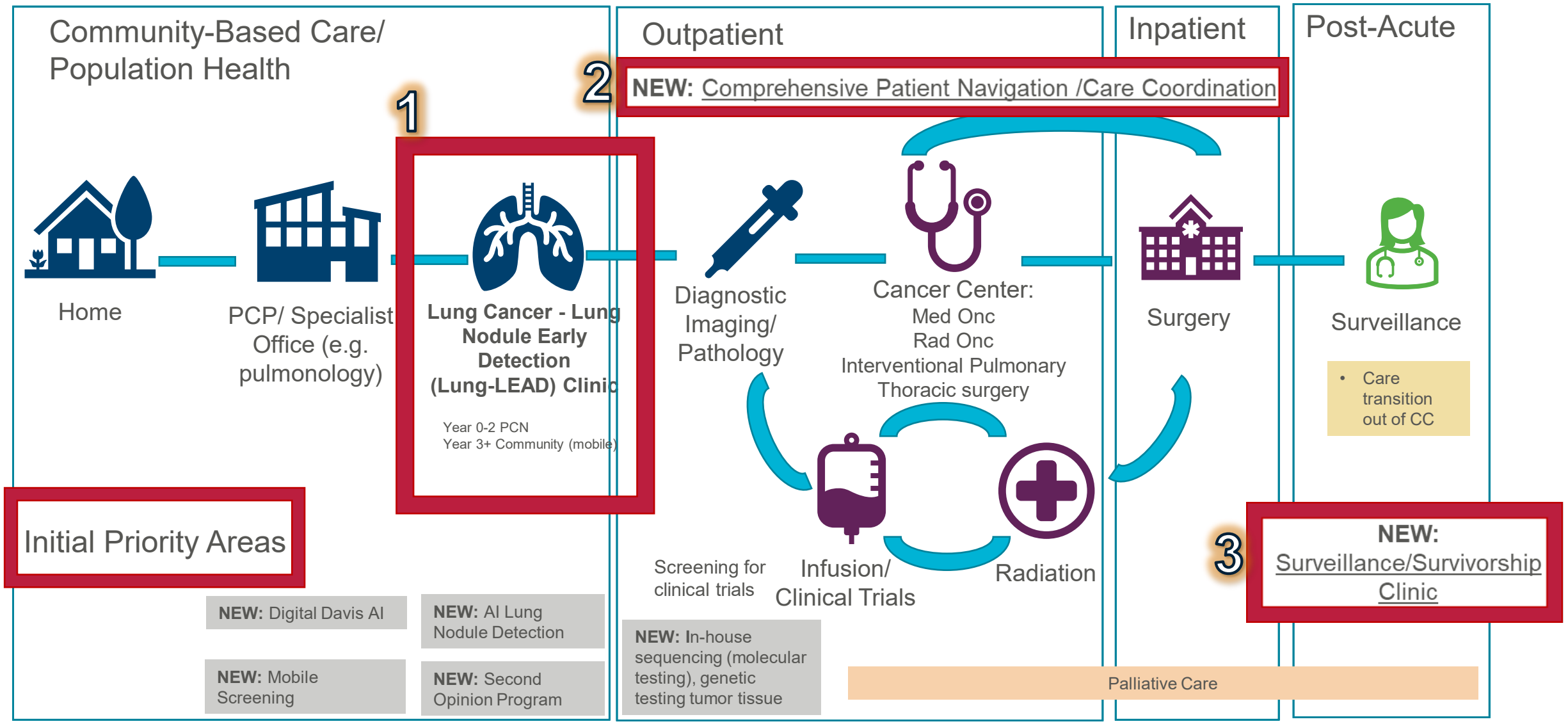
Kristin Mensonides, MHA, MLS
Executive Director

# Top-Level Areas of Friction

**This visual is designed to highlight areas of fiction patients faced in their experiences. These colors correspond to report details and highlight areas of emotional stress specific to their experiences.**



# Lung Cancer ISL Care Continuum



# Initial Priority Areas

1. Community-Based Care/Population Health
   - Lung Cancer - Lung Nodule Early Detection (Lung-LEAD) Clinic

     Increase the LDCT screening rate of patients, centralize management of incidental lung nodules, encourage active surveillance of LDCT screening patients and incidental findings, improve upon smoking cessation efforts.

2. Outpatient
   - Comprehensive Patient Navigation – Care Coordination

     Align and expedite testing and results to ensure meaningful treating provider and accelerated path from new patient referral, initiation of treatment, and navigation of care. Focused on patients **diagnosed** with lung cancer, and patients **highly suspected of having** lung cancer.

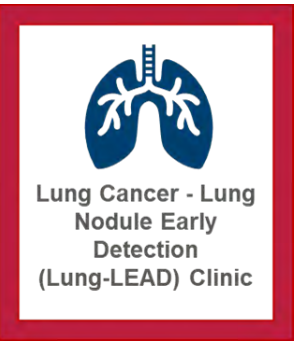
3. Post-Acute
   - Surveillance/Survivorship Clinic

     Transition long-term follow-up/surveillance patients from the treating provider schedule to APP, opening provider template to new patient appointments and expand access to the Cancer Center.

# Lung Cancer - Lung Nodule Early Detection (Lung-LEAD) Clinic

1

1. Patient Review Criteria
   - Established patients with an upcoming PCP appointment with UCDH will be flagged for review if they are aged 50-80 (77 Medicare) and have a history of smoking (as reported in EPIC)
2. Dedicated Lung Cancer ISL Care Navigators
   - Our Lung Cancer ISL Care Navigators will proactively engage with patients to update smoking history, determine patients for lung cancer screening eligibility (age, pack year history, current smoker/quit date), and schedule appointments with the Lung ISL APP in the Lung Early Detection Clinic.




3. Dedicated Lung Cancer ISL APPs
   - The Lung Cancer ISL APP will conduct a shared-decision making (SDM) visit and order a Low Dose CT (LDCT) for eligible patients who want to proceed with screening.
   - The Lung Cancer ISL APP will complete a follow-up visit with all patients to communicate results, ongoing follow-up (immediate or annual), and will order additional tests / referrals as needed based standardized clinical criteria
4. Communication and Results
   - The patient's primary care physician will be cc'd on the Lung Cancer ISL APP provider chart note if the patient meets with the Lung Cancer ISL APP
   - If the LDCT shows significant screening results, these will be directly communicated to the patient's primary care physician

# Workflow: Lung - LEAD Clinic (Comprehensive Lung Cancer Screening Program)

1

## Patient Review Criteria

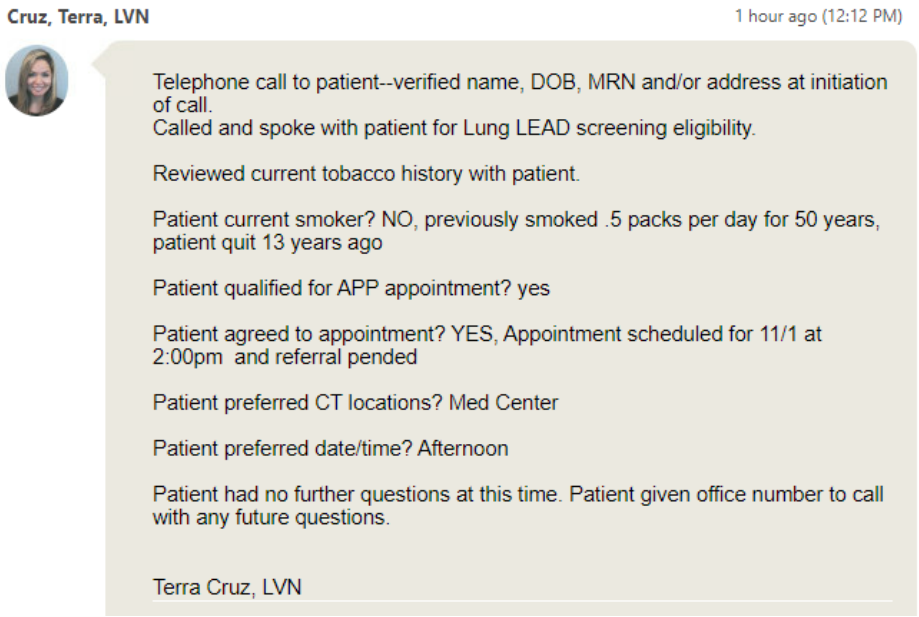
- Established patients with an upcoming PCP appointment with UCDH are flagged for review if they are aged 50-80 (77 Medicare) and have a history of smoking (as reported in EPIC)

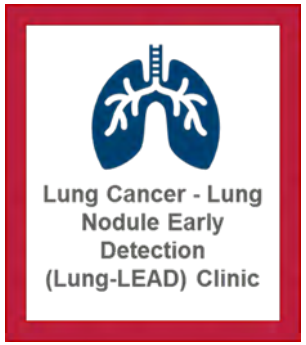
## Dedicated Lung Cancer ISL Care Navigators

- Our Lung Cancer ISL Care Navigators proactively engage with patients to update smoking history, determine patients for lung cancer screening eligibility (age, pack year history, current smoker/quit date), and schedule appointments with the Lung ISL APP in the Lung – LEAD Clinic.

LVNs

- Terra Cruz
- Keilani Guevarra
- Ananeiri Medina
- Maria Quadra
- Christine Ramil-Francisco




Chak EW, et al. Am J Med. 2022 Jul;135(7):840-843.

# Workflow: Lung - LEAD Clinic (Comprehensive Lung Cancer Screening Program)

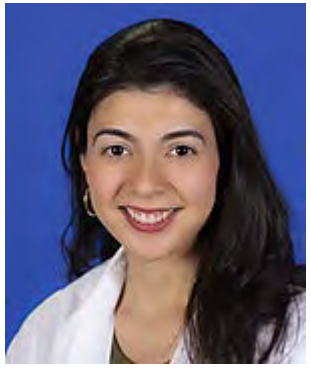
1

Dedicated Lung Cancer ISL APPs

- The Lung Cancer ISL APP conduct a shared-decision making (SDM) visit and order a Low Dose CT (LDCT) for eligible patients who want to proceed with screening.
- The Lung Cancer ISL APP complete a follow-up visit with all patients to communicate results, ongoing follow-up (immediate or annual), and order additional tests / referrals as needed based standardized clinical criteria.

APPs

- Paola Velosa, NP
- Jennifer Aldred, NP
- Jaspreet Dhillon, NP



Lung Cancer - Lung Nodule Early Detection (Lung-LEAD) Clinic

Chak EW, et al. Am J Med. 2022 Jul;135(7):840-843.

# Workflow: Suspected Lung Cancer, Lung-LEAD Clinic patient w/ Findings

1, 2

Comprehensive Patient Navigation/Care Coordination

- The patient's primary care physician is cc'd on the Lung Cancer ISL APP provider chart note if the patient meets with the Lung Cancer ISL APP
- If the LDCT shows significant screening results, these are directly communicated to the patient's primary care physician
- Highly suspicious nodules and suspected masses are managed by the Lung Cancer ISL and its Comprehensive Patient Navigation Team, including DGIM clinician, Nurse Coordinator/Patient Navigator and MA II Care Navigator.

Erin Noren, MD, MS
Assistant Director,
DGIM Cancer Center Initiatives

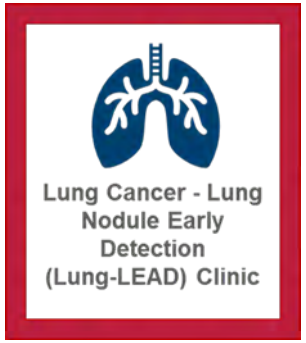
Angela Mackie, RN, Nurse Coordinator/Patient Navigator

Shalini Paul, MAII Navigator

Lung Cancer - Lung Nodule Early Detection (Lung-LEAD) Clinic

# Lung - LEAD Clinic Results

| To Date | Total |
|---|---|
| Calls Made | 1147 |
| Patients Called | 721 |
| Agree to SDM Appointment & Screening | 169 (48.29%) |



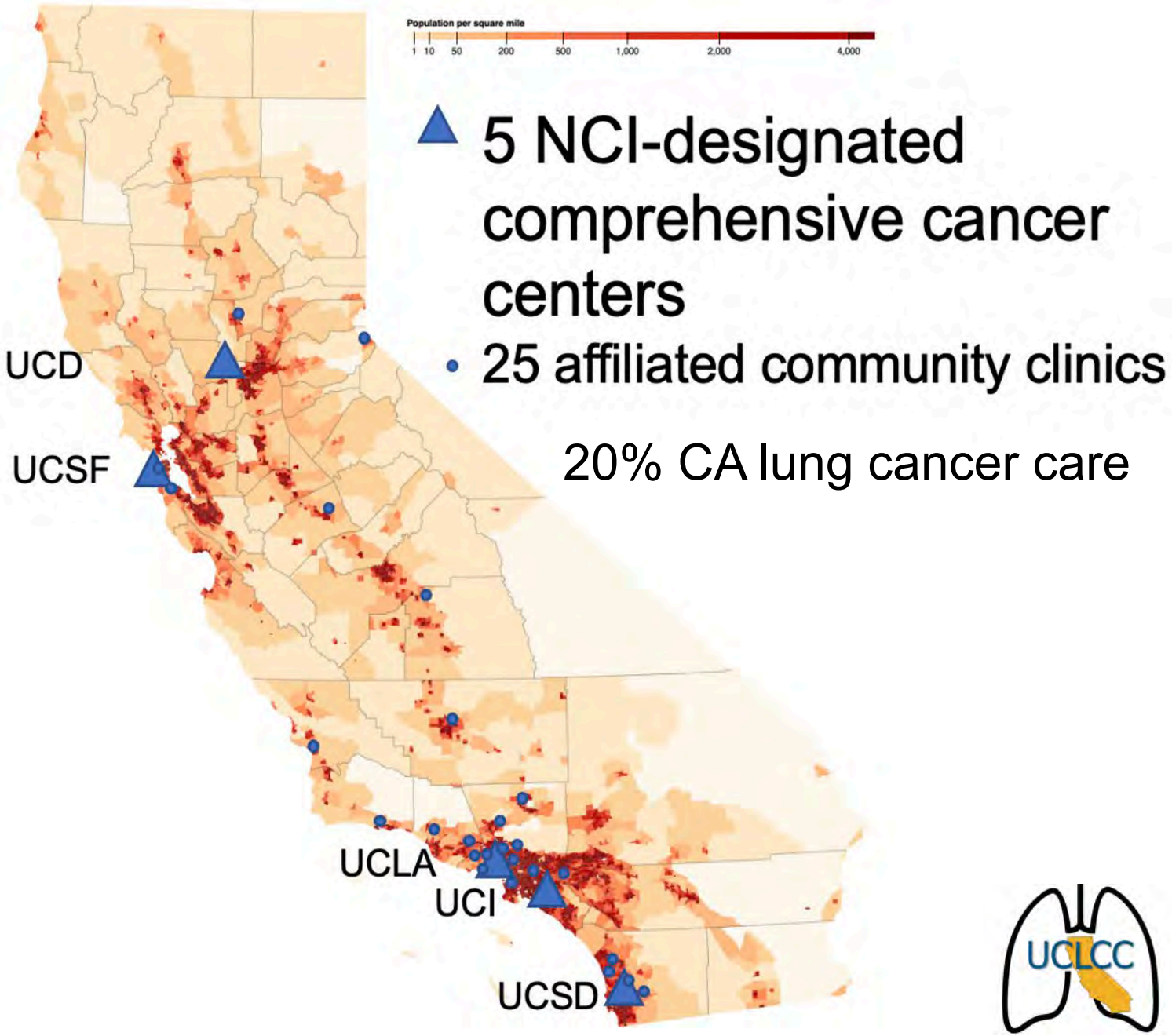
As of 10/31/2023

Current smokers with LCS (CPT 71271) in the last 12 months

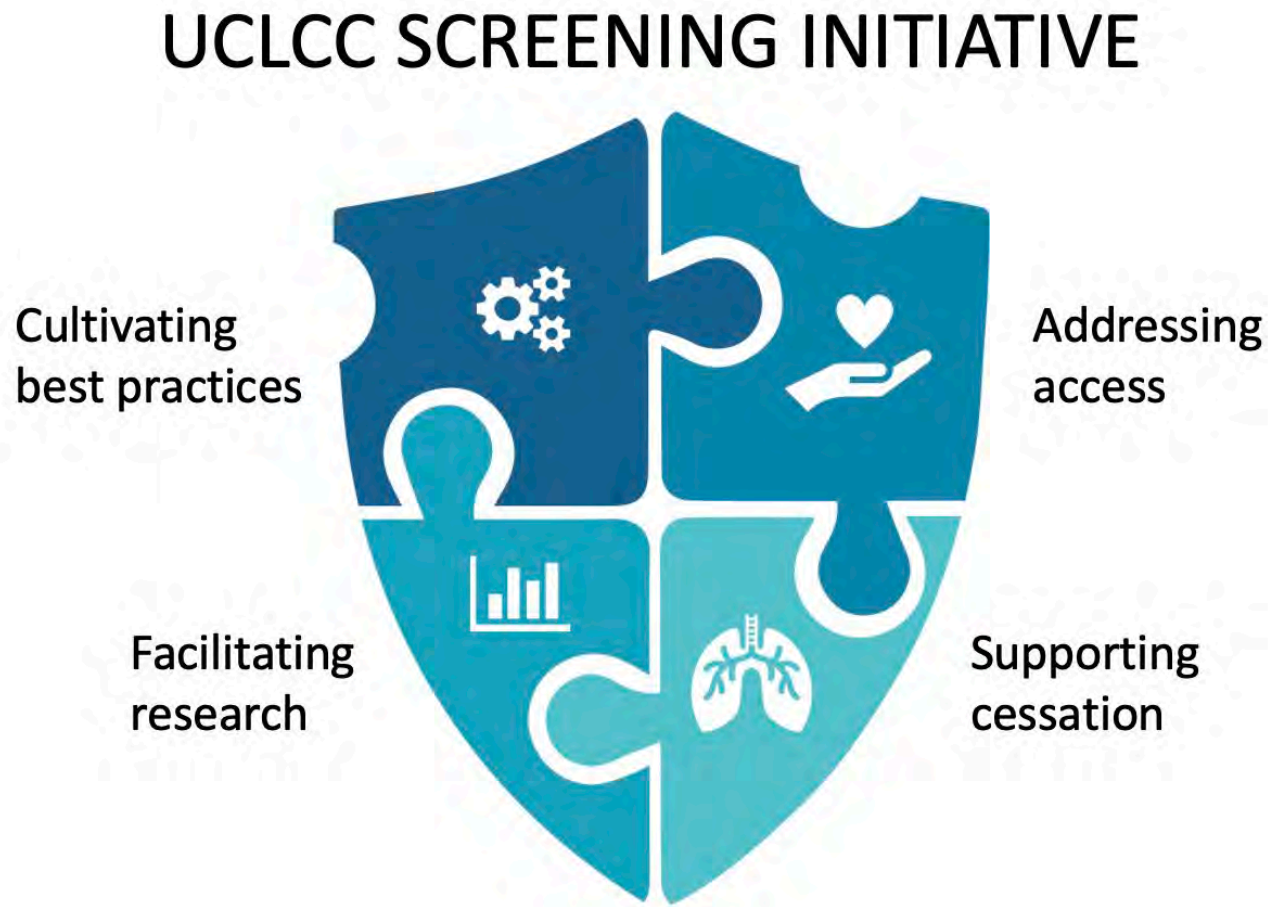

Former smokers with LCS (CPT 71271) in the last 12 months

# Take Lessons Learned and Disseminate Statewide

# University of California Lung Cancer Consortium (UCLCC)



# Specific Aims – Strategic Plan



# Next: Project Deep Dive

- 5 Campus Screening and Tobacco Cessation Dashboard Project
- California Digital Health Project

UNIVERSITY OF CALIFORNIA Lung Cancer Consortium

About | Screening Locations | Resources | Languages | Login

# Take the Lung Cancer Screening Questions

Two minutes could save your life. Find out if you should screen for lung cancer through UC Screen CA.

Start UC Screen CA  Learn More →

**https://www.ucscreenca.org**

UC DAVIS HEALTH

# Summary

- Lung cancer screening saves lives
- Eligible patients are not being screened
- Intentional efforts can move the needle to increase screening

# Patient Promise: **Patients are** at the center of everything we do.


UC DAVIS HEALTH

# Advances in Smoking Cessation

**Elisa Tong, MD, MA**
**Professor**
**UC Davis**

Elisa Tong is a Professor of Internal Medicine at UC Davis. Her research focus is in tobacco cessation and policy, with special interests in cancer and population health. She completed her medical degree at Stanford University, residency training at Santa Clara Valley Medical Center, and research fellowship at UCSF. She is the Principal Investigator for CA Quits and Director for the Tobacco Cessation Policy Research Center.

# ADVANCING TOBACCO CESSATION TREATMENT

Elisa Tong, MD, MA

Director, Tobacco Cessation Policy Research Center

Medical Director, Stop Tobacco Program, UC Davis Comprehensive Cancer Center

Professor of Internal Medicine, UC Davis

California Thoracic Society

# RELEVANT FINANCIAL DISCLOSURES

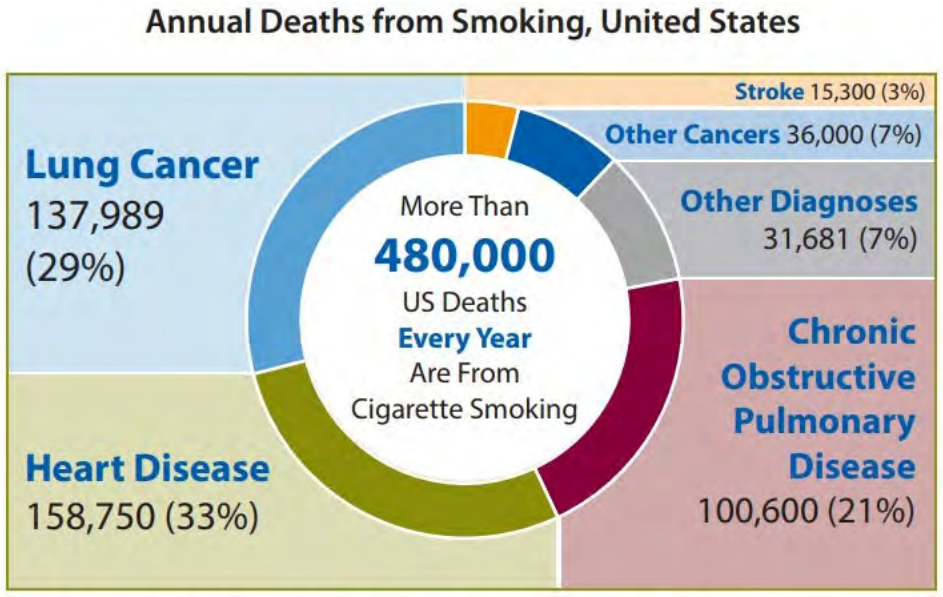
- I do not have relationships with ACCME defined ineligible companies
- I WILL NOT discuss off-label use and/or investigational use of any drugs or devices.
- Funding:
  - "CA Quits", California Tobacco Prevention Program, California Department of Public Health 22-10340
  - "Tobacco Cessation Policy Research Center", Tobacco-Related Disease Research Program T33PC6880

California Thoracic Society

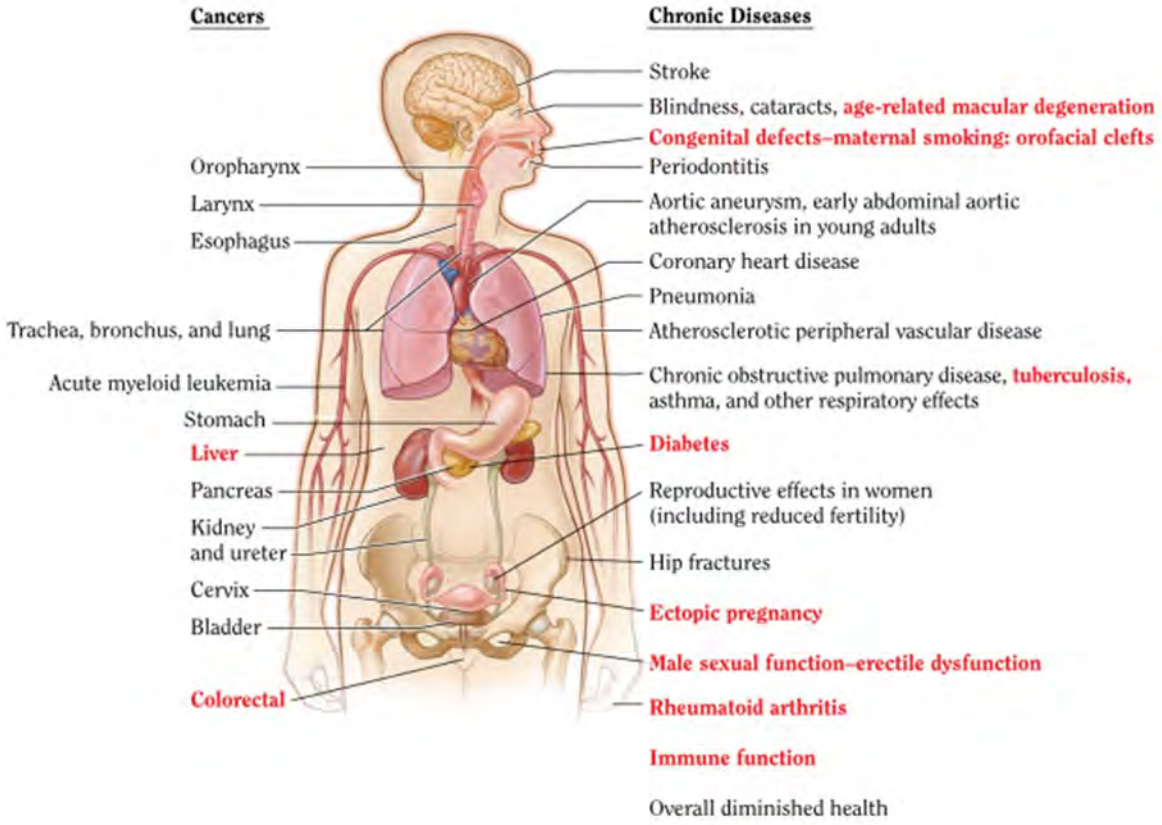
# OBJECTIVES

- **Understand the tobacco industry impact on public health**
- Describe a framework for tobacco assessment and treatment
- Identify strategies for improving tobacco assessment and treatment

# LEADING CAUSE OF DEATH AND DISEASE



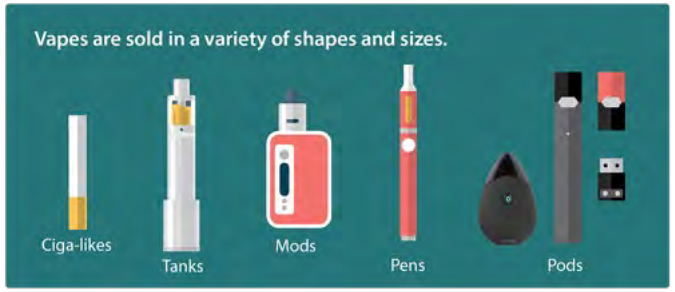

Note: Average annual number of deaths for adults aged 35 or older, 2005–2009.
Source: 2014 Surgeon General's Report, Table 12.4, page 660.




www.cdc.gov; Surgeon General 2014 https://www.hhs.gov/surgeongeneral/reports-and-publications/tobacco/consequences-smoking-factsheet/index.html

California Thoracic Society

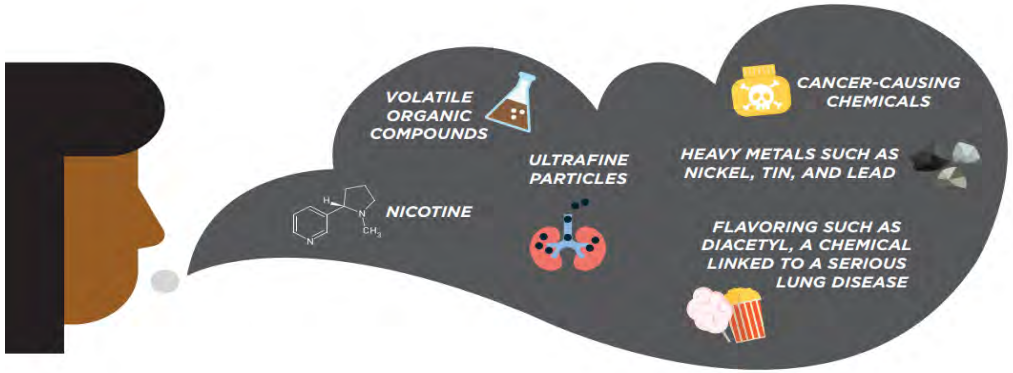
# NEW PRODUCTS, NEW PROBLEMS



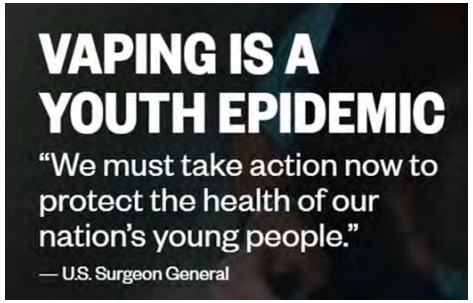

## New Nicotine Salts

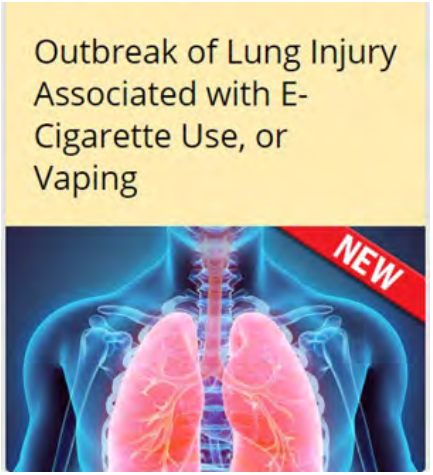
Nicotine salts, which have a lower pH than free base nicotine, allow particularly high levels of nicotine to be inhaled more easily and with less irritation to the throat than freebase nicotine.

THE E-CIGARETTE AEROSOL THAT USERS BREATHE FROM THE DEVICE AND EXHALE CAN CONTAIN HARMFUL AND POTENTIALLY HARMFUL SUBSTANCES:




It is difficult for consumers to know what e-cigarette products contain. For example, some e-cigarettes marketed as containing zero percent nicotine have been found to contain nicotine.




https://www.cdc.gov/tobacco/basic_information/e-cigarettes/index.htm

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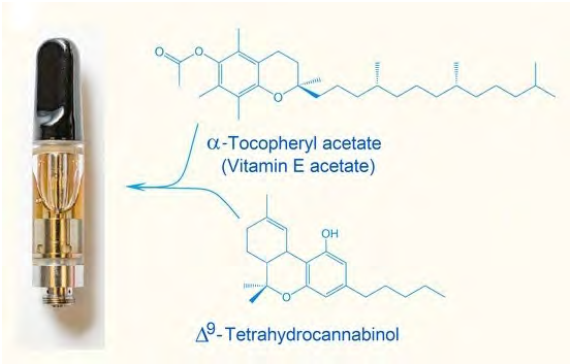
# BIOLOGICAL EFFECTS






RESEARCH ARTICLE | CHEMISTRY

**Potential for release of pulmonary toxic ketene from vaping pyrolysis of vitamin E acetate**

Dan Wu and Donal F. O'Shea | Authors Info & Affiliations

Edited by Scott H. Randell, The University of North Carolina at Chapel Hill, and accepted by Editorial Board Member Brigid L. Hogan February 11, 2020 (received for review December 3, 2019)

March 10, 2020 | 117 (12) 6349-6355 | https://doi.org/10.1073/pnas.1920925117

*Am J Physiol Lung Cell Mol Physiol* 316: L470–L486, 2019.
First published January 3, 2019; doi:10.1152/ajplung.00304.2018.

RESEARCH ARTICLE | *Electronic Cigarettes: Not All Good News?*

**Cinnamaldehyde in flavored e-cigarette liquids temporarily suppresses bronchial epithelial cell ciliary motility by dysregulation of mitochondrial function**

Phillip W. Clapp,[1,2] Katelyn S. Lavrich,[1] Catharina A. van Heusden,[4] Eduardo R. Lazarowski,[4] Johnny L. Carson,[2,3] and Ilona Jaspers[1,2,3]

September 16, 2019

**Risk Analysis for the Carcinogen Pulegone in Mint- and Menthol-Flavored e-Cigarettes and Smokeless Tobacco Products**

Sairam V. Jabba, DVM, PhD[1]; Sven-Eric Jordt, PhD[1]

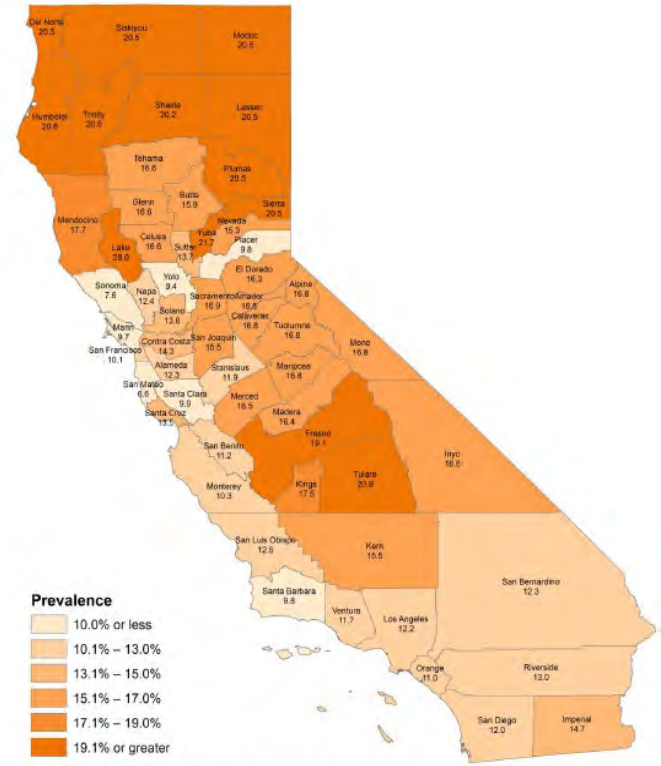
» Author Affiliations | Article Information

*JAMA Intern Med.* 2019;179(12):1721-1723. doi:10.1001/jamainternmed.2019.3649

Duffy et al. Toxics 2020 www.mdpi.com/2305-6304/8/1/8; CDC 2024, IARC Monograph 2016; Vol. 108;

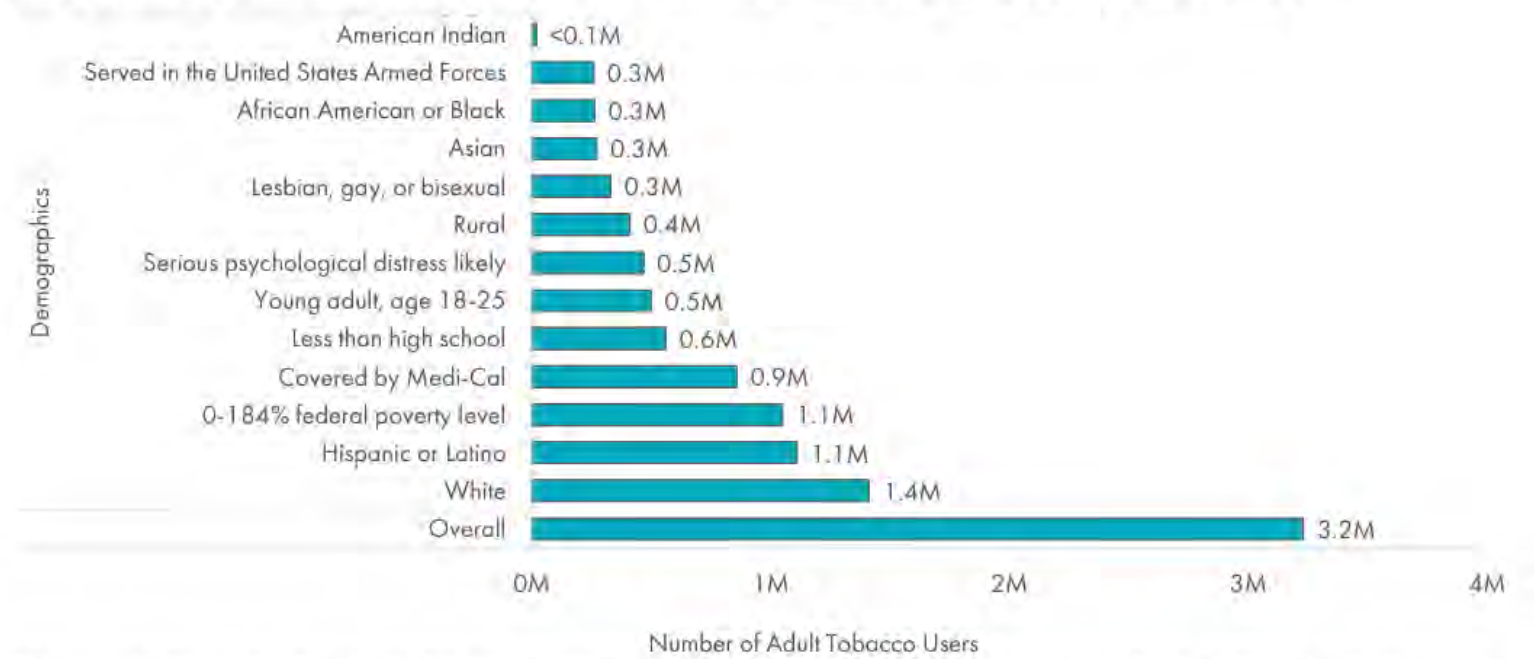
California Thoracic Society

# CALIFORNIA: 3.2 MILLION TOBACCO USERS




Note: Respondents aged 18+ were asked to report current cigarette smoking behavior.
Source: California Health Interview Survey, 2012–2014.

**Figure 3. Number of adults ≥18 years who reported current tobacco use—California Health Interview Survey, 2020-21**




Tobacco use includes cigarettes, cigars, hookah, little cigars or cigarillos, smokeless tobacco products, or vapes. Racial groups include only non-Hispanic or Latino of a single race unless otherwise noted. Hispanic or Latino includes all racial groups. See Additional Notes section for more information.

Source: California Health Interview Survey. CHIS 2020 and CHIS 2021 Adult Files. Los Angeles, CA: UCLA Center for Health Policy Research; October 2022.

https://www.cdph.ca.gov/Programs/CCDPHP/DCDIC/CTCB/CDPH%20Document%20Library/ResearchandEvaluation/FactsandFigures/CaliforniaTobaccoFactsAndFigures2022.pdf

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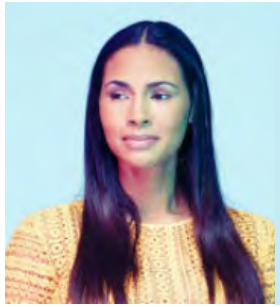
# TOBACCO USE = A HEALTH EQUITY ISSUE

## African American/Black

There are up to 10 times more tobacco ads in **African American/Black** neighborhoods than in others.



## American Indian

The tobacco industry appropriates **American Indian** cultures in marketing, using valued traditions to promote tobacco use.

## Hispanic/Latino

Big Tobacco gave $75,000 to the **Hispanic American** Chamber of Commerce to mail 92,000 letters urging businesses to protest tobacco tax increases.

## Asian/Pacific Islander

A Tobacco executive stated that **Asian American** populations would be a profitable target due to "this community being generally predisposed toward smoking."

## Low-income

Big Tobacco targeted children living **in low-income** housing projects by handing our free packs of cigarettes in the 50s.

## LGBTQ

In 1995, a tobacco company created a targeted marketing plan for **Lesbian, Gay, Bisexual, Transgender, Queer (LGBTQ) communities** called "Project SCUM".

## People with Mental Challenges

Big Tobacco promoted cigarettes as a medicinal substance in **behavioral** health treatment facilities.

## Rural Communities

Big Tobacco warps rural masculine ideals by depicting rugged images of cowboys, hunters, and racecar drivers in their advertising, making people living in **rural communities** some of Big Tobacco's best customers.

https://tobaccofreeca.com/story-of-inequity/

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# HARM TO NONSMOKERS & ENVIRONMENT

**The U.S. Surgeon General has concluded that breathing even a little secondhand smoke poses a risk to your health.**

- Scientific evidence indicates that there is no risk-free level of exposure to secondhand smoke.

The U.S. Surgeon General Concluded that Aerosol from E-Cigarettes Can Contain Harmful Substances





tobaccofreeca.com; https://www.cdc.gov/tobacco/infographics/secondhand-smoke/index.htm; sacbreathe.org/tobacco-litter/; https://www.cdph.ca.gov/Programs/CCDPHP/DCDIC/CTCB/CDPH%20Document%20Library/Community/EducationalMaterials/DisposalofE-CigarettesPUBLIC.pdf

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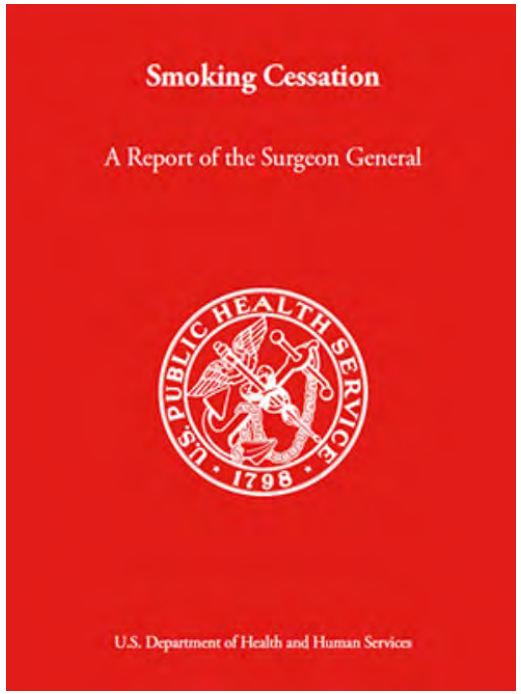
# QUITTING HAS IMMEDIATE HEALTH BENEFITS





www.cdc.gov/tobacco/sgr/2020-smoking-cessation/index.html

https//smokefree.gov

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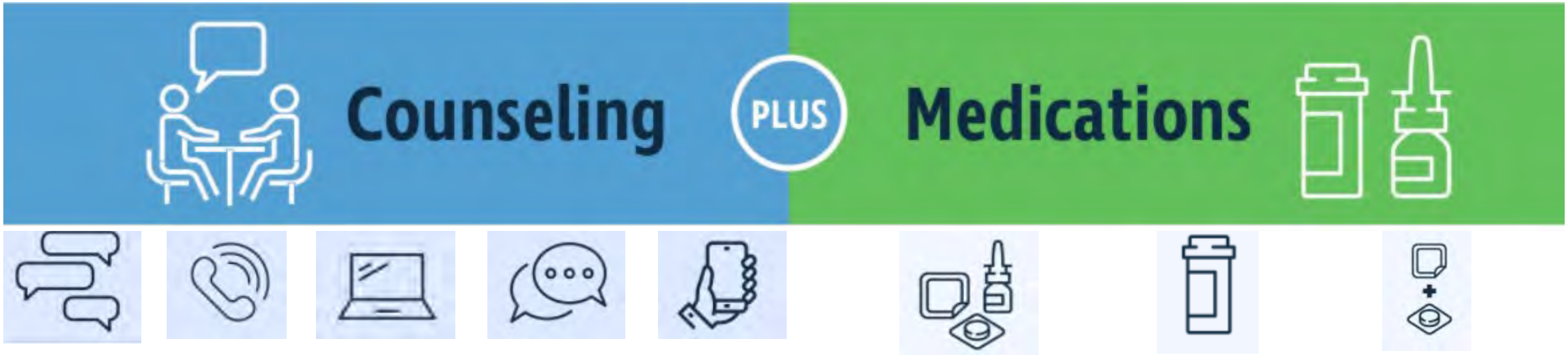
# OBJECTIVES

- Understand the tobacco industry impact on public health
- **Describe a framework for tobacco assessment and treatment**
- Identify strategies for improving tobacco assessment and treatment

# STRONG EVIDENCE FOR TOBACCO TREATMENT




U.S. Preventive Services
TASK FORCE

https://www.cdc.gov/tobacco/quit_smoking/how_to_quit/index.htm; https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/tobacco-use-in-adults-and-pregnant-women-counseling-and-interventions

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# THE FIVE A'S → ASK ADVISE REFER

**ASK** → about tobacco USE and EXPOSURE

**ADVISE** → tobacco users to QUIT

**REFER** to quitline or other resource

- **ASSESS** → READINESS to make a quit attempt
- **ASSIST** → with the QUIT ATTEMPT
- **ARRANGE** → FOLLOW-UP care

Adapted from rxforchange.ucsf.edu

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# **ASK:** "HAVE YOU EVER USED TOBACCO OR NICOTINE PRODUCTS?" (CURRENT=PAST MONTH)

## SMOKING

Blunt = tobacco leaf + cannabis

## SMOKELESS

Moist snuff

Dry snuff

Snus


Loose Chewing Tobacco

Plug Chewing Tobacco

## ECIGS or VAPES


***Now included in the CMS eCQI Tobacco quality metric**

**"Do you use nicotine, cannabis (THC, CBD), or flavors?"**

CA Quits; Images: CDC, FDA, California Youth Advocacy Network

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# ASK: WITH LUNG CANCER SCREENING ABOUT RECENT USE AND EXPOSURE

**Assessment and Counseling Gaps Among Former Smokers Eligible for Lung Cancer Screening in US Adults**

**A Cross-Sectional Analysis of National Health and Nutrition Examination Surveys (NHANES), 2013–2018**

*Eve Angeline Hood-Medland, MD[1], Melanie S. Dove, ScD[2], and Elisa K. Tong, MD, MA[1]*

J Gen Intern Med
DOI: 10.1007/s11606-022-07542-0


If you ask: "**Do you smoke now**?"

Patient answers: "**No**" → Former smoker?

Actually, nearly 1.5 million "Former Smokers" may be misclassified by asking this way and are actually "Current Tobacco Users"

- About 1 in 5 "Former Smokers" had recent tobacco use past 5 days or higher **cotinine**
- 53% of Former Smokers *without* recent tobacco use had recent exposure by cotinine

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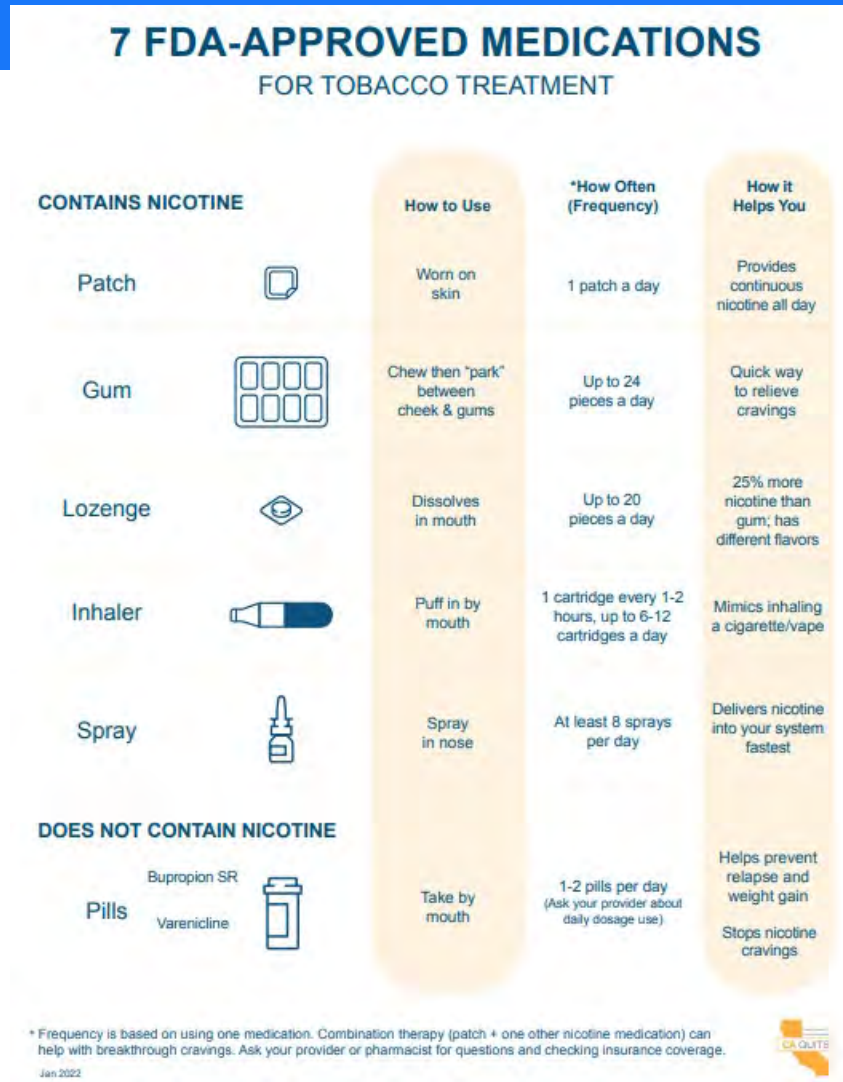
# **ASSIST:** CESSATION MEDICATIONS



## 7 FDA-APPROVED MEDICATIONS
FOR TOBACCO TREATMENT

| | How to Use | *How Often (Frequency) | How it Helps You |
|---|---|---|---|
| **CONTAINS NICOTINE** | | | |
| Patch | Worn on skin | 1 patch a day | Provides continuous nicotine all day |
| Gum | Chew then "park" between cheek & gums | Up to 24 pieces a day | Quick way to relieve cravings |
| Lozenge | Dissolves in mouth | Up to 20 pieces a day | 25% more nicotine than gum; has different flavors |
| Inhaler | Puff in by mouth | 1 cartridge every 1-2 hours, up to 6-12 cartridges a day | Mimics inhaling a cigarette/vape |
| Spray | Spray in nose | At least 8 sprays per day | Delivers nicotine into your system fastest |
| **DOES NOT CONTAIN NICOTINE** | | | |
| Pills: Bupropion SR, Varenicline | Take by mouth | 1-2 pills per day (Ask your provider about daily dosage use) | Helps prevent relapse and weight gain<br>Stops nicotine cravings |

* Frequency is based on using one medication. Combination therapy (patch + one other nicotine medication) can help with breakthrough cravings. Ask your provider or pharmacist for questions and checking insurance coverage.

Jan 2022

CA QUITS

1 mg nicotine ~ 1 cigarette

20 cigarettes in 1 pack

1 smokeless can/week ~ 1 pack

Dose higher for "eye-opener" use (1st 5 min)

## Combination Nicotine

Long-acting patch (7, 14, 21 mg)

Short-acting lozenge/gum (2 or 4 mg)

Rxforchange.ucsf.edu; veterans.smokefree.gov/tools-tips-vet/quit-for-good-with-nrt

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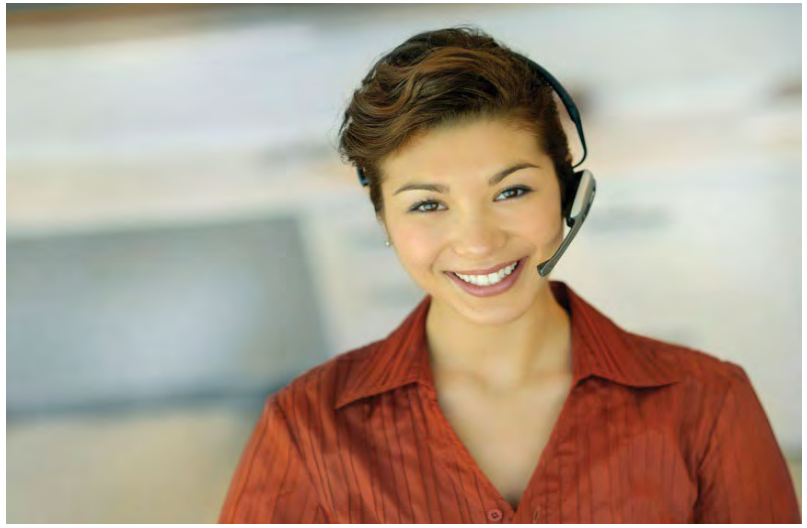
# **REFER:** "I'M GOING TO HAVE OUR FREE STATE QUITLINE CALL YOU"



UCDAVIS HEALTH

CALIFORNIA SMOKERS' HELPLINE 1-800-NO-BUTTS

KICK IT California

Web-based referral: kickitca.org/patient-referral

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# REFER: FREE QUITLINE

CALIFORNIA SMOKERS' HELPLINE 1-800-NO-BUTTS → KICK IT California


The NEW ENGLAND JOURNAL of MEDICINE

**EVIDENCE OF REAL-WORLD EFFECTIVENESS OF A TELEPHONE QUITLINE FOR SMOKERS**

SHU-HONG ZHU, PH.D., CHRISTOPHER M. ANDERSON, B.A., GARY J. TEDESCHI, PH.D., BRADLEY ROSBROOK, M.S., CYNTHIA E. JOHNSON, B.A., MICHAEL BYRD, M.A., AND ELSA GUTIÉRREZ-TERRELL, M.A.

N Engl J Med, Vol. 347, No. 14 · October 3, 2002

Counseling doubles long-term abstinence rates (12 months)

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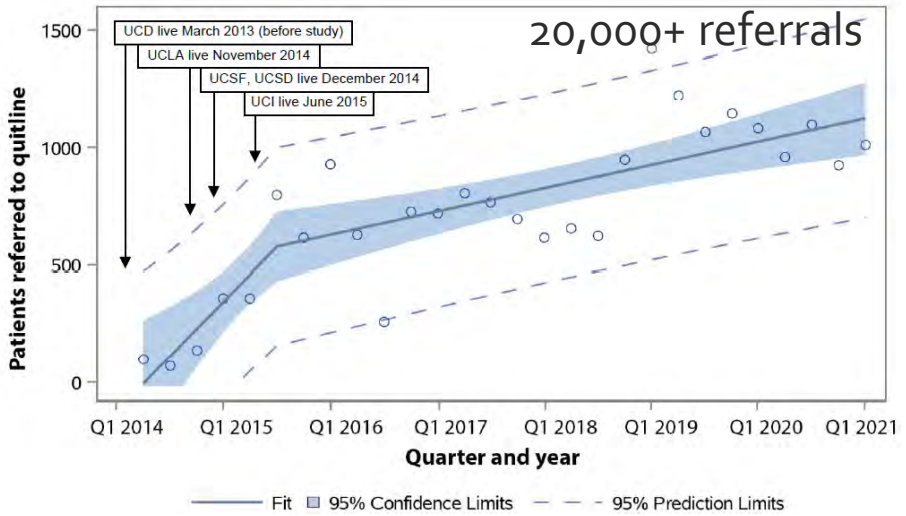
# **REFER:** UC CLINIC AND HOSPITAL REFERRALS

## Implementation, Maintenance, and Outcomes of an Electronic Referral to a Tobacco Quitline Across Five Health Systems

Elisa K. Tong MD[1], Shu-Hong Zhu PhD[2,3], Christopher M. Anderson BA[3], Mark V. Avdalovic MD[1], Alpesh N. Amin MD[4], Allison L. Diamant MD[5], Timothy W. Fong MD[6], Brian Clay MD[7], Robert El-Kareh MD[7], Sujatha Sankaran MD[8], Catherine Bonniot BA[9], Carrie A. Kirby MS[3], Antonio Mayoral MA[3], Linda Sarna PhD[10]

*Nicotine and Tobacco Research*, 2023, **25**, 1135–1144
https://doi.org/10.1093/ntr/ntad008
Advance access publication 29 March 2023


Referred UC patients who completed intake (n=4264)

- 46% non-white
- 59% Medicaid
- 59% chronic disease
- 49% behavioral health condition

Quit rate of random sample

- 13% at 7-month follow-up

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# OBJECTIVES

- Understand the tobacco industry impact on public health
- Describe framework for tobacco assessment and treatment
- **Identify strategies for improving tobacco assessment and treatment**

# QUALITY METRIC: TOBACCO

**NCQA Quality Metric for Lung Cancer Screening (in process, late 2024)**

$$\frac{\text{Non-users* + Current users}}{\text{Clinic patients seen past year}}$$

National Quality Forum metric 0028

1) % Patients Assessed

2) % Current Users Counseled

3) % Non-users* Assessed + Current Users Counseled
(Reflects the Non-user majority)

*Non-users = Never Users + Former Users

ecqi.healthit.gov/ecqm/ec/2024/cms0138v12

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# POPULATION PROMOTION & INCENTIVES

American Journal of
Preventive Medicine

RESEARCH ARTICLE

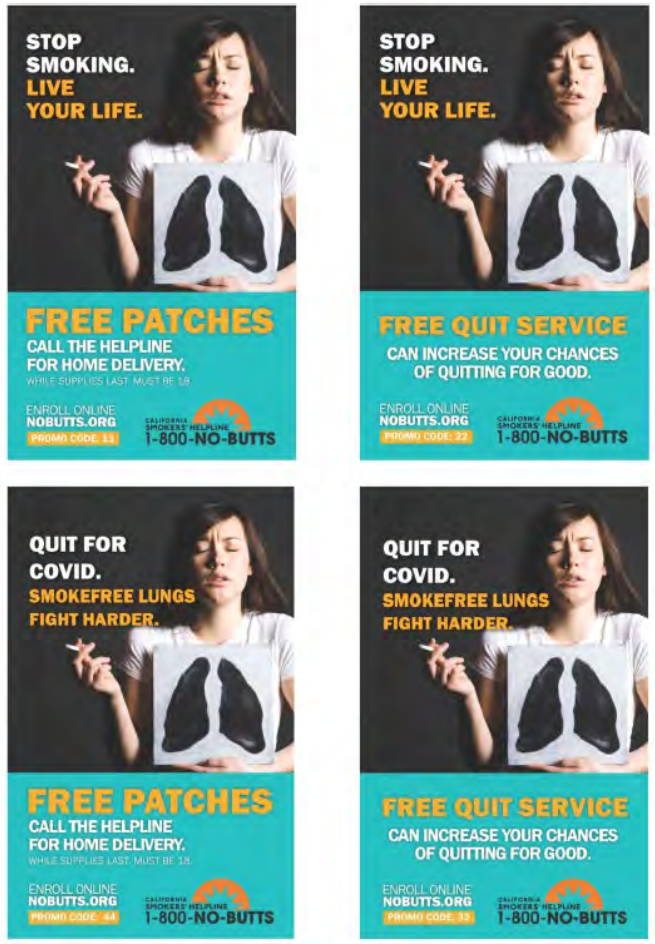
Quitline Promotion to Medicaid Members Who Smoke: Effects of COVID-19–Specific Messaging and a Free Patch Offer

Elisa K. Tong, MD,[1] Sharon E. Cummins, PhD,[2] Christopher M. Anderson, BA,[2] Carrie A. Kirby, MS,[2] Shiushing Wong, PhD,[2] Shu-Hong Zhu, PhD[2,3]

https://doi.org/10.1016/j.amepre.2022.09.009

- Free nicotine patch message got >6x more engagement than free help
  - Health messaging no difference

- 13,000 Californians got free nicotine patches mailed home during COVID shutdown

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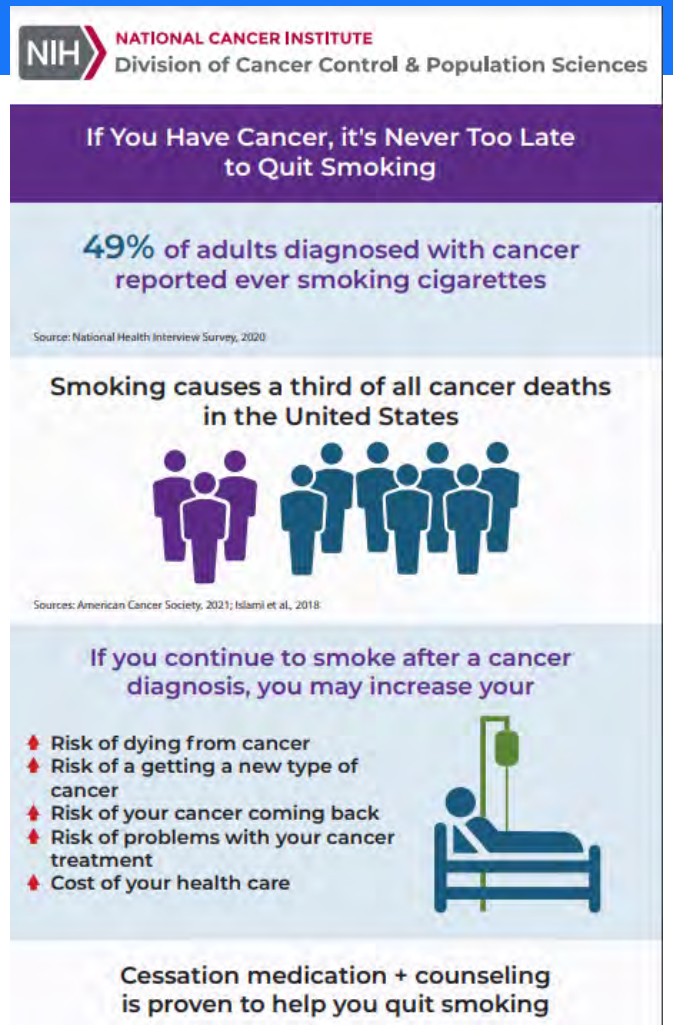
# TOBACCO TREATMENT IN CANCER CARE




- Among Californians diagnosed with 12 tobacco-related cancers (2014-2019), nearly 70,000 are current users (Maguire et al. *JAMA Network Open* 2023)
- NCI Cancer Center Cessation Initiative (3 of 5 UC, Stanford, City of Hope, USC)
- Commission on Cancer's "Just ASK" and "Beyond ASK" tobacco QI projects

California Thoracic Society

# POLICY RESEARCH CENTER

Mission

- Build capacity for health care **access**
- Promote excellence in health care **delivery**
- Facilitate health care **engagement**
- Achieve health plan coverage **equity**

Tobacco Cessation
POLICY RESEARCH CENTER

American Cancer Society Cancer Action Network

UCDAVIS HEALTH | COMPREHENSIVE CANCER CENTER

UCLA Health

UC CENTER SACRAMENTO

Funding: Tobacco-Related Disease Research Program T33PC6880

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# ENGAGE ON POLICY: SHARE YOUR VOICE

THE SACRAMENTO BEE

VIEWPOINTS

*To save African American lives, flavored tobacco ban must include menthol cigarettes*

BY DAVID TOM COOKE AND PHILLIP GARDINER *SPECIAL TO THE SACRAMENTO BEE*
UPDATED MARCH 14, 2019 12:15 PM

PUBLIC HEALTH

Join the Fight Against Underage Vaping

"No, I don't smoke, I just vape." For pediatricians, this response is all too familiar from our adolescent patients during routine health maintenance visits.

We are currently in an epidemic of teen vaping, with as many as one in five teens saying they have used e-cigarettes. The 2019-2020 California Student Tobacco Survey revealed 96% of high schoolers in California who vape use flavored vape products. Candy-flavored tobacco and nicotine products can lead to addiction and hook customers for a lifetime.

E-cigarette use in teens can have significant detrimental effects to their health, prime the developing brain for future addiction and increase the likelihood that they will use traditional cigarettes later in life. Ninety percent of adult smokers smoked their first cigarette before the age of 18, and more than one half of young adults who smoke daily started smoking between ages 6 to 12.

Fruit and candy flavors like bubble gum, blue raspberry and root beer have been used in vape pens and electronic cigarettes, making them more attractive to underage users. Colorful and convenient packaging work to glamorize nicotine use. Moreover, while flavorings may seem innocuous, some flavoring chemicals have been found to be toxic and damage lungs.



As many as one in five teens say they have used e-cigarettes. Some flavoring chemicals have been found to be toxic and damage lungs.

Menthol is a common flavor that makes it easier to start, harder to quit and increases the risk of harm. Big Tobacco's years of targeted marketing has resulted in significant health disparities for African Americans and many other groups. The U.S. Food and Drug Administration's recent ruling to take menthol out of cigarettes has been years overdue.

What's even worse is these new products with nicotine salts, which are more bioabsorbable and can contain as much nicotine as a pack of 20 cigarettes, amplifying the opportunity for addiction and disease. Vaping is associated with up to a seven-fold increase in getting COVID. New disease epidemics like EVALI are still sidelining young people locally during COVID.

How do we keep these dangerous products out of the hands of children? Limiting the retail sale of flavored tobacco products is one first step to reduce access. Addiction among children and young adults will decrease when tobacco tastes and smells like tobacco. A study of children and young adults in Texas in 2017 revealed 75% of flavored tobacco users reported they would no longer use the product if it wasn't flavored.

California has a state law restricting the sale of flavored tobacco products, including menthol, but it has been on hold. In August 2020, California passed Senate Bill 793, with bipartisan support, to prohibit the sale of flavored tobacco products. The tobacco industry spent over $20 million to place a referendum on SB 793, and the law's implementation has been on hold pending the outcome of a vote by Californians on the November 2022 ballot.

At the local level, over 125 cities and counties in California have passed restrictions on the sale of flavored tobacco products. The City of Sacramento has had a policy since 2020 and unincorporated Sacramento County will implement a similar policy in July 2022. Several other cities in the Sacramento region have been actively considering policies.

Local physicians who work at UC Davis Health have joined public health groups to help educate policymakers and the community. The Sacramento Sierra Valley Medical Society and its Public and Environmental Health Committee have helped with local education and support, consistent with the California Medical Association's official position.

There are several ways for SSVMS physicians to get involved and make a difference. One way to become more active in the campaign is to contact the Greater Sacramento Smoke & Tobacco Free Coalition at greatersactfcoalition@gmail.com or call (916) 879-5869 about opportunities to join upcoming policy meetings and a speakers' bureau training.

Patients who smoke or vape can be referred to Kick It California (www.kickitca.org), previously the California Smokers' Helpline, for free help to quit. The 2% Quits series also offers free, brief tobacco treatment training modules worth up to 3.0 CME credits at www.cmecalifornia.com. More information can be found at the California Tobacco Control Program's public website at www.cctcp.org.

When Big Tobacco wins, our children and communities lose. As physicians, we can help the next generation from suffering through more tobacco epidemics.

*Dr. Lina Tong contributed to this article. The opinions expressed are those of Drs. Cayrak and Tong and not of the University of California.*

32 | Sierra Sacramento Valley Medicine

July/August 2022 | 33


Tobacco Cessation
POLICY RESEARCH CENTER

tcprc.ucdavis.edu

California Thoracic Society

# SUMMARY

- The tobacco industry has new products, new problems

- Ask about tobacco and nicotine use
- Assist with FDA-approved cessation medications
- Refer to quitline or tobacco treatment program

- Tobacco assessment & treatment is a quality measure
- Engage by sharing your voice

California Thoracic Society

# Multidisciplinary Approach to Lung Cancer

## Justine Ko, MD
## Fellow
## UC San Francsico-Fresno

Dr. Justine Ko received her medical degree from the Keck School of Medicine of USC. She completed her internal medicine esidency at USC and was awarded resident of the year. Currently, she is a second year fellow at the UCSF-Fresno Pulmonary and Critical Care Fellowship Program. She has focused her education and research in interventional pulmonology under the mentorship of Dr. Pravachan Hegde. She will be applying for a fellowship position in interventional pulmonology this coming cycle.

## David Tom Cooke, MD
## Professor

## UC Davis

Dr. David Tom Cooke is a Professor at the University of California, Davis School of Medicine.  He is the founding Chief of the Division of General Thoracic Surgery, Director of the General Thoracic Surgery Robotics Program, the Vice Chair for Faculty Development and Wellness for the Department of Surgery, the Associate Director for the Office of Inclusivity, Diversity, Equity and Accessibility (IDEAL) and the Interim Physician-in-Chief, UC Davis NCI designated Comprehensive Cancer Center. Dr. Cooke specializes in the surgical treatment of malignant and benign lung and esophageal disease and is a national leader in robotic thoracic surgery. Dr. Cooke's research includes oncologic trials, surgical outcomes/health services research, patient-centered outcomes research, surgical education, medical social media, and public medical communication. He has authored over 100 peer-reviewed publications. He is president of the Thoracic Surgery Directors Association, a director of the American Board of Thoracic Surgery, a director of the Accreditation Council for Graduate Medical Education (ACGME), member of the American Surgical Association and an associate member of the American College of Surgeons Academy of Master Surgeon Educators. Dr. Cooke currently serves on the American Lung Association National Lung Cancer Expert Medical Advisory Panel. Dr. Cooke completed his cardiothoracic surgery training at the University of Michigan in Ann Arbor, general surgery residency at the Massachusetts General Hospital in Boston, medical school at Harvard Medical School and undergraduate at UC Berkeley.

## Elisa Tong, MD, MA
## Professor
## UC Davis

Elisa Tong is a Professor of Internal Medicine at UC Davis. Her research focus is in tobacco cessation and policy, with special interests in cancer and population health.
She completed her medical degree at Stanford University, residency training at Santa Clara Valley Medical Center, and research fellowship at UCSF. She is the Principal Investigator for CA Quits and Director for the Tobacco Cessation Policy Research Center.

## Brian Shaller, MD
## Assistant Professor
## Stanford

Brian Shaller is a Clinical Assistant Professor in the Division of Pulmonary, Allergy & Critical Care Medicine at Stanford University. He trained in Interventional Pulmonology at the Cleveland Clinic and helped establish Stanford's Interventional Pulmonology fellowship program in 2022, for which he currently serves as Associate Program Director. Dr. Shaller's clinical and academic interests include advanced diagnostics for lung nodules, endoscopic management of central airway diseases, and procedural education.

# Multidisciplinary Approach to Lung Cancer

California Thoracic Society
Friday, March 8, 2024

Brian Shaller, MD
David Tom Cooke, MD, FACS
Elisa Tong, MD, MA
Justine Ko, MD, MPH

California Thoracic Society
ATS Chapter

# COI/Disclosures

None

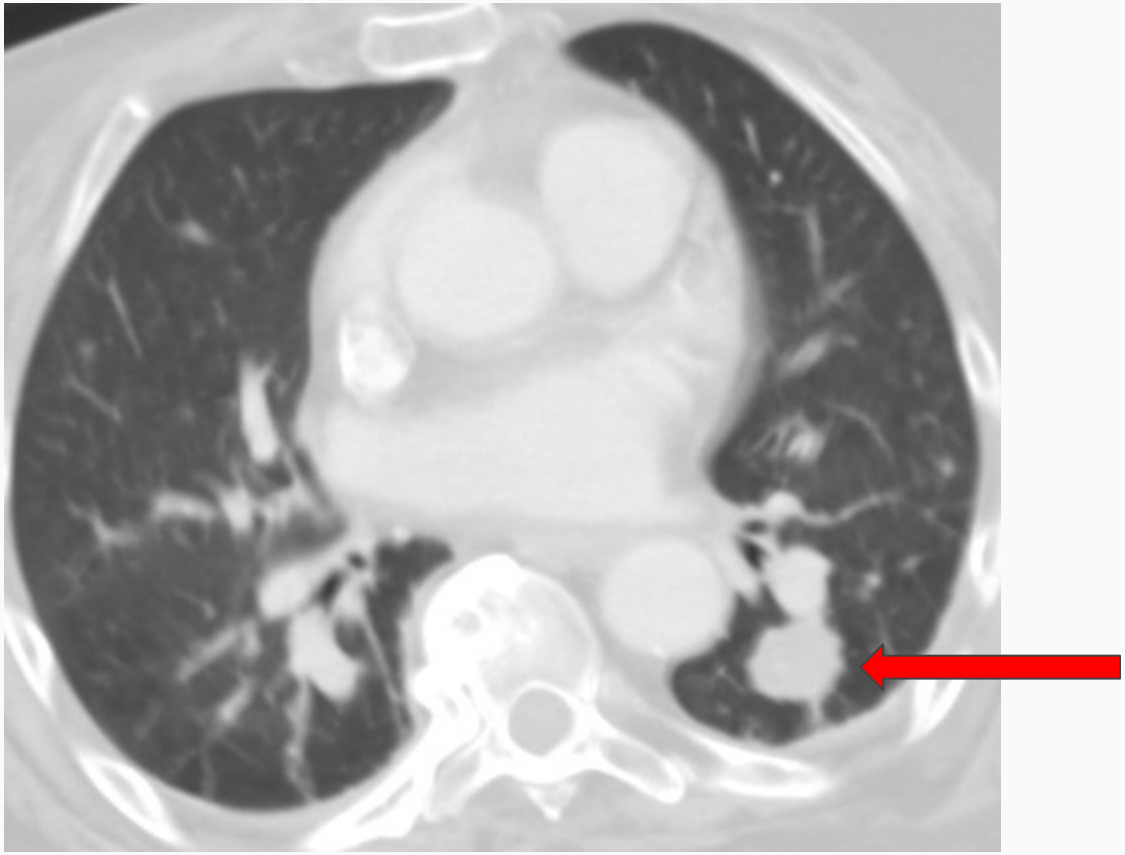
# Case 1

A 71 yo female is found to have an incidental nodule in the LLL during imaging for abdominal pain. Dedicated chest imaging is obtained and there is a 1.7 x 2.3 cm nodule with no hilar or mediastinal lymphadenopathy with no other nodules seen on imaging. Comparison to prior scan from 7 months prior show that there has been interval increase in size.

She is an active smoker and has a >20 pack year smoking history.

# Case 1 Imaging

1.7 x 2.3 cm nodule in the left lower lobe



# Fleischner Society 2017 Guidelines for Management of Incidentally Detected Pulmonary Nodules in Adults (*Radiology*)

**A: Solid Nodules***

| Nodule Type | Size | | | Comments |
|---|---|---|---|---|
| | <6 mm (<100 $mm^3$) | 6–8 mm (100–250 $mm^3$) | >8 mm (>250 $mm^3$) | |
| Single | | | | |
| Low risk† | No routine follow-up | CT at 6–12 months, then consider CT at 18–24 months | Consider CT at 3 months, PET/CT, or tissue sampling | Nodules <6 mm do not require routine follow-up in low-risk patients (recommendation 1A). |
| High risk† | Optional CT at 12 months | CT at 6–12 months, then CT at 18–24 months | Consider CT at 3 months, PET/CT, or tissue sampling | Certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A). |
| Multiple | | | | |
| Low risk† | No routine follow-up | CT at 3–6 months, then consider CT at 18–24 months | CT at 3–6 months, then consider CT at 18–24 months | Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A). |
| High risk† | Optional CT at 12 months | CT at 3–6 months, then at 18–24 months | CT at 3–6 months, then at 18–24 months | Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A). |

Note.—These recommendations do not apply to lung cancer screening, patients with immunosuppression, or patients with known primary cancer.

* Dimensions are average of long and short axes, rounded to the nearest millimeter.

† Consider all relevant risk factors (see Risk Factors).

# Question for Dr. Tong

- How does this patient’s smoking history change your approach to management?

# Question for Dr. Shaller

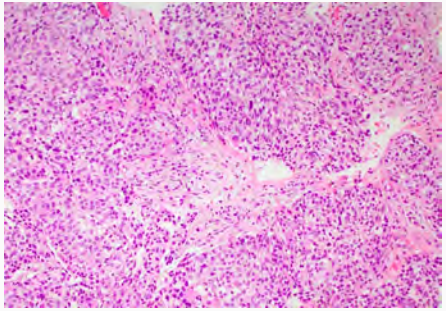
- Who does the biopsy – IR or IP?

# Question for Dr. Cooke

- When is empiric surgical resection appropriate for both diagnosis and treatment?

# Case 1 Outcome

- Patient received a CT guided biopsy of the LLL nodule and was found to have squamous cell carcinoma of the lung
- Lymph node biopsies did not show hilar or mediastinal disease
- Due to her comorbidities, surgery was not offered
- She is currently seeing radiation oncology with plans for definitive SBRT with Cyberknife

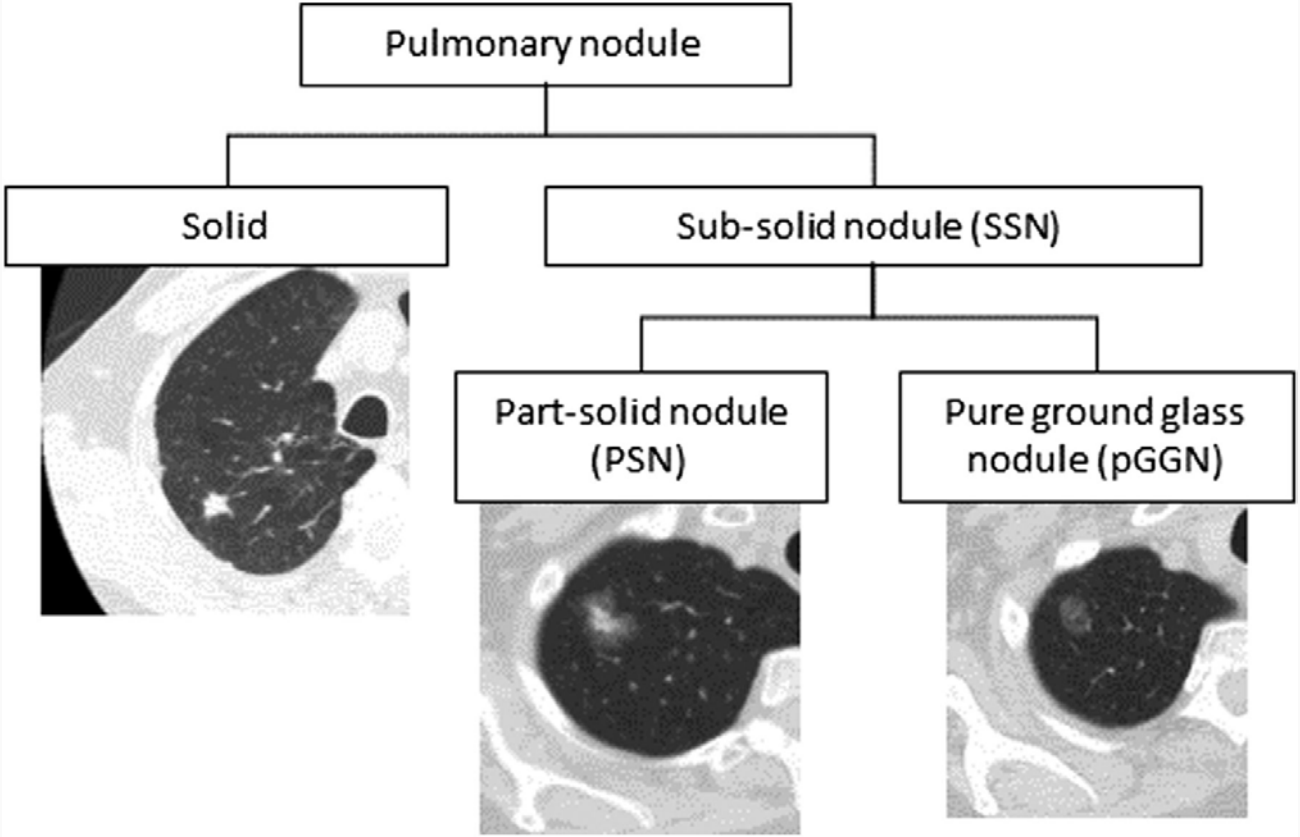


https://www.pathologyoutlines.com/topic/lungtumorscc.html

# Case 2

A 69 yo female with GOLD 1A COPD and 75 pack year smoking history has multiple subsolid lesions in her right lung. Her nodules were first detected on low dose CT in 2019 and have been slowly growing through 2023.

# Classification and CT Appearance of Pulmonary Nodules




https://doi.org/10.1136/thoraxjnl-2015-207221

# Fleischner Society 2017 Guidelines for Management of Incidentally Detected Pulmonary Nodules in Adults (*Radiology*)

**B: Subsolid Nodules***

| Nodule Type | Size | | Comments |
|---|---|---|---|
| | <6 mm (<100 $mm^3$) | ≥6 mm (>100 $mm^3$) | |
| Single | | | |
| Ground glass | No routine follow-up | CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years | In certain suspicious nodules < 6 mm, consider follow-up at 2 and 4 years. If solid component(s) or growth develops, consider resection. (Recommendations 3A and 4A). |
| Part solid | No routine follow-up | CT at 3–6 months to confirm persistence. If unchanged and solid component remains <6 mm, annual CT should be performed for 5 years. | In practice, part-solid nodules cannot be defined as such until ≥6 mm, and nodules <6 mm do not usually require follow-up. Persistent part-solid nodules with solid components ≥6 mm should be considered highly suspicious (recommendations 4A-4C) |
| Multiple | CT at 3–6 months. If stable, consider CT at 2 and 4 years. | CT at 3–6 months. Subsequent management based on the most suspicious nodule(s). | Multiple <6 mm pure ground-glass nodules are usually benign, but consider follow-up in selected patients at high risk at 2 and 4 years (recommendation 5A). |

Note.—These recommendations do not apply to lung cancer screening, patients with immunosuppression, or patients with known primary cancer.

* Dimensions are average of long and short axes, rounded to the nearest millimeter.

† Consider all relevant risk factors (see Risk Factors).

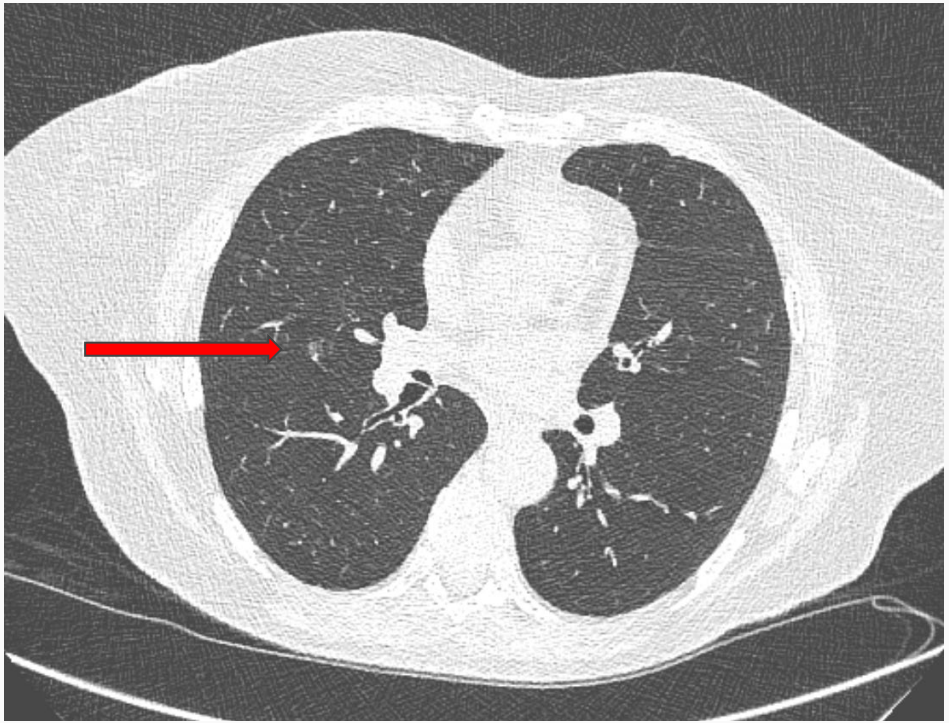
# Case 2

Nodules are measured as following:

- RLL anterior basal segment cystic ground glass nodule, 25 x 20 mm
- RLL superior segment subsolid nodule, 9 x 8 mm
- RML lateral segment subsolid nodule, 10 x 9 mm

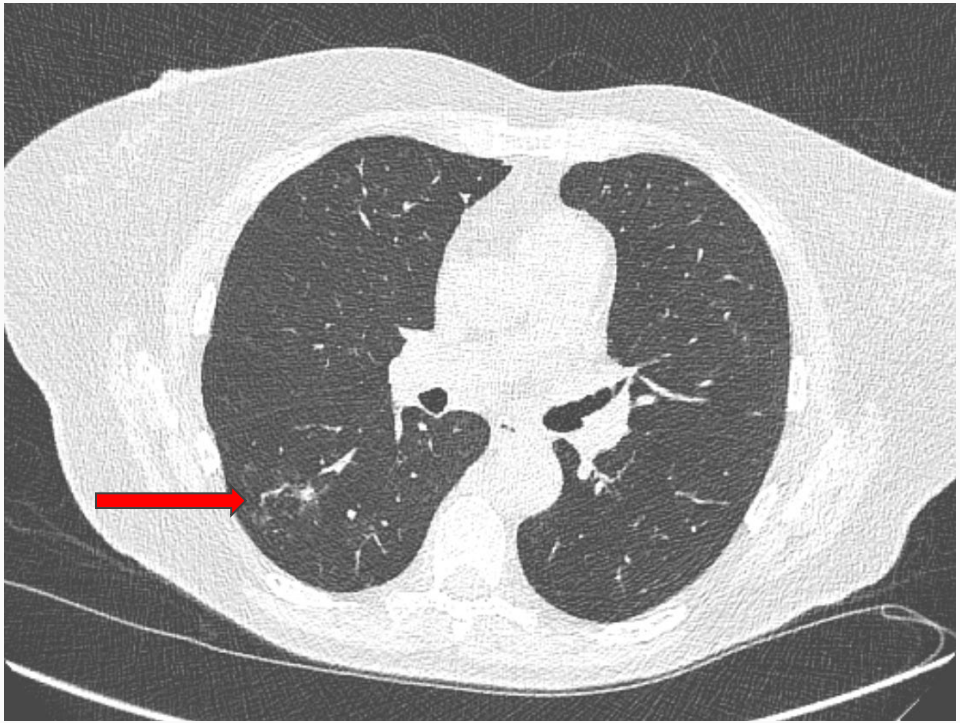
# Case 2 Imaging

- RML lateral segment subsolid nodule, 10 x 9 mm



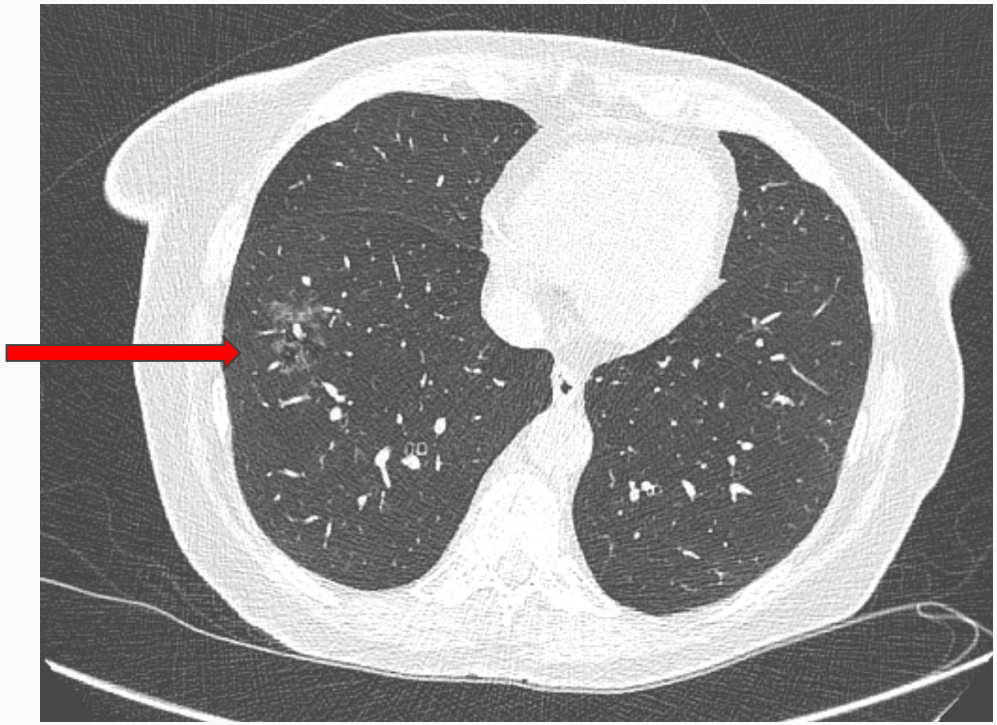
# Case 2 Imaging

- RLL superior segment subsolid nodule, 9 x 9 mm



# Case 2 Imaging

- RLL anterior basal segment cystic ground glass nodule, 25 x 20 mm



# Question for Dr. Tong

- What is your next step when you see a patient with ground glass nodules?

# Case 2

The patient is referred to Thoracic Surgery for evaluation of the nodules.

# Question for Dr. Cooke

- When should a patient be referred to thoracic surgery for management of lung nodules?

# Case 2 Continued

The patient’s case was reviewed by the thoracic surgeon and the patient was referred to interventional pulmonology. She underwent robotic assisted, cone beam CT-guided bronchoscopy with biopsy of the nodules.

All 3 targets showed adenocarcinoma with acinar growth on pathology. Lymph nodes sampled from stations 7, 11R, and 11Ri were negative for malignancy.

# Question for Dr. Shaller

- How does the management of ground glass nodules differ from the management of solid nodules?

# Case 2 Continued

The patient underwent a VATS-RLL lobectomy with lymph node dissection. Nodes were again confirmed negative on surgical pathology.

The patient was discharged home with plans to undergo SBRT to the RML nodule following recovery from surgery.

# Case 3

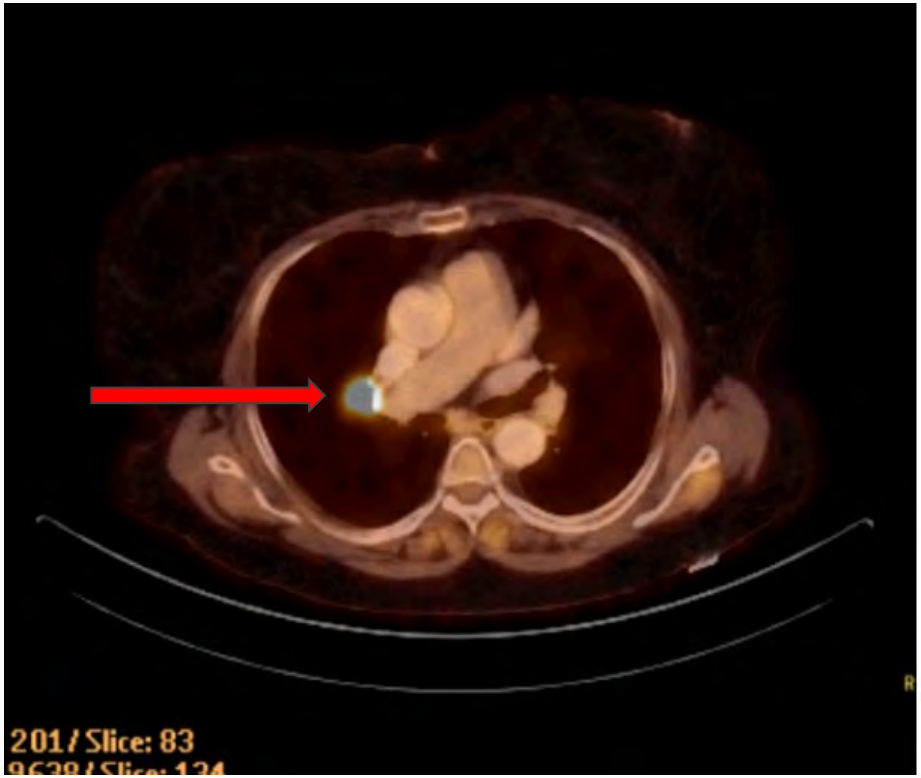
A 82 yo female is referred to the lung nodule clinic for evaluation of a new PET avid right hilar lymph node identified on surveillance imaging.

Her medical history is significant for diagnosis of RUL squamous cell carcinoma in 2019 with bony metastases to the ribs. She has been treated with carboplatin, taxol, and Keytruda with restaging imaging showing excellent response to treatment. She was then maintained on Keytruda alone for several years before stopping in 2022 due to development of pneumonitis.

She has a prior 20 pack year smoking history but quit in 2007. Over the past few months, she has noted 10 lb weight loss.

# Case 2 Imaging

- PET avid right hilar lymph node



# Question for Dr. Tong

- How frequently do you get surveillance imaging after treatment of the malignancy?

# Question for Dr. Shaller

- When is a biopsy indicated vs presuming recurrence of a prior confirmed diagnosis?

# Question for Dr. Cooke

- Is there a role for surgery in recurrent disease?

# Case 3 Outcome

- Stations 11R and 7 were sampled using EBUS and negative for malignancy
- Station 10R biopsy using EBUS contains atypical cells positive for p40 and panCK which are suspicious for metastatic squamous cell carcinoma
- Patient is referred by her oncologist to radiation oncology for consideration of CyberKnife radiation therapy

# Guideline Recommendations and Invasive Mediastinal Staging (*CHEST* 2021)

**TABLE 1** ] Guideline Recommendations and Invasive Mediastinal Staging

| Variable | CHEST | NCCN | CCO | NICE | ESTS/ERS/ESGE |
|---|---|---|---|---|---|
| Publication year | 2013 | 2020 | 2011 | 2019 | 2015 |
| Indications for invasive mediastinal staging | | | | | |
| Tumor > 3 cm | Yes | Yes | Yes | NS | Yes |
| Central tumor | Yes | Yes | Yes | NS | Yes |
| Tumor without PET uptake | NS | NS | NS | NS | Yes |
| Lymphadenopathy | Yes | Yes | Yes | Yes | Yes |
| Nodes showing positive PET results | Yes | Yes | Yes | Yes | Yes |
| Definition of central tumor | | | | | |
| Inner one third | Yes | ... | Yes | NS | Yes |
| Inner two thirds | ... | Yes | ... | NS | ... |
| First-line invasive mediastinal staging method | | | | | |
| EBUS | Yes | ... | ... | Yes | Yes |
| EBUS/EUS | Yes | ... | ... | Yes | Yes |
| Mediastinoscopy | ... | ... | Yes | ... | ... |
| Any method[a] | ... | Yes | ... | ... | ... |
| Indication for repeat invasive mediastinal staging | | | | | |
| Negative or nondiagnostic first-line endosonography findings | Yes | Yes | NS | Yes | Yes |
| Minimum extent of lymph node evaluation | | | | | |
| Three mediastinal lymph node stations | NS | NS | ... | NS | Yes |
| Five mediastinal lymph node stations | ... | NS | Yes | NS | ... |

CCO = Cancer Care Ontario; CHEST = American College of Chest Physicians; EBUS = endobronchial ultrasound; ESGE = European Society of Gastrointestinal Endoscopy; ERS = European Respiratory Society; ESTS = European Society of Thoracic Surgeons; EUS = esophageal ultrasound; NCCN = National Comprehensive Cancer Network; NICE = National Institute for Health and Care Excellence; NS = not specified.

[a]EBUS, EUS, mediastinoscopy, mediastinotomy, CT scanning-guided nodal aspiration, or a combination thereof.

# References


- Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. *Radiology* vol. 284,1 (2017)
- Mediastinal Staging for Lung Cancer. *Chest* vol. 160,4 (2021): 1552-1559
- Lababede O, Meziane MA. The Eighth Edition of TNM Staging of Lung Cancer: Reference Chart and Diagrams. Oncologist. 2018 Jul;23(7):844-848. doi: 10.1634/theoncologist.2017-0659. Epub 2018 Apr 12. PMID: 29650687; PMCID: PMC6058324.

# Q&A with the Audience

# Thank you for joining us!

# TNM Staging

| Primary tumor (T) | |
|---|---|
| **T category** | **Definition** |
| Tx | Tumor that is proven histopathologically (malignant cells in bronchopulmonary secretions/washings) but cannot be assessed or is not demonstrable radiologically or bronchoscopically. |
| T0 | No evidence of primary tumor. |
| Tis | Carcinoma in situ: |
| | Squamous cell carcinoma in situ. |
| | Adenocarcinoma in situ (pure lepidic pattern and $\leq$3 cm in greatest dimension). |
| T1 | Size: $\leq$3 cm. |
| | Airway location: in or distal to the lobar bronchus. |
| | Local invasion: none (surrounded by lung or visceral pleura). |
| | Subdivisions: T1mi: Minimally invasive adenocarcinoma (pure lepidic pattern, $\leq$3 cm in greatest dimension and $\leq$5 mm invasion)—T1a (size $\leq$1 cm)[a]—T1b (1 cm $<$ size $\leq$ 2 cm)—T1c (2 cm $<$ size $\leq$ 3 cm). |
| T2 | Any of the following characteristics: |
| | Size: >3 cm but $\leq$5 cm. |
| | Airway location: invasion of the main bronchus (regardless the distance to the carina) or presence of atelectasis or obstructive. |
| | Pneumonitis that extends to hilar region (whether it is involving part or the entire lung). |
| | Local invasion: visceral pleura (PL1 or PL2). |
| | Subdivisions: T2a (3 cm $<$ size $\leq$ 4 cm or cannot be determined) and T2b (4 cm $<$ size $\leq$ 5 cm). |
| T3 | Any of the following characteristics: |
| | Size: >5 cm but $\leq$7 cm. |
| | Local invasion: direct invasion of chest wall (including superior sulcus tumors), parietal pleura (PL3), phrenic nerve, or parietal pericardium. |
| | Separate tumor nodule(s) in the same lobe of the primary tumor. |
| T4 | Any of the following characteristics: |
| | Size >7 cm. |
| | Airway location: invasion of the carina or trachea. |
| | Local invasion: diaphragm, mediastinum, heart, great vessels, recurrent laryngeal nerve, esophagus or vertebral body. |
| | Separate tumor nodule(s) in an ipsilateral different lobe of the primary tumor. |

# TNM Staging

| Lymph nodes (N) | |
|---|---|
| **Descriptor** | **Definition** |
| Nx | Regional lymph nodes cannot be evaluated. |
| N0 | No regional lymph nodes involvement. |
| N1 | Involvement of ipsilateral peribronchial and/or ipsilateral hilar lymph nodes (includes direct extension to intrapulmonary nodes). |
| N2 | Involvement of the ipsilateral mediastinal and/or subcarinal lymph nodes. |
| N3 | Involvement of any of the following lymph node groups: contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular nodes. |
| **Distant metastasis (M)** | |
| **Descriptor** | **Definition** |
| M0 | No distant metastasis. |
| M1 | Presence of distant metastasis. |
| | Subdivisions: M1a (separate tumor nodule(s) in a contralateral lobe to that of the primary tumor or tumors with pleural or pericardial nodules or malignant effusion); M1b (single extrathoracic metastasis); M1c (multiple extrathoracic metastases to one or more organs). |

Note: Tumor's size is determined by the greatest dimension of the lesion.

[b]The uncommon superficial spreading tumor with invasive component limited to bronchial wall is classified as T1a regardless of size or extent to main bronchus.

# Dyssynchronous Waveforms

**Rob Bautista, BSRT, RRT, RRT-ACCS**
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**UC San Francisco**

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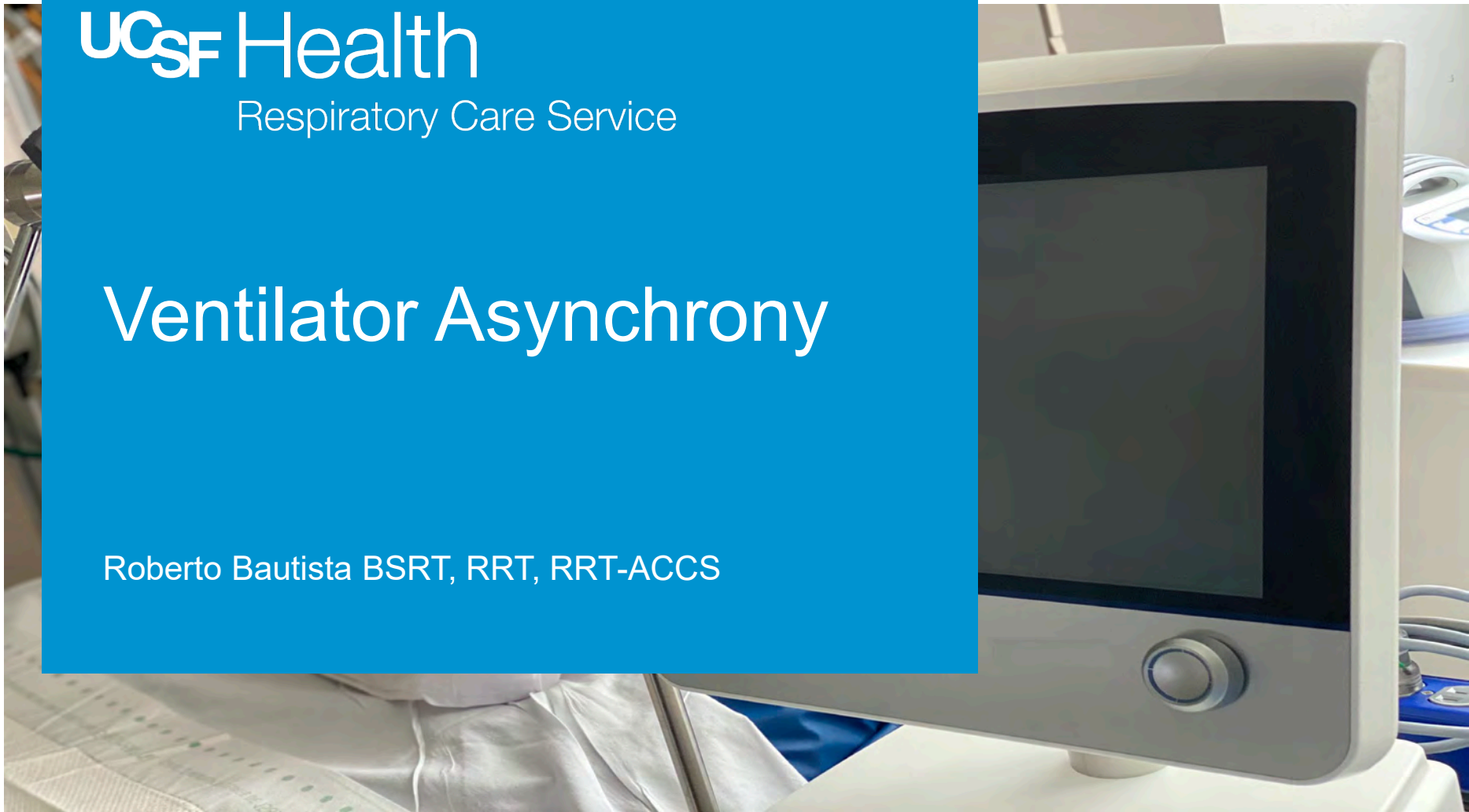
# Ventilator Asynchrony

Roberto Bautista BSRT, RRT, RRT-ACCS



# Relevant Financial Disclosure(s)

## Roberto Bautista BSRT, RRT, RRT-ACCS

- I have no conflicts of interest.

# Ventilator Asynchrony

## Introduction

- Mechanical ventilation is a supportive treatment for improving oxygenation and/or ventilation, unloading the respiratory muscles, and gaining time until the patient's condition improves.
- Patient-ventilator asynchrony can be defined as a mismatch between the patient and ventilator timing and/or effort.

# Ventilator Asynchrony

Asynchronies can result in dyspnea, anxiety, delirium, cognitive alterations, and self-inflicted lung injury; they could also induce vigorous inspiratory efforts leading to high stress (i.e., elevated transpulmonary pressure), strain (i.e., global or regional lung overdistention), and consequent diaphragm and lung injury. Asynchronies are also associated with longer duration of mechanical ventilation.

Esperanza, JA, Respiratory Care 2020

# Objectives

# Ventilator Asynchrony

## Objectives

- Interpret waveforms
- Identify and define type of asynchrony
- Discuss possible interventions and/or adjustments
- Evaluate efficacy of current plan

# Physiology

# Ventilator Asynchrony

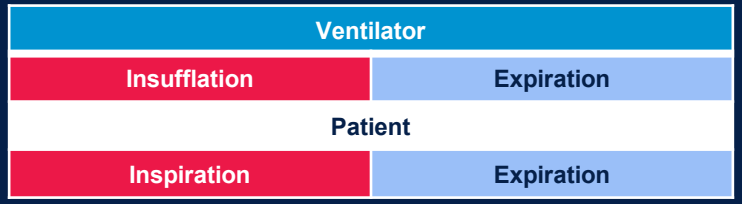
## Mechanisms

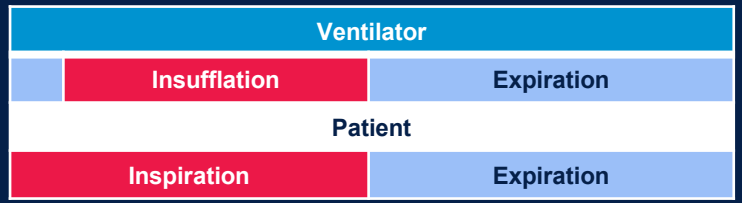
### Main mechanisms of Asynchrony

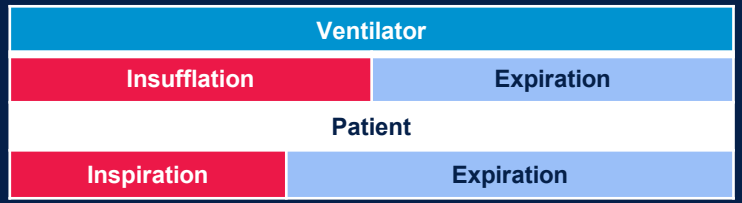
Timing of the patient is mismatched with the timing of the ventilator

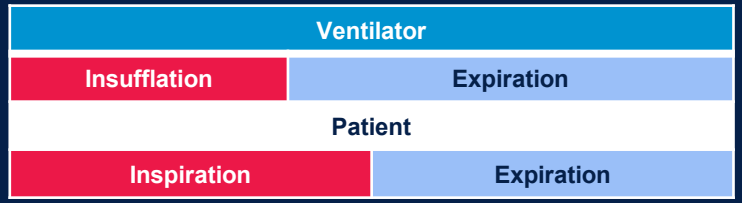
Imbalances in the amount work of breathing by the patient and the amount mechanical assist delivered during inspiration.

# Neural/Ventilator Timing Mismatch



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# Respiratory Drive/Mechanical Assist Mismatch

## High Respiratory Drive

(CNS, Metabolic, Respiratory Failure)

Insufficient ventilatory assist

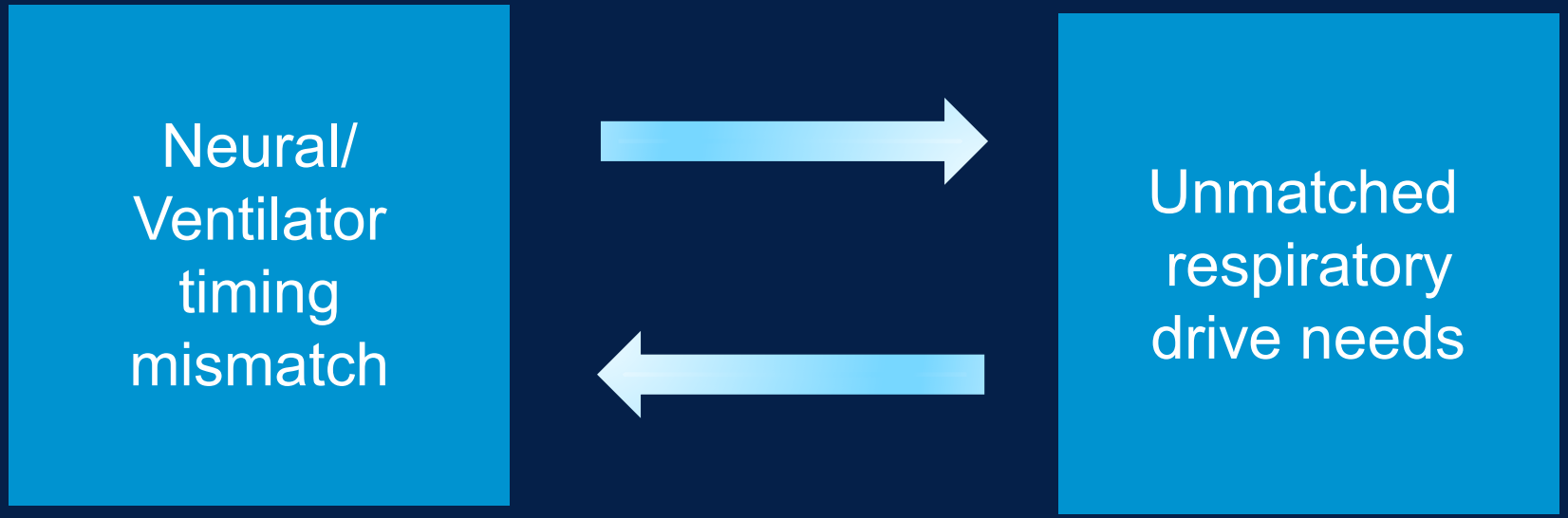
Intrinsic to patient's disease state

## Low Respiratory Drive

Excessive ventilatory assist

Excessive sedation

# Asynchrony Interactions



# Ventilator Asynchrony

## What Phase?

- When does the asynchrony occur?
  - Inspiratory Trigger
  - Inspiratory Limit
  - Inspiratory Cycle
  - Expiratory

# Cases

# #1

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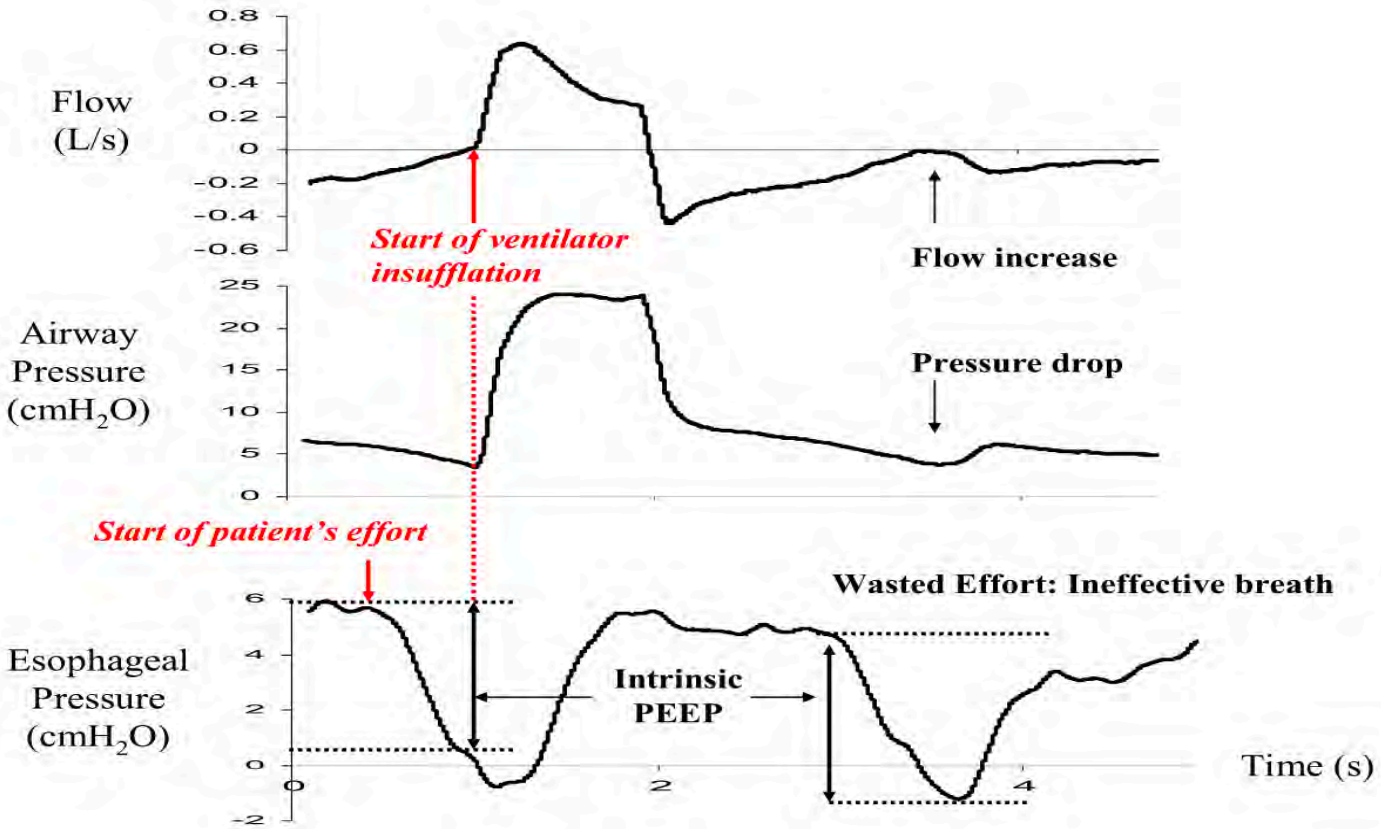


Thille, AW, Intensive Care Medicine 2008



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# Missed/Ineffective Trigger

- What phase is this in?
  - Inspiratory trigger
- Causes
  - Trigger sensitivity high
  - High set inspiratory pressure
  - Set frequency and/or I-time set too high
  - Presence of AutoPEEP
  - Low respiratory drive
  - Weak inspiratory effort
  - Sedation

# Missed/Ineffective Trigger

- Interventions
  - Decrease trigger sensitivity
  - Decrease set inspiratory pressure
  - Increase PEEP
  - Decrease sedation
  - Increase pt strength

# #2




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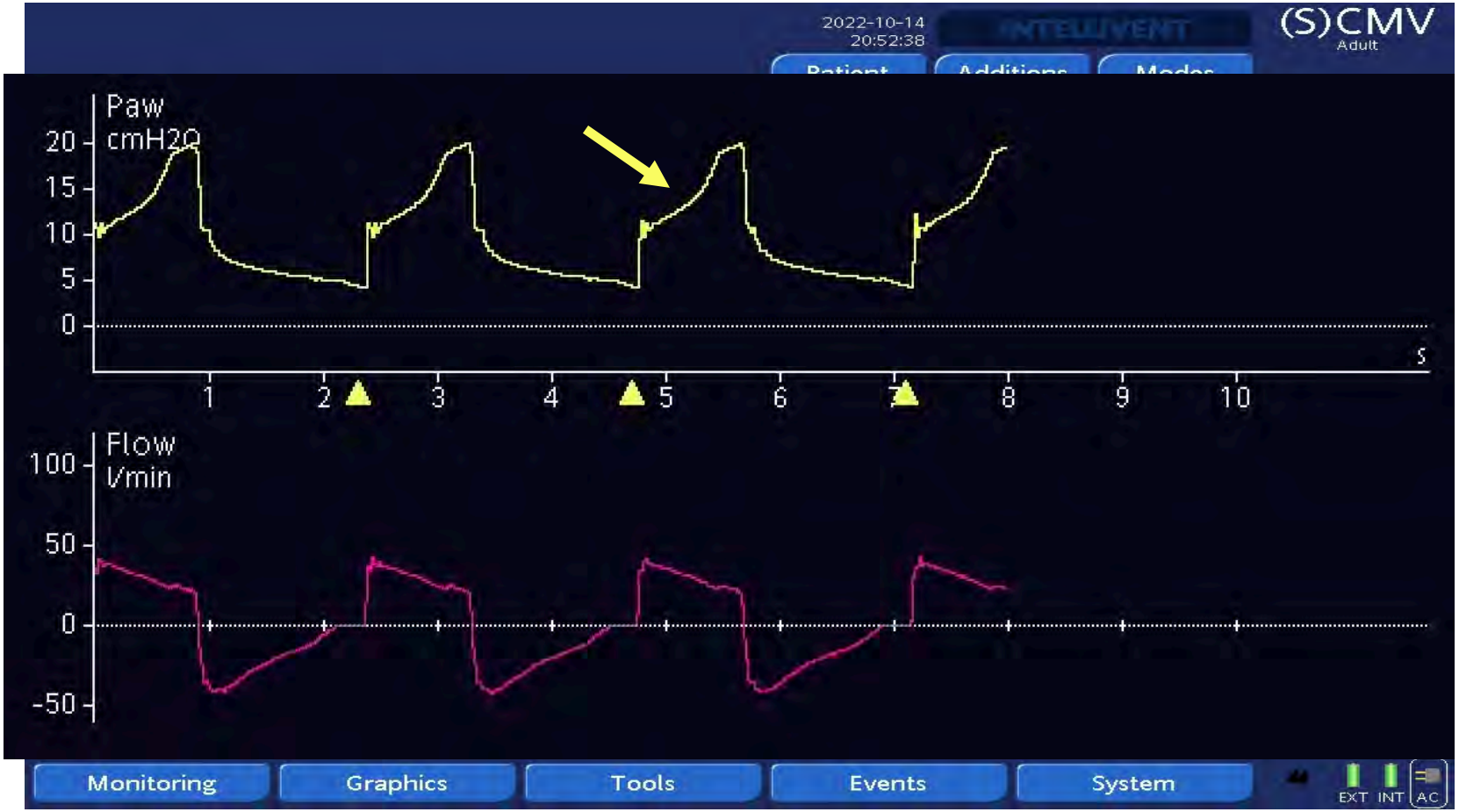
# #2



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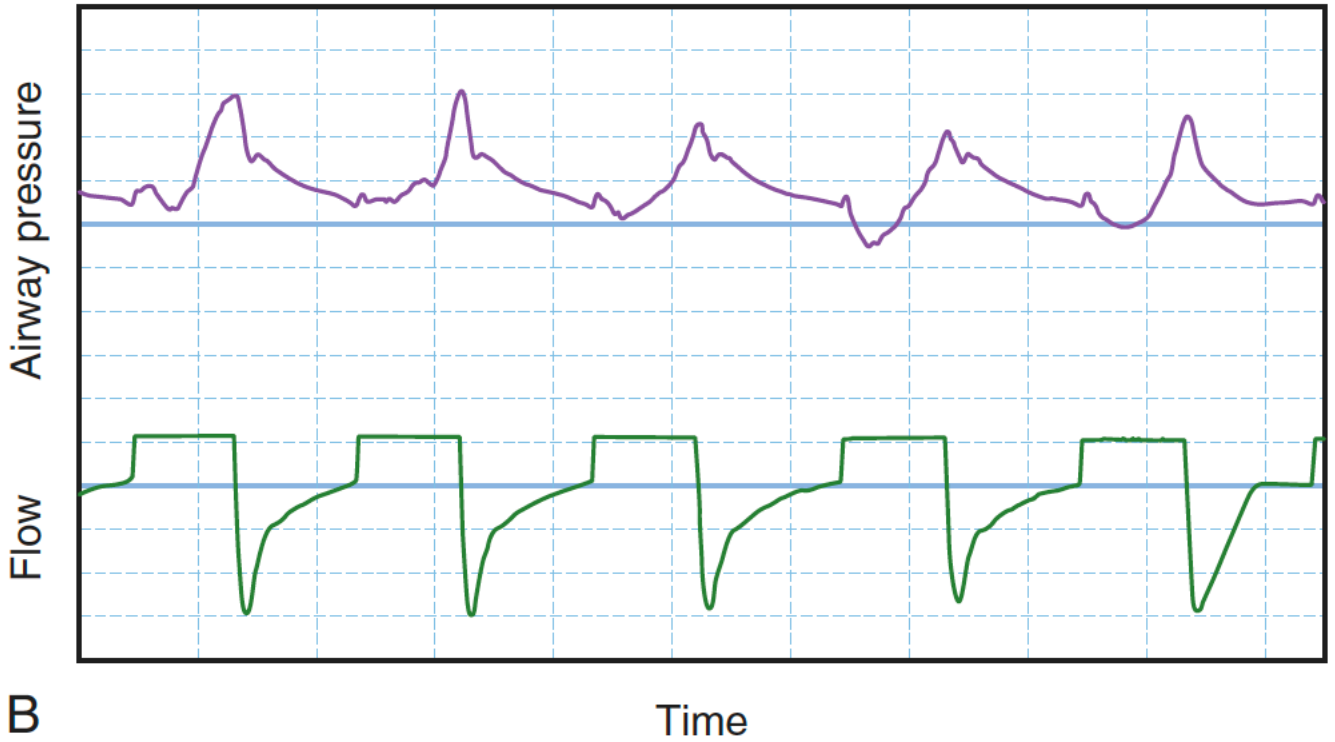
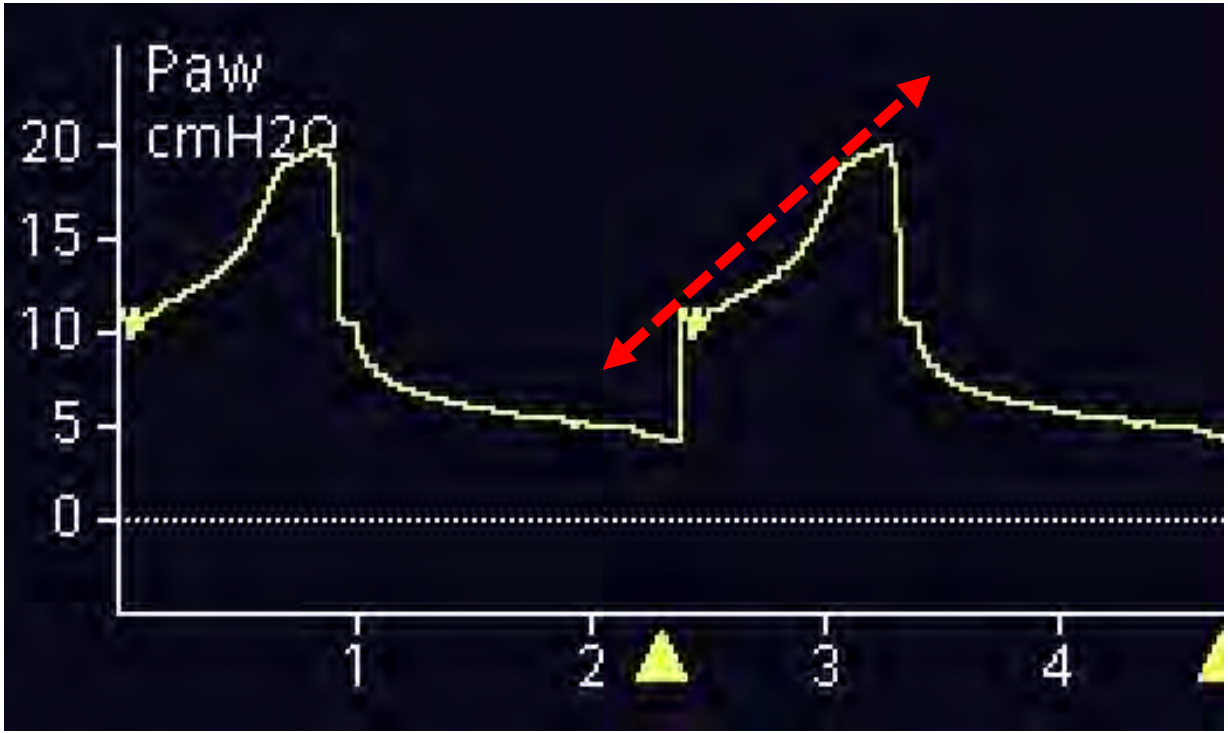
Flow asynchrony occurs when the set ventilator flow does not meet the patient inspiratory flow demand



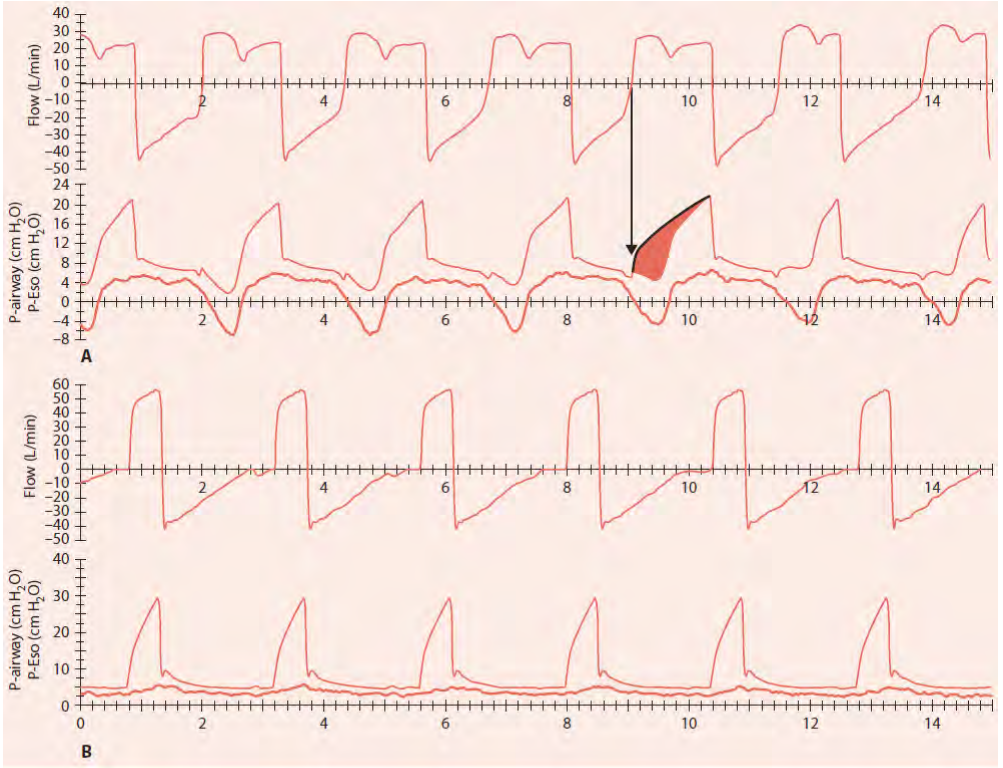

Kacmarek, R, Egan's Fundamentals of Respiratory Care 2021

Generally recognized by concave pressure-time scalar. Also termed “Air Hunger”



# Flow Asynchrony

- What phase is this in?
  - Inspiratory Limit
- Causes
  - Inappropriate vent mode
  - High Inspiratory Effort
  - Inappropriate Flow/ Time setting
  - Decreased Vt

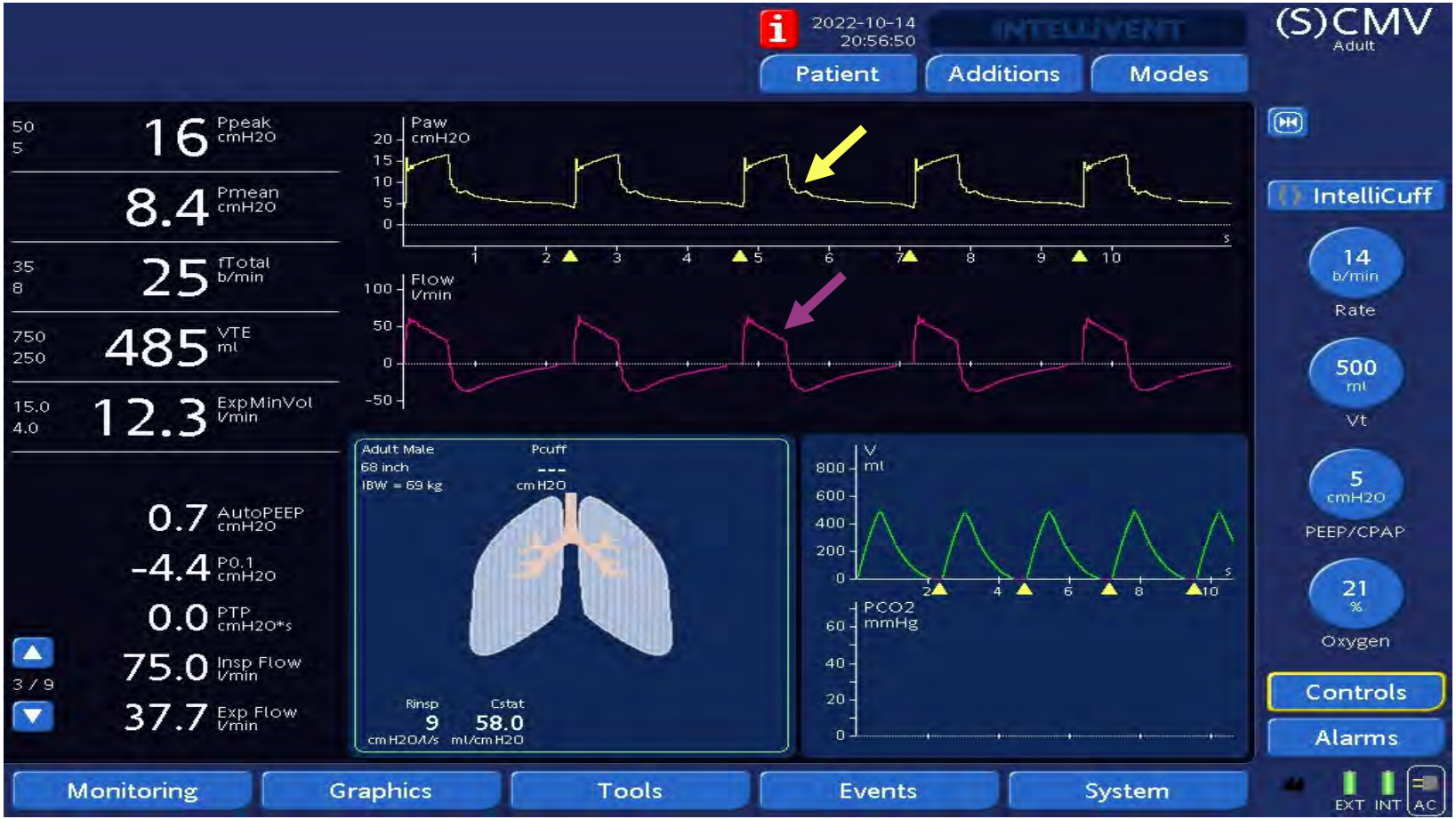


# Flow Asynchrony

- Interventions
  - Select appropriate mode
  - Increase Flow and/or Vt
  - Adjust time setting

# #3

**0.6s**



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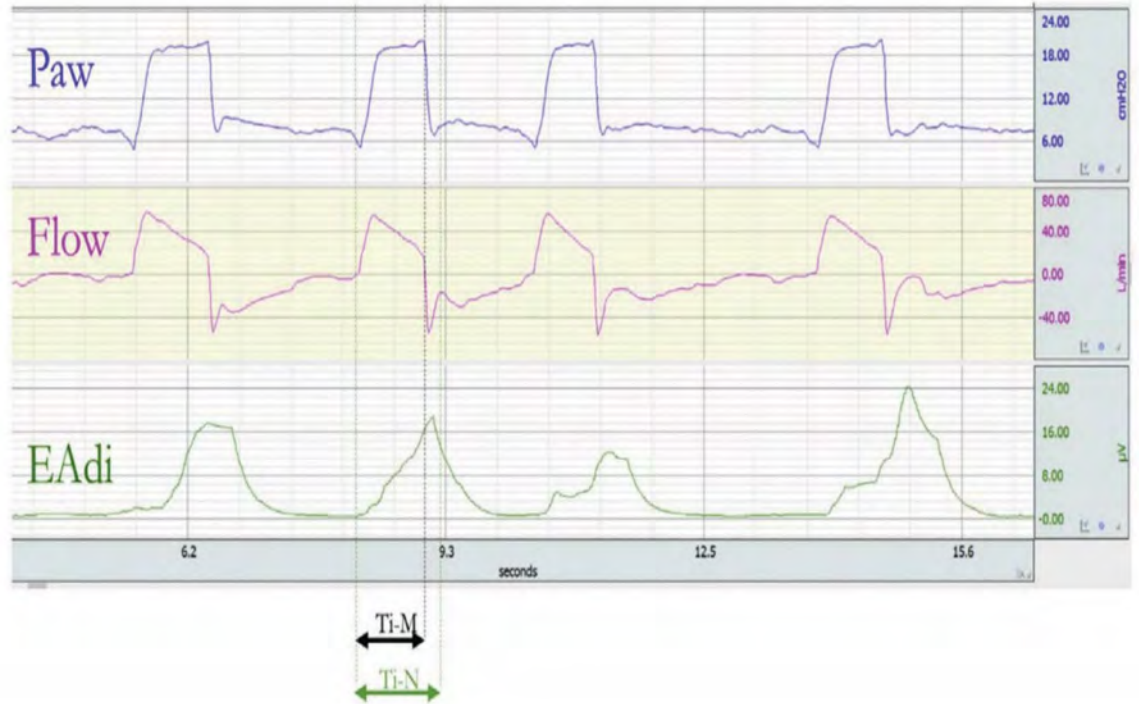
# Premature/Short Cycling

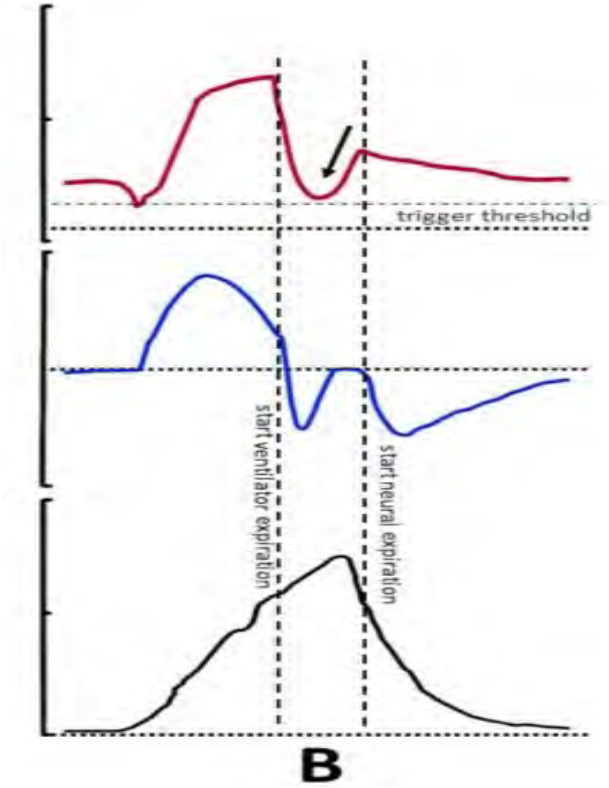
Short cycling occurs when the inspiratory time set by the ventilator is less than the neural timing of the patient.




De Oliveira, B, Journal of Clinical Medicine 2021

# Premature/Short Cycling

- When does this occur?
  - Inspiratory Cycle
- Causes
  - I-time set too low
  - High Inspiratory Effort
  - Vt set too low




Enrico, B, Acta Biomedica 2018

# Premature/Short Cycling

- Interventions
  - Adjust I-time
  - Increase Vt
  - Select to appropriate mode
  - Decrease cycle criterion

# #4

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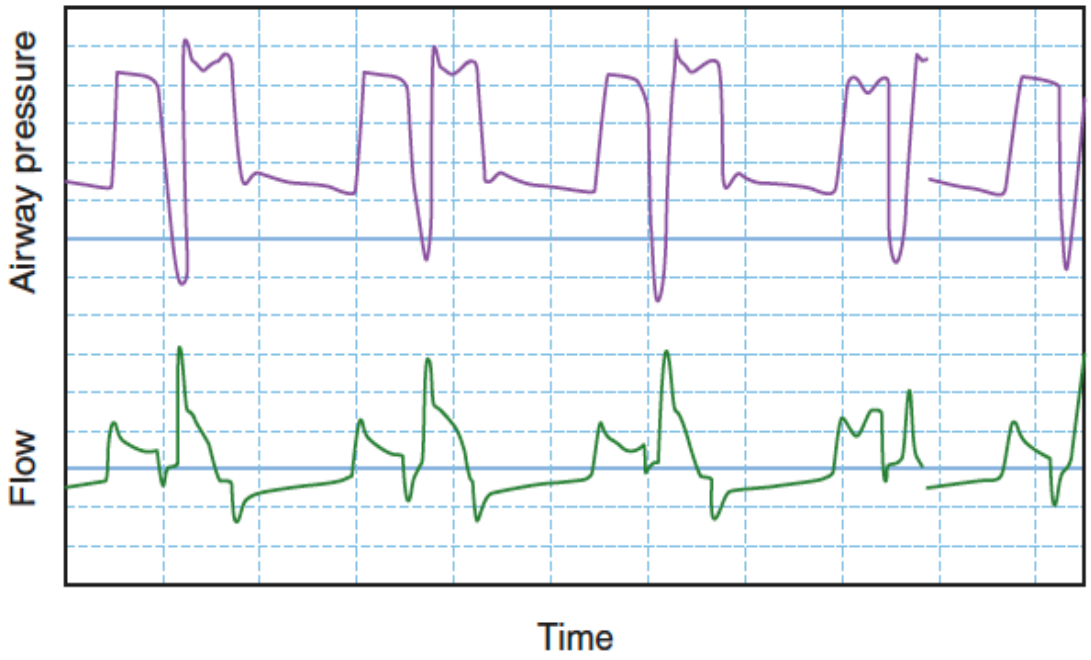
# Double Triggering

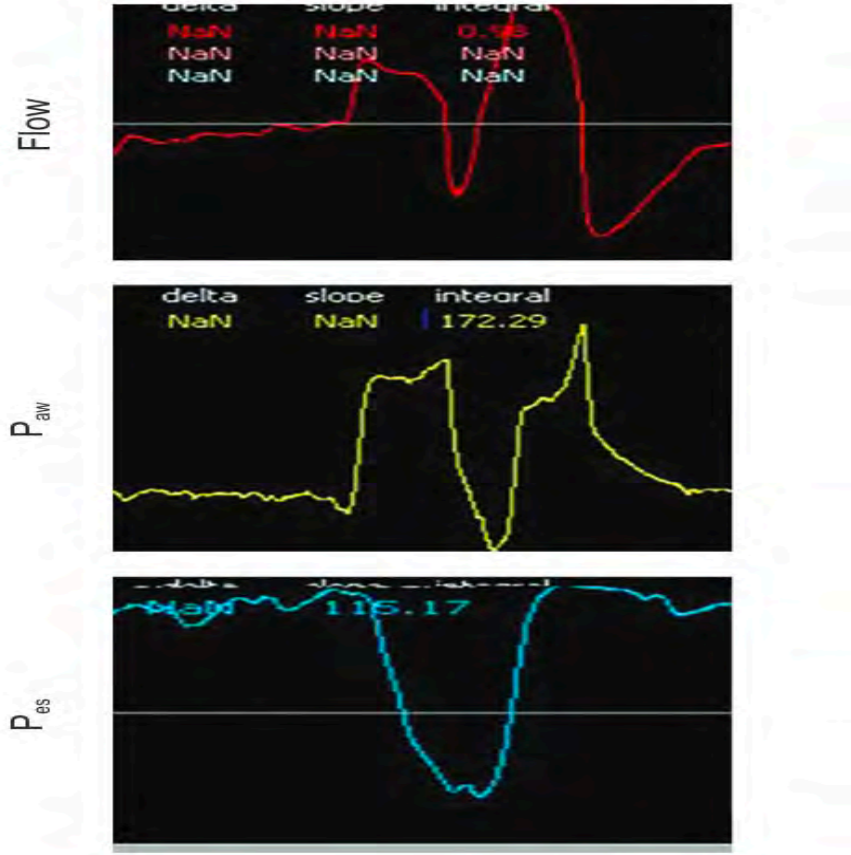
Aka Breathstacking occurs when there is no expiration or very little expiration between breaths.




Kacmarek, R, Egan's Fundamentals of Respiratory Care 2021

# Double Triggering

- What phase is this in?
  - Inspiratory cycle
- Causes
  - High inspiratory demand
  - Inspiratory time too short
  - Vt too low
  - Cycle criterion too high




Mirabella, L, Respiratory Care 2020



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# Double Triggering

- Interventions
  - Increase Vt
  - Increase peak flow to match demand
  - Increase I-time to match patient's neural timing
  - Mode change to Pressure Support
  - Increase sedation

# #5




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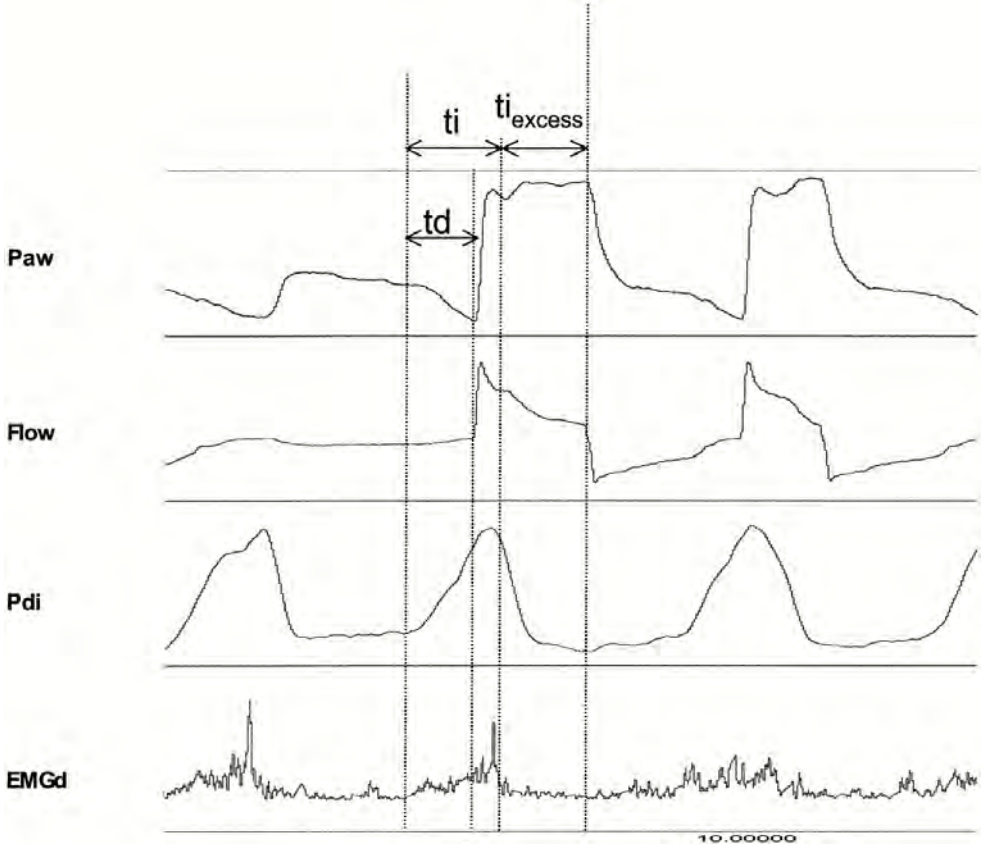
# Delayed Cycling

- What phase is this in?
  - Inspiratory Cycle
- Causes
  - Cycle % set too low
  - I-time too long
  - Too much support/volume




Tassaux, D, AJRCCM 2005



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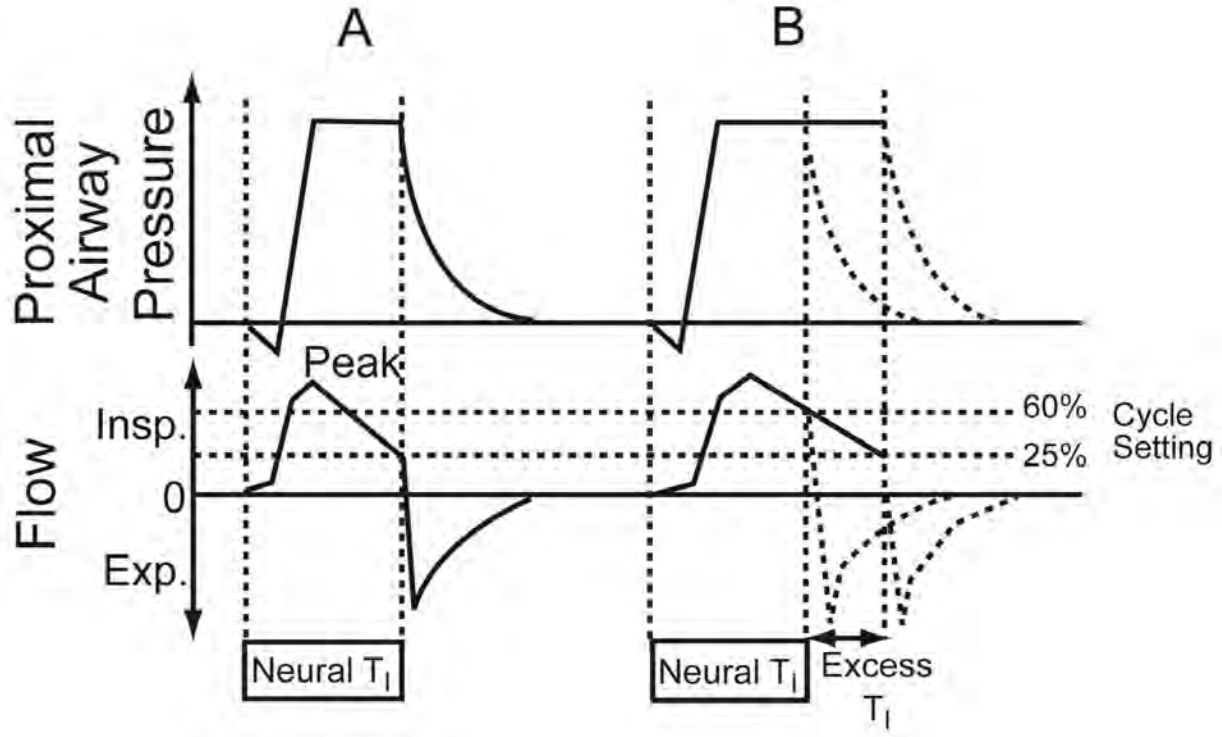
# Delayed Cycling

Delayed Cycling is active expiratory effort before the cycling criterion is met.




Gentile, MA, Respiratory Care 2011

# Delayed Cycling

- Interventions
  - Increase cycling criterion
  - Decrease I-time
  - Decrease support/volume

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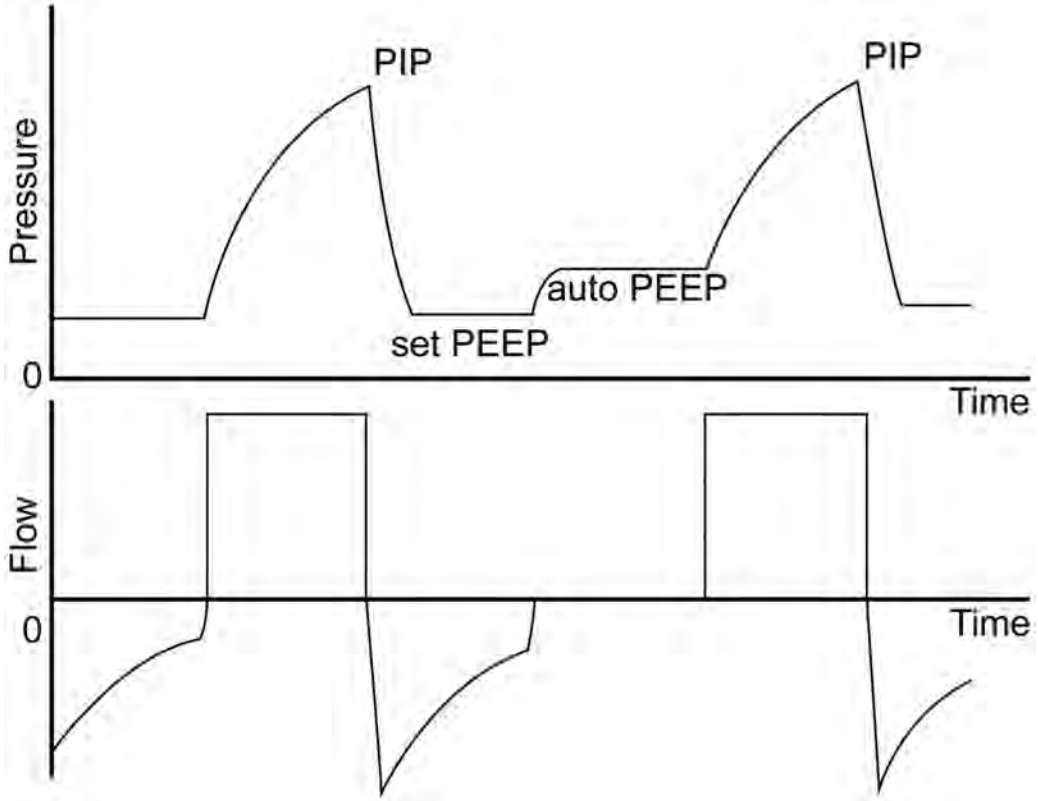
# Auto-PEEP

Auto-PEEP (Intrinsic PEEP) is incomplete emptying of the lungs occurs if the expiratory phase is terminated prematurely.




Hess, D, Respiratory Care 2014



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# Auto-PEEP

- What phase is this in?
  - Expiratory
- Causes
  - Inappropriate E-time
  - Inappropriate RR
  - Inappropriate Vt


Total PEEP = Set PEEP + AutoPEEP



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# Auto-PEEP

- Interventions
  - Adjust E-time
  - Adjust RR
  - Adjust Vt
  - Increase PEEP
  - Bronchodilators

# Summary

- Asynchronies are common
- Must be able to identify type of asynchrony
- Some can be resolved with vent interventions, others require chemical interventions
- Asynchronies if left untreated can be harmful

**The capacity to learn is a GIFT; the ability to learn is a SKILL; the willingness to learn is a CHOICE.**

**Brian Herbert**

UCSF Health

Respiratory Care Service

# Questions

Roberto.Bautista@ucsf.edu

# Optimizing Lung Recruitment in Challenging Populations Post-Intubation

**Alex Kristine Pearce, MD**
**Associate Physician Diplomate**
**UC San Diego**

Dr. Alex Pearce received her medical degree from Tulane School of Medicine followed by residency in Internal Medicine at UC San Diego. She subsequently completed her clinical fellowship in Pulmonary and Critical Care and research fellowship at UC San Diego. She currently works as an intensivist at UC San Diego with a research focus on mechanical ventilation and Acute Respiratory Distress Syndrome.

# OPTIMIZING LUNG RECRUITMENT IN CHALLENGING POPULATIONS POST-INTUBATION: INTRODUCTION TO ELECTRICAL IMPEDANCE TOMOGRAPHY (EIT)

CTS March 2024

Alex Kristine Pearce MD

UC San Diego, Division of Pulmonary and Critical Care

California Thoracic Society

# RELEVANT FINANCIAL DISCLOSURES

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

- I WILL discuss off-label use and/or investigational use of any drugs or devices.

California Thoracic Society

# Outline/Objectives

- Review pertinent background in VILI, pleural pressure gradients, distribution of ventilation.
- Recognize challenges in lung protective ventilation
- Introduction to principles of EIT
- Understand how EIT can be used in a clinical/research setting

# Background: VILI (Ventilator induced lung injury)

- Several mechanisms
  - volutrauma: injury from high volumes
  - Barotrauma: injury from high pressures
  - Atelectrauma: injury from repetitive opening/closing
  - Dys-synchrony: injury from pendelluft

Lung strain

(Tidal volume/FRC)

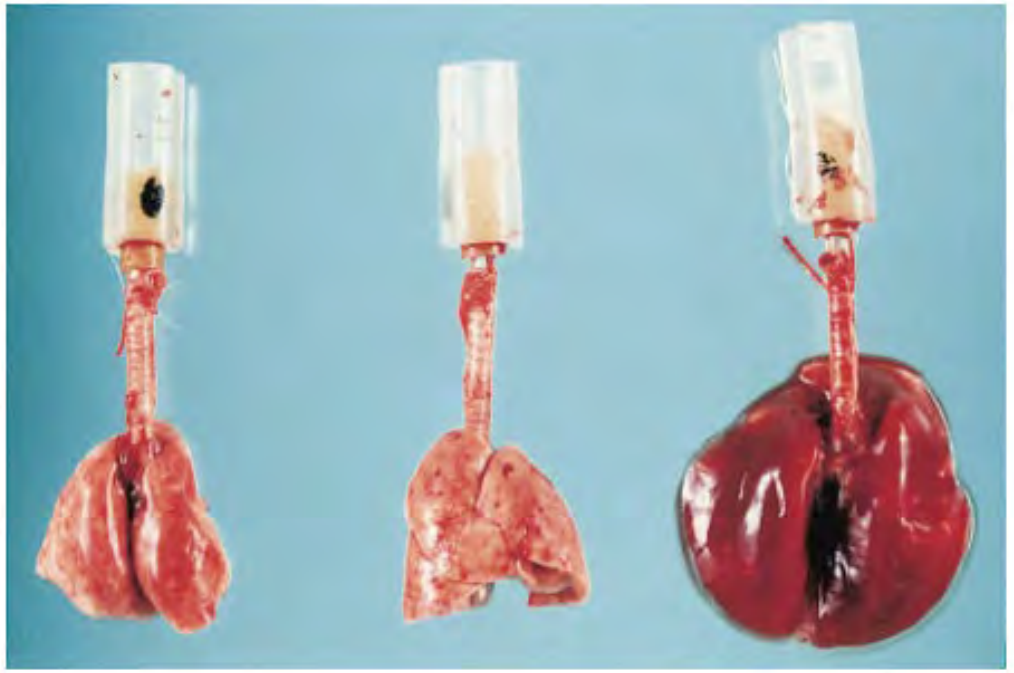
Lung Stress

(plateau or transpulmonary pressure)

Volu-trauma

Baro-trauma

↑ Mortality& morbidity



**Dreyfuss and Saumon. AJRCCM 1998.**

# Background: Lung Protective Ventilation

Lung protection (traditional)
Low tidal volumes→ 6 cc/kg IBW
Plateau Pressure <30, Low Driving pressure <15 cmH2O
Open lung strategy (avoid cyclical atelectasis)
Prone positioning

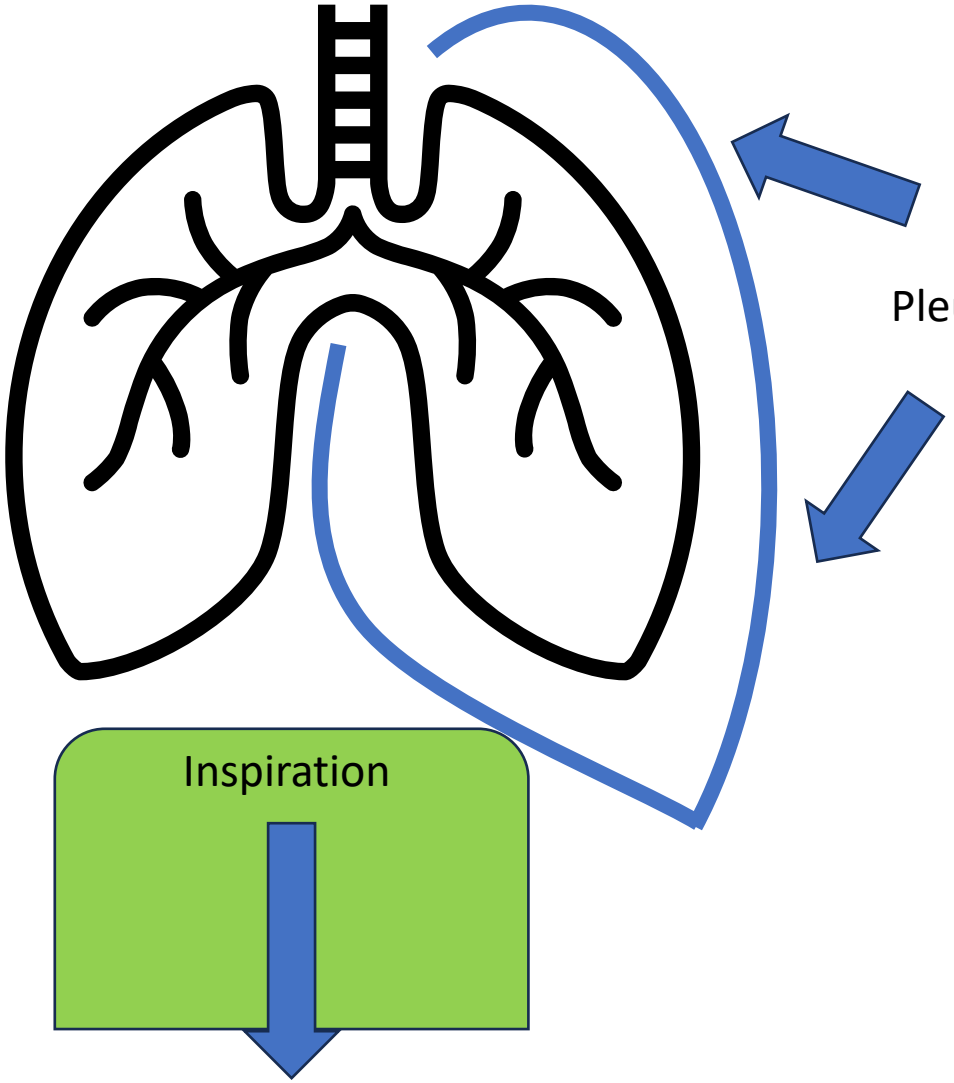
Is this always enough? No
Can harm/VILI still occur? Yes

Why?– Current approaches only focus on global metrics and neglect assessment of regional stress/strain

# Background: regional ventilation in health and disease

- Time-constants (resistance x compliance)
- Airway closure below FRC
- Pleural pressure gradients (transpulmonary pressure)
- Parenchymal heterogeneity

# Pleural pressure




**Perfect world**: transpulmonary pressure would be the same throughout the lung

Pleural pressure (-10 cmH2O)

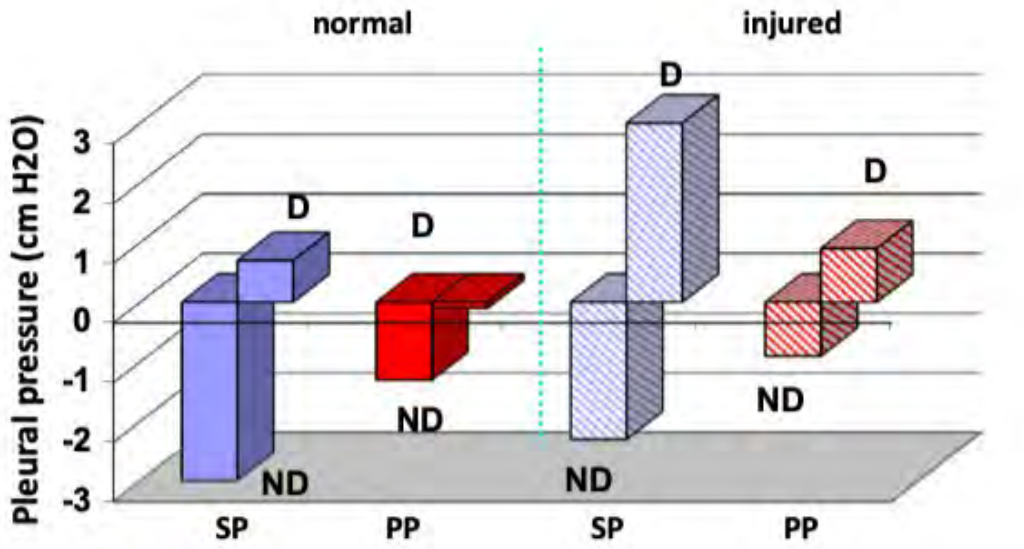
Transpulmonary pressure= Airway Pressure – Pleural Pressure

# Pleural pressure gradients are complicated

## Real world: Pleural pressure is WAY MORE complicated

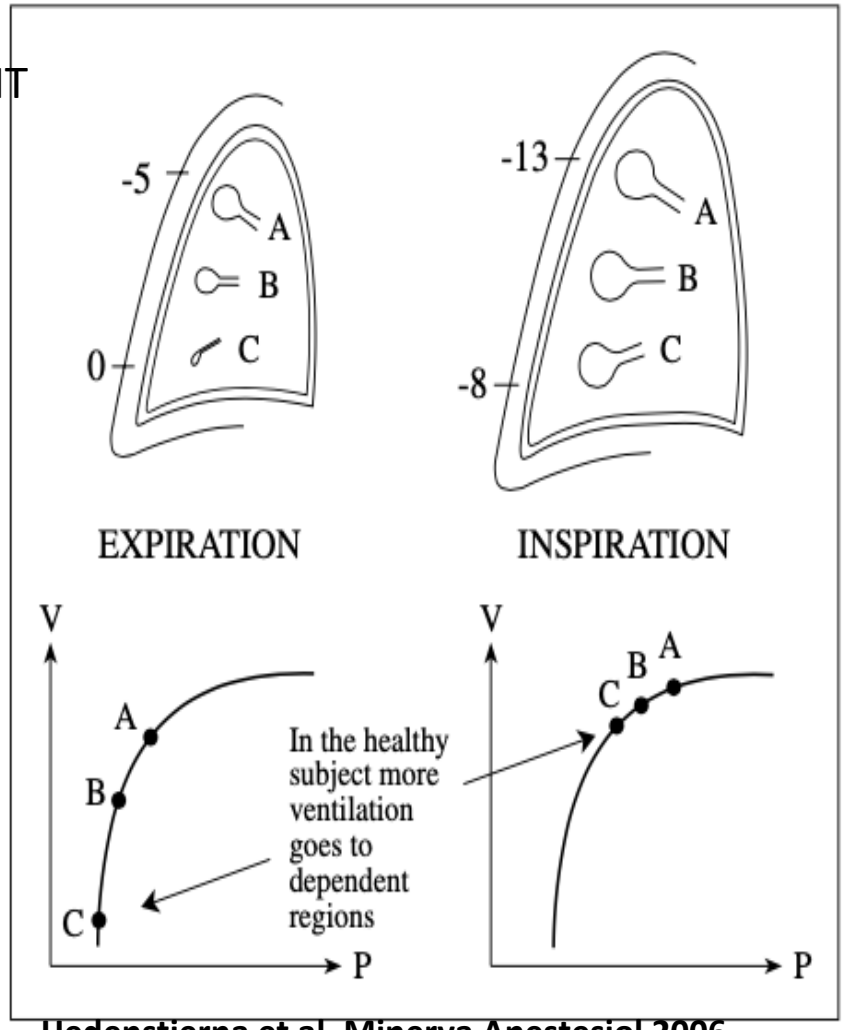
Pleural pressure gradients + heterogeneity in lung injury

1. Gravity (both apical/basilar and Ventral/dorsal)
2. Lung injury make gradients worse




Guerin et al. Intensive Care Med 2014.

UPRIGHT



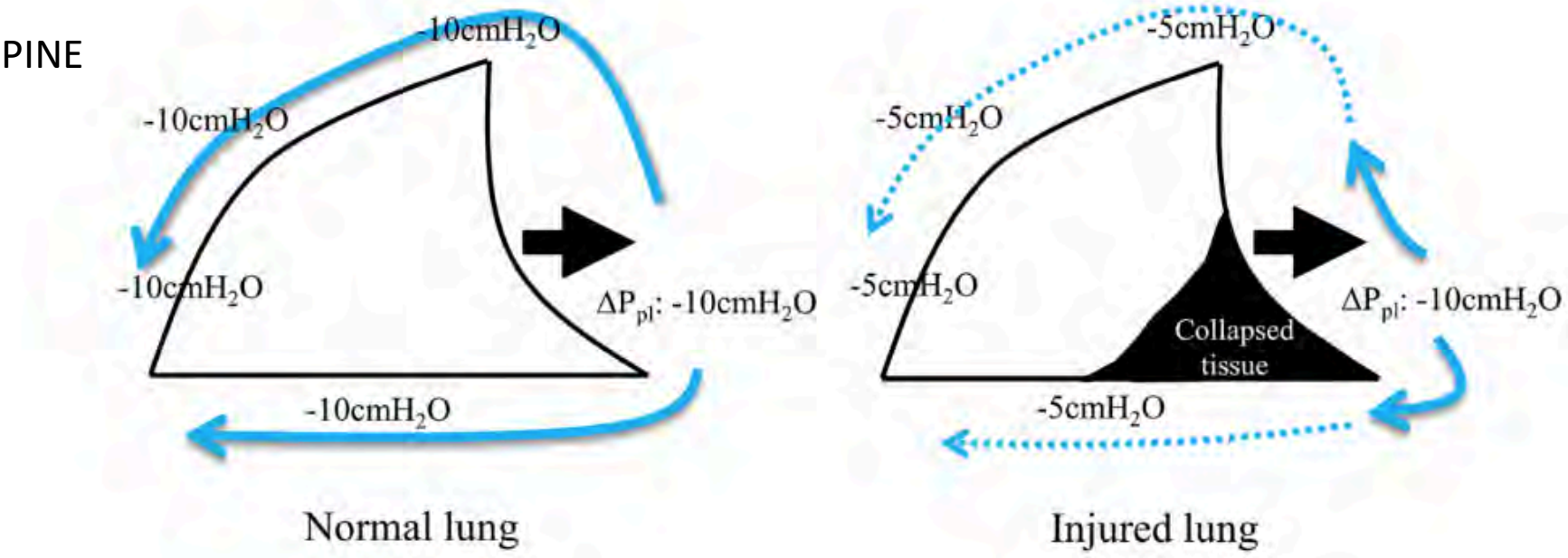

Hedenstierna et al. Minerva Anestesiol 2006.

# Pleural pressure gradients are complicated

Why does this matter?

heterogeneous lung parenchyma+ uneven distribution of pleural pressure→ variable transpulmonary pressure in different parts of the lung
→difficult to ventilate all parts of lung safely

SUPINE




**Yoshida et al J Intensive Care. 2015. PMID: 27408729.**

# Options in a patient who is difficult to ventilate/oxygenate?

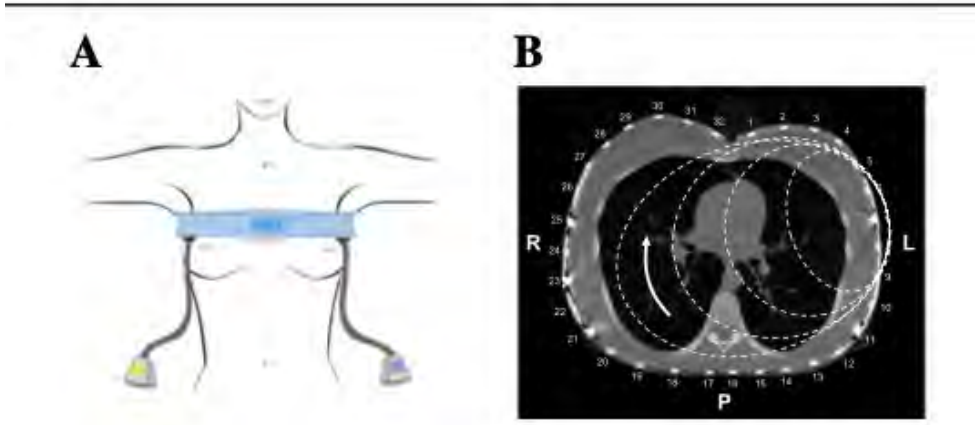
1. Esophageal manometry
2. Pressure volume curves
3. Recruitment maneuvers and best compliance

Only estimates pleural pressure at mid-thorax (at best the mid to dorsal lung- misses ventral, apex, base)

Treat the lung as a whole/average→ but injured lung tends to be heterogenous with complex pleural pressure gradients

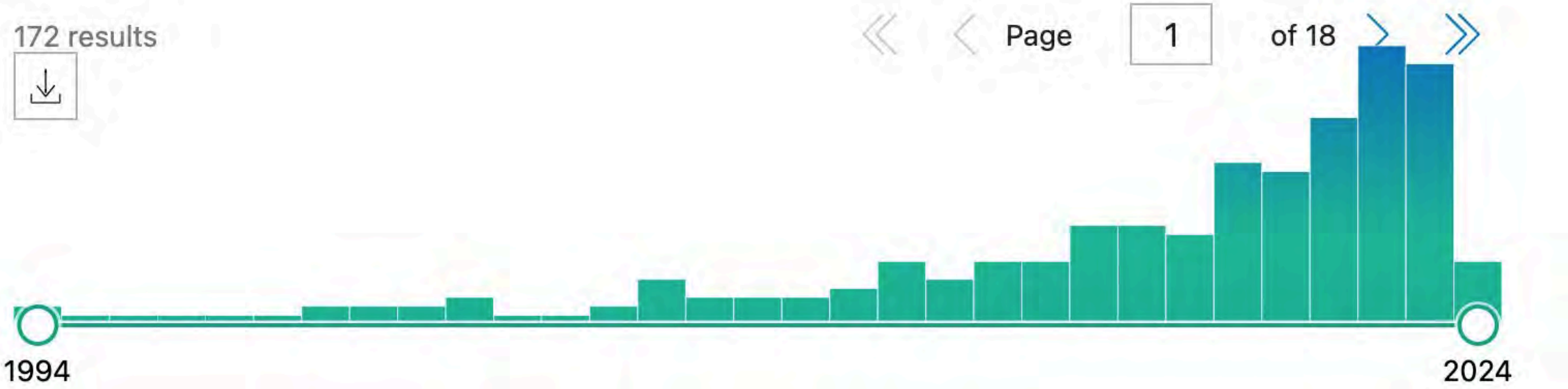
4. Electrical impedance Tomography? (EIT)

# EIT in ARDS: growing interest



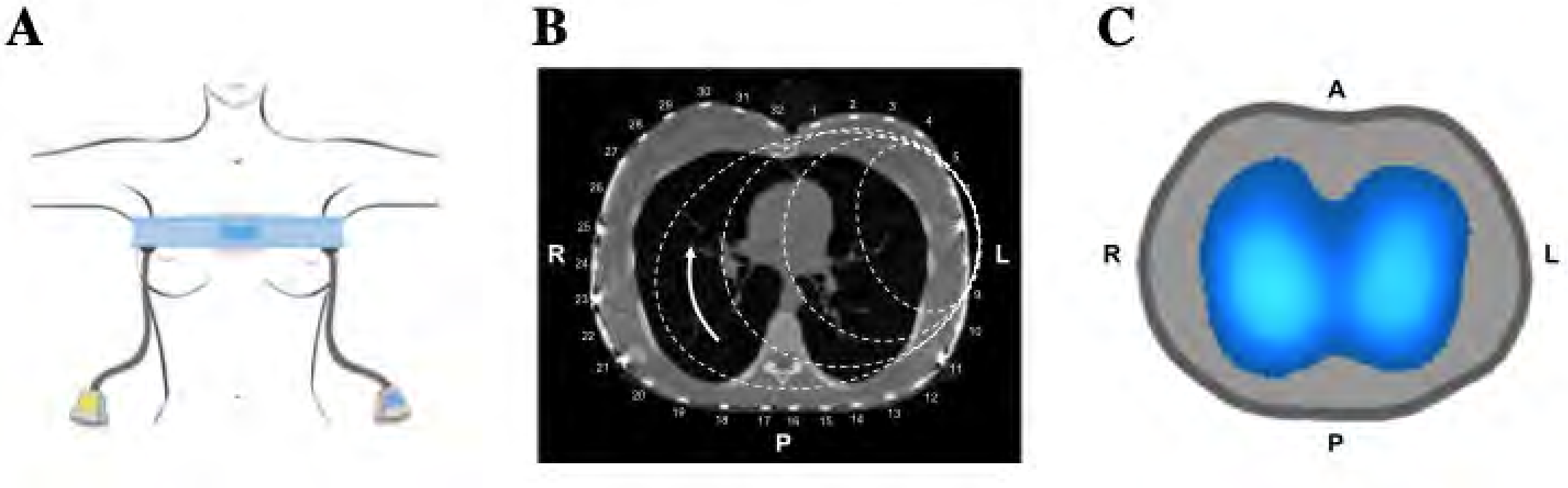

**Bachmann et al. Crit Care 2018.**

Pubmed (EIT AND ARDS)



# EIT: general principles

- Noninvasive real-time bedside technology




**Bachmann et al. Crit Care 2018.**

# EIT General principles

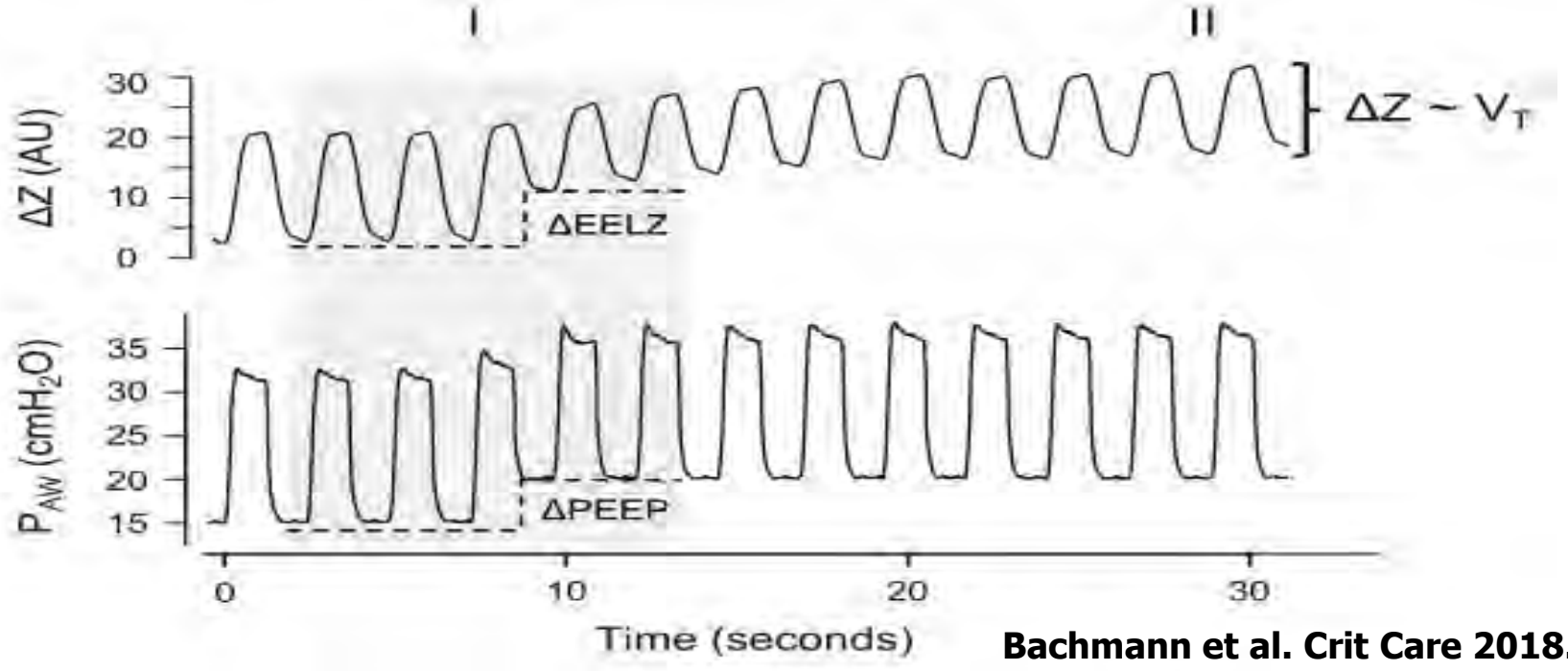
- Every tissue has a different resistivity to current
- Estimates resistivity changes across lungs while breathing
  - Inspiration= ⬆️ Resistivity
  - Expiration= ⬇️ Resistivity

**Table 2** Body tissue resistivity to passage of current (50 Hz)

| Tissue | Resistivity (Ωm) |
|---|---|
| Lung during expiration | 12.5 |
| Lung during inspiration | 25 |
| Blood (50% hematocrit) | 1.4–1.7 |
| Cardiac muscle | 2.5–5 |

**Tomicic V and Cornejo R. Journal of Thoracic Disease, 2019**

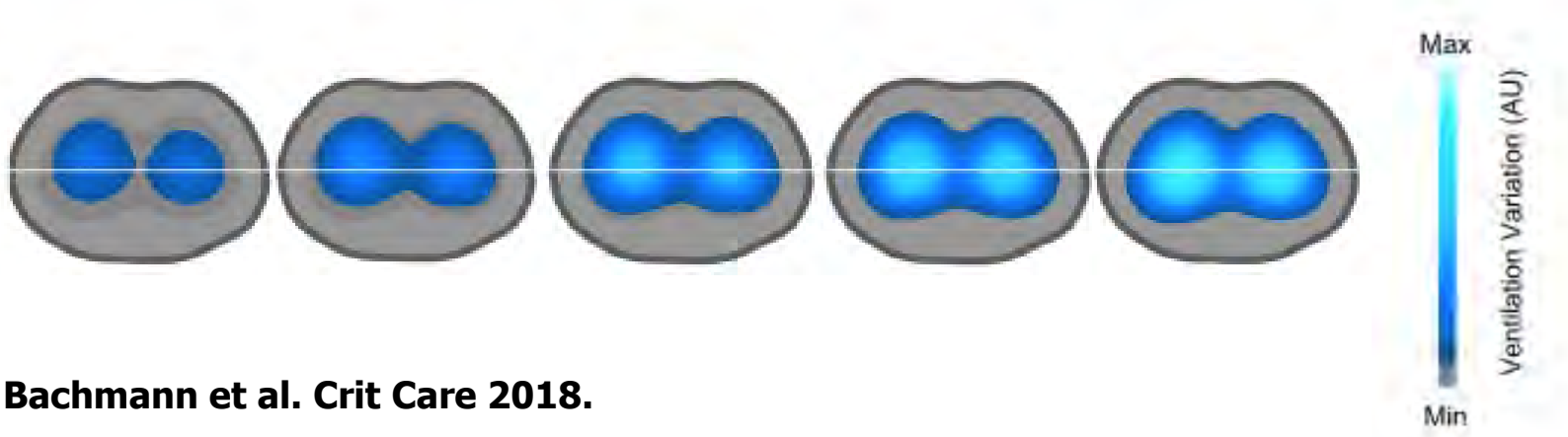
EIT plethysmogram



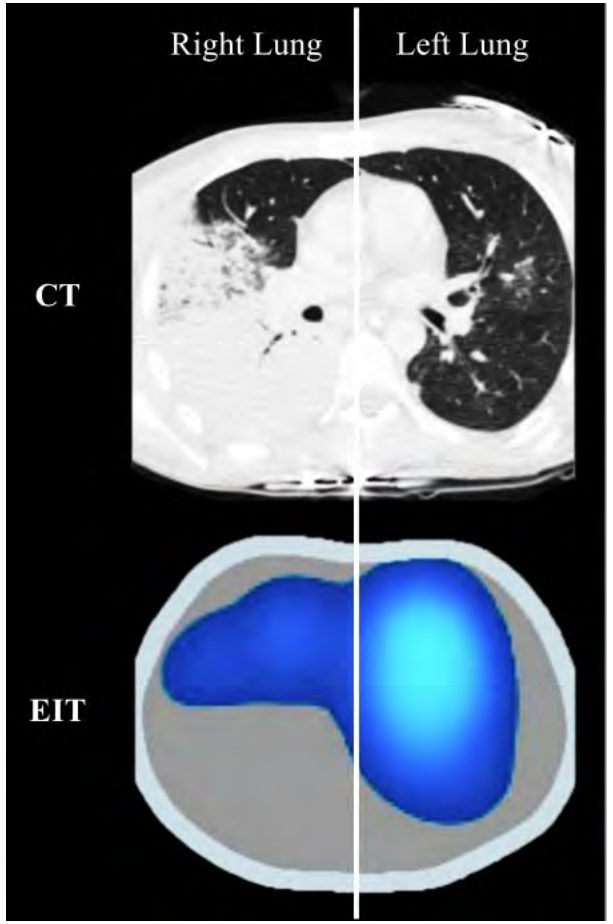

**Bachmann et al. Crit Care 2018.**

# EIT: General principles

- Resistivity/change in resistivity correlates with volume of air that enters the lung
- Creates image and way to quantify/assess distribution of ventilation




**Bachmann et al. Crit Care 2018.**

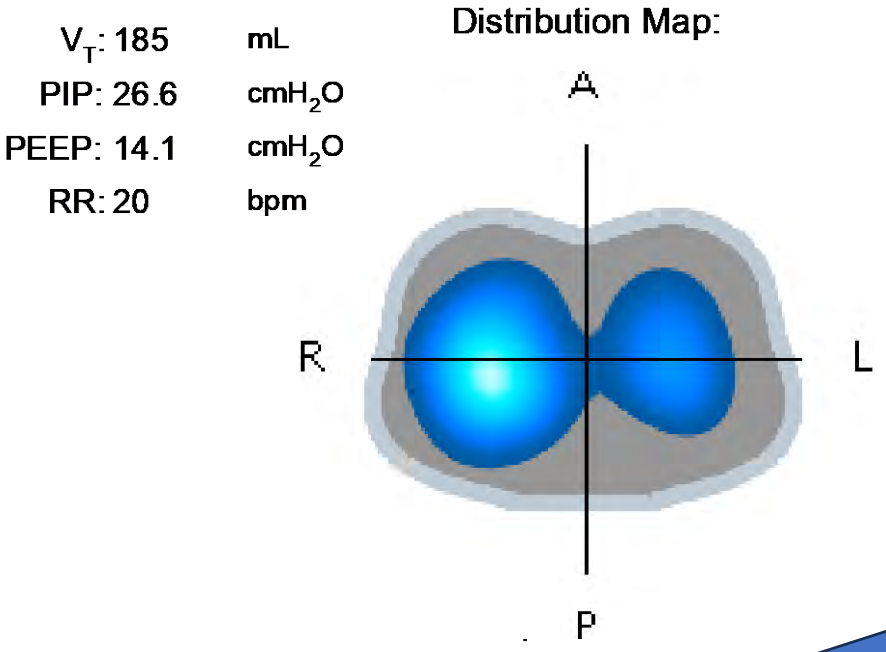



**Bachmann et al. Crit Care 2018.**

# Clinical/Research Applications

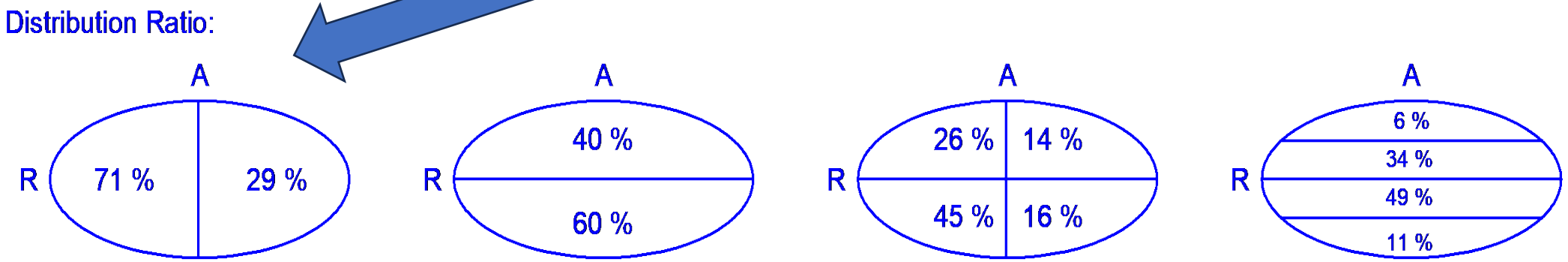
- Distribution of ventilation
- PEEP titration
- Pendelluft
- Other: patient-ventilator asynchrony, Ventilation/perfusion, NIPPV

# Distribution of Ventilation




- EIT provides a ventilation map: can quantify distribution of ventilation several ways
- Can use to identify heterogeneity in distribution of ventilation
-Impedance change correlates with changes in air content

Example of mucus plugging on the left side

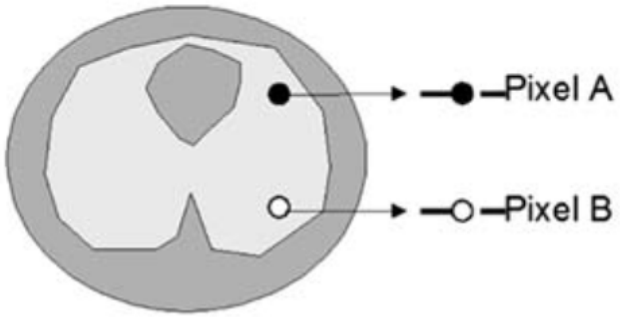


# PEEP Titration

- How should we titrate PEEP?
  - Esophageal manometry: EP-VENT3 planning in progress= TBD
  - PEEP tables?
  - Best compliance?
  - WHO KNOWS?
  - What about EIT?

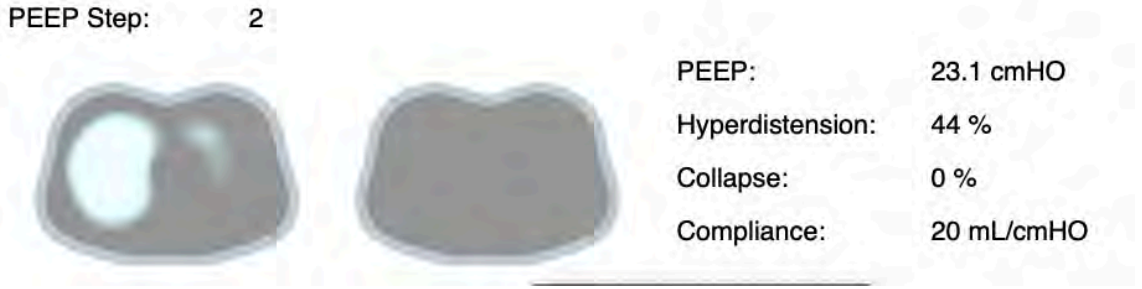
# PEEP Titration with EIT

Balance between overdistension and collapse (Costa Method)



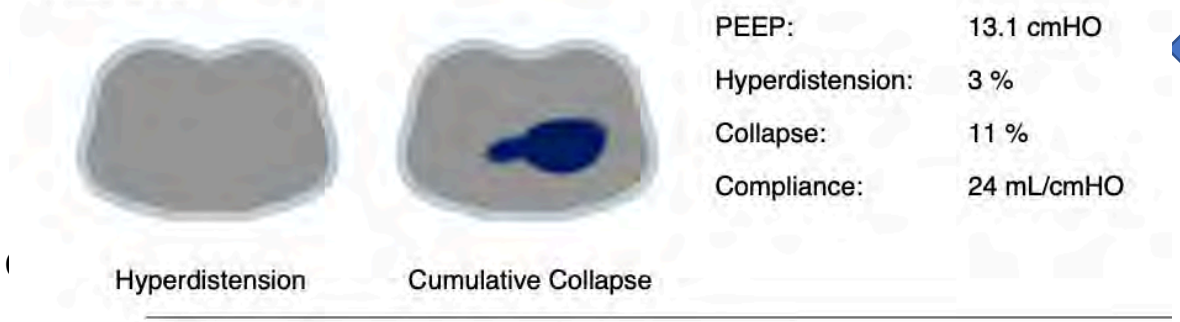

**Costa EL et al. Intensive Care Medicine 2009.**


**PEEP 25**




**PEEP 23**

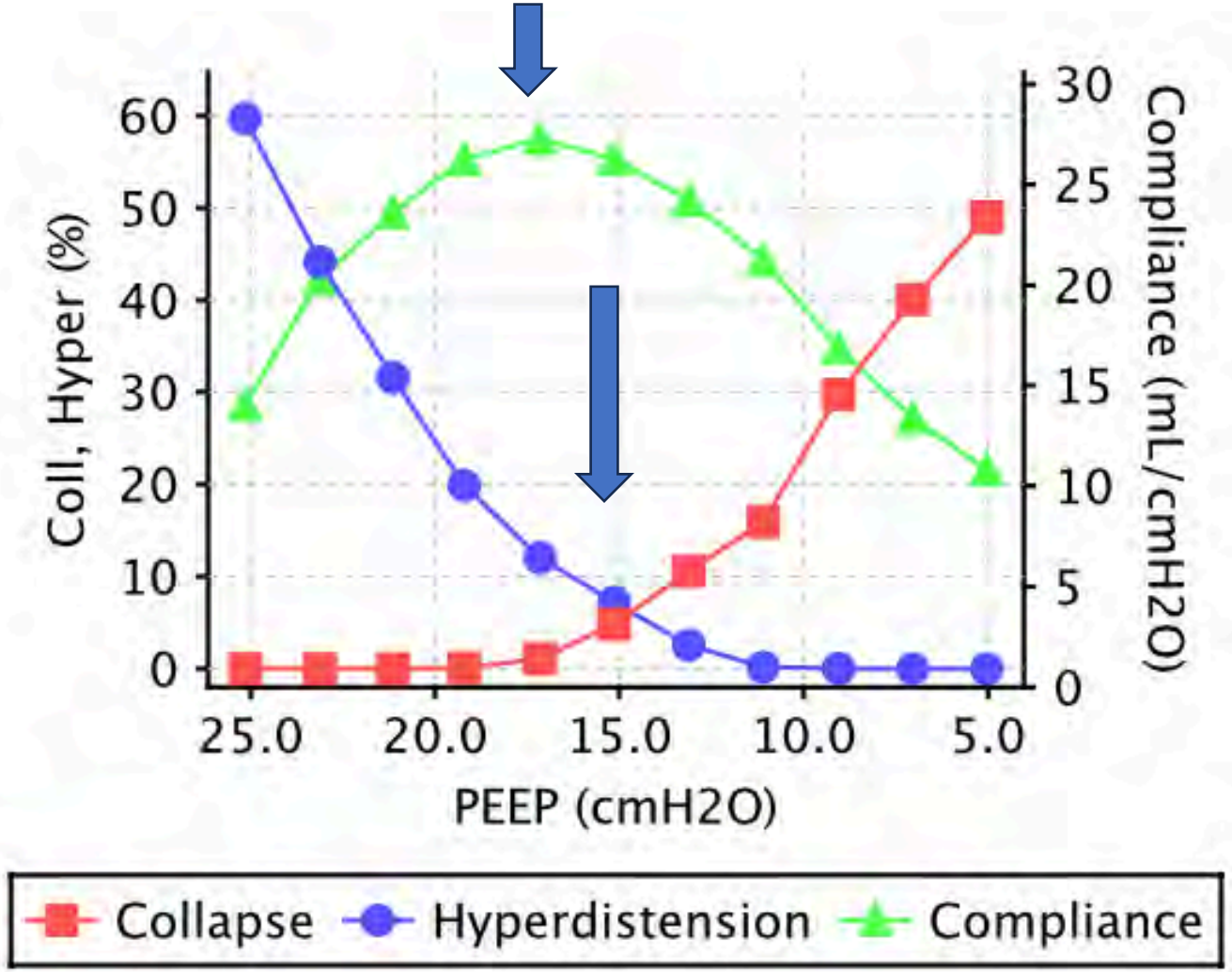

**PEEP 15**




**PEEP 13**

White= overdistention
**Blue**=collapse

# PEEP Titration (example)




| PEEP ($cmH_2O$) | Compliance ($mL/cmH_2O$) | Hyperdist. (%) | Collapse (%) |
|---|---|---|---|
| 25.1 | 14 | 60 | 0 |
| 23.1 | 20 | 44 | 0 |
| 21.1 | 24 | 32 | 0 |
| 19.2 | 26 | 20 | 0 |
| 17.2 | 27 | 12 | 1 |
| 15.1 | 26 | 7 | 5 |
| 13.1 | 24 | 3 | 11 |
| 11.1 | 21 | 0 | 16 |
| 9.0 | 17 | 0 | 30 |
| 7.0 | 13 | 0 | 40 |
| 5.0 | 11 | 0 | 49 |

# PEEP Titration with EIT offers individualized approach and may improve outcomes?

**RECRUIT study (2023): Jonkman and Alcala et al. *AJRCCM***

- 171 Patients with ARDS due to COVID-19
- Used EIT based PEEP selection (Costa method) versus best compliance
- in 81% of patients EIT based PEEP selection yielded PEEP selection different from best compliance
- Offers personalized way to adjust PEEP in patients with different responses to PEEP

*Non COVID recruitment ongoing

**EIT-Guided PEEP titration reduces mechanical power: a randomized crossover pilot study (2023): Jimenez et al. *Critical Care***

- High PEEP/FiO2 table versus EIT guided PEEP selection
- 16 patients with moderate to severe ARDS
- EIT guided PEEP titration resulted in lower mechanical power

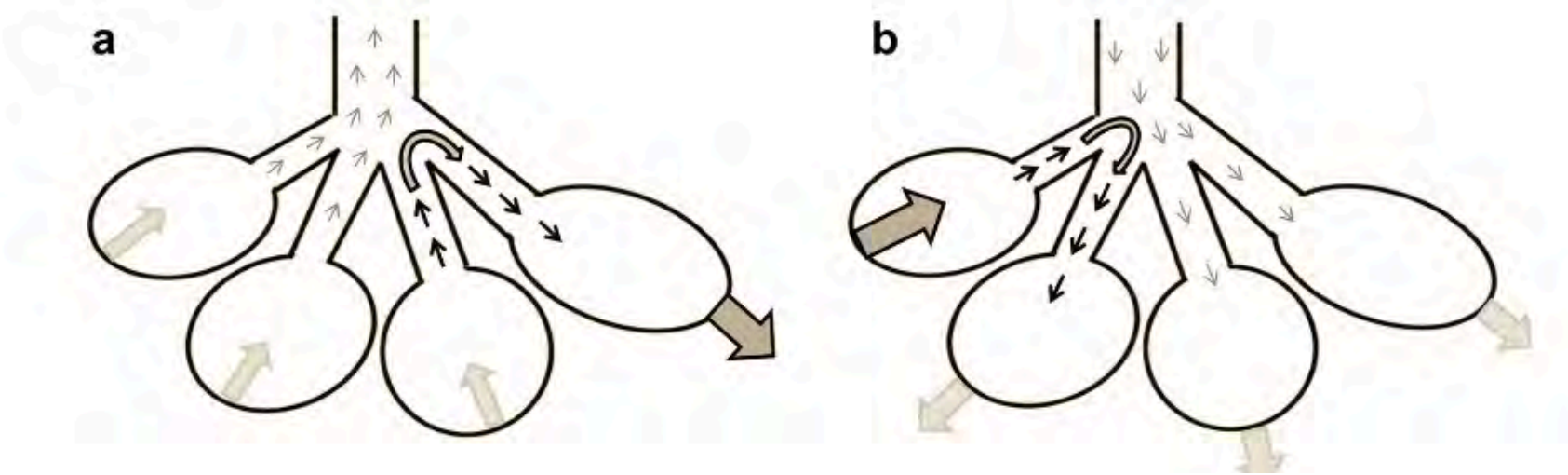
**Early Individualized PEEP guided by EIT in ARDS: a randomized controlled clinical trial (2021): He et al. *Critical Care***

- ARDS net PEEP/FiO2 table versus EIT guided PEEP selection
- 117 patients with moderate to severe ARDS
- Absolute mortality 27% (PEEP/FiO2 table) versus 21% (EIT guided)

**Additional EIT studies upcoming**

# Pendelluft

General definition: movement of air from one region of the lung to another during a tidal breath



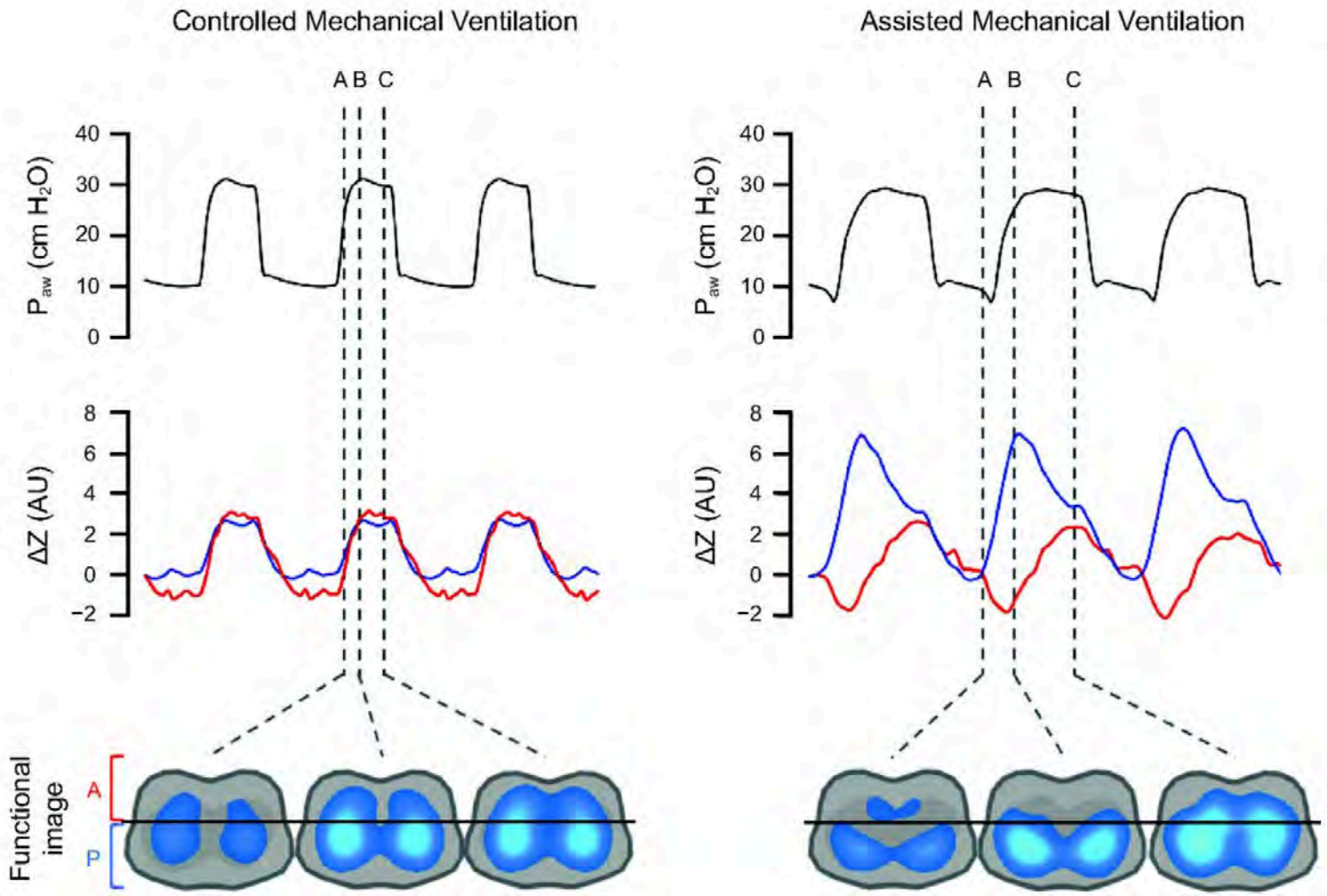

- Can lead to occult overdistension (potentially harmful)

**Coppadoro A et al. Occurrence of pendelluft under pressure support ventilation in patients who failed a spontaneous breathing trial: an observational study.** ***Ann Intensive Care*** **2020.**

# Pendelluft

- EIT can be used to identify pendelluft

* Can use NMB or increase PEEP to minimize pendelluft



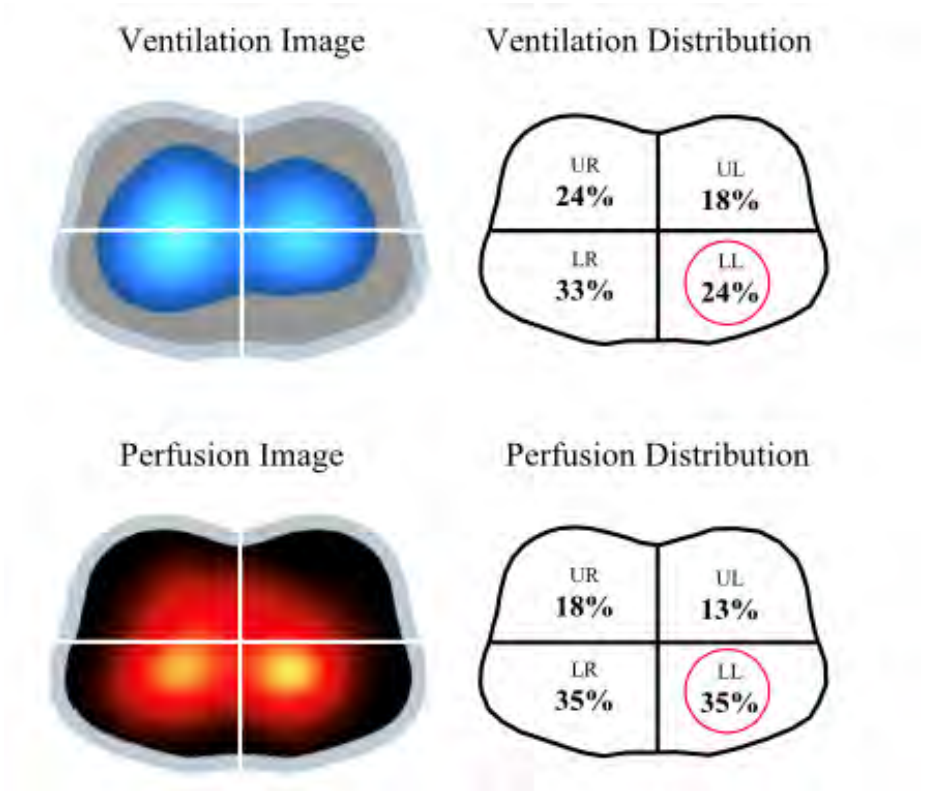

**Kacmarek R et al. Consequences to the Lungs When Gas Swings Between Lung Units during Patient triggered mechanical ventilation.** ***Respiratory Care*** **2021.**

# Future Directions

- Ventilation/perfusion mapping

- Asynchrony detection features

- HHFB, NIPPV, HFOV (measuring tidal volume, collapse/overdistention)




**Bachmann et al. Crit Care 2018.**

# Take home messages

- EIT offers a continuous non-invasive bedside assessment of regional ventilation (and perfusion)
- Offers good temporal resolution; can see dynamic changes over time
- Can measure responses to changes like PEEP or paralytics
- Allows individualized patient management (when one-size fits all approaches have failed)
- Ongoing research will determine impact on clinical outcomes

# Thank you!

- Special thank you to....
  - Marcelo Amato
  - Eduardo Costa
  - Caio Morais
  - Glasiele C. Alcala
  - Ewan Goligher
  - Atul Malhotra
  - Kim Prisk
  - Jim Butler
  - Stephen Loring

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# Pro: Non-Ventilator Based Techniques are Necessary for Optimization of Lung Mechanics in Ventilated Patients?

**Brian M. Daniel, RRT, TCO**
**Respiratory Therapist**
**UC San Francisco**

Brian M. Daniel is a respiratory care practitioner with more than 35 years of experience in academic health care, education, and research. Currently, he is a clinical specialist for Respiratory Care Services at UCSF Health as well as a clinical research coordinator for UCSF's Cardiovascular Research Institute. Brian also serves as Director for Clinical Education, at Skyline College's Respiratory Care Program.

# Let’s NOT forget the basics!

Non-Ventilator based techniques ARE necessary when optimizing lung mechanics…

# Disclosures

- None relative to this presentation


2021-11-11
14:26:45
INTELLiVENT
P-CMV
Adult
Patient
Additions
Modes
40
5
31
Ppeak
cmH2O
11
Pmean
cmH2O
40
8
22
fTotal
b/min
800
250
297
VTE
ml
18.0
4.0
6.6
ExpMinVol
l/min
Paw
cmH2O
Flow
l/min
IntelliCuff
18
b/min
Rate
16
cmH2O
Pcontrol
7
cmH2O
PEEP/CPAP
100
%
Oxygen
Adult Male
172 cm
IBW = 68 kg
Pcuff
---
cmH2O
22
fTotal
b/min
---
fSpont
b/min
0.60
TI
s
2.13
TE
s
1:3.6
I:E
5 / 11
Rinsp
5
cmH2O/l/s
Cstat
11.8
ml/cmH2O
V
ml
PCO2
mmHg
Controls
Alarms
Monitoring
Graphics
Tools
Events
System
INT
AC


1:51
2021-07-21
09:08:27
INTELLIVENT
SPONT
Adult
Backup
Patient
Additions
Modes
45
5
29
Ppeak
cmH2O
18
Pmean
cmH2O
55
8
45
fTotal
b/min
900
100
445
VTE
ml
25.0
4.0
19.9
ExpMinVol
l/min
Paw
cmH2O
40
30
20
10
0
s
1
2
3
4
5
6
7
8
9
10
Flow
l/min
100
50
0
-50
-100
IntelliCuff
16
cmH2O
Psupport
10
cmH2O
PEEP/CPAP
100
%
Oxygen
1:55
Controls
Alarms
Adult Male
172 cm
IBW = 68 kg
Pcuff
---
cmH2O
45
fTotal
b/min
45
fSpont
b/min
0.47
TI
s
0.83
TE
s
1:1.8
I:E
5 / 9
Rinsp
23
cmH2O/l/s
Cstat
22.7
ml/cmH2O
PCO2
mmHg
60
40
20
0
2
4
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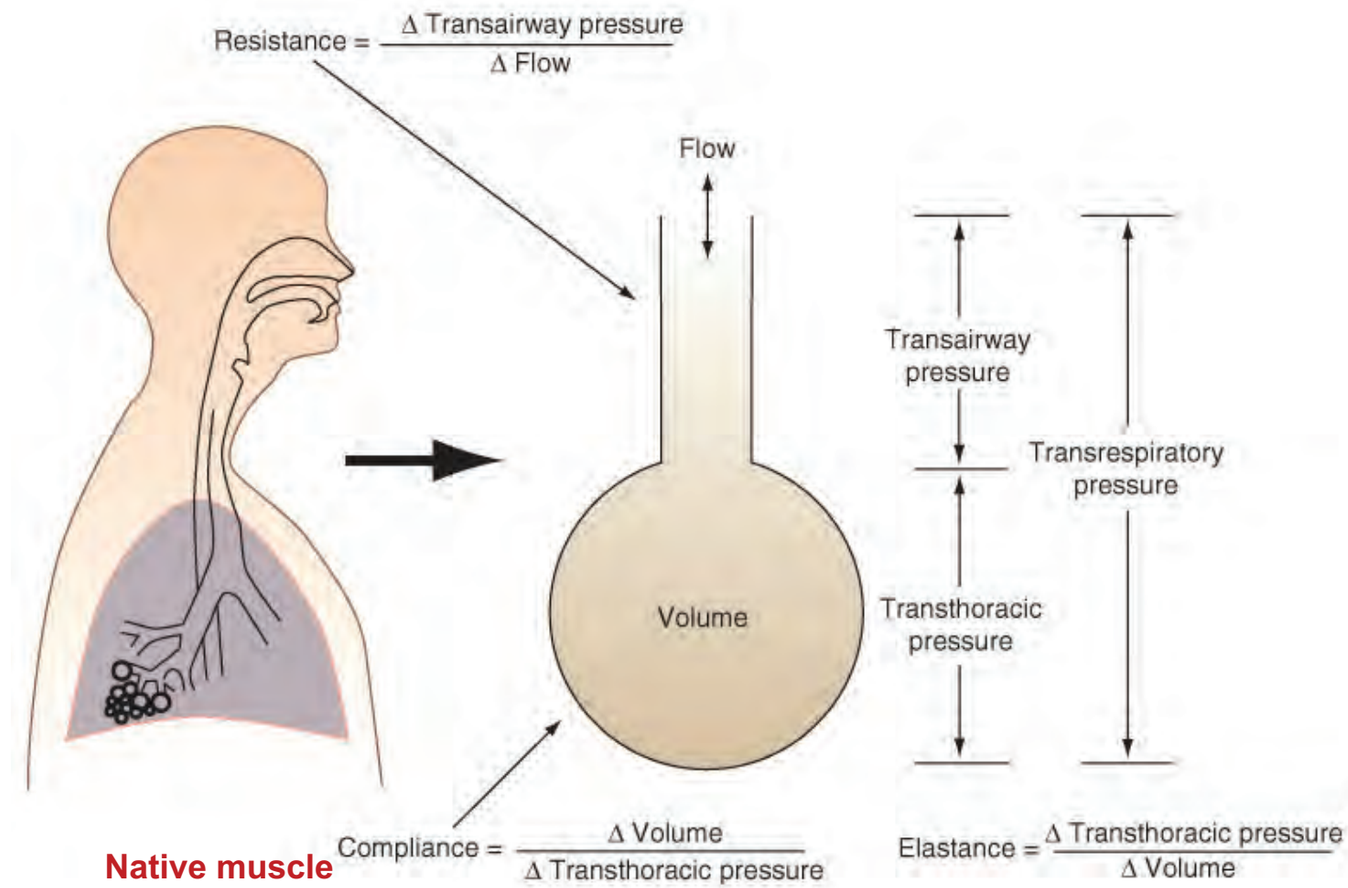
8
V
ml
1600
1200
800
400
0
Monitoring
Graphics
Tools
Events
System
INT
AC

# Control System

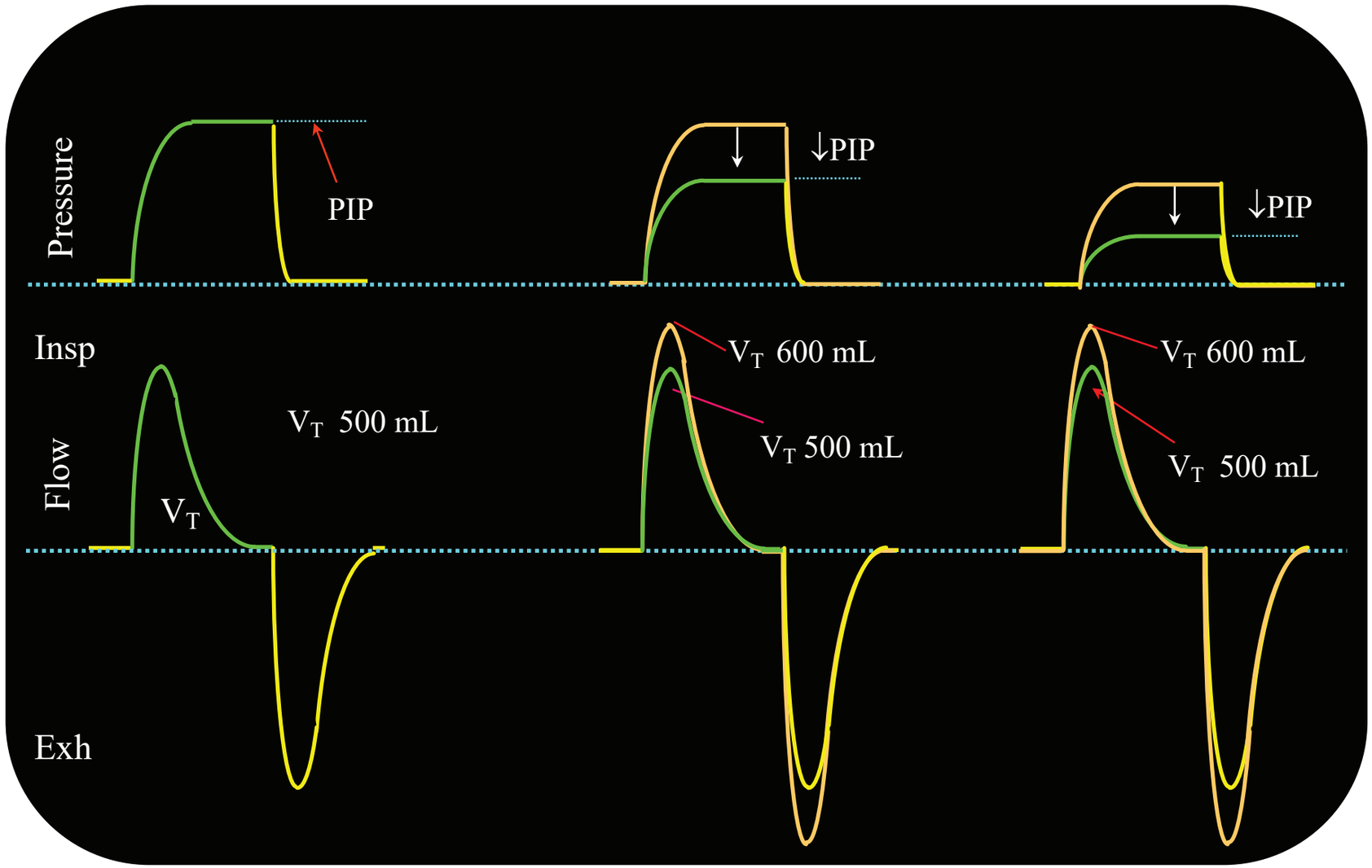


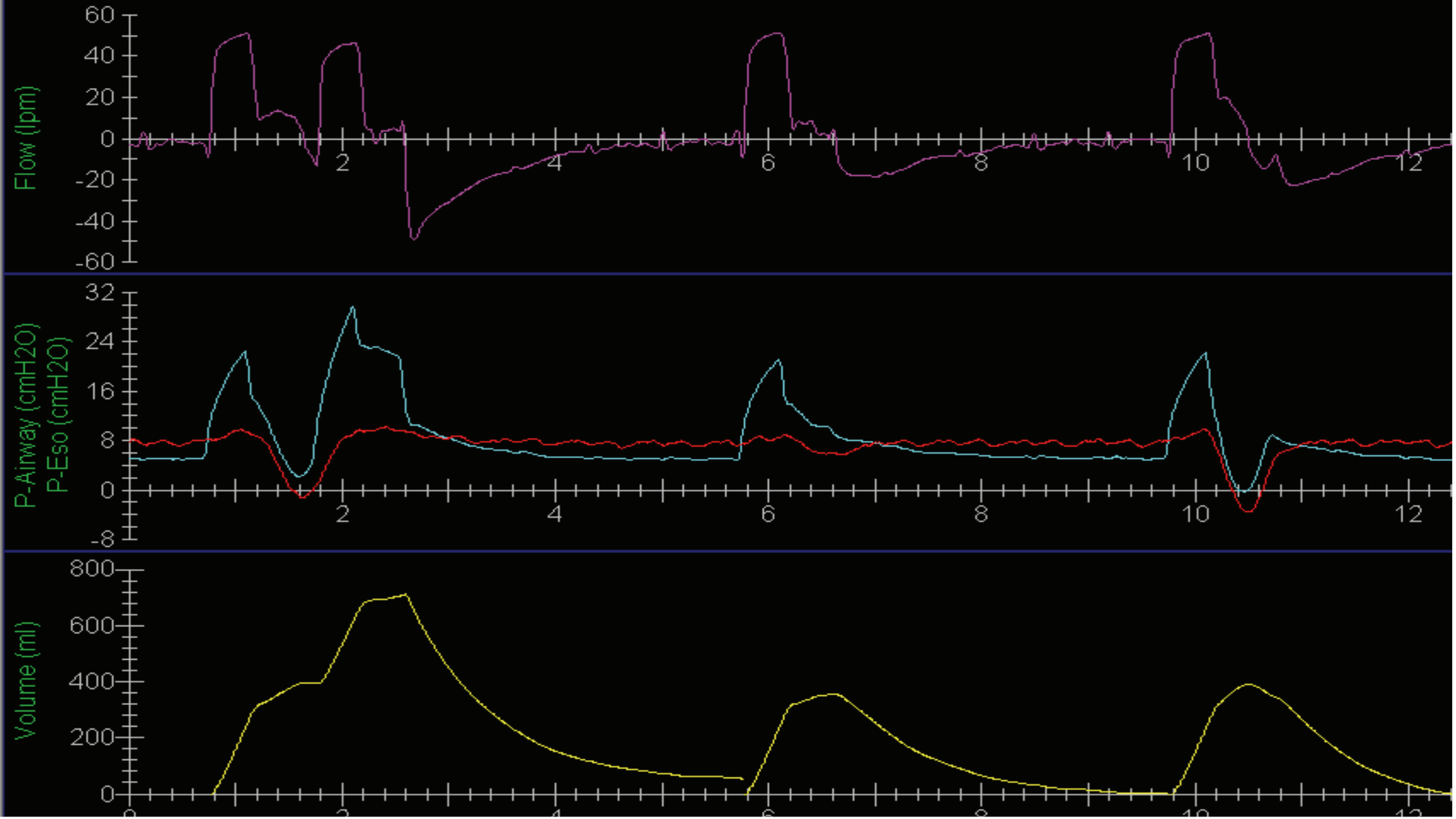

Native muscle

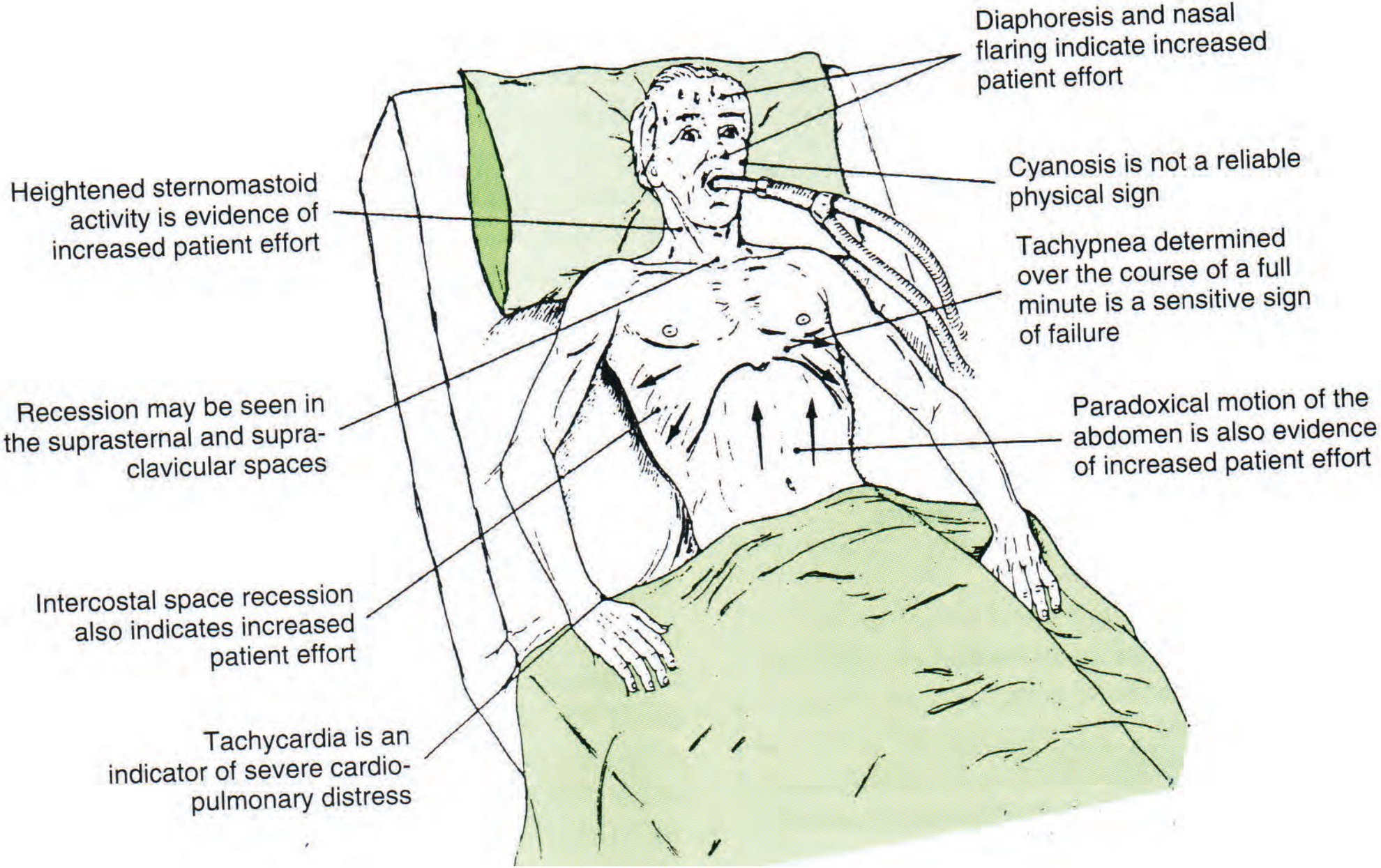
New muscle

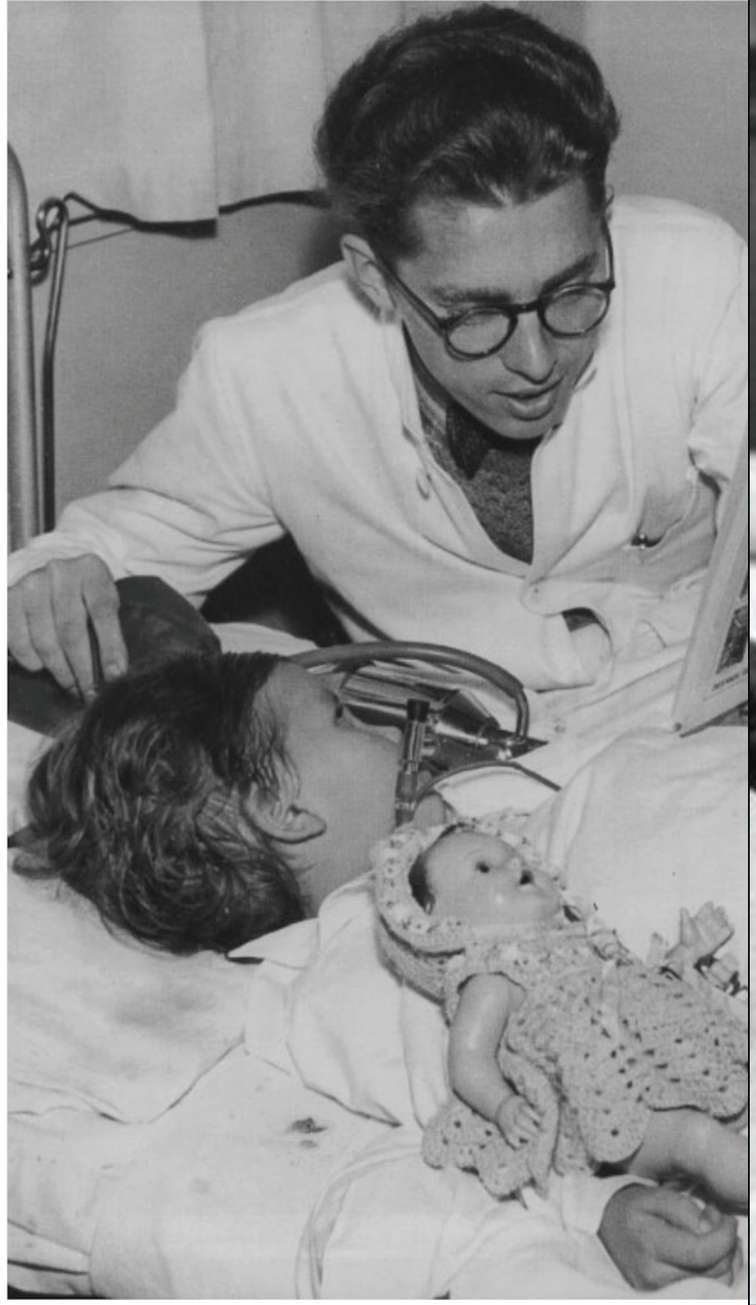
Equation of Motion for the Respiratory System

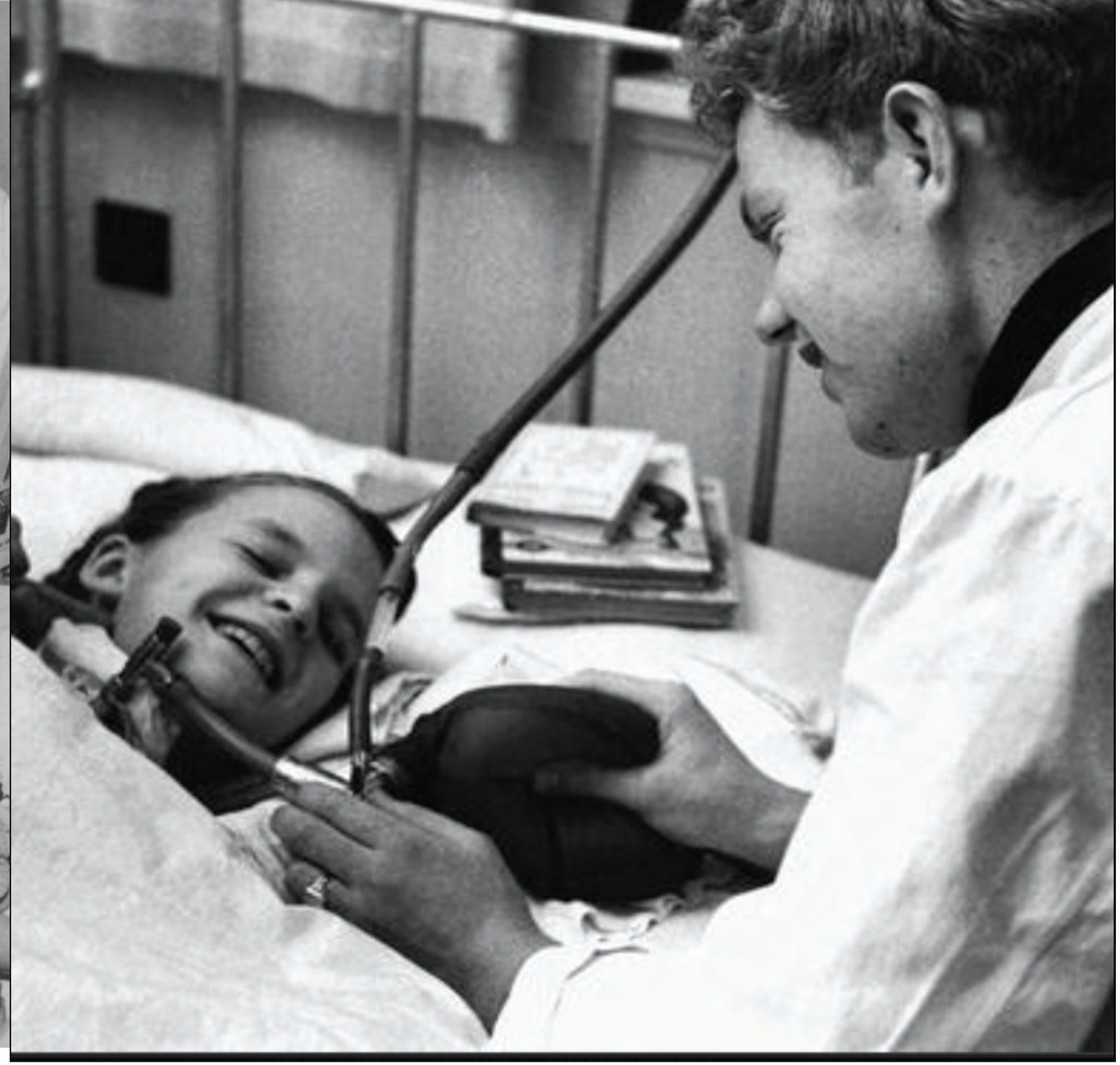
$P_{vent} + P_{muscles} = \text{elastance} \times \text{volume} + \text{resistance} \times \text{flow}$

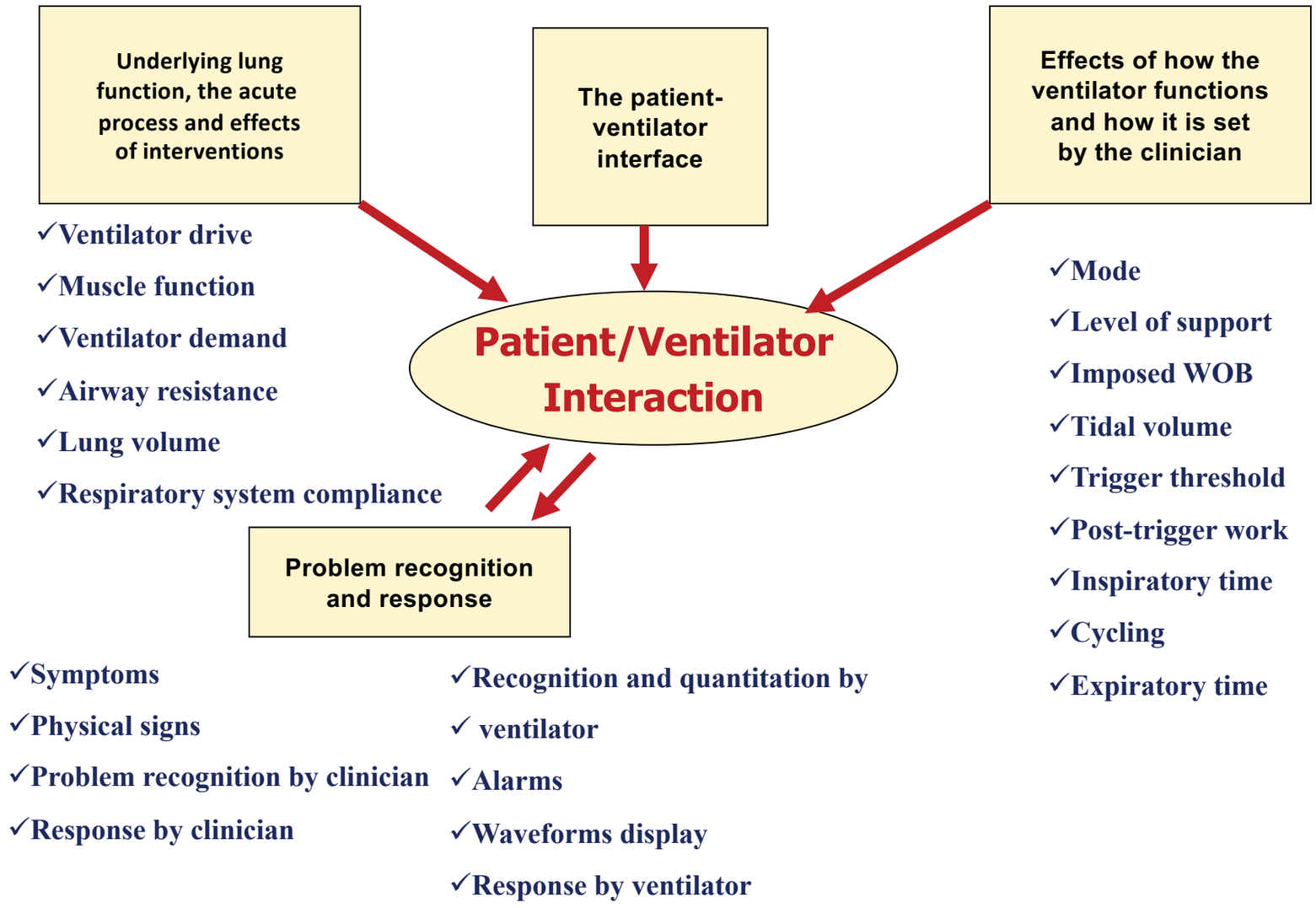

Pressure
PIP
↓PIP
↓PIP
Insp
Flow
Exh
$V_T$ 500 mL
$V_T$
$V_T$ 600 mL
$V_T$ 500 mL
$V_T$ 600 mL
$V_T$ 500 mL


Flow (lpm)
60
40
20
0
-20
-40
-60
2
4
6
8
10
12
P-Airway (cmH2O)
P-Eso (cmH2O)
32
24
16
8
0
-8
2
4
6
8
10
12
Volume (ml)
800
600
400
200
0


Diaphoresis and nasal flaring indicate increased patient effort
Cyanosis is not a reliable physical sign
Tachypnea determined over the course of a full minute is a sensitive sign of failure
Paradoxical motion of the abdomen is also evidence of increased patient effort
Heightened sternomastoid activity is evidence of increased patient effort
Recession may be seen in the suprasternal and supra-clavicular spaces
Intercostal space recession also indicates increased patient effort
Tachycardia is an indicator of severe cardio-pulmonary distress






Underlying lung function, the acute process and effects of interventions
The patient-ventilator interface
Effects of how the ventilator functions and how it is set by the clinician
✓Ventilator drive
✓Muscle function
✓Ventilator demand
✓Airway resistance
✓Lung volume
✓Respiratory system compliance
Patient/Ventilator Interaction
✓Mode
✓Level of support
✓Imposed WOB
✓Tidal volume
✓Trigger threshold
✓Post-trigger work
✓Inspiratory time
✓Cycling
✓Expiratory time
Problem recognition and response
✓Symptoms
✓Physical signs
✓Problem recognition by clinician
✓Response by clinician
✓Recognition and quantitation by
✓ ventilator
✓Alarms
✓Waveforms display
✓Response by ventilator


Circuit Type: Adult
Humidification Type: HME
PLOT SETUP
FREEZE
P CIRC
cmH2O
80
60
40
20
0
-20
0
2
4
6
8
10
12s
INSP
120
90
60
30
0
V̇
L/min
30
60
90
EXP
120
MANUAL EVENT

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 2022-02-14 | 21:11:41 | Sigh Off | Special | | 509 | | | |
| 2022-02-14 | 21:11:41 | Disable TRC | Special | | 510 | | | |
| 2022-02-14 | 21:11:41 | FlowPattern 4 | Setting | | 312 | | | |
| 2022-02-14 | 21:11:41 | Flowtrigger 5.0 l/min | Setting | | | 304 | | |
| 2022-02-14 | 21:11:41 | Pause 0 % | Setting | | 308 | | | |
| 2022-02-14 | 21:11:41 | TI 0.90 s | Setting | | 317 | | | |
| 2022-02-14 | 21:11:41 | Oxygen 100 % | Setting | | 302 | | | |
| 2022-02-14 | 21:11:41 | PEEP/CPAP 5.0 cmH2O | Setting | | | 301 | | |
| 2022-02-14 | 21:11:41 | Vt 450 ml | Setting | | 315 | | | |
| 2022-02-14 | 21:11:41 | Rate 28 b/min | Setting | | 314 | | | |
| 2022-02-14 | 21:11:41 | Ventilation mode (S)CMV | Setting | | | 224 | | |
| 2022-02-14 | 21:11:41 | Standard setup | Setting | | 200 | | | |
| 2022-02-14 | 21:11:41 | Oxygen high is off | Setting | | | 132 | | |
| 2022-02-14 | 21:11:41 | SpO2 right Off | Setting | | 118 | | | |
| 2022-02-14 | 21:11:41 | SpO2 left Off | Setting | | 117 | | | |
| 2022-02-14 | 21:11:41 | PetCO2 low 30 mmHg | Setting | | | 112 | | |
| 2022-02-14 | 21:11:41 | PetCO2 high 60 mmHg | Setting | | | 113 | | |
| 2022-02-14 | 21:11:41 | CO2 is on | Setting | | 116 | | | |
| 2022-02-14 | 21:11:41 | O2 is on | Setting | | 111 | | | |
| 2022-02-14 | 21:11:41 | Apnea time 20 s | Setting | | 110 | | | |
| 2022-02-14 | 21:11:41 | Leak is off | Setting | | 109 | | | |
| 2022-02-14 | 21:11:41 | Vt low 250 ml | Setting | | 108 | | | |
| 2022-02-14 | 21:11:41 | Vt high 750 ml | Setting | | 107 | | | |
| 2022-02-14 | 21:11:41 | Rate low 8 b/min | Setting | | | 106 | | |
| 2022-02-14 | 21:11:41 | Rate high 23 b/min | Setting | | | 105 | | |
| 2022-02-14 | 21:11:41 | ExpMinVol low 4.00 l/min | Setting | | | | 104 | |
| 2022-02-14 | 21:11:41 | ExpMinVol high 10.00 l/min | Setting | | | | 103 | |
| 2022-02-14 | 21:11:41 | Pressure low 5 cmH2O | Setting | | | 102 | | |
| 2022-02-14 | 21:11:41 | Pressure high 40 cmH2O | Setting | | | 101 | | |
| 2022-02-14 | 21:11:40 | Reset Ventilation time 2856 min | Special | | | | 554 | |
| 2022-02-14 | 21:11:40 | ETS 25 % | Setting | | 319 | | | |
| 2022-02-14 | 21:11:40 | Standby Off | Special | | 507 | | | |
| 2022-02-14 | 21:09:57 | TE : 1897 1896 | Tech fault | | | 1897 | | |

**Causes, clinical features, and management of respiratory distress in mechanically ventilated patients**

| Etiology of respiratory distress | Clinical features, ventilator mechanics, bedside testing | Treatment |
|---|---|---|
| **Ventilator and ventilator circuit** | | |
| Incorrect ventilator settings (eg, tidal volume, fraction of inspired oxygen, inspiratory flow or pressure rate, positive end expiratory pressure, trigger sensitivity) | ▪ Can occur when settings are inadequate or too high.<br>▪ Commonly found when ventilator settings are initiated or changed (eg, after intubation, procedures, or transport).<br>▪ May be less common with modern ventilators that automatically revert to previous settings when patients are temporarily removed from mechanical ventilation or settings are temporarily changed. | ▪ Disconnect the ventilator from the ETT.<br>▪ If respiratory distress resolves, examine the ventilator including settings and connections for problems.<br>▪ Once resolved, resume mechanical ventilation.<br>▪ If distress recurs, consider altering ventilator settings attempting to "match" patient effort (eg, increase the tidal volume or respiratory rate or switch to pressure support or pressure-controlled mode), ensuring new settings do not place the patient at risk of volutrauma or barotrauma.<br>▪ Consider replacement of the ventilator if distress persists. |
| Ventilator circuit leak or obstruction (including HME) | ▪ Volume-controlled ventilation:<br>• Low peak pressures and low expired tidal volume may suggest a leak in the absence of a balloon cuff leak or cephalad displacement of the ETT (refer to below).<br>• High peak pressures, with widened delta Ppeak-Pplat*, may suggest obstruction.<br>▪ Pressure-controlled ventilation:<br>• Airway pressure unchanged, increase in tidal volume, and expiratory flow that does not return to baseline may suggest an air leak.<br>• Airway pressure unchanged, a decrease in tidal volume, and expiratory flow that is slow to return to baseline, suggest increased airway resistance from obstruction.<br>▪ A sawtooth pattern on ventilator graphics may suggest secretions or water in ventilator tubing as a source of obstruction.<br>▪ If no secretions are present in ventilator tubing, consider an obstruction at the level of the HME. | ▪ Replace the tubing if a leak is suspected.<br>▪ Empty the ventilator tubing of secretions.<br>▪ Replace the HME, if necessary. |
| Ventilator malfunction | ▪ This issue is unusual but may be suspected when respiratory distress recurs despite resuming ventilation with the correct settings and no intrinsic parenchymal, airway, pleural, or extrapulmonary issues are suspected. May be determined during ventilator interrogation. | ▪ Consider replacing components of the ventilator or the ventilator itself. |
| **Airway** | | |
| | ▪ **Most conditions are associated with the following ventilatory mechanics:**<br>• Increased Ppeak and a widened delta Ppeak-Pplat (volume-controlled ventilation).*<br>**or**<br>• Unchanged airway pressure, decreased tidal volume, expiratory flow slow to return to baseline (pressure-controlled ventilation). | |
| ETT obstruction – Mucus, blood, foreign body, kinking, or biting | ▪ Known thick and voluminous secretions or hemoptysis.<br>▪ Foreign body such as a tooth may have been inhaled during intubation.<br>▪ Kinking in the ETT or biting may be obvious.<br>▪ Resistance to manual ventilation and passage of a suction catheter through the ETT.<br>▪ Maintenance of tidal volume, unless obstruction is complete. | ▪ Attempt to identify and remove the obstruction.<br>▪ Suctioning thick secretions often sufficient.<br>▪ Reposition the head especially if a kinked tube is suspected.<br>▪ Place bite block if biting of the ETT is suspected.<br>▪ If above measures fail, replace ETT.<br>▪ Bronchoscopy if problem persists. |
| Bronchospasm | ▪ Often occurs in those with underlying obstructive lung disease but can also occur due to trauma in the airways (eg, suctioning, bronchoscopy), or medications (eg, beta blockers, allergies).<br>▪ Respiratory distress with wheeze or rhonchi.<br>▪ Maintenance of tidal volume. | ▪ Urgent bronchodilation with beta-2 agonists.<br>▪ Glucocorticoids, antihistamine, histamine receptor blockade, and epinephrine and may be administered if allergy is suspected. |
| Obstruction of lower airways by secretions, blood, airway mass, or foreign object | ▪ Secretions of blood may be evident.<br>▪ Respiratory distress with wheeze or rhonchi (may be unilateral or focal).<br>▪ Tidal volume is maintained. Increased Ppeak* with widened delta Ppeak-Pplat.* | ▪ Attempt suctioning.<br>▪ Saline bullets sometime required to break up thick mucus plugs.<br>▪ Urgent bronchoscopy may be needed for foreign body retrieval, preferably with adequate suction channel and the ability to retrieve a foreign body if necessary. |
| Caudal migration of the ETT to mainstem bronchus (typically right-sided) | ▪ Suspect in patients with agitation or in patients who have been repositioned.<br>▪ Air entry may be limited on the unaffected side and trachea may deviate away from the affected side. | ▪ Deflate the cuff and pull the ETT back by a predetermined amount.<br>▪ Re-image with chest radiography to confirm appropriate placement. |

# Summary

- Basic (non-ventilator based) patient assessment is essential when optimizing lung mechanics.

- Emerging mechanical ventilator tools and adjuncts lack significant evidence and consistency.

# Con: Non-Ventilator Based Techniques are NOT Necessary for Optimization of Lung Mechanics in Ventilated Patients?

**Pablo Gonzalez, RRT**
**Respiratory Therapist**
**Scripps Health**

Pablo Gonzalez is currently a neonatal/pediatric/adult respiratory therapist at Scripps Memorial Hospital in La Jolla, San Diego, CA.

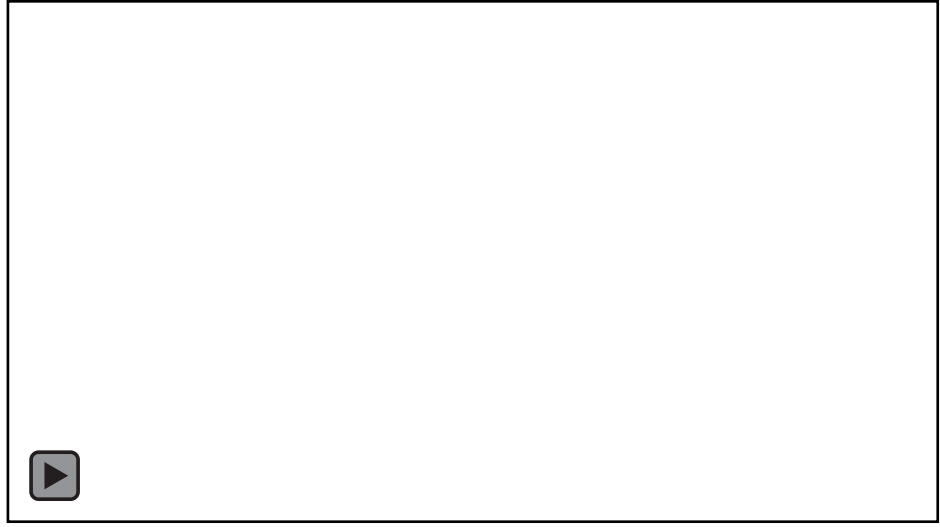
He has worked at a few facilitates: Cedar Sinai Medical Center, CHOC, Loma Linda, Sharp Mary Birch, Sanford MN, and Regions Hospital in St Paul MN where he worked alongside Dr. John J. Marini which drove him to work at the Mayo Clinic and worked alongside Dr. Gustavo Cortes Puentes and worked along renowned physicians/nurses and respiratory therapist as a ECMO specialist.

While he worked at the renowned Mayo Clinic in Rochester Minnesota, St. Mary's Hospital in the CVICU. He was a clinical preceptor, utilizing the advanced modalities in respiratory care, from ventilator management and ventilator waveform management, esophageal balloon monitoring, APRV, caring for ECMO patients, A-line insertion, bladder pressure monitoring, and HFJV in the neonatal population to name a few.

He has continued development of his skills and has started the Advanced Mechanical Ventilation Conference in San Diego. Bringing renowned speakers from all over the world. Currently he is working on a respiratory book that will help clinicians in the ICU.

Pablo earned a B.A. from laguna College of Art and Design in Laguna Beach, CA., and his associate science from California College San Diego.

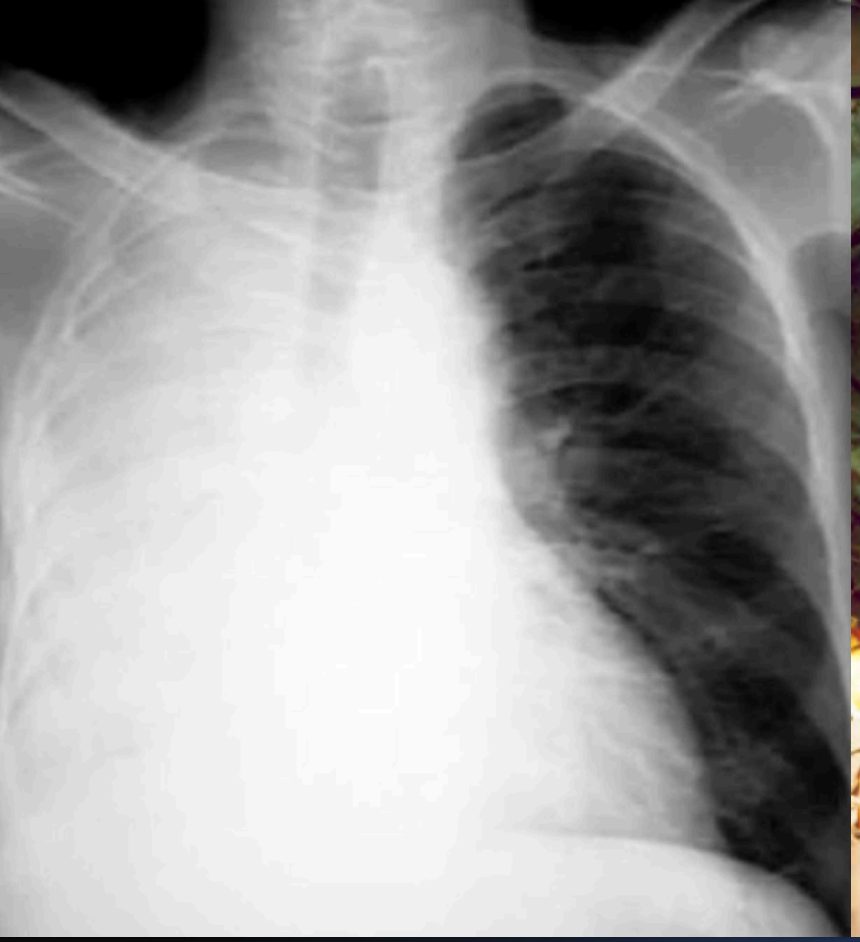
# “Ventilating Blindly
# The Cons of External Tools”

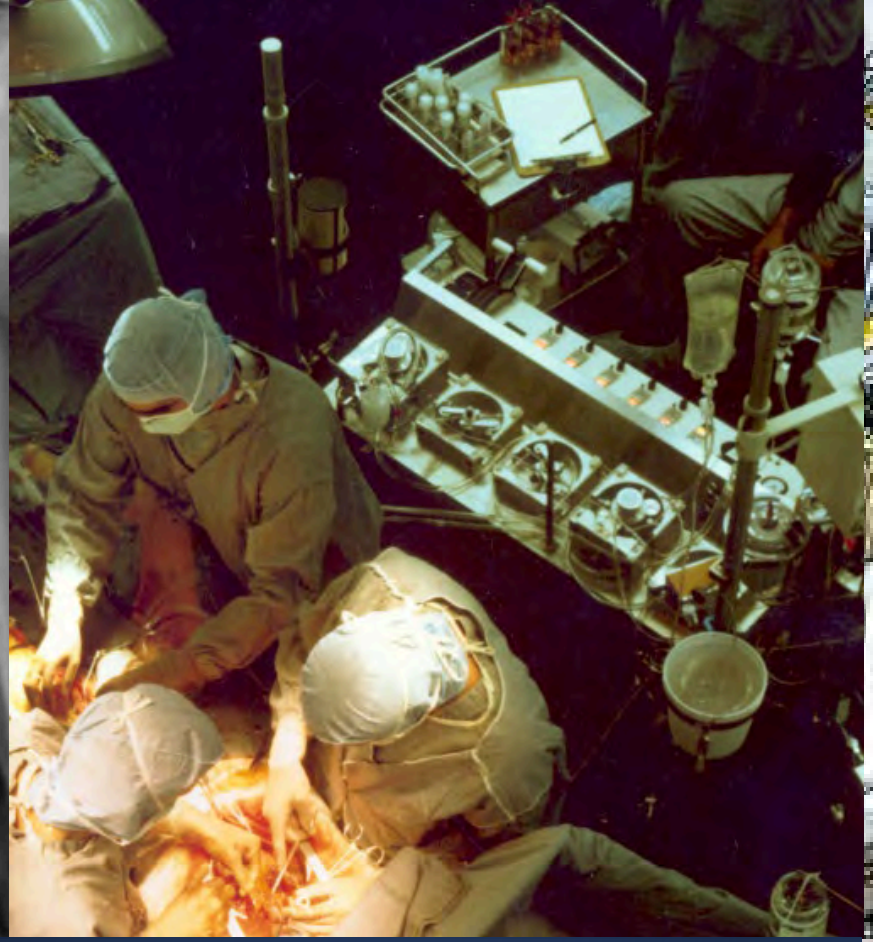


**My own religion has been to do all the good I could to my fellow man, and as little harm as possible.”**

**William Worrall Mayo**

Pablo Gonzalez-RRT-ACCS, NPS, ECMO Specialist





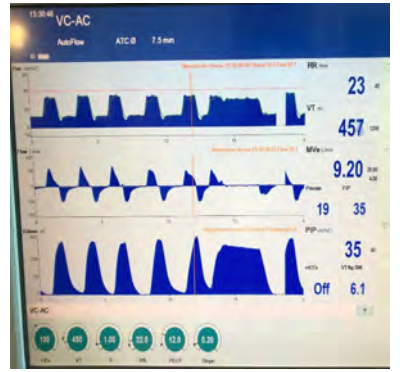
# Conflict of interest

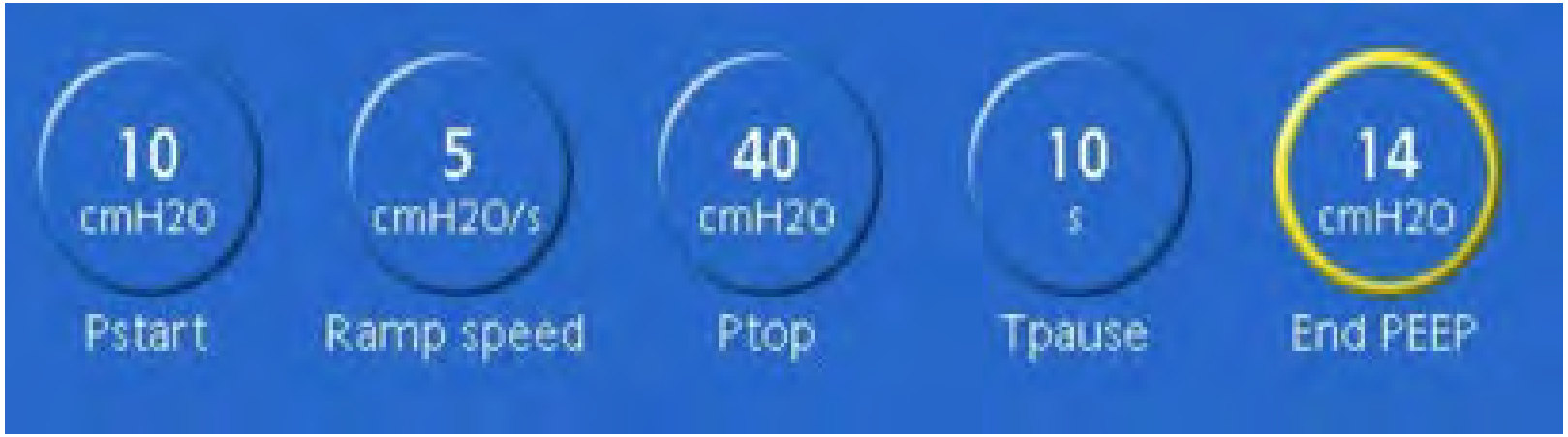
None

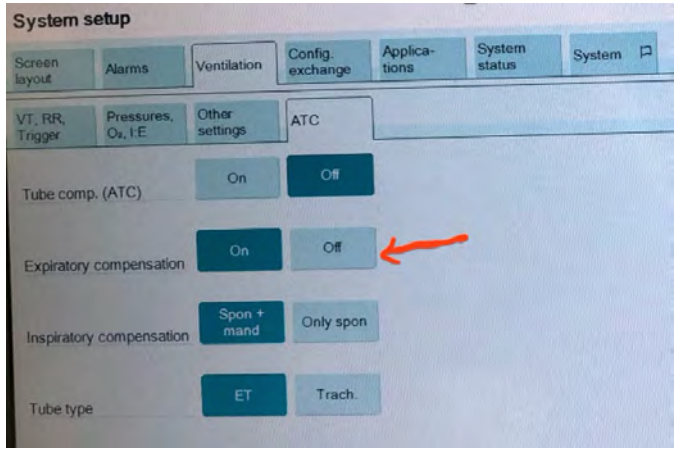
# Objectives

1. Observe and understand ventilator settings and waveforms.
2. The cons of the advanced non and invasive ventilator tools.
3. Complexity of mechanical ventilation.





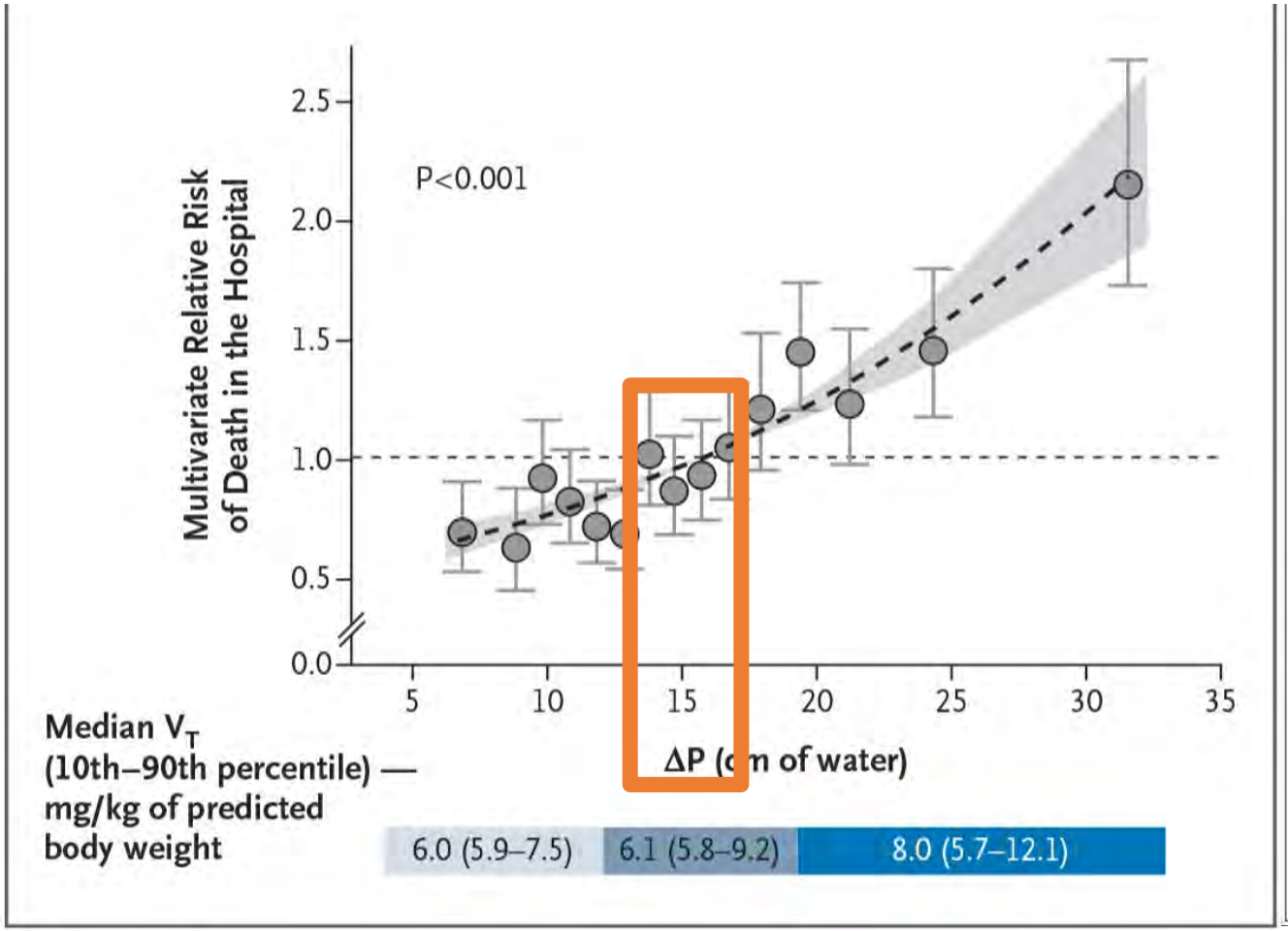



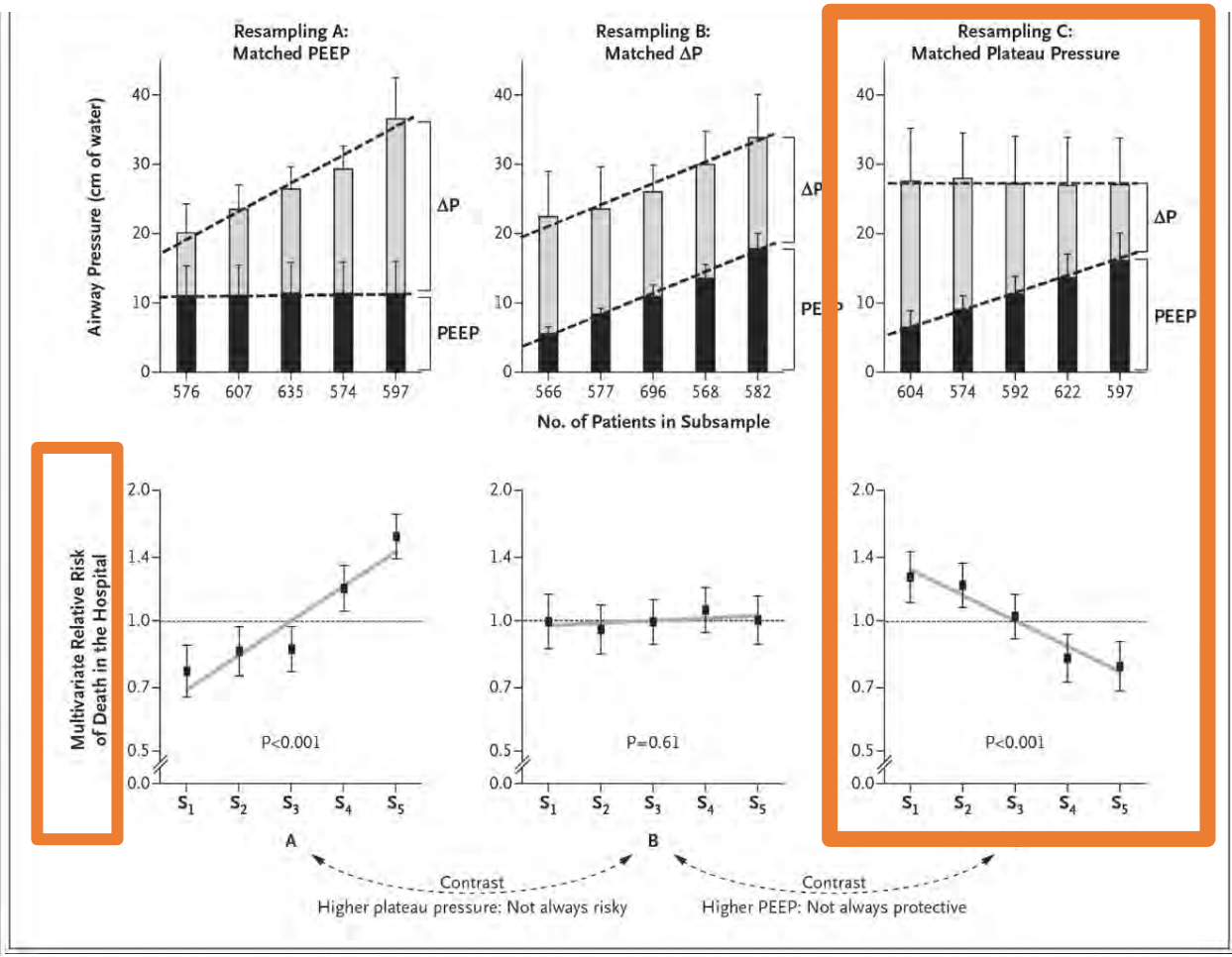




# Lung settings

# Driving Pressure and Survival in the Acute Respiratory Distress Syndrome

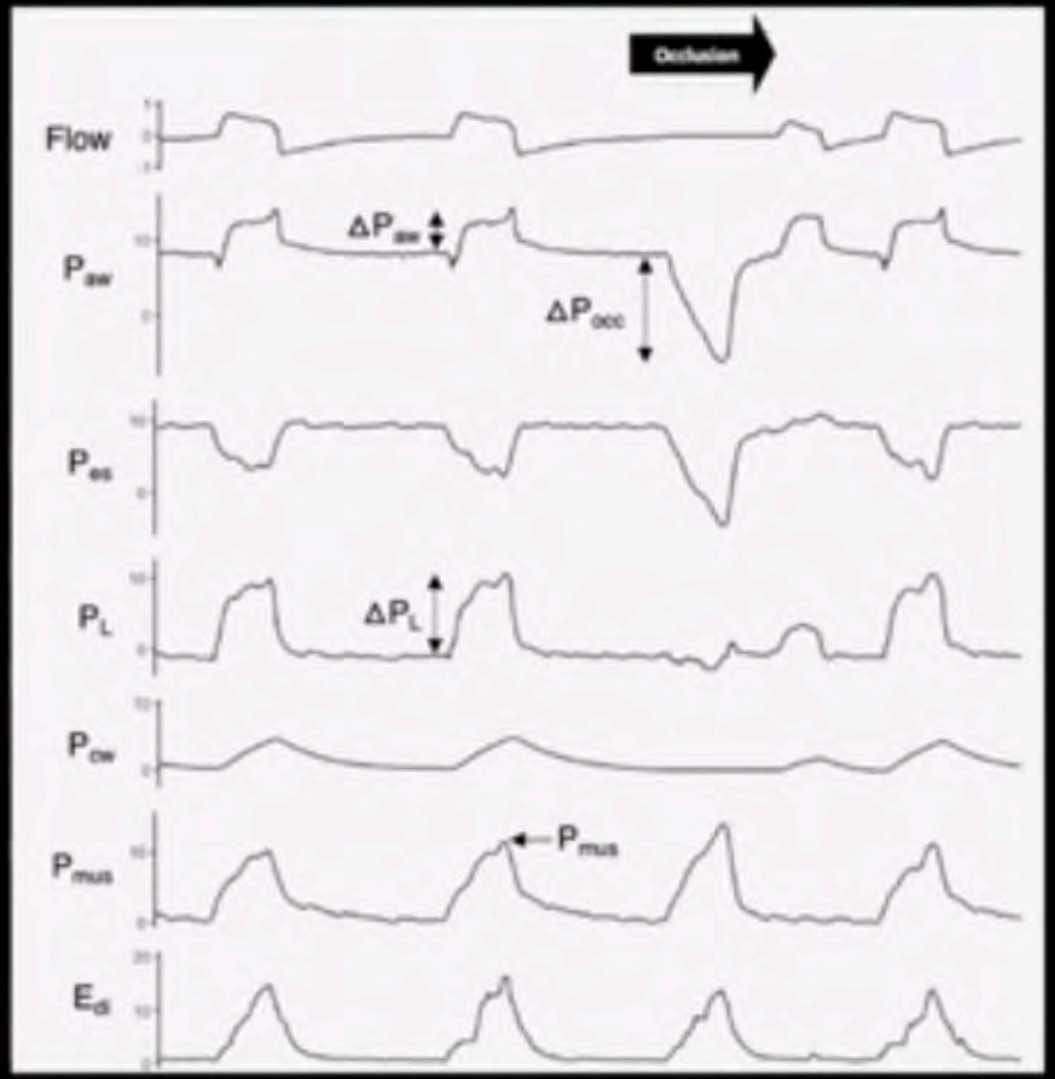
Marcelo B.P. Amato, M.D., Maureen O. Meade, M.D., Arthur S. Slutsky, M.D., Laurent Brochard, M.D., Eduardo L.V. Costa, M.D., David A. Schoenfeld, Ph.D., Thomas E. Stewart, M.D., Matthias Briel, M.D., Daniel Talmor, M.D., M.P.H., Alain Mercat, M.D., Jean-Christophe M. Richard, M.D., Carlos R.R. Carvalho, M.D., et al.

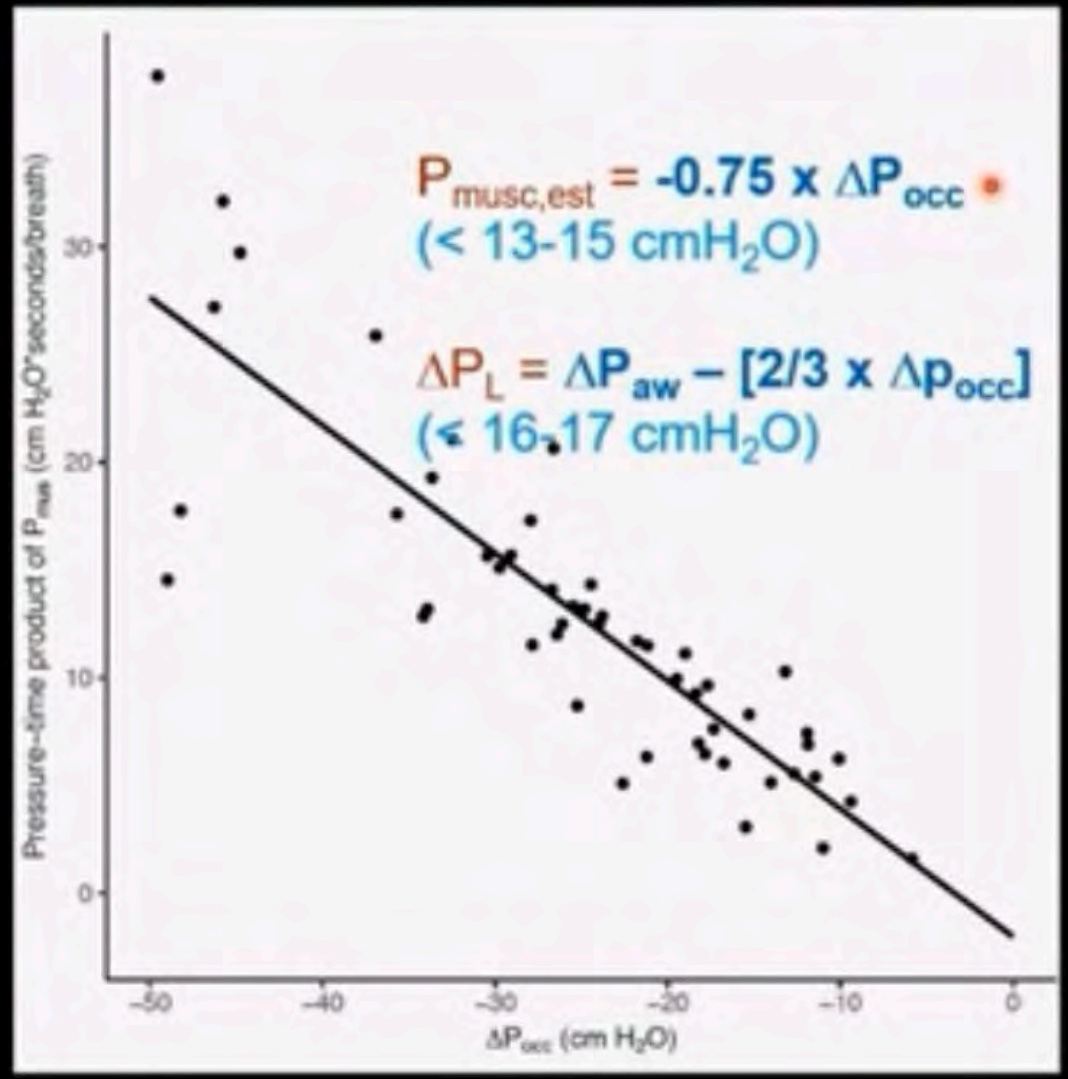


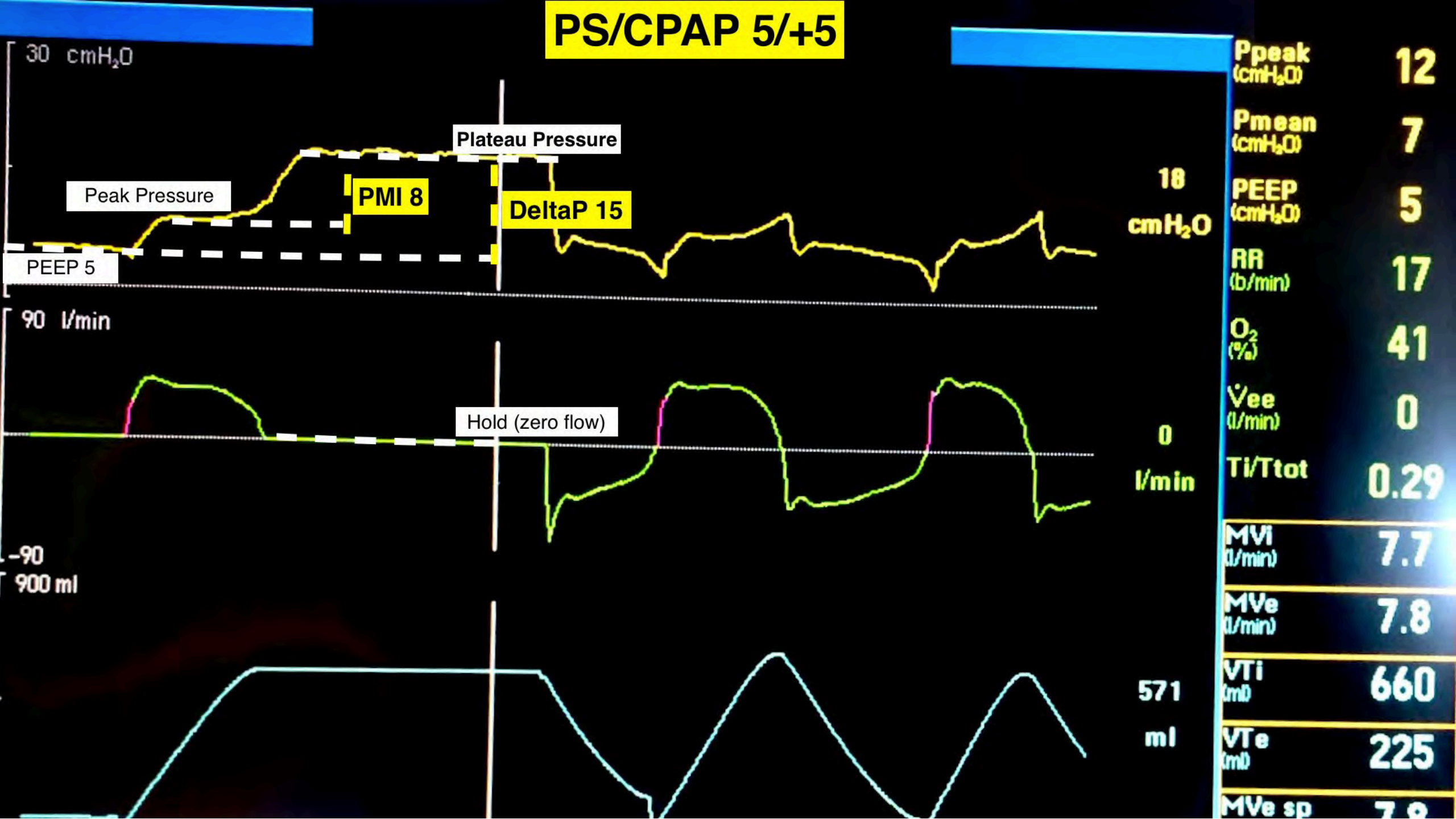

February 19, 2015, N Engl J Med 2015; 372:747-755 DOI: 10.1056/NEJMsa1410639

# Estimation of Respiratory Muscle Pressure ($P_{musc,est}$) and dynamic transpulmonary Pressure ($\Delta P_L$ )



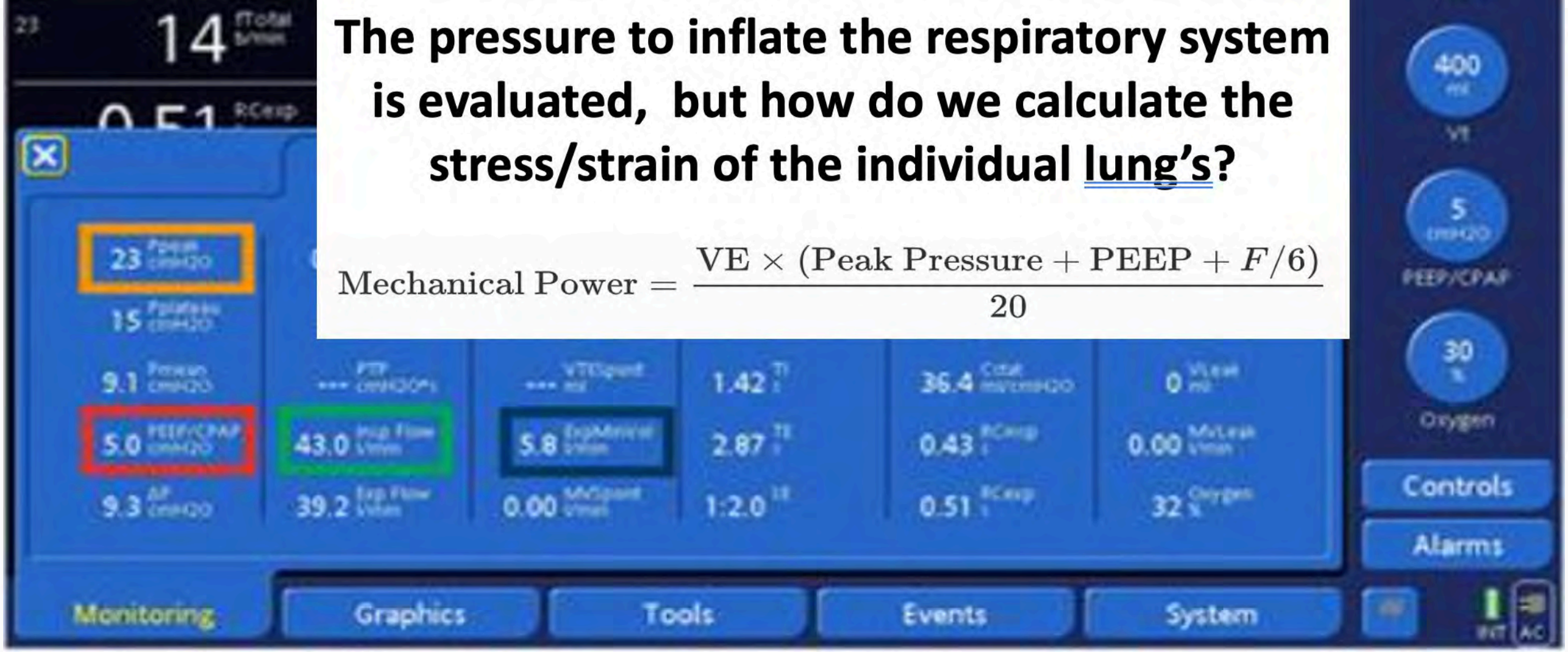




Bertoni et al. Critical Care (2019) 23;346


PS/CPAP 5/+5
30 cmH2O
Plateau Pressure
Peak Pressure
PMI 8
DeltaP 15
PEEP 5
18
cmH2O
90 l/min
Hold (zero flow)
0
l/min
-90
900 ml
571
ml
Ppeak (cmH2O) 12
Pmean (cmH2O) 7
PEEP (cmH2O) 5
RR (b/min) 17
O2 (%) 41
Vee (l/min) 0
Ti/Ttot 0.29
MVi (l/min) 7.7
MVe (l/min) 7.8
VTi (ml) 660
VTe (ml) 225
MVe sp 7.8

# Lung Parameters

- *VT/Pplat - totalPEEP= **Crs**
- *VT/DP= **Crs**
- *VT/PL=**Crs**
- *Pplat – totPEEP= **DP**
- *[(PaO2*10)/(FiO2*totPEEP)]
- *PaO2/FiO2 ratio
- *(PEEP1+PEEP2)/2=Average totPEEP (APRV)
- *PHigh -Average totPEEP= **DP** (APRV)
- Pmusc, estimated = - 0.75 x deltaPocc (<13-15 cmH2O)
- Dynamic deltaPL= deltaPaw – [2/3 x deltaPocc] (<13-15 cmH2O)
- **Expiratory hold during APRV will give you totalPEEP (do not do this on Drager vents)*
- **Note-Without an Esophageal Balloon Monitoring device, driving pressure is an estimating number ±3-4 cmH2O when compared with a true PL.*




$$\frac{5.8 \times (23 + 5 + 43/6)}{20} = 10.2 \text{ J/min}$$ Mechanical Power in Volume Control

(Mode PC) MP J/min= 0.098xRRxVTx( DeltaP + totalPEEP)

Giosa, L., Busana, M., Pasticci, I. *et al.* Mechanical power at a glance: a simple surrogate for volume-controlled ventilation. *ICMx* **7**, 61 (2019). https://doi.org/10.1186/s40635-019-0276-8

# Mechanical Power in the Setting of Positive End-Expiratory Pressure (PEEP) Titrated by Esophageal Pressure

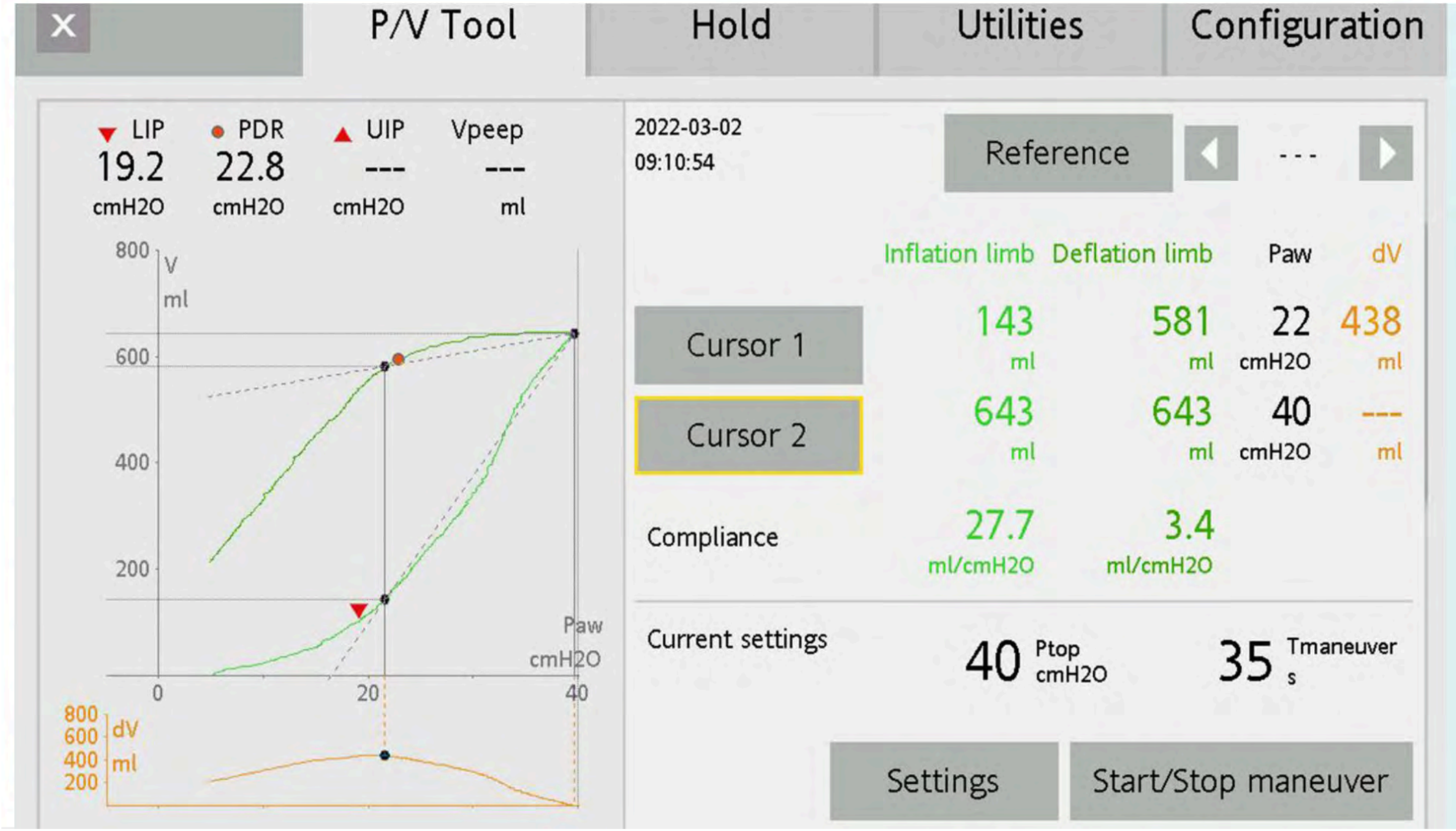
**CONCLUSIONS:**

In our study sample, mechanical ventilation with PEEP titrated by esophageal pressure monitoring resulted in unexpectedly high values of PEEP among patients with mild ARDS. Additionally, both $MP_{RS}$ and $MP_{L}$ seemed to track the higher mortality rate observed in the moderate ARDS group.

Cortes-Puentes GA, Oeckler RA. ATS 2018

MAYO CLINIC

# What is the local volume distribution? Using pressure-volume curves to set proper PEEP in acute lung injury




Nurs Crit Care 2007 Sep-Oct;12(5):231-41. doi: 10.1111/j.14785153.2007.00224.x.

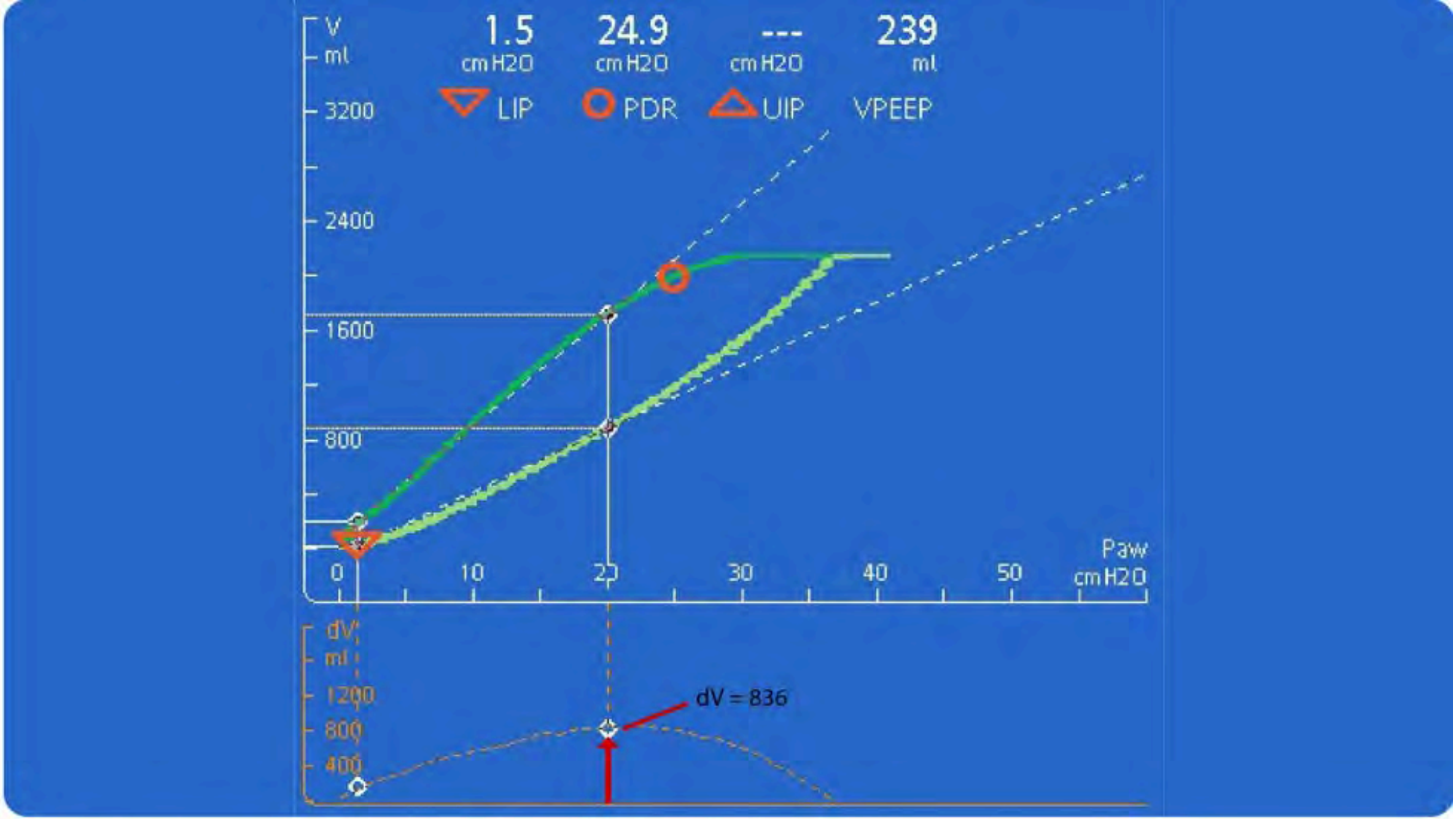



Figure 4: Difference > 500 ml - high potential for recruitment

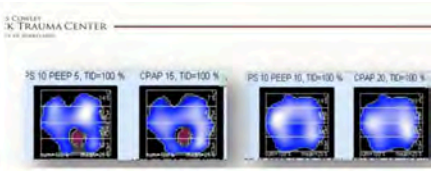
## Electrical Impedance Tomography (EIT)

**Pros**

- EIT is noninvasive, radiation-free monitoring tool to assess and visualize regional ventilation and perfusion.
- EIT is currently predominantly a research tool, but rapidly emerging data are helping to define its clinical role.
- EIT may prove to be a key component of a multimodal approach to individualizing ventilator management, as has been demonstrated by the Lung Rescue Team (MGH).

**Cons**

- >60 BMI: larger belt in development
- Implanted electronic devices (neurostimulators, cardioverter defibrillators or pacemakers)
- Pregnant or lactating patients
- Fragile skin, spinal cord injury (e.g. Burns)

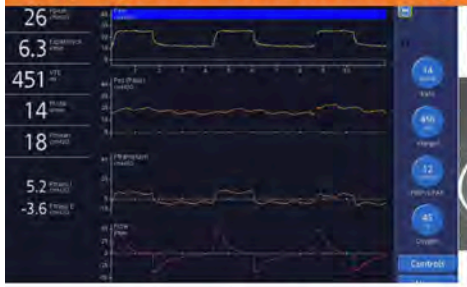


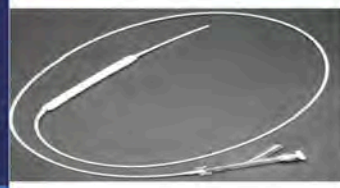
| PS 10 cm H2O + PEEP 5 cm H2O | CPAP 15 cm H2O + ATC | RESULTS | | PS 10 cm H2O + PEEP 10 cm H2O | CPAP 20 cm H2O + ATC |
|---|---|---|---|---|---|
| 14% | 7% | Decreased by 15% | Ventral | 14% | 20% |
| 51% | 43% | | Mid-Ventral | 40% | 37% |
| 26% | 32% | Increased by 13% | Mid-Dorsal | 31% | 38% |
| 10% | 17% | | Dorsal | 15% | 15% |

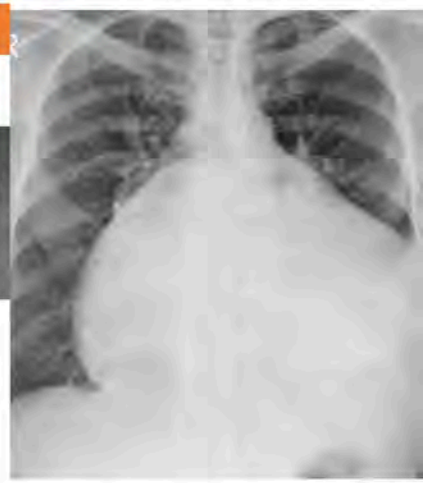
**Pros**

- The goal of a Pes-based PEEP setting is to have sufficient transpulmonary pressure (PL) to keep (part of) the lung open at the end of expiration.
- EPVent-2 revealed in patients with lower APACHE II score and when PEEP setting resulted in end-expiratory PL values close to 0 ± 2 cmH2O instead of higher or more negative values.
- Calibration of the balloon should be repeated regularly.
- Too low PEEP setting in patients with airway closure will result in misleading respiratory mechanics assessment. Pes readings should always be checked.

## Esophageal Balloon Monitoring



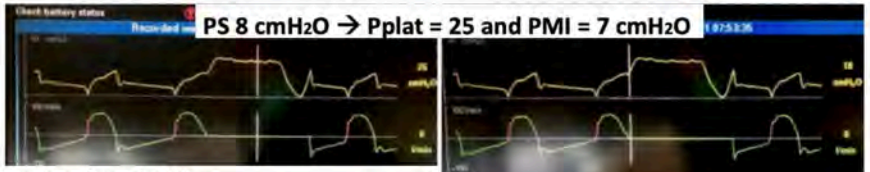





**Cons**

- Excessive secretions
- Enlarge congenital anomalies
- Leakage in chest
- Anomaly in the esophagus
- Pneumonectomy?

*The esophageal balloon for respiratory monitoring in ventilated patients:* European Respiratory Review 2023 32: 220186; DOI: 10.1183/16000617.0186-2022


**Pros**

- Easy to perform at bedside
- Reflects changes in respiratory muscle output
- Helpful for detecting asynchronies in PSV mode

## Electrical Activity of the Diaphragm (EAdi)

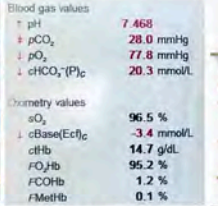
**Cons**

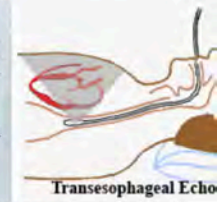
Any condition that limits the respiratory drive or any diaphragmatic anatomical defect in cases of an intact respiratory drive may be contraindicated, including:

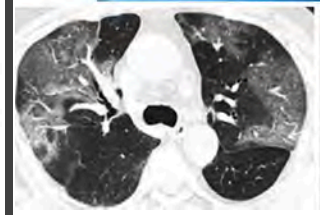
1. Central: paralytics, suppressed respiratory drive due to heavy sedation or brain injury
2. Peripheral: phrenic nerve injury or use of paralytic agent
3. Structural: esophageal atresia and diaphragmatic hernia
4. Target values may be difficult to achieve in patients with excessive respiratory drive

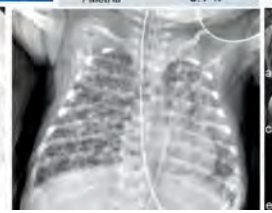
Foti G., Cereda M., Banfi G., Pelosi P., Pesenti A. End-inspiratory airway occlusion: a method to assess the pressure developed by inspiratory muscles in patients with acute lung injury undergoing pressure support. Am J Respir Crit Care Med. 1997;156(4 Pt 1):1210-1216

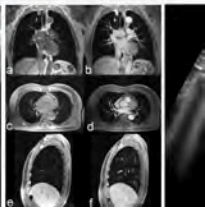
How do I know edema is not developing in the depend
reabsorption of intra-alveolar edema in nondepenc

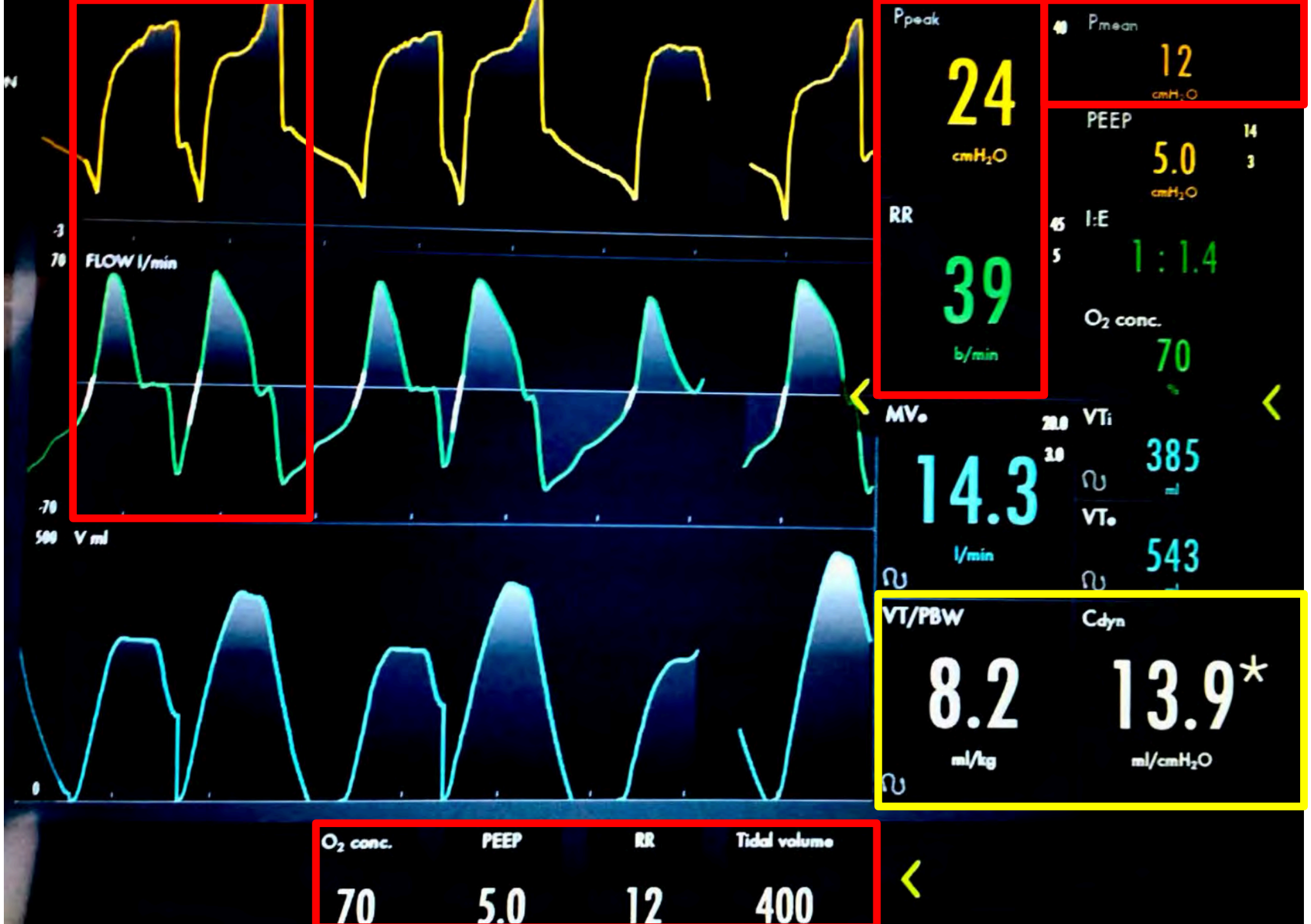


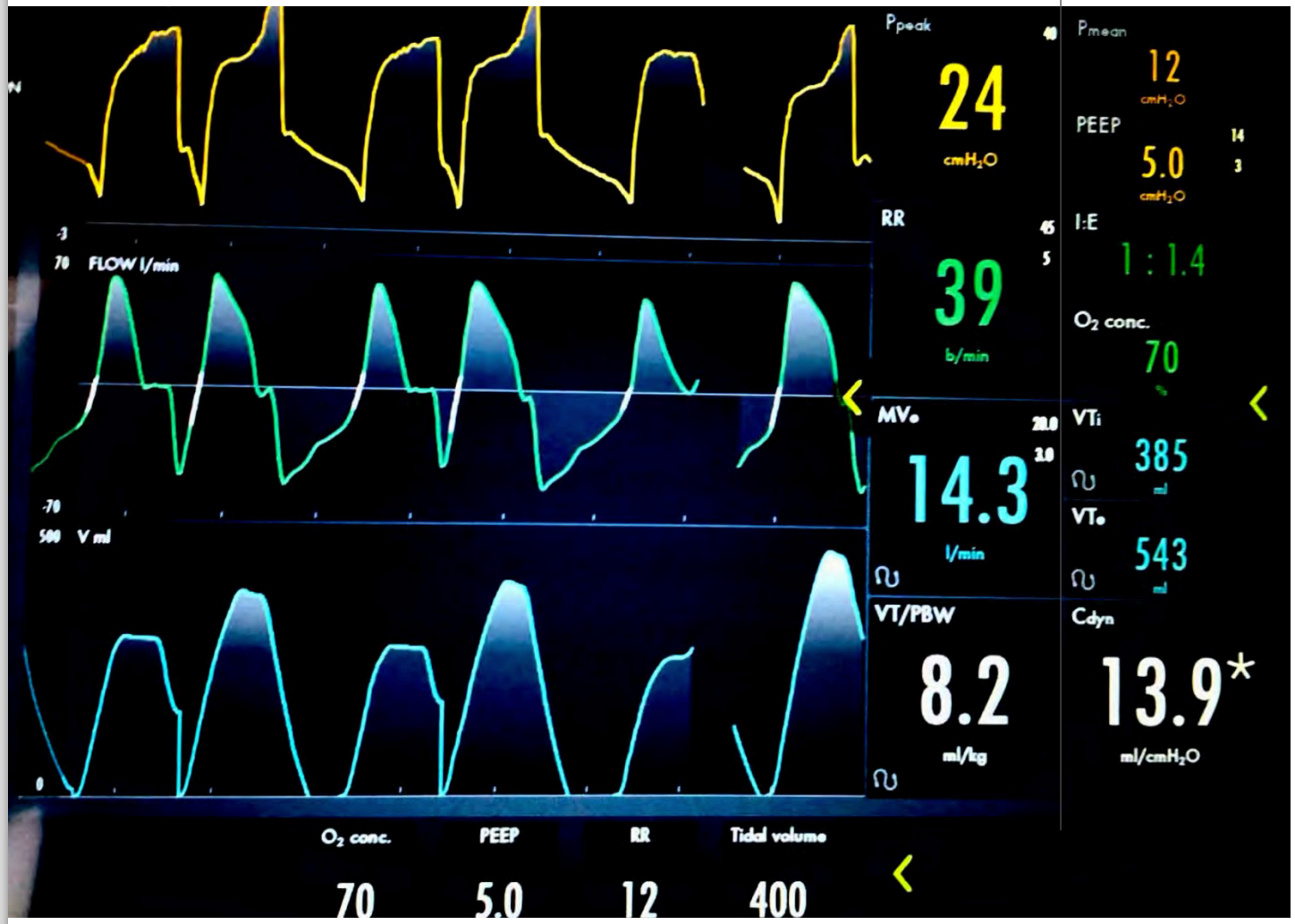








Ppeak
24
cmH2O
RR
39
b/min
Pmean
12
cmH2O
PEEP
5.0
cmH2O
I:E
1 : 1.4
O2 conc.
70
FLOW l/min
V ml
MV
14.3
l/min
VTi
385
VT
543
VT/PBW
8.2
ml/kg
Cdyn
13.9*
ml/cmH2O
O2 conc.
PEEP
RR
Tidal volume
70
5.0
12
400

# 75yr. Male, PNA, Covid on (PC-CMVa) PRVC 12/400/+5/70%

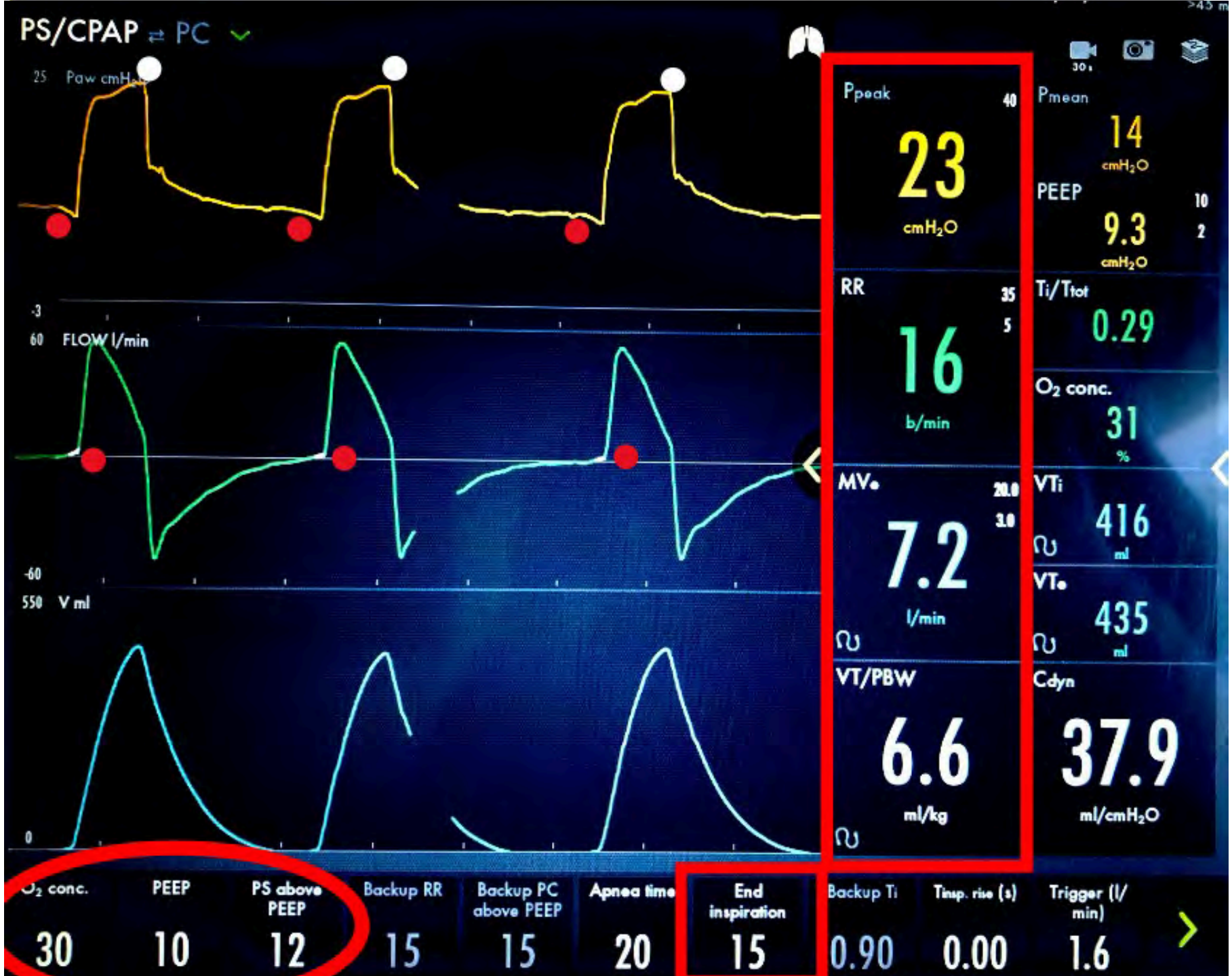



What would be your best clinical decision?

A. Change to PC-CMVs
B. Increase Vt up to 8ml/kg PBW
C. Decrease RR
D. Increase PEEP, prone, possibly sedate/paralyze
E. If ARDS, prone, sedate/paralyze
F. Lengthen i-Time
G. Change to PS/CPAP

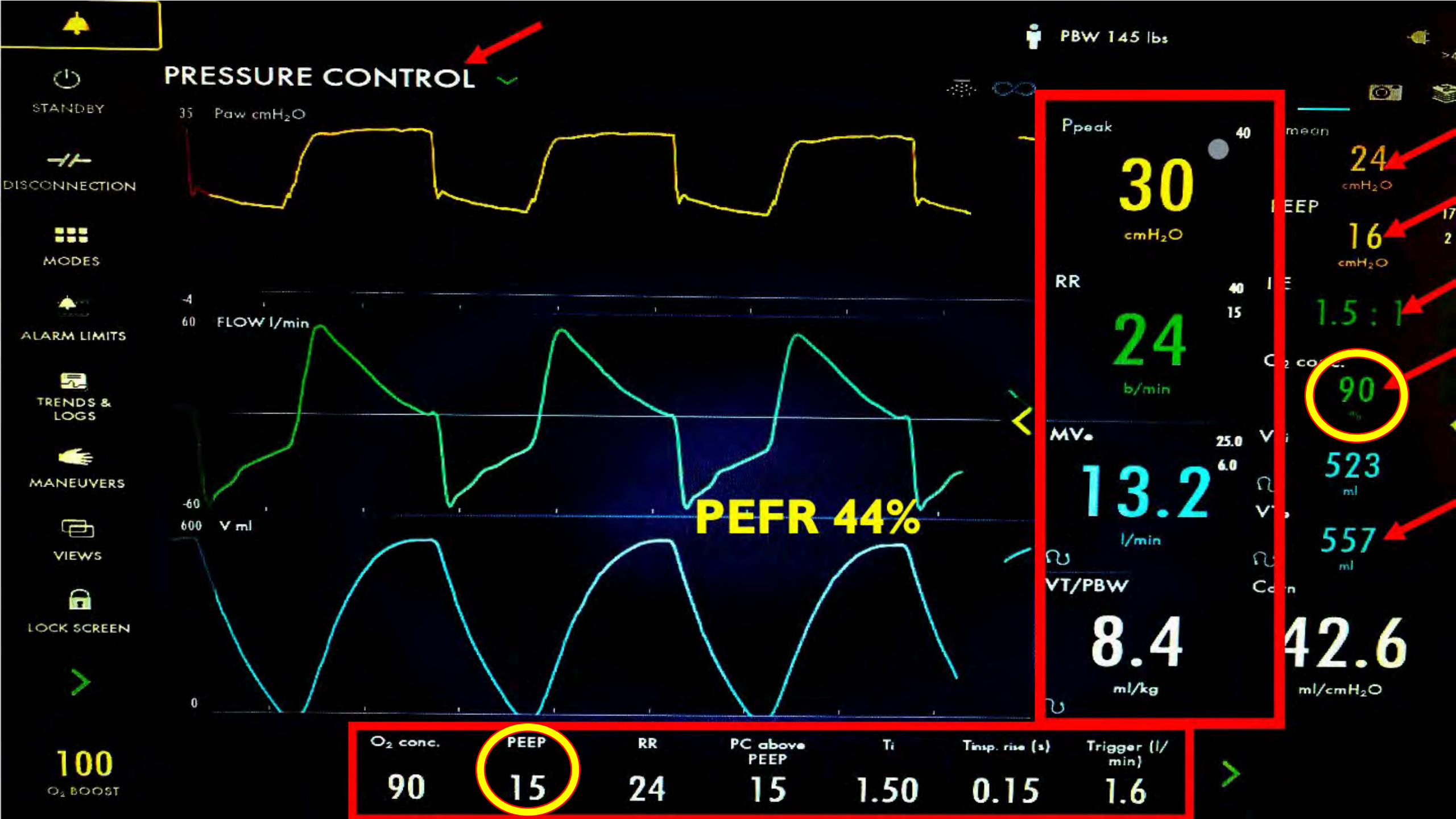
# High Positive End–Expiratory Pressure Renders Spontaneous Effort Noninjurious

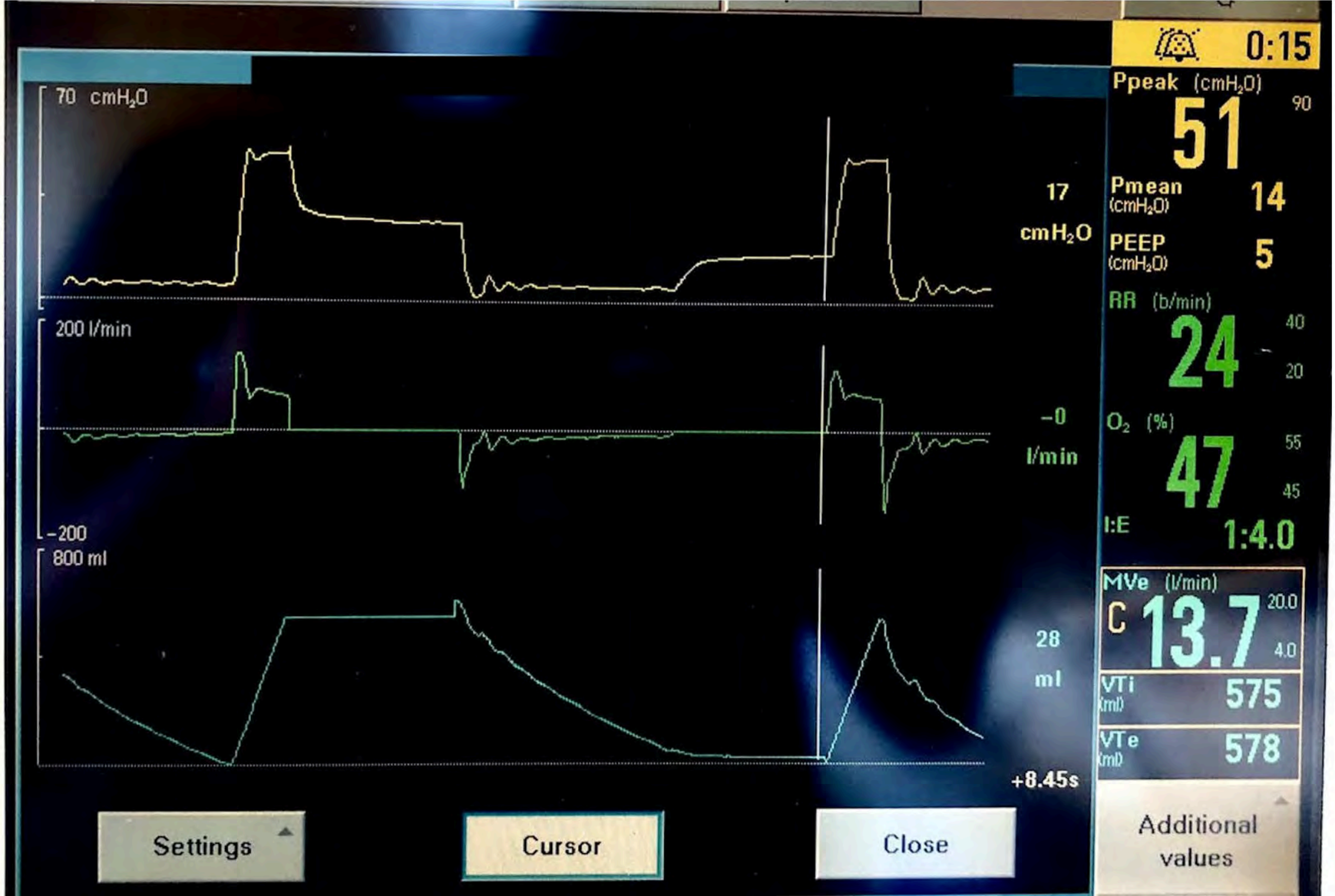
Morais, Am J Respir Crit Care Med, 2018


PS/CPAP ⇄ PC
25 Paw cmH2O
-3
60 FLOW l/min
-60
550 V ml
0
Ppeak 40
23
cmH2O
Pmean
14
cmH2O
PEEP 10
9.3 2
cmH2O
RR 35
16 5
b/min
Ti/Ttot
0.29
O2 conc.
31
%
MV• 20.0
7.2 3.0
l/min
VTi
416
ml
VT•
435
ml
VT/PBW
6.6
ml/kg
Cdyn
37.9
ml/cmH2O
O2 conc. 30
PEEP 10
PS above PEEP 12
Backup RR 15
Backup PC above PEEP 15
Apnea time 20
End inspiration 15
Backup Ti 0.90
Tinsp. rise (s) 0.00
Trigger (l/min) 1.6


| Blood gas values | 100% FiO2 | |
|---|---|---|
| pH | 7.429 | |
| ↓ $pCO_2$ | 34.9 | mmHg |
| ↑ $pO_2$ | 251 | mmHg |
| $cHCO_3^-(P)_c$ | 23.1 | mmol/L |
| **Oximetry values** | | |
| ↑ $sO_2$ | 100.0 | % |
| $cBase(Ecf)_c$ | -1.2 | mmol/L |
| $ctHb$ | 13.4 | g/dL |
| ↕ $FO_2Hb$ | > 98.5 | % |

| Blood gas values | 40% FiO2 |
|---|---|
| ↑ pH | 7.468 |
| ↕ $pCO_2$ | 28.0 mmHg |
| ↓ $pO_2$ | 77.8 mmHg |
| ↓ $cHCO_3^-(P)_c$ | 20.3 mmol/L |
| **Oximetry values** | |
| $sO_2$ | 96.5 % |
| ↓ $cBase(Ecf)_c$ | -3.4 mmol/L |
| $ctHb$ | 14.7 g/dL |
| $FO_2Hb$ | 95.2 % |
| $FCOHb$ | 1.2 % |
| $FMetHb$ | 0.1 % |


PRESSURE CONTROL
PBW 145 lbs
STANDBY
DISCONNECTION
MODES
ALARM LIMITS
TRENDS & LOGS
MANEUVERS
VIEWS
LOCK SCREEN
100
O2 BOOST
35 Paw cmH2O
-4
60 FLOW l/min
-60
600 V ml
0
PEFR 44%
Ppeak
40
30
cmH2O
RR
40
15
24
b/min
MV
25.0
6.0
13.2
l/min
VT/PBW
8.4
ml/kg
mean
24
cmH2O
PEEP
16
cmH2O
I:E
1.5 : 1
O2 conc.
90
%
Vti
523
ml
VTe
557
ml
Cdyn
42.6
ml/cmH2O
O2 conc.
PEEP
RR
PC above PEEP
Ti
Tinsp. rise (s)
Trigger (l/min)
90
15
24
15
1.50
0.15
1.6


0:15
70 cmH2O
17
cmH2O
200 l/min
-0
l/min
-200
800 ml
28
ml
+8.45s
Ppeak (cmH2O)
51
90
Pmean
(cmH2O)
14
PEEP
(cmH2O)
5
RR (b/min)
24
40
20
O2 (%)
47
55
45
I:E
1:4.0
MVe (l/min)
C
13.7
20.0
4.0
VTi
(ml)
575
VTe
(ml)
578
Settings
Cursor
Close
Additional
values

# Summary

1. Monitoring ventilator settings and parameters
2. Mechanical Power in PC and VC
3. PV tool maneuver
4. Driving pressure
5. Management of ventilator waveform asynchronies
6. Cons of external tools to assist ventilator management

# PABLO85.GONZALEZ@GMAIL.COM

## Mayo Clinic Mechanical Ventilation Conference 2024

Oceanside, CA US
October 16, 2024 to October 19, 2024

Overview Location Faculty Accreditation Register

**This course offers Live (in-person) and Livestream (virtual) attendance options.**

**Course summary**

**Available credit:**

**19.25** *AMA PRA Category 1 Credit™*

**19.25** ANCC

**19.25** Attendance

**Event starts:** 10/16/2024 - 6:15am

**Event ends:** 10/19/2024 - 12:00pm

Scripps

## 2nd Advanced Mechanical Ventilation Conference 2024

June 29, 2024 – 8 CEU Event

"Sleep and Circadian Rhythm Disturbances: Respiratory Care in the Intensive Care Unit"
*"Advanced Ventilation", "Advances in Neonatal Respiratory Support"*
*"Precision medicine in critical care medicine: the implementation of a lung rescue team"*
*"Heart-Lung Interaction During Spontaneous and Passive Ventilation"*
*"Electrical Impedance Tomography Neonate/Peds/Adults"*

***Scripps Memorial Hospital La Jolla***
*Schaetzel Great Hall*
*9890 Genesee Ave*
*San Diego, CA 92037*

https://www.csrc.org/

# Mortality rate is cut in half by a Lung Rescue Team at Mass General focused on patients with obesity and acute respiratory failure

Debate

patients with obesity and ARF within 24 hours of ICU admission. The intervention tools they employ include esophageal manometry to determine the intrapleural pressure inside the chest; trans-thoracic echocardiography to determine cardiac function during mechanical ventilation manipulation; and electrical impedance tomography (EIT) to measure the regional distribution of ventilation and assess the degree of lung collapse and overdistension.

Berra, L., Lung Rescue Team. Development of a Lung Rescue Team to Improve Care of Subjects With Refractory Acute Respiratory Failure. Respir Care. 2020 Apr;65(4):420-426.

DOI: 10.4187/respcare.07350. Epub 2020 Feb 4. PMID: 32019849

# References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2. Jonkman, H. A., Alacla, C. G., Brochard, J. L. *Lung Recruitment Assessed by Electrical Impedance Tomography (RECRUIT): A Multicenter Study of COVID-19 Acute* Respiratory Distress Syndrome. https://doi.org/10.1164/rccm.202212-2300OC PubMed: 37097986 (April 24, 2023).
3. Amato, B.P. M., Meade, O. M., Brochard, L. Slutsky, S. A., *Driving Pressure and Survival in the Acute Respiratory Distress Syndrome.* DOI: 10.1056/NEJMsa1410639 February 19, 2015 N Engl J Med 2015; 372:747-755
4. LaFollette, R., Hojnowski, K., Norton, J. *Using pressure-volume curves to set proper PEEP in acute lung injury.* Nurs Crit Care 2007 Sep-Oct;12(5):231-41. doi: 10.1111/j.1478-5153.2007.00224.x.
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6. Annemijn H. Jonkman, Irene Telias, Elena Spinelli, Evangelia Akoumianaki, Lise Piquilloud. *The esophageal balloon for respiratory monitoring in ventilated patients: updated clinical review and practical aspects.* European Respiratory Review 2023 32: 220186; DOI: 10.1183/16000617.0186-2022
7. Foti G., Cereda M., Banfi G., Pelosi P., Pesenti A. End-inspiratory airway occlusion: a method to assess the pressure developed by inspiratory mucsles in patients with acute lung injury undergoing pressure support. Am J Respir Crit Care Med. 1997;156(4 Pt 1):1210-1216
8. Sanket D. Shah; Fatima Anjum. *Neurally Adjusted Ventilatory Assist (NAVA).* May 22, 2023.
9. Berra, L., Lung Rescue Team. Development of a Lung Rescue Team to Improve Care of Subjects With Refractory Acute Respiratory Failure. Respir Care. 2020 Apr;65(4):420-426. DOI: 10.4187/respcare.07350. Epub 2020 Feb 4. PMID: 32019849
10. Jansen, D., Keijzer, C., Heunks, L., Positive end-expiratory pressure affects geometry and function of the human diaphragm. J Appl Physiol (1985). 2021 Oct 1;131(4):1328-1339. doi: 10.1152/japplphysiol.00184.2021.Epub 2021 Sep 2. PMID: 34473571
11. Morais, C. , Lima, C., Ramos, O., Amato, M., Tucci, M., Pereira, S., Plens, G., Gomes, S., Costa, E., Yoshida, T. High Positive End-Expiratory Pressure Renders Spontaneous Effort Noninjurious. Am J Respir Crit Care Med. 2018 May 15;197(10):1285-1296. doi: 10.1164/rccm.201706- 1244OC. PMID: 29323536
12. Somhorst, P., Mousa, A., Jonkman, A. Setting positive end-expiratory pressure: the use of esophageal pressure measurements. Current Opinion in Critical Care 30 (1):p 28-34, February 2024. DOI: 10.1097 / MCC. 0000000000001120
13. Frerichs, I., Schadler, D., Becher, Tobias. Setting positive end-expiratory pressure by using electrical impedance tomography. Current Opinion in Critical Care 30(1):p 43-52, February 2024. DOI: 10.1097 / MCC. 0000000000001117

# Hands-on Session:
# ICU Ventilators and Ventilator Waveforms

## Rob Bautista, BSRT, RRT, RRT-ACCS
## Respiratory Therapist
## UC San Francisco

Roberto Bautista received his Baccalaureate Degree from Boise State University and is pursuing his Masters Degree at UCSF. He is a Clinical Specialist for the Respiratory Care Services department at UCSF with a focus on Adult Critical Care. Roberto is the CSRC-AARC Delegate and is a member of the CSRC Executive Committee.

## Lena Scotto, MD
## Assistant Professor
## VA Palo Alto/Stanford

After earning a B.S. from Stanford University, Dr. Scotto attended Johns Hopkins School of Medicine. She then returned to her native Bay Area to train in the combined Stanford University Anesthesiology Residency/Critical Care Fellowship program and served as a Chief Fellow in Critical Care Medicine (CCM). Following graduation, Dr. Scotto worked in private practice at a local hospital as an Anesthesiologist and Intensivist and later joined the Palo Alto VA in 2019 as an Attending in Anesthesiology and Critical Care Medicine. She is the hospital-wide Resuscitation Committee Co-Chair and heads the newly formed Green Anesthesia Committee. Furthermore, she is a member of the Anesthesia Patient Safety Foundation Advisory Group on Perioperative Brain Health. Outside of work, when she's not chasing after her toddler, she enjoys trail running, reading mystery novels, and trying new cooking recipes.

# Hands-on Session:
# Esophageal Manometry

**Pablo Gonzalez, RRT**
**Respiratory Therapist**
**Scripps Health**

Pablo Gonzalez is currently a neonatal/pediatric/adult respiratory therapist at Scripps Memorial Hospital in La Jolla, San Diego, CA.

He has worked at a few facilitates: Cedar Sinai Medical Center, CHOC, Loma Linda, Sharp Mary Birch, Sanford MN, and Regions Hospital in St Paul MN where he worked alongside Dr. John J. Marini which drove him to work at the Mayo Clinic and worked alongside Dr. Gustavo Cortes Puentes and worked along renowned physicians/nurses and respiratory therapist as a ECMO specialist.

While he worked at the renowned Mayo Clinic in Rochester Minnesota, St. Mary's Hospital in the CVICU. He was a clinical preceptor, utilizing the advanced modalities in respiratory care, from ventilator management and ventilator waveform management, esophageal balloon monitoring, APRV, caring for ECMO patients, A-line insertion, bladder pressure monitoring, and HFJV in the neonatal population to name a few.

He has continued development of his skills and has started the Advanced Mechanical Ventilation Conference in San Diego. Bringing renowned speakers from all over the world. Currently he is working on a respiratory book that will help clinicians in the ICU.

Pablo earned a B.A. from laguna College of Art and Design in Laguna Beach, CA., and his associate science from California College San Diego.

# Hands-on Session:
# Electrical Impedance Tomography

**Alex Kristine Pearce, MD**
**Associate Physician Diplomate**
**UC San Diego**

Dr. Alex Pearce received her medical degree from Tulane School of Medicine followed by residency in Internal Medicine at UC San Diego. She subsequently completed her clinical fellowship in Pulmonary and Critical Care and research fellowship at UC San Diego. She currently works as an intensivist at UC San Diego with a research focus on mechanical ventilation and Acute Respiratory Distress Syndrome.

# Hands-on Session:
# Portable Bronchoscopy

## Lindsey John, RRT
## Respiratory Therapist
## UC San Francisco

Lindsey John received her Associate of Respiratory Care in 2004 from Milwaukee Area Technical College and Bachelors of Psychology from Trinity International University in Deerfield, IL 2016. Over her 20 year career in Respiratory Care, Ms. John has worked in Level 1 and 3 Trauma Centers, Regional Burn Units, Level 3 NICUs and Critical Care ICUs. Currently, she is the Bronchoscopy Services Manager at UCSF for the Lung Transplant, Interventional Pulmonology and Pulmonary Consult Services.


## Joon Chang, MD
## Assistant Professor
## Stanford University

Dr. Joon Chang received his medical degree from UCLA David Geffen school of medicine. He did her post-graduate medicine residency at NYU and pulmonary and critical care fellowship at Stanford. He completed his interventional pulmonology fellowship at the Hospital of University of Pennsylvania in 2022. Currently, he serves as an Assistant Professor of Medicine at Stanford and a member of interventional pulmonology group at Stanford.

# Single-Use Bronchoscopy Cheat Sheet

Single-Use (Portable) Bronchoscope vs. Reusable Olympus Bronchoscope Considerations

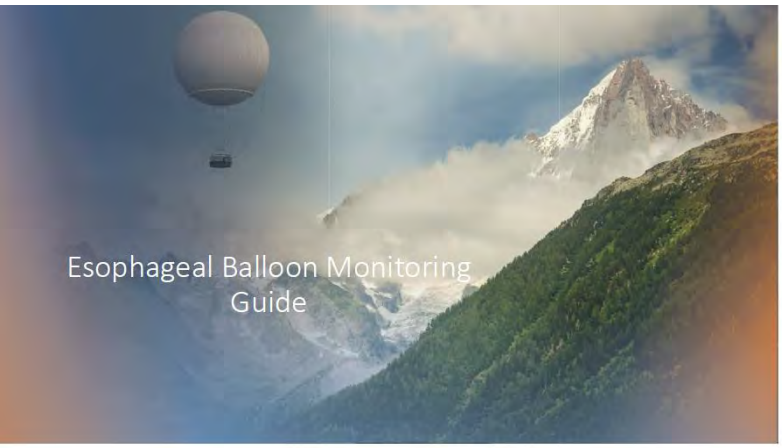
- **Cost** of single use bronchoscope vs. repairing reusable bronchoscope
- Single use vs. sterile **reprocessing** for reusable
- **Workflow**: monitor and tower set up with processor
- **Bronchosampler**- single operator ease of use
- Infection risk
- **Environmental factors** (water, chemical energy)
- Location of working channel

| Single-Use Bronchoscopes | Working Channel Diameter (mm) | Scope Outer Diameter (mm) | Minimum Endotracheal (ET) Tube Size* | |
|---|---|---|---|---|
| Ambu aScope 4 Regular | 2.2 | 5.0 | 6.0 | Bronchosampler Swivel |
| Ambu aScope 4 Large | 2.8 | 5.8 | 7.0 | |
| Ambu aScope 5 Ultra-Thin | 1.2 | 2.7 | 4.0 | |
| Ambu aScope 5 Therapeutic | 2.8 | 5.6 | 6.0 | |
| Boston Scientific EXALT Model B Slim | 1.0 | 3.8 | 5.0 | Clamshell design working channel |
| Boston Scientific EXALT Model B Regular | 2.0 | 5.0 | 6.0 | |
| Boston Scientific EXALT Model B Large | 2.6 | 5.8 | 7.0 | |
| Verathon BFlex 2 Slim | 1.2 | 3.8 | 5 | GlideScope ET tube retainer |
| Verathon BFlex 2 Regular | 2.2 | 5.0 | 6 | |
| Verathon BFlex 2 Large | 3.0 | 5.8 | 7 | |

| Reusable Olympus Bronchoscopes | Working Channel Diameter (mm) | Scope Outer Diameter (mm) | Minimum Endotracheal (ET) Tube Size* |
|---|---|---|---|
| Therapeutic Bronchoscope (BF-1TH190) | 2.8 | 6.2 | 7.5 |
| Diagnostic Bronchoscope (BF-H190) | 2.0 | 5.5 | 7.0 |
| Diagnostic Bronchoscope (BF-P190) | 2.0 | 4.2 | 5.5 |

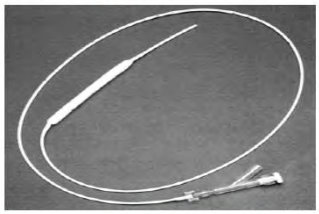
**<u>Bronchosampler for Ambu</u>**

1. Attach the flat portion of the sampler bridge to the flat portion of the Ambu scope.
2. Clamp the attachment lock into place for secure connection.
3. Attach the sample container to the port on the sampler bridge – it will click into place.
4. Place an introducer on the open port on top of the scope.
5. Connect IV Extension tubing to the introducer to allow for lidocaine to be administered through a 35cc syringe.
6. Attach suction tubing to the suction connector located on the sampler bridge.
7. The direction of the “Flow Switch” on the sampler bridge directs where sample is collected.
8. Press downward on the “Flip Top” of the sampler container and pull away to remove the sample from the bridge.




## Catheter

Cooper Surgical

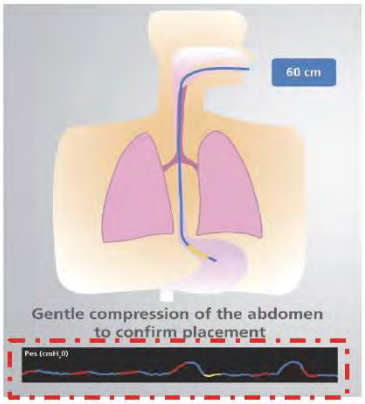


5 FR Esophageal Catheter www.coopersurgical.com

- ✓5 FR catheter
- ✓Closed End
- ✓Removable guide wire
- ✓Extension tubing
- ✓3 way stopcock

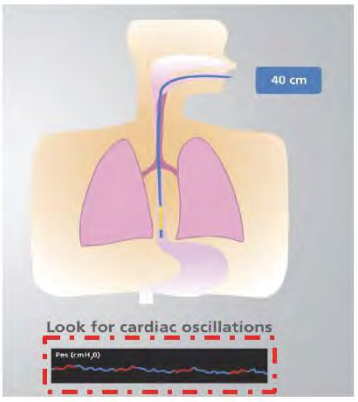
## Insertion

- Oral or Nasal Route (preference)
- Advance gently 1-2 cm at a time (avoids coiling)
- Don't advance during coughing, gagging, esophageal spasm.
- Apply Jaw thrust or head tilt if needed
- Insert to 55-60 cm in gastric space
- Insert air into balloon
  - Cooper- 1 ml
  - Smartcath-
- Perform stomach push




## Withdrawal

- Withdraw catheter slowly until cardiac oscillations appear (25-40 cm at the incisor)




**Indications**

- ✓Persistent Hypoxemia
- ✓Prone to Atelectasis
- ✓Intraabdominal Hypertension
- ✓Early onset ARDS
- ✓Morbid Obesity-Low chest wall compliance

**Contraindications**

- ✓Contraindication to NG/OG tube
- ✓Esophageal Varices, trauma, tumor
- ✓Nasal/facial Fractures
- ✓TE Fistula
- ✓Severe Coagulopathy

## Scalar Waveforms

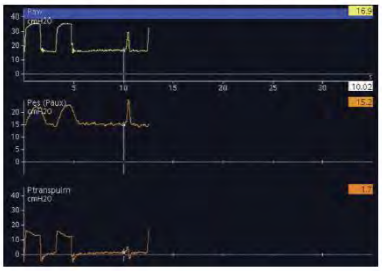
Pressure/Time

Pes (Paux)

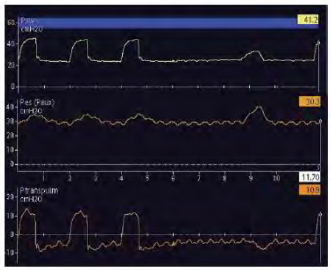
Ptranspulmonary

## Occlusion Test (Chest Push)

**Adequate Depth**

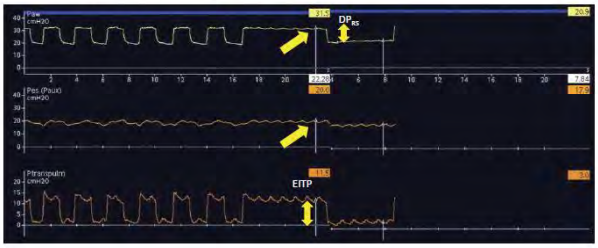


**Balloon To Low**



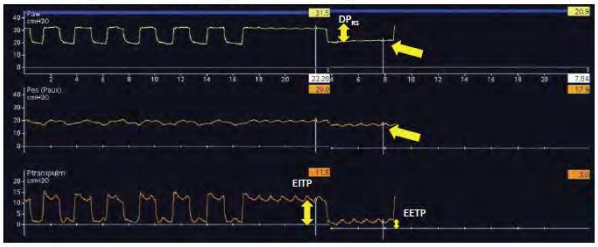
## $P_{plat} - P_{es}$ = Transpulmonary Plateau (Insp. Hold)

31.5 $cmH_2O$—20 $cmH_2O$ = 11.5 cm $H_2O$



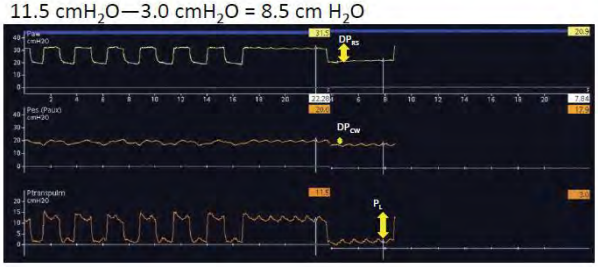

## $P_{PEEP} - P_{es}$ = Transpulmonary PEEP (Exp. Hold)

20.9 $cmH_2O$—1 7.9 $cmH_2O$ = +3 cm $H_2O$




## TP Plateau – Transpulmonary PEEP = Transpulmonary $DP_L$

11.5 $cmH_2O$—3.0 $cmH_2O$ = 8.5 cm $H_2O$




## PEEP 12

Ptrans I= 9.6
Ptrans E= -2.6


## PEEP 15

Ptrans I= 12
Ptrans E= +.03


Ptrans I goal= ≤10 Ptrans E goal= ≥ 0

## Tidal Volume Adjustment

- Tidal Volume decreased to lower Ptrans I (Inspiratory Transpulmonary Pressure) to ≤ 10 cm H2O.
- Ptrans E remained ≥ 0 cm H2O
- Goals for optimal Lung Protective Ventilation were optimized

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ATS Chapter

**CTS 2024 Annual Education Conference**
Hands-On Session: Ventilators and Ventilator Waveforms
March 8, 2024

# Hamilton C6 Ventilator

Features:

- Turbine driven – can transport patients on it, no air inlet necessary
- IntelliCuff – automated cuff manometer
    - Set desired cuff pressure & measure continuously
    - Cuff leak detection and compensation
- P/V tool – Protective Ventilation Tool
    - Generates a quasi-static P-V curve
    - Lung recruitability assessed by the differential volume between inspiration and expiration
    - Optional buy-in tool
- Esophageal manometry
    - Allows determination of transpulmonary pressure and appropriate PEEP titration
- ASV mode – Adaptive Support Ventilation, closed-loop ventilation
    - Adjusts rate & tidal volume based on Otis' least work of breathing equation
    - Minimizes chance of autoPEEP, volutrauma, and barotrauma
    - Decreases work of breathing
- Intellisync+
    - Real-time measurements of patient effort and adjusts flow trigger and inspiratory/expiratory cycling to optimize patient comfort
    - Used for spontaneous or non-invasive modes
- Support $HFO_2$ up to 60 L/m

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# Draeger V800 Ventilator

Features:

- Tablet-like touch screen
- Supports HFNC up to 80 L/min
- Automatic weaning through SmartCare/PS
    - Automatically adjusts pressure support during spontaneous breathing
- Low Flow P-V loop maneuver
    - Determination of lung recruitability from inflation and deflation curves
    - Lower inflection point utilized for optimal PEEP
- Smart Pulmonary View
    - Graphic view of compliance and resistance
    - Displays ratio between spontaneous and mandatory ventilation
- PressureLink
    - Coupling of Pinsp and PEEP
    - Setting one parameter will adjust the other automatically
- Spontaeneous-Proportional Pressure Support
    - Level of pressure support self-titrates based on patient inspiratory effort through Flow Assist and Volume Assist parameters

# Small Airways Disease and Oscillometry

**Catherine Sassoon, MD**
**Professor in Residence**
**UC Irvine/VA Long Beach**

Dr. Sassoon is Emeritus Professor of Medicine at UC Irvine with specialty in Pulmonary, Critical Care and Sleep Medicine. She did her postgraduate work at Cook County Hospital, Chicago, and UCLA School of Medicine. She had previously served as Chief of Pulmonary and Critical Care Medicine at the VA Long Beach Healthcare System, and as member of the Editorial Board of the American Journal of Respiratory and Critical Care Medicine, CHEST, and Respiratory Care. Her research interest is in mechanical ventilation, lung physiology, and diaphragmatic structure and function.

# SMALL AIRWAYS DISEASE AND OSCILLOMETRY

Catherine S. Sassoon, MD

Emeritus Professor of Medicine

University of California, Irvine

VA Long Beach Healthcare System

California Thoracic Society

# RELEVANT FINANCIAL DISCLOSURES

- I have no relationships with any ACCME defined ineligible companies.

- I will not discuss off-label use and/or investigational use of any drugs or devices.

# OUTLINE

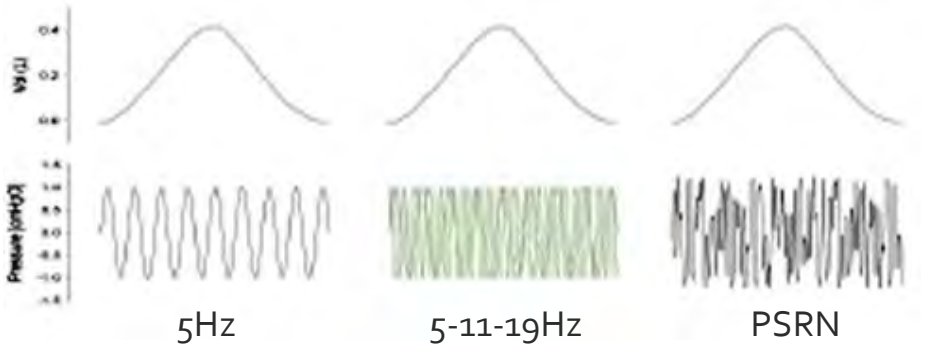
- What is Oscillometry?
- Physiology of Oscillometry
- Measured Variables and Interpretation
- Case presentation
- Clinical Application
- Limitation
- Summary

# WHAT IS OSCILLOMETRY?

- Oscillometry is a **noninvasive method** to assess respiratory mechanics, by superimposing external small oscillatory pressure generated by a loudspeaker to the airway opening of **spontaneously breathing** subject.

- The delivered pressure waveform is a sine wave of a single frequency (e.g, 5 Hz), a combination of sine waves of multiple frequencies (5 Hz, 10/11 Hz, 19/20 Hz), pseudo-random noise, or a train of pulses (5 pulses/s).

- Two commercially available oscillometry instruments based on superimposed pressure delivery:
  - Forced oscillation technique (FOT, sine waveform)
  - Impulse oscillometry (IOS, train of pulses)




*Adapted from Smith HJ et al. Eur Respir Mon, 2005, 31, 72-105*
*Kostorz-Nosal S et al. Respir Physiol Neurobiol 2023; 316:104135*

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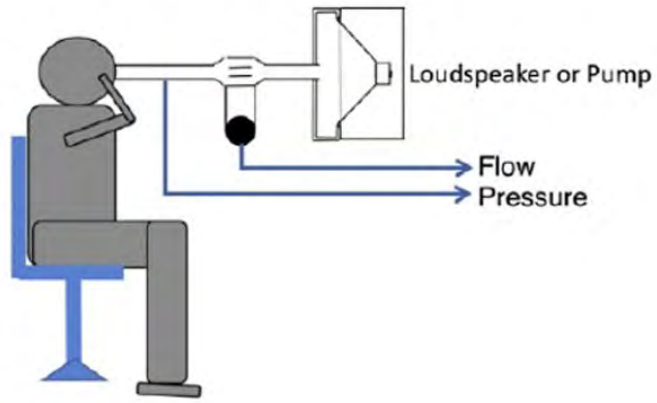
# BRIEF HISTORY OF OSCILLOMETRY

- Oscillometry was first introduced by A. Dubois and coworkers: Oscillatory mechanics of the lung and chest in man. J. Appl. Physiol. 1956; 8:587-594.
- Oscillometry has evolved from bulky equipment, manual calculation, paper tracings to plain mouth-piece and a small equipment of the size of a medium shipping box




- Pressure generator (loudspeaker)
- Pressure
- Flow

*Courtesy of C. Irvin, Ph.D. with permission; adapted from Oscillometry 101, ERS Channel 2022*

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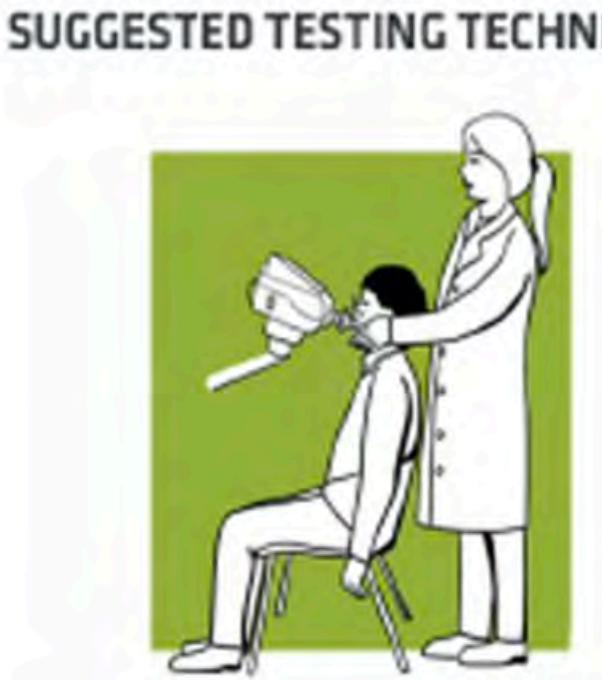
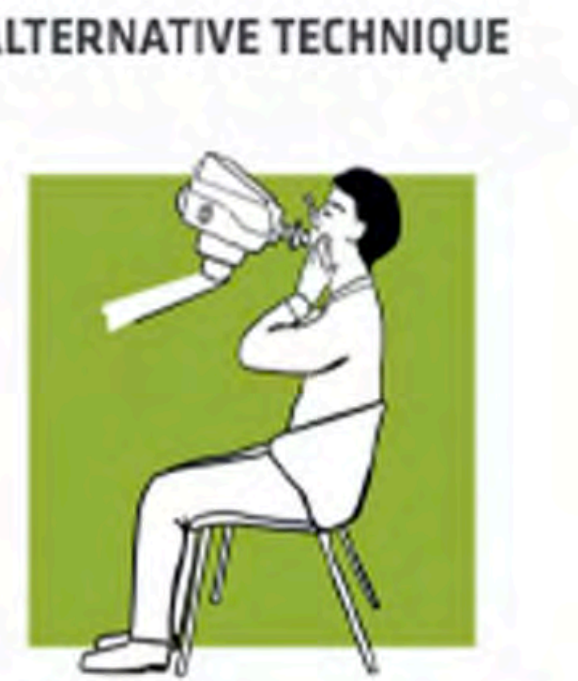
# METHOD OF MEASUREMENT WITH FORCED OSCILLATION TECHNIQUE

**FOT**


- Measured prior to spirometry
- Three acceptable tests, each of ≥ 30 sec duration
- Coefficient of variations <10% (adults); <15% (pediatrics)

*Courtesy of R. Perissin, with permission MGC Diagnostic International, Italy*
*Kostorz-Nosal S et al. Respir Physiol Neurobiol 2023; 316:104135*

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# PHYSIOLOGY OF OSCILLOMETRY

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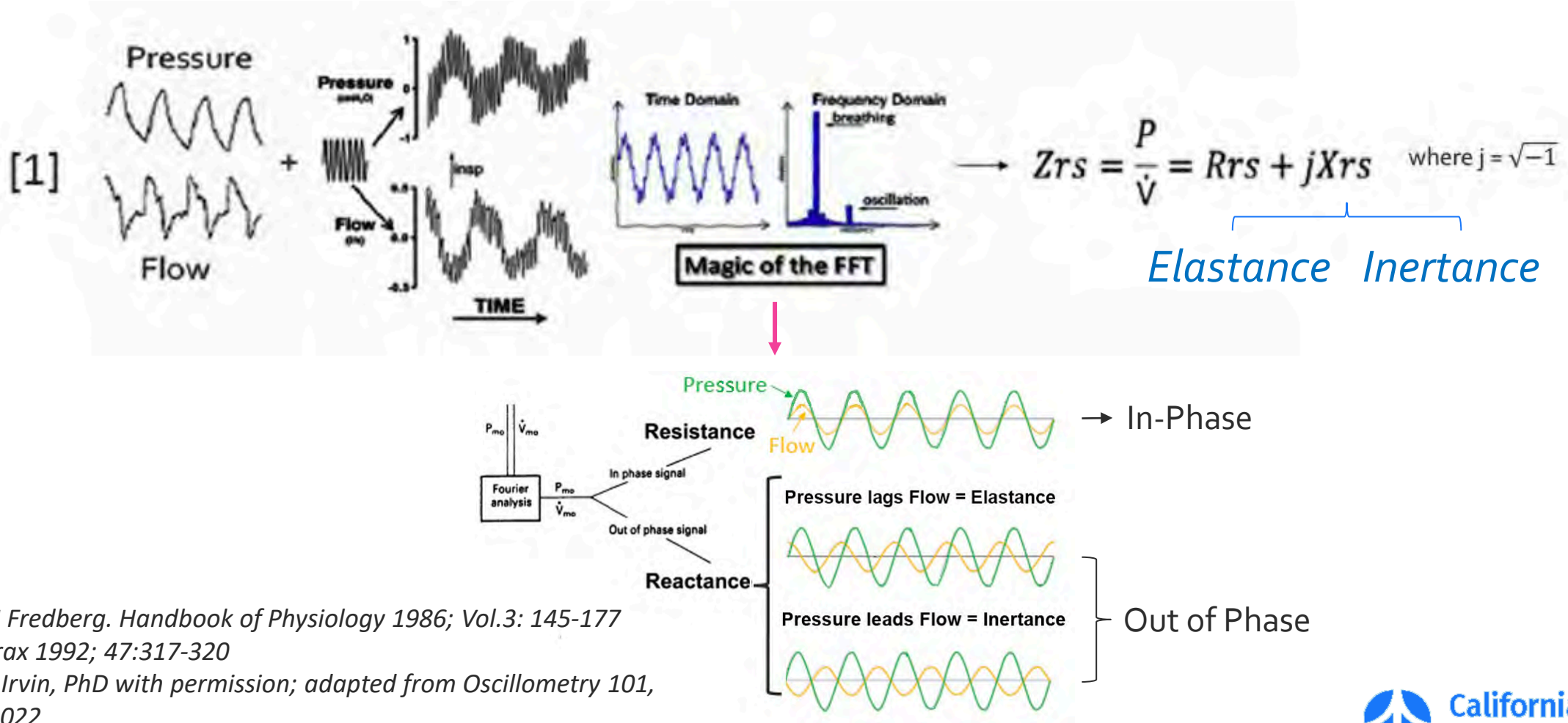
# BASIC SIGNAL PROCESSING




*R Peslin and JJ Fredberg. Handbook of Physiology 1986; Vol.3: 145-177*
*NB Pride. Thorax 1992; 47:317-320*
*Courtesy of C. Irvin, PhD with permission; adapted from Oscillometry 101, ERS Channel 2022*

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# MEASURED VARIABLES AND INTERPRETATION

# PHYSICAL PROPERTIES OF THE RESPIRATORY SYSTEM

**IMPEDANCE (Zrs)**

**The ratio of effective Pressure to effective Flow ($\frac{P}{\dot{V}}$)**

**1. RESISTANCE (Rrs)** (Real Component)

- Ratio of Pressure to Flow
- Pressure and Flow are in-phase
- Measure resistance of airways, tissue and chest wall

**2. REACTANCE (Xrs)** (Imaginary component)

- Ratio of Pressure to Flow
- Pressure and Flow are out of phase

$Zrs = \frac{P}{\dot{V}}$ = Rrs + jXrs  where j = $\sqrt{-1}$

*Zrs ~ Rrs '+' Ers '+' Irs (Equation of motion)*

**2.a. ELASTANCE (Ers)**
**(*Capacitance*)**

- Elastic properties of peripheral airways, lung parenchyma, and chest wall
- Negative component
- Dominates at low frequency

**2.b. INERTANCE (Irs)**

- Inertive force moving air column
- Positive component
- Dominates at high frequency

*Courtesy of C Cooper, MD, with permission; adapted from presentation at Spiromics 2022*
*Adapted from Kaminsky DA et al. Eur Respir Rev 2022; 31:210208*
*Pride NB. Thorax 1992; 47:317*

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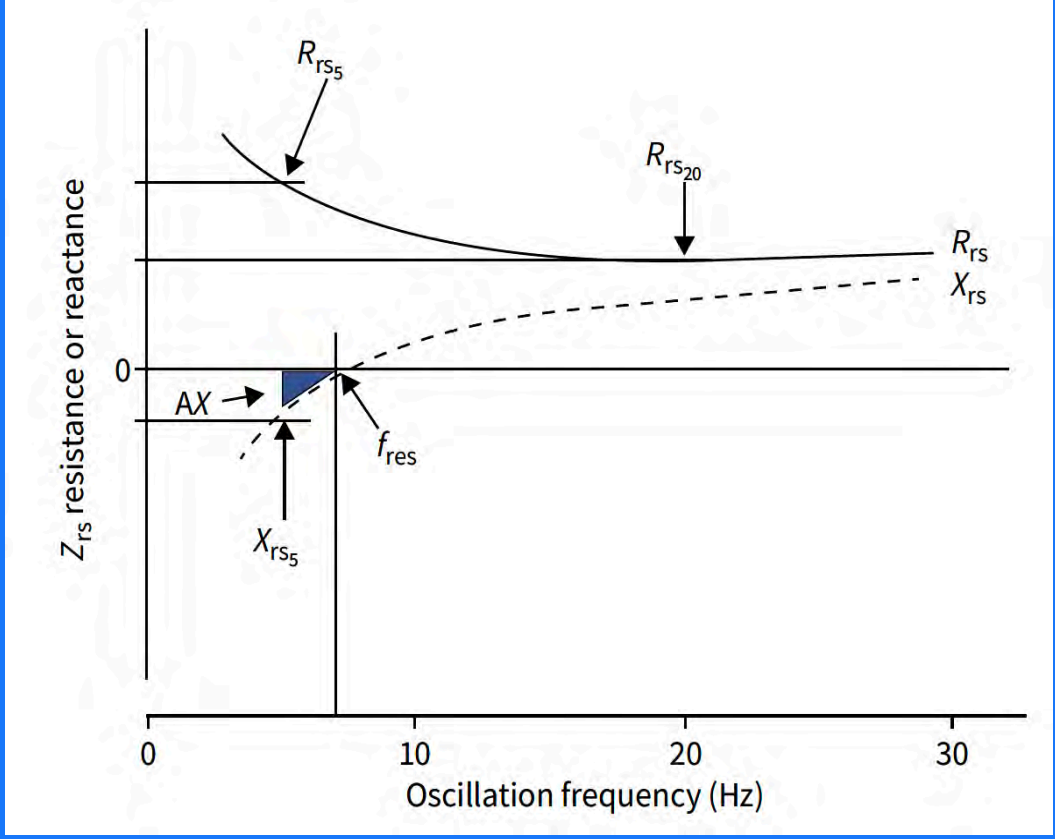
# OSCILLOMETRIC VARIABLES IN MEDIUM FREQUENCY RANGE (5-40 HZ) USED IN CLINICAL PRACTICE

## OSCILLOGRAM




- Zrs = Impedance of the respiratory system
- Rrs = Resistance of the respiratory system
- Frequency dependence of resistance (R5-R19/20Hz)
- Xrs = Reactance of the respiratory system

  (subscript numbers denote frequency in Hz)
- fres = Resonant frequency is the frequency where respiratory system elastance (Ers) and Inertance (Irs) make equal and opposite contributions to impedance (frs of healthy subjects is ~8-12 Hz; increases in lung disease
- AX = Area under the reactance curve subtended by the Xrs curve at the lowest frequency (5Hz) and fres

*Adapted from Kaminsky DA et al. Eur Respir Rev 2022; 31:210208*

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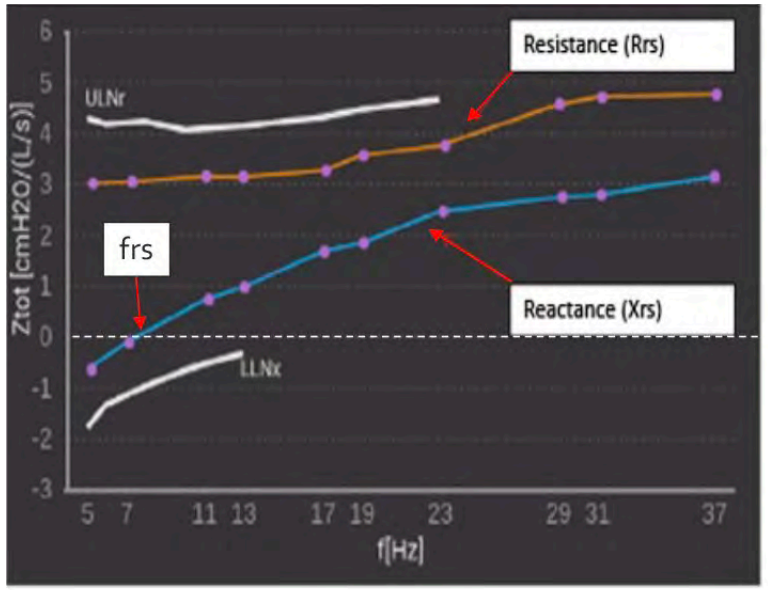
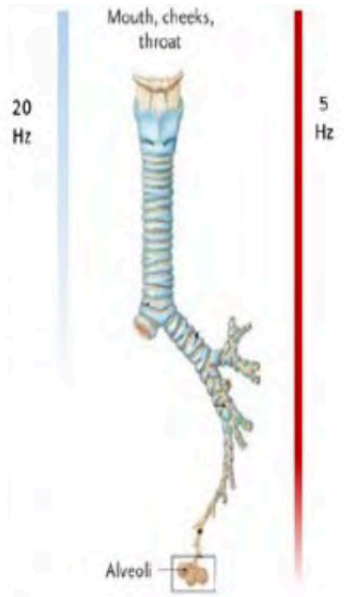
# RESISTANCE OF THE RESPIRATORY SYSTEM




Low frequencies travel all the way to the small airways, thus, reflect the resistive properties of the entire airway tree, while high frequencies travel only proximally, reflecting mainly central airways.

*Rentzhog CH et al. Clin Exp Allergy 2017; 47:1546*

- Respiratory system resistance (Rrs)reflects frictional losses of gas flow along the airways, and in tissues of the lung and chest wall as they are stretched and deformed.
- Rrs **5 Hz** reflects **total** airway resistance, increases in **both peripheral and central airway obstruction**.
- **Rrs 19/20 Hz** reflects changes in airway caliber (bronchoconstriction, mucus plug, airway inflammation) – **central airways**.
- **Rrs 5-19/20 Hz** considered to reflect small airway disease; but is not recommended given the lack of specificity. Impairment in **Xrs 5Hz** is more sensitive to peripheral airway disease.

*Kaminsky DA et al. Eur Respir Rev 2022; 31:210208*

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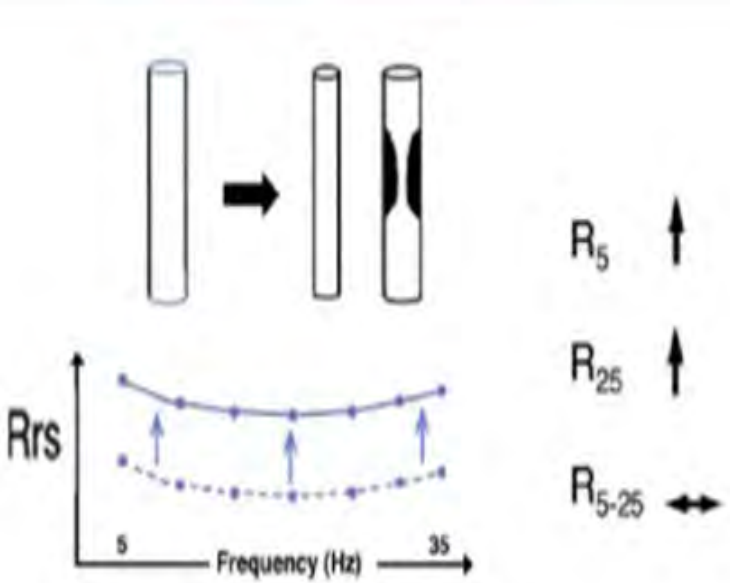
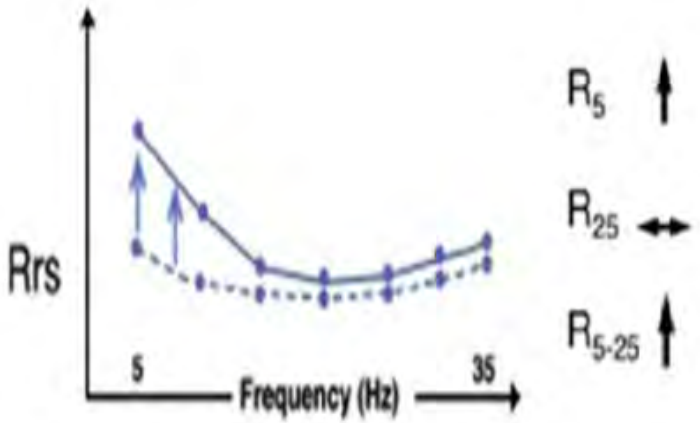
# INTERPRETATION OF RESISTANCE

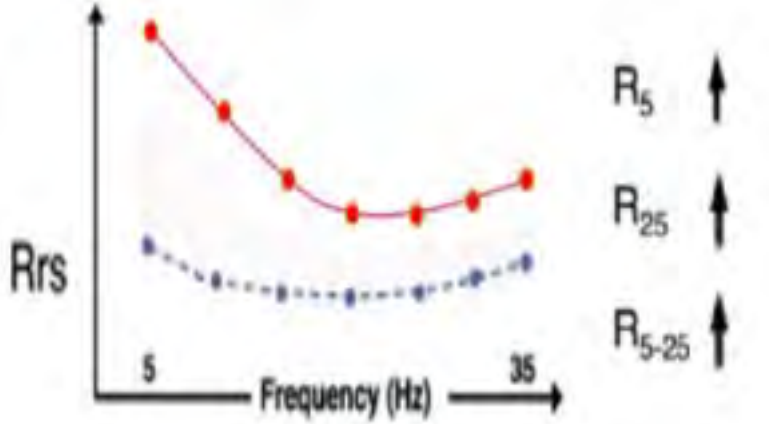
Increased Central Airway Resistance




Increased Peripheral Airway Resistance




Increased Central and Peripheral Airway Resistance




*Courtesy of C. Irvin, Ph.D. with permission; adapted from Oscillometry 101, ERS Channel 2022*

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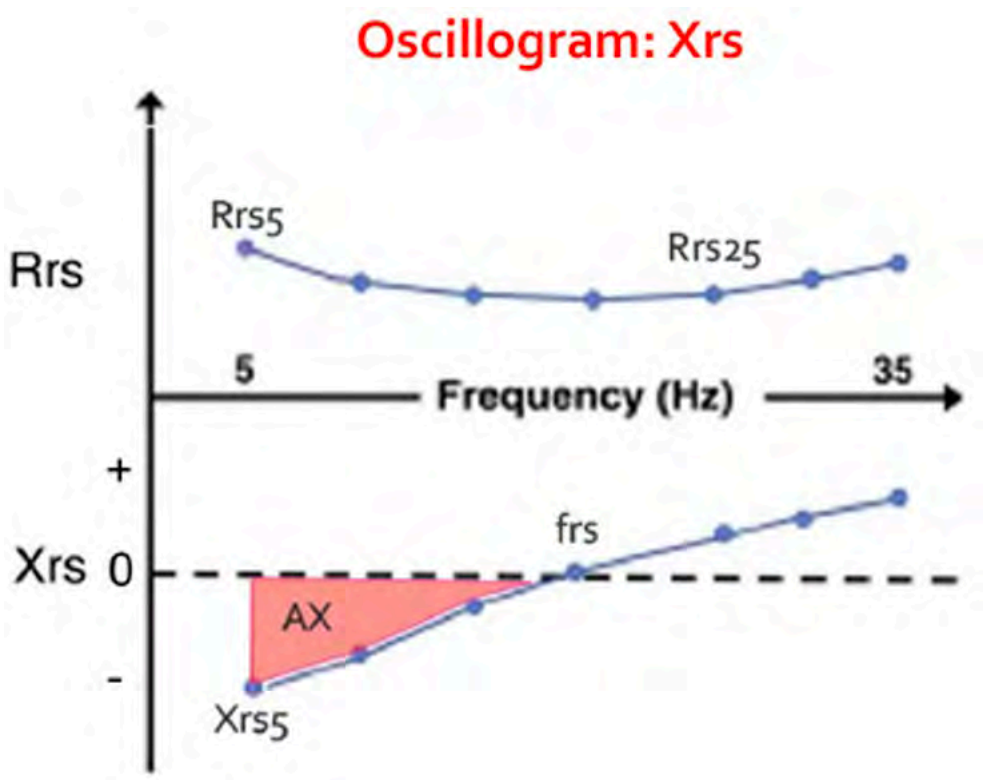
# REACTANCE OF THE RESPIRATORY SYSTEM




- Reactance (Xrs) expresses the energy storage, below the frs reflects respiratory system elastance (Ers) due to stifness of the lung tissue, airways and chest wall and above frs reflects respiratory system inertance (Irs) due to the mass of gas in the central airways → [ Xrs = Ers + Irs ].
- Xrs 5 Hz becomes more negative in lung disease, indicating the respiratory system becomes stiffer; reflects also small airway heterogeneity in obstructive lung disease.
- AX (cm H2O/L): The area AX reflects the stiffness of the lung parenchyma, potentially more sensitive to changes in the elastic properties of the respiratory system than Xrs at single frequency.

*Kaminsky DA et al. Eur Respir Rev 2022; 31:210208*
*Kostorz-Nosal S et al. Respir Physiol Neurobiol 2023; 316:104135*

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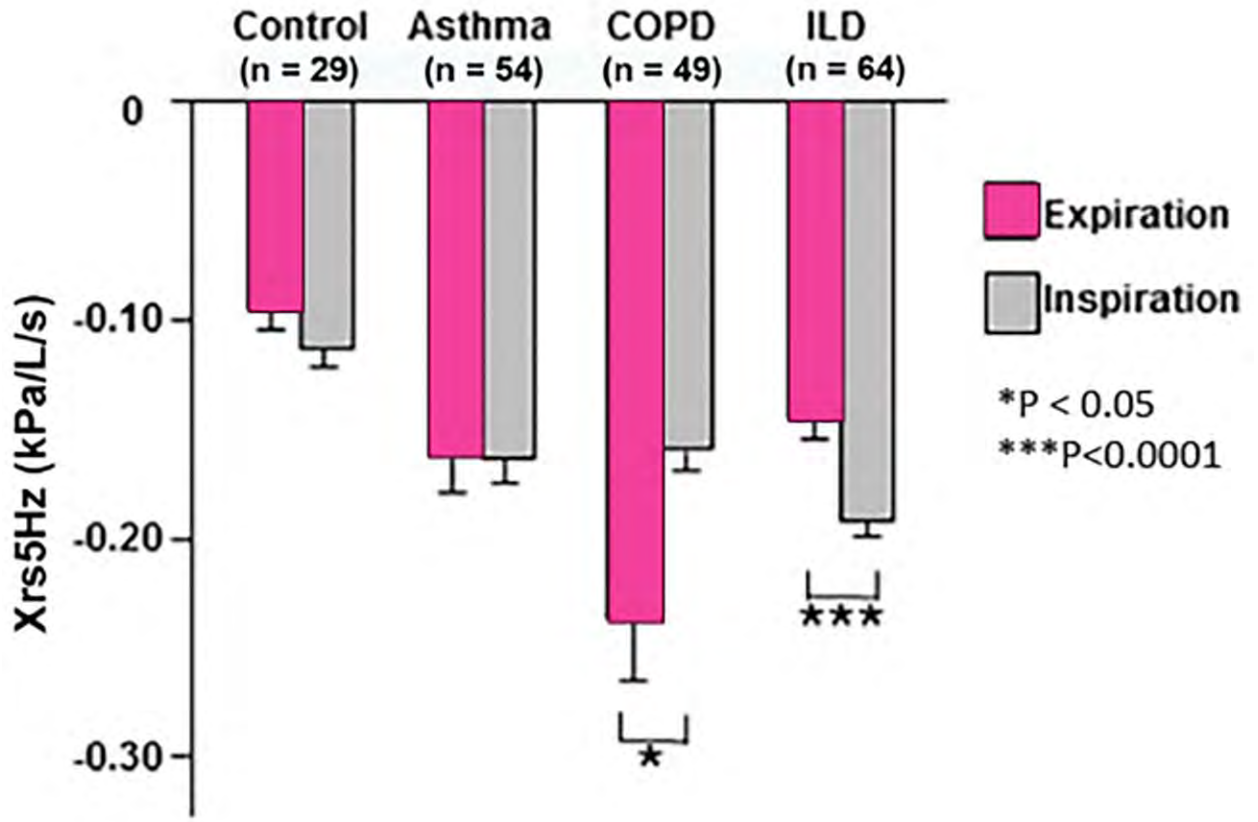
# INTRABREATH INSPIRATORY AND EXPIRATORY XRS-5HZ IN COPD AND ILD




*Adapted from Sugiyama A et al: Respir Med 2013; 107:875*
*Kostorz-Nosal S et al. Respir Physiol Neurobiol 2023; 316:104135*

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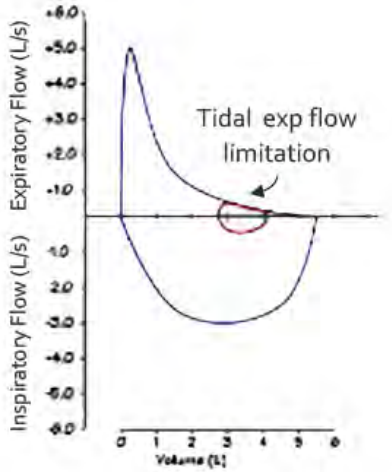
# REACTANCE OF THE RESPIRATORY SYSTEM IN COPD

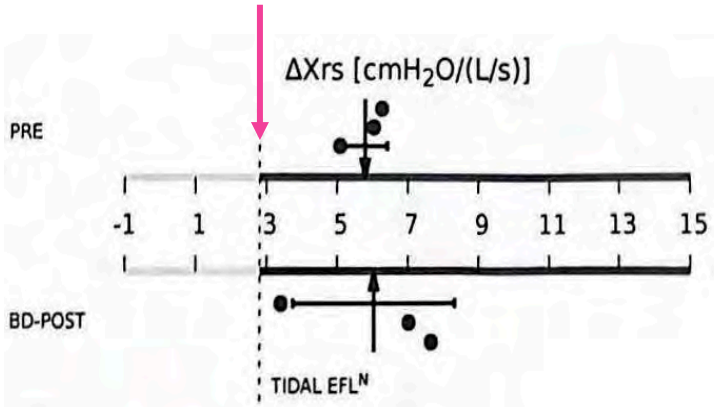
- Changes in intra-breath Xrs at 5Hz between inspiration and expiration are useful to detect **expiratory flow-limitation**.



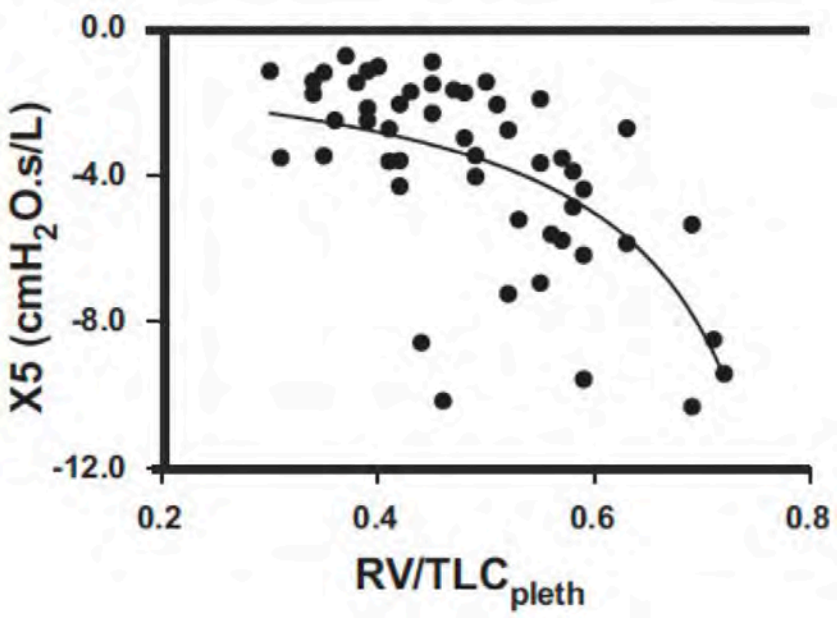

$\Delta Xrs_{5Hz} = Xrs_{5Hz}$ insp - $Xrs_{5Hz}$ exp

Threshold tidal EFL:

$\Delta Xrs_{5Hz} \geq 2.8$ cm H2O/L/s




- Xrs 5Hz is sensitive to airway closure, reflecting communicating lung volume (i.e., air trapping).




*Dellaca RL et al. Eur Respir J 2004;23:232*

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# BRONCHODILATOR RESPONSE CRITERIA

## Significant Bronchodilator Response Threshold:

- **ADULTS and CHILDREN**

  - Rrs5Hz: 40% decrease from baseline
  - Xrs5Hz: 50% increase
  - AX: 80% decrease

*King GG et al: Eur Respir J 2020;55:1900753*

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# CASE PRESENTATION NO. 1

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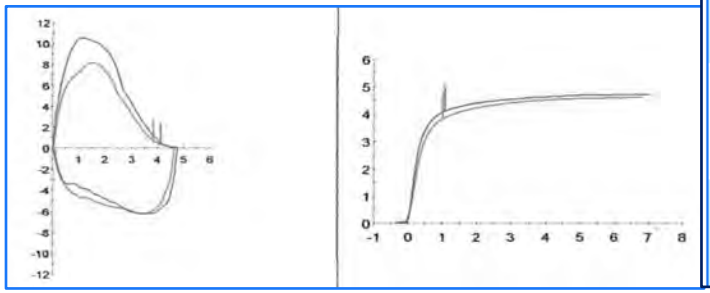
# CASE # 1: NORMAL SPIROMETRY WITH SYMPTOMS OF ASTHMA, DOES PATIENT HAVE ASTHMA?

32 yr old Hispanic Male
H 172 cm W 72 Kg
BMI 24.3 Kg/$m^2$
**Dyspnea**: walking < 91 m
**Cough**: non-productive
**Tobacco**: never smoke
**Wheeze**: frequent
**Recent illness**: Asthma exacerbation 3 months ago
**Medications**: Albuterol
**ACT score**: 9



**SPIROMETRY**

| | Pre-BD | | | | | Post-BD | | |
|---|---|---|---|---|---|---|---|---|
| | Actual | LLN | Z-Score | Pred | %Pred | Actual | %Pred | %Chng |
| FVC (L) | 4.63 | 4.01 | -0.61 | 4.99 | 92 | 4.74 | 94 | +2 |
| FEV1 (L) | 3.84 | 3.28 | -0.56 | 4.12 | 93 | 4.12 | 99 | +7 |
| FEV1/FVC (%) | 82.96 | 71.97 | +0.03 | 82.81 | 100 | 96.84 | 104 | +4 |
| **SLOW VITAL CAPACITY** | | | | | | | | |
| SVC (L) | 4.74 | 4.01 | -0.42 | 4.99 | 94 | | | |

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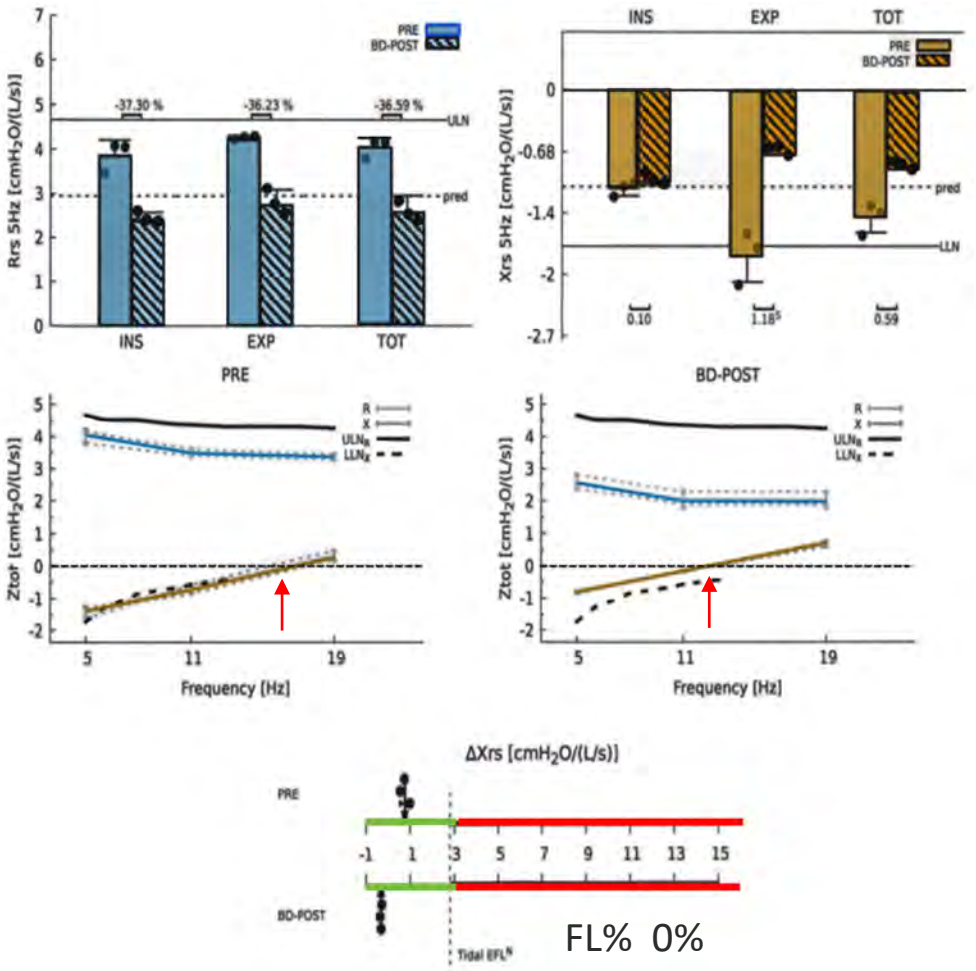
# CASE # 1 OSCILLOMETRY DATA




FL% 0%

| | PRE-BD | | | POST-BD | | | |
|---|---|---|---|---|---|---|---|
| Rrs 5Hz (cmH2O/L/s) | Mean±SD | Zscore | %Pred | Mean±SD | Zscore | %Pred | CHG% |
| Rinsp | 3.86±0.35 | 0.97 | 131.27% | 2.42±0.14 | -0.69 | 82.31% | -37.30% |
| Rexp | 4.26±0.04 | 1.32 | 144.90% | 2.72±0.36 | -0.28 | 92.40% | -36.23% |
| Rtot | 4.04±0.21 | 1.13 | 137.22% | 2.56±0.23 | -0.50 | 87.01% | -36.59% |
| Xrs5Hz (cm H2O/L/s) | | | | | | | |
| Xinsp | -1.09±0.08 | -0.04 | 101.29% | -0.99±0.06 | 0.23 | 92.08% | 9.09% |
| Xexp | -1.84±0.29 | -1.89 | 170.79% | -0.66±0.06 | 1.17 | 60.95% | 64.31% |
| Xtot | -1.41±0.17 | -0.88 | 131.58% | -0.82±0.05 | 0.69 | 76.43% | 41.92% |
| Tidal EFL (cm H2O/L/s) | | | | | | | |
| ΔXrs insp-exp | 0.75±0.22 | | | -0.33±0.04 | | | |

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# CASE # 1 INTERPRETATION

- $Rrs_{5Hz}$ is within normal limits with no significant response to bronchodilator.
- $Xrsexp_{5Hz}$ increased (more negative), suggests impaired mechanical properties of the peripheral airways due to peripheral airways inflammation, and/or ventilation inhomogeneities.
- Following bronchodilator administration, $Xrsexp_{5Hz}$ decreased >50% (less negative), with frs shifted to lower frequency, suggests a significant response to bronchodilator.
- Poor control asthma symptoms together with abnormal reactance ($Xrsexp_{5Hz}$) and response to bronchodilator are consistent with asthma.

# RELATIONSHIP OF ABNORMAL SPIROMETRY AND ABNORMAL OSCILLOMETRY TO POOR ASTHMA CONTROL

| Lung Function Variable | | Poor Asthma Control (ACT <20) | | | |
|---|---|---|---|---|---|
| (n = 90) | | Present (n) | Absent (n) | Sensitivity | Specificity |
| Spirometric FAO | Present | 30 | 13 | 55% | 63% |
| | Absent | 25 | 22 | | |
| Abnormal $R_{5Hz}$ | Present | 23 | 5 | 82% | 86% |
| | Absent | 32 | 30 | | |
| Abnormal $X_{5Hz}$ | Present | 38 | 9 | 81% | 74% |
| | Absent | 17 | 26 | | |
| Abnormal AX | Present | 43 | 14 | 75% | 60% |
| | Absent | 12 | 21 | | |

FAO: Fixed airflow obstruction; ACT: asthma control test

*Adapted from Cottee AM et al. J Allergy Clin Immunol Pract 2022;10:1260*

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# CASE PRESENTATION NO. 2

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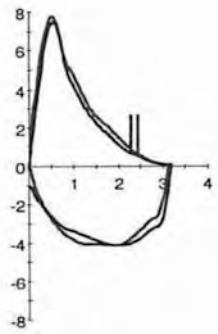
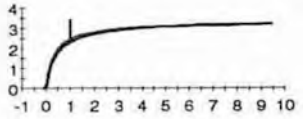
# CASE #2: NORMAL SPIROMETRY, MILD OBESITY WITH AIR TRAPPING, DOES PATIENT HAVE COPD?

63 yrs old Caucasian Male
H 169 cm W 97 Kg
BMI 34 Kg/$m^2$
**Dyspnea**: with exertion
**Cough**: yes, productive
**Tobacco**: 5 pkyrs, quit 6 yrs ago
**Wheeze**: no
**Recent illness**: no
**Medications**: Spiriva, ± Fluticasone/Salmeterol, ± Albuterol prn.





| SPIROMETRY | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Pre-BD | | | | | | Post-BD | | |
| | Actual | LLN | ULN | Z-Score | Pred | %Pred | Actual | %Pred | %Chng |
| FVC (L) | 3.13 | 3.03 | 4.99 | -1.48 | 4.00 | 78 | 3.18 | 79 | +1 |
| FEV1 (L) | 2.43 | 2.31 | 3.85 | -1.40 | 3.11 | 78 | 2.30 | 74 | -5 |
| FEV1/FVC (%) | 77.88 | 65.15 | 88.58 | +0.03 | 77.65 | 100 | 72.18 | 92 | -7 |
| **SLOW VITAL CAPACITY** | | | | | | | | | |
| SVC (L) | 3.57 | 3.03 | 4.99 | -0.74 | 4.00 | 89 | | | |
| ERV (L) | 0.22 | | | | 1.35 | 16 | | | |
| **LUNG VOL (PLETH)** | | | | | | | | | |
| TLC (L) | 6.80 | 5.12 | 7.70 | +0.51 | 6.40 | 106 | | | |
| FRC (L) | 3.45 | 2.23 | 4.47 | +0.33 | 3.22 | 107 | | | |
| RV (L) | 3.24 | 1.26 | 3.01 | +2.00 | 2.06 | 157 | | | |
| RV/TLC (%) | 47.58 | 21.62 | 42.01 | +2.50 | 31.59 | 150 | | | |
| sGaw (L/cmH2O*s) | 0.17 | 0.08 | 0.32 | -0.49 | 0.20 | 82 | | | |

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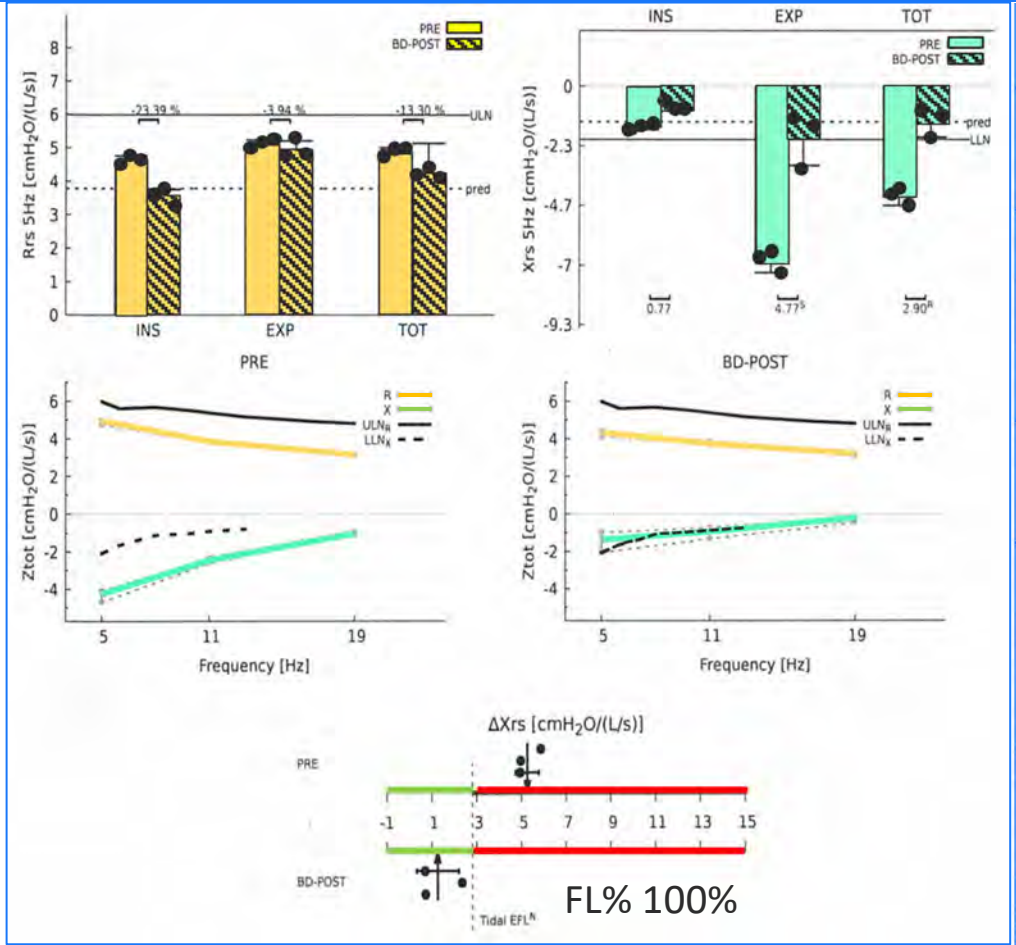
# CASE #2 OSCILLOMETRY DATA




FL% 100%

| | PRE-BD | | | POST-BD | | | |
|---|---|---|---|---|---|---|---|
| Rrs 5Hz (cmH2O/L/s) | Mean±SD | Zscore | %Pred | Mean±SD | Zscore | %Pred | CHG% |
| Rinsp | 4.62±0.14 | 0.72 | 122.23% | 3.54±0.21 | -0.23 | 93.64% | -23.39% |
| Rexp | 5.14±0.10 | 1.09 | 135.92% | 4.94±0.27 | 0.95 | 130.57% | -3.94% |
| Rtot | 4.89±0.12 | 0.92 | 129.39% | 4.24±0.20 | 0.41 | 112.19% | -13.30% |
| Xrs5Hz (cm H2O/L/s) | | | | | | | |
| Xinsp | -1.58±0.12 | -0.47 | 113.78% | -0.81±0.14 | 1.53 | 58.51% | 48.58% |
| Xexp | -6.84±0.45 | -9.50 | 492.45% | -2.07±1.02 | -1.61 | 149.07% | 69.73% |
| Xtot | -4.34±0.33 | -5.93 | 312.70% | -1.44±0.55 | -0.14 | 103.9% | 66.76% |
| Tidal EFL (cm H2O/L/s) | | | | | | | |
| ΔXrs insp-exp | 5.26±0.53* | | | 1.26±0.95 | | | -76.08% |

*EFL Threshold ≥ 2.8 cmH2O/L/s

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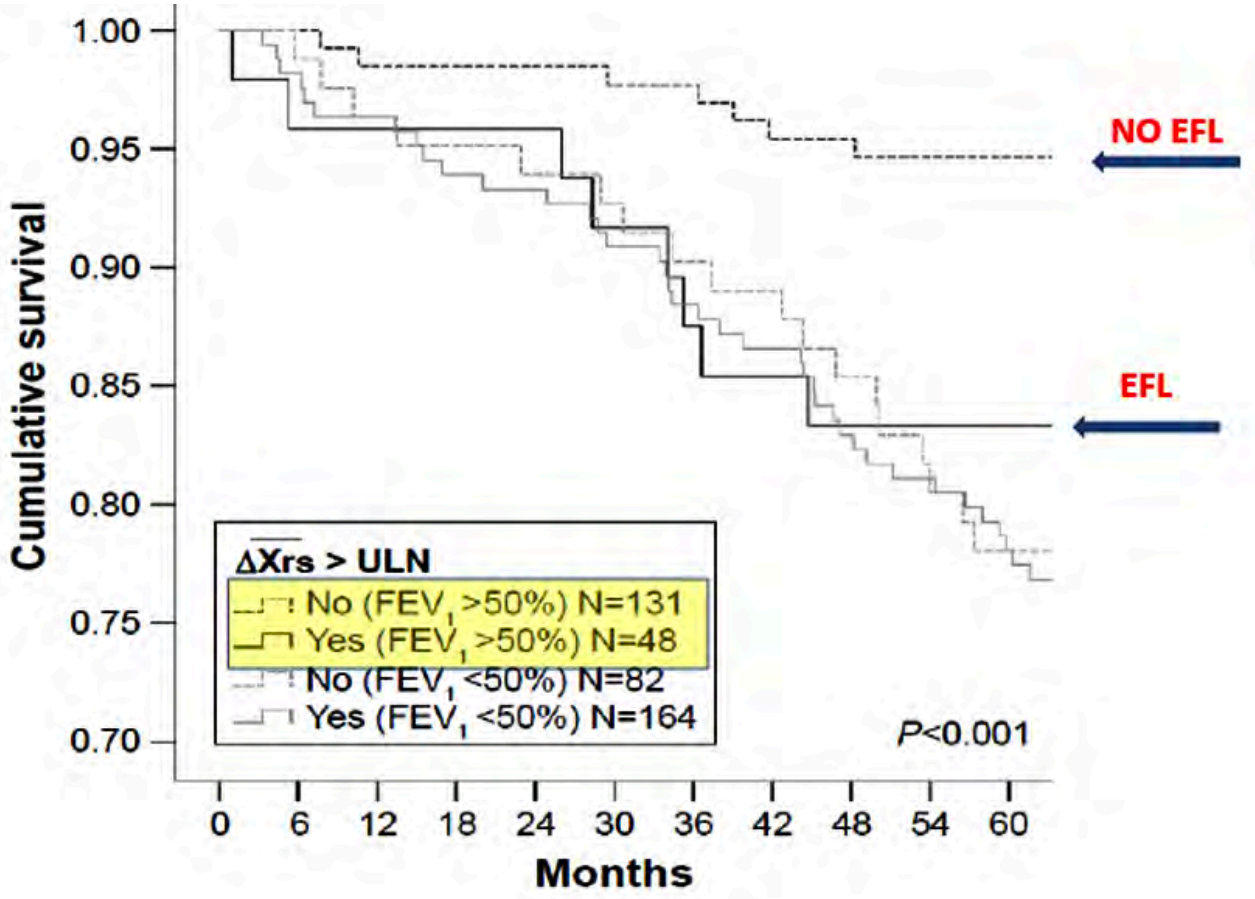
# CASE #2 INTERPRETATION

- $Rrs_{5Hz}$ is within normal limits with no significant response to bronchodilator.
- $Xrsexp_{5Hz}$ and $Xrstot_{5Hz}$ increased (more negative) suggests impaired mechanical properties of peripheral airways, ventilation inhomogeneity, airway closure, and increased chest wall stiffness (obesity).
- The presence of EFL leads to air trapping (increased RV/TLC).
- Following bronchodilator administration, both $Xrsexp_{5Hz}$ and $Xrstot_{5Hz}$ decreased >50% (less negative), with frs shifted to lower frequency, suggests a significant response to bronchodilator.
- The above findings are consistent with Chronic Bronchitis or Asthma

# INTRA-BREATH EFL DISCRIMINATE SURVIVAL IN MODERATELY SEVERE COPD (ECLIPSE TRIAL)




- In moderately severe COPD (FEV1 > 50% pred), oscillometry detected ~27 % of patients with EFL.
- In this group of patients, EFL predicts high risk for mortality
- In severe or very severe COPD (FEV1 <50% pred), FEV1 predicts high risk of mortality irrespective of EFL.
- Detection of EFL leads to early intervention, e.g., pulmonary rehabilitation may be of benefit.

*Aarli BB et al. Inter J COPD 2017; 12: 2179*

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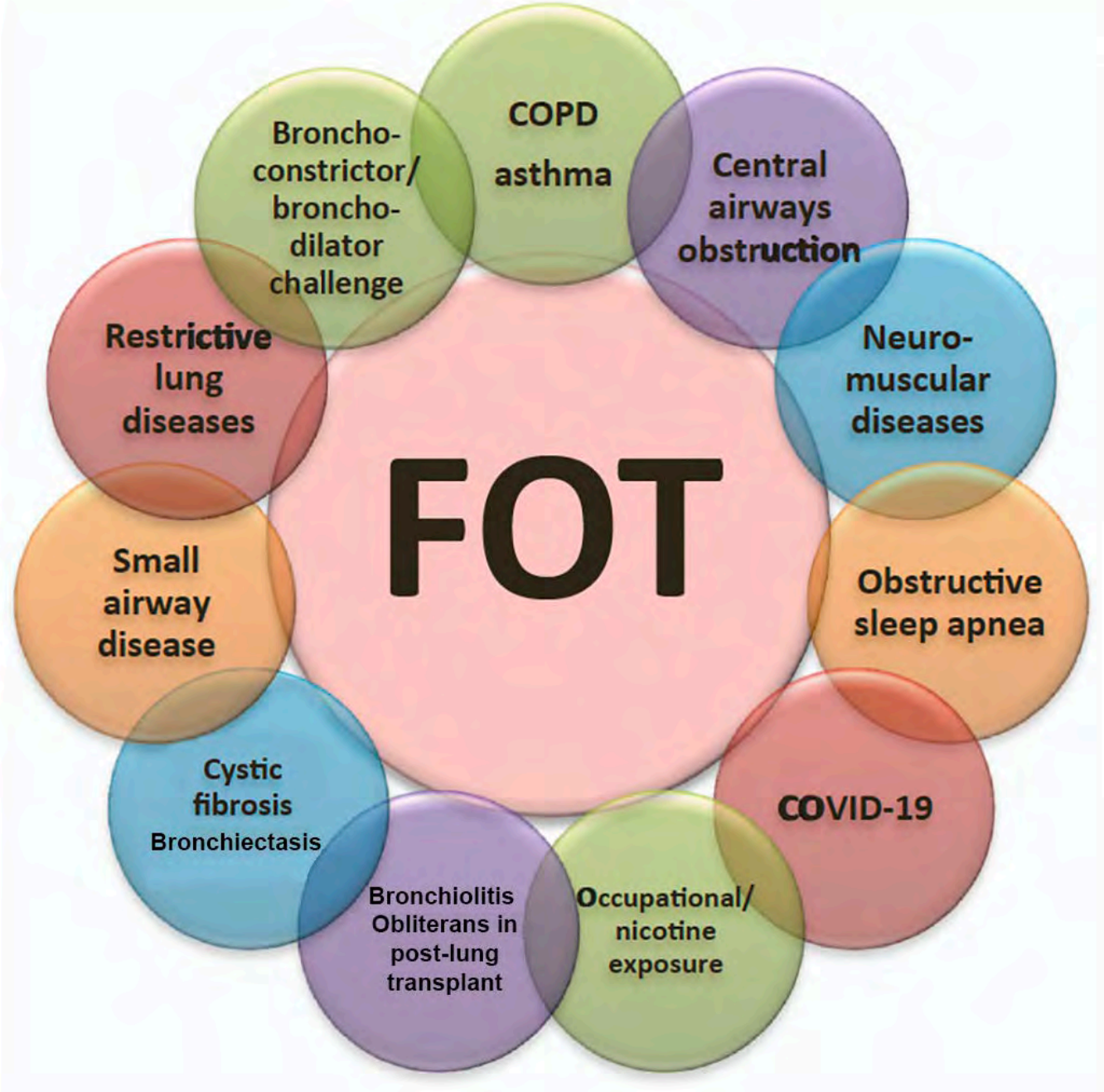
# CLINICAL APPLICATION IN OSCILLOMETRY




*Kostorz-Nosal S et al. Respir Physiol Neurobiol 2023; 316:104135*

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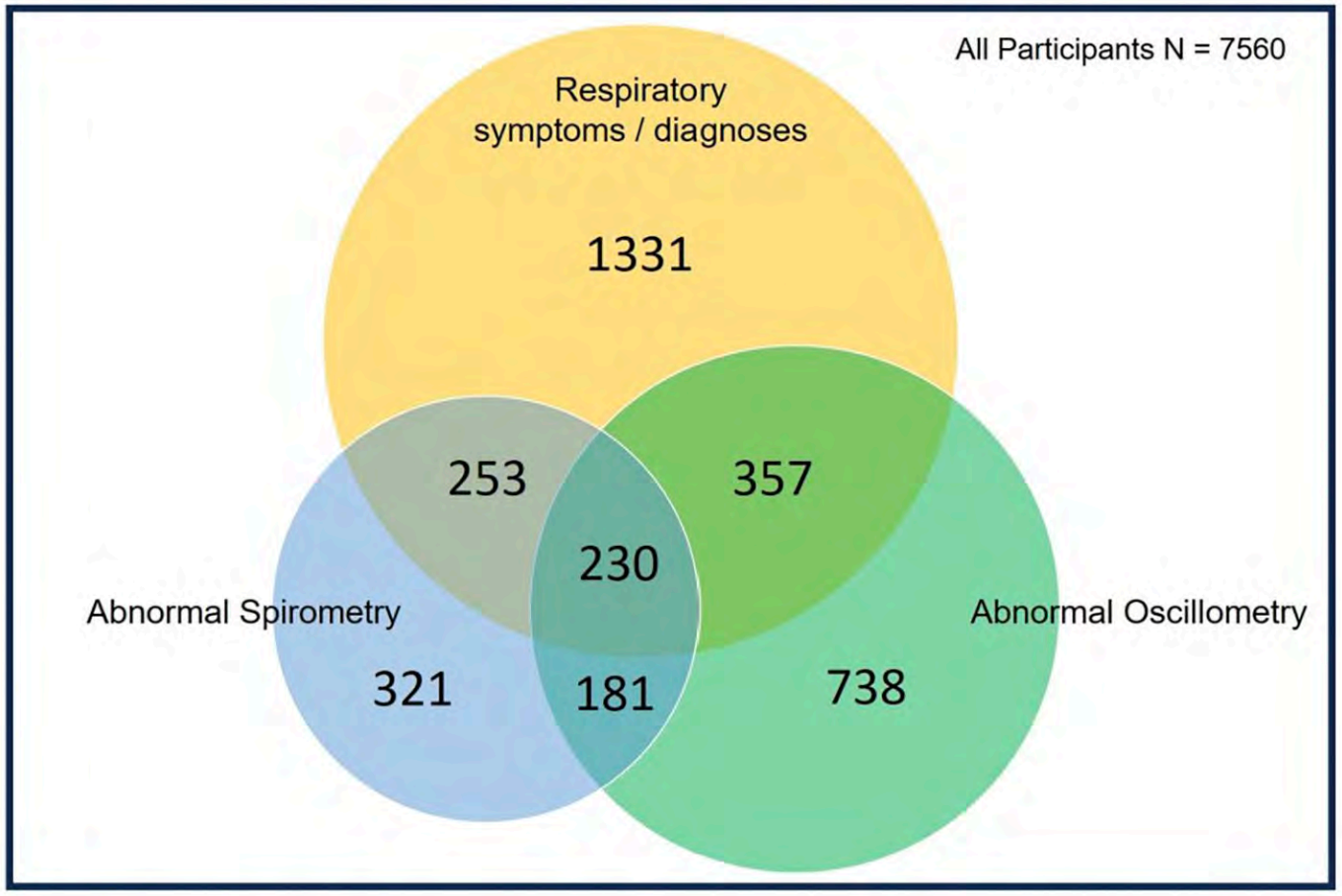
# DIAGNOSTIC POTENTIAL OF OSCILLOMETRY
## LEAD [LUNG HEART SOCIAL BODY] STUDY




- General population 18-90 yrs (total n: 7560; with symptoms /disease n = 2171)
- Abnormal Oscillometry detected in 20% (1506/7560) of population
- Abnormal Spirometry detected in 13% (985/7560) of population
- Abnormal oscillometry alone identified 27% (587/2171) of subjects with respiratory symptoms/disease
- Abnormal spirometry alone identified 22.2% (483/2171) of subjects with respiratory symptoms/disease
- Combined abnormal oscillometry and spirometry identified 38.8% (840/2171) of subjects with respiratory symptoms/disease

*Veneron C et al. Am J Repir Crit Care Med 2024; 209: 444*

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# LIMITATIONS OF OSCILLOMETRY

- No extensive reference normal values comparable to Global Lung Function Initiative (GLI) reference values for spirometry, lung volumes and DLCO [e.g., Rrs5-19Hz].
- Unable to determine the degree of severity similar to the degree of obstruction with GOLD's percent predicted FEV1.
- Resistance and Reactance are volume dependent, yet, unable to correct for lung volume. Since bronchodilation reduces lung hyperinflation, this would potentially cause paradoxical increase in Rrs and decrease Xrs, therefore, the interpretation of bronchodilator responses of Rrs and Xrs may not be straightforward and could cause some disparity with spirometry response.

# SUMMARY

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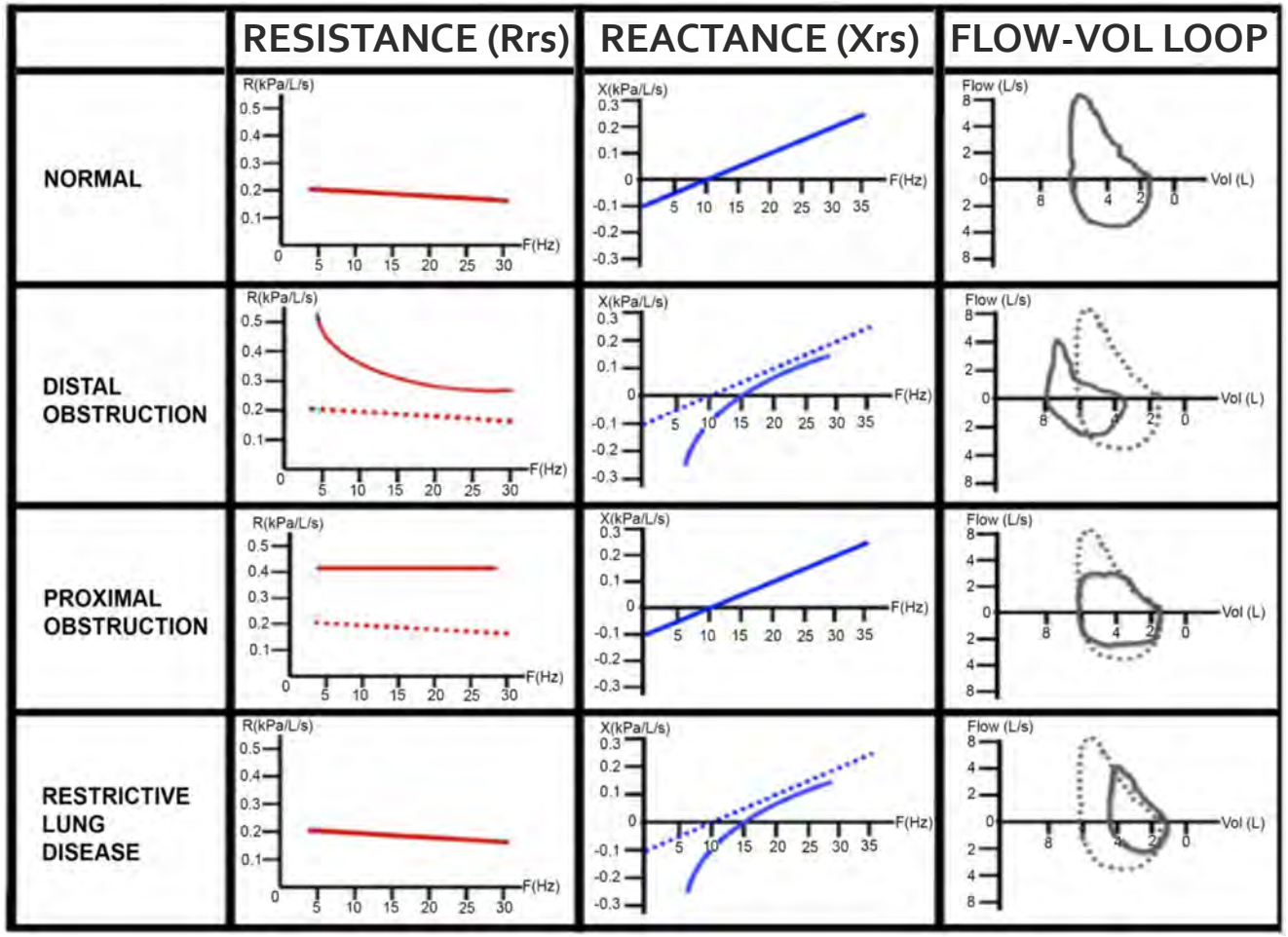
# SUMMARY OF OSCILLOMETRIC RESISTANCE AND REACTANCE PATTERN IN NORMAL AND DISEASE




*Adapted from Komarow HD et al. Ann Allergy Asthma Immunol 2011; 106: 191*

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# TAKE HOME MESSAGE

- Oscillometry complements existing conventional pulmonary function tests.
- Oscillometry is useful for longitudinal monitoring of lung function from the very young to the very old, essentially throughout life.
- Increased Rrs5Hz is consistent with peripheral airway obstruction.
- Increased Rrs at all frequencies is consistent with central airway obstruction
- Reactance at 5 Hz is sensitive to detect impaired mechanical properties of the peripheral airways, however, it increases (more negative) in both obstructive disease (due to parenchymal inhomogeneity, peripheral airway wall stiffness, or air trapping from dynamic airway closure) and restrictive disease (due to increased stiffness of lung parenchyma or chest wall), hence clinical correlation is necessary.

# REFERENCES


- Veneroni C et al. Diagnostic potential of oscillometry: A population-based approach. Am J Respir Crit Care Med 2024; 209: 444-453.
- Kaminsky DA. Real world application of oscillometry: Taking the LEAD. [Editorial]. Am J Respir Crit Care Med 2024; 209: 356-357.
- Kostorz-Nosal S et al. Window of opportunity for respiratory oscillometry: A review of recent research. Respir Physiol Neurobiol 2023; 316: 104135.
- Kaminsky DA et al. Clinical significance and application of oscillometry. Eur Respir Rev 2022; 31: 210208. doi: 10.1183/16000617.0208-2021.
- King GG et al. Technical standards for respiratory oscillometry. Eur Respir J 2020; 55: 1900753. doi: 10.1183/13993003.00753-2019.
- Oostveen E et al. Respiratory impedance in healthy-subjects baseline values and bronchodilator response. Eur Respir J 2013; 42:1513-1523.


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# Resmon Pro Full V3
# DEMONSTRATION VIDEO :

**"Measuring FOT with the Resmon Pro Full V3 FOT-Oscillometry system, a product demonstration, 7:30 minutes (Jan 2023)"**

LINK : ***https://vimeo.com/788556136***

**Password : "ResmonV3DEMO"**


*"DESCRIPTION : Two good acceptable FOT and one one non-acceptable measurements have been already performed, and to complete the **FOT session** (as per 2020 ERS international guidelines) a THIRD acceptable measurement is now added. This video shows how to perform a measurement, complete a session, and analyze the results.*

*NOTE : This is an extract from the video (OPEN ACCESS, no password required) :* ***Intro to Forced Oscillation Technique (FOT) or Oscillometry, using the Resmon PRO FULL V3 System*** *– JAN 2023 (35 min)*
***https://www.youtube.com/watch?v=mpdcqvP0jtU***

*Perissin R. With permission.*

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# Biologics for COPD

**Stephanie Christenson, MD, MAS**
**Associate Professor**
**UC San Francisco**

Dr. Christenson is an Associate Professor at the University of California, San Francisco in the Division of Pulmonary, Critical Care, Allergy, and Sleep Medicine. She serves as an attending physician on the Pulmonary Consult Service and in the Pulmonary Clinic. Dr. Christenson obtained her undergraduate degree at the University of Wisconsin, Madison and her medical degree at the Medical College of Wisconsin. She completed her residency training as well as a year of research training in computational biology at Boston Medical Center. She then came to UCSF for fellowship in Pulmonary and Critical Care Medicine where she also obtained a Master's in Clinical Research, after which she joined faculty.

Dr. Christenson's research program integrates her expertise in genomics/bioinformatics and clinical research to study chronic airway disease and the associated risk factors. Her research emphasizes innovative computational tools, systems biology approaches, and 'omics biomarkers to better inform our understanding of the biology underlying clinical traits and outcomes in asthma, smoking, and COPD. Dr. Christenson also serves in multiple leadership roles for multi-center studies and advises industry on trials of biologic and inhaled therapies for COPD. Leadership roles include co-director of the Genetics and Genomics Subcommittee for the multi-center SPIROMICS and SOURCE studies, the UCSF site PI for the American Lung Association (ALA) Airway Clinical Research Consortium, and a Disease Study Site PI for the NHGRI-funded Multi-Omics in Health and Disease (MOHD) Consortium.

UCSF
University of California
San Francisco

# Biologic Therapies in COPD

Stephanie Christenson, MD MAS
California Thoracic Society
March 8th, 2024

# Faculty Disclosures

I have the following relationships with ACCME defined ineligible companies:

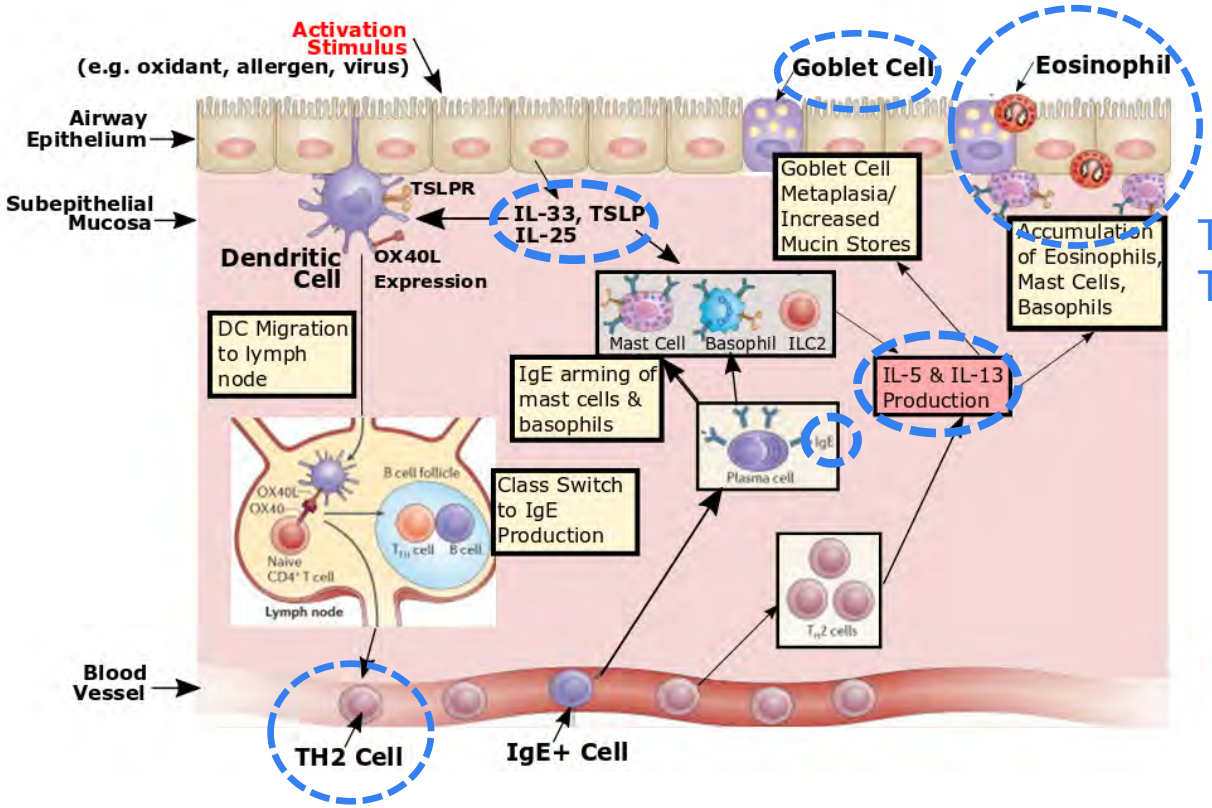
- AstraZeneca: Consultant, Speaker (non-branded)
- GlaxoSmithKline: Consultant, Speaker (non-branded)
- Glenmark: Consultant
- Sanofi: Consultant, Speaker (non-branded)
- Regeneron: Consultant, Speaker (non-branded)
- UpToDate: writer
- Verona: Consultant

I WILL discuss off-label use and/or investigational use of any drugs or devices.

# Outline

- Overview of T2 inflammation
- Evidence for T2 inflammation in COPD before biologics: **blood eosinophils and corticosteroids**
- Biologics in COPD

# Type 2 Inflammation in the Airway






*Fahy, Nat Rev Immun. 2015*

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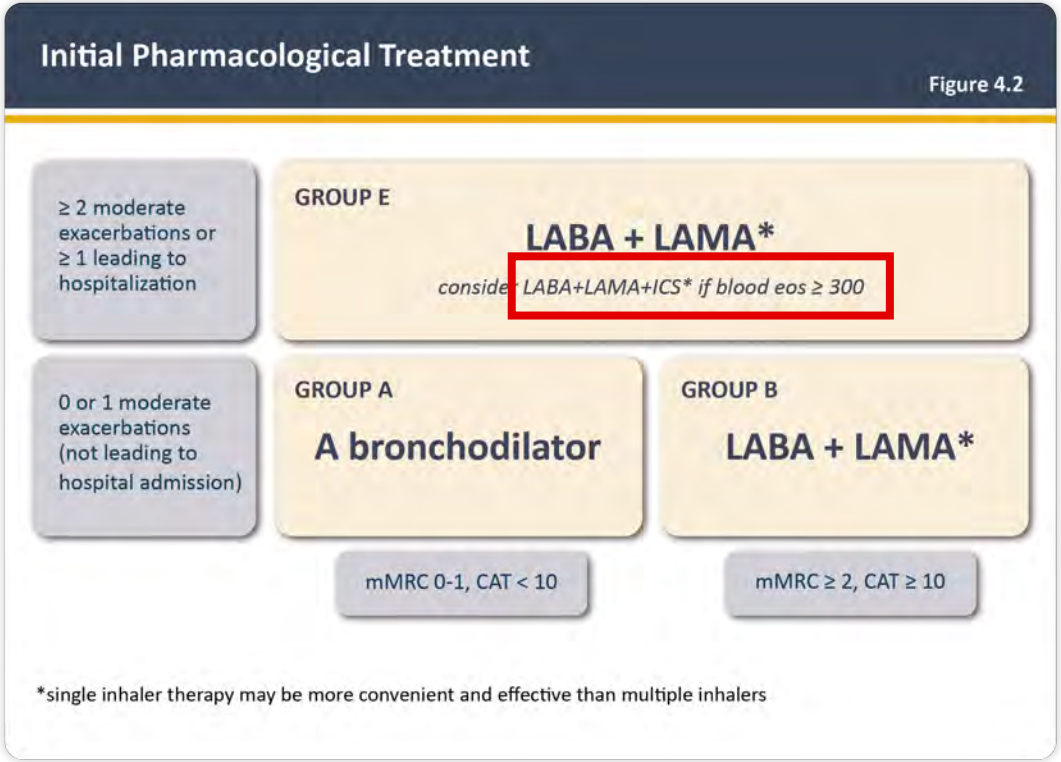
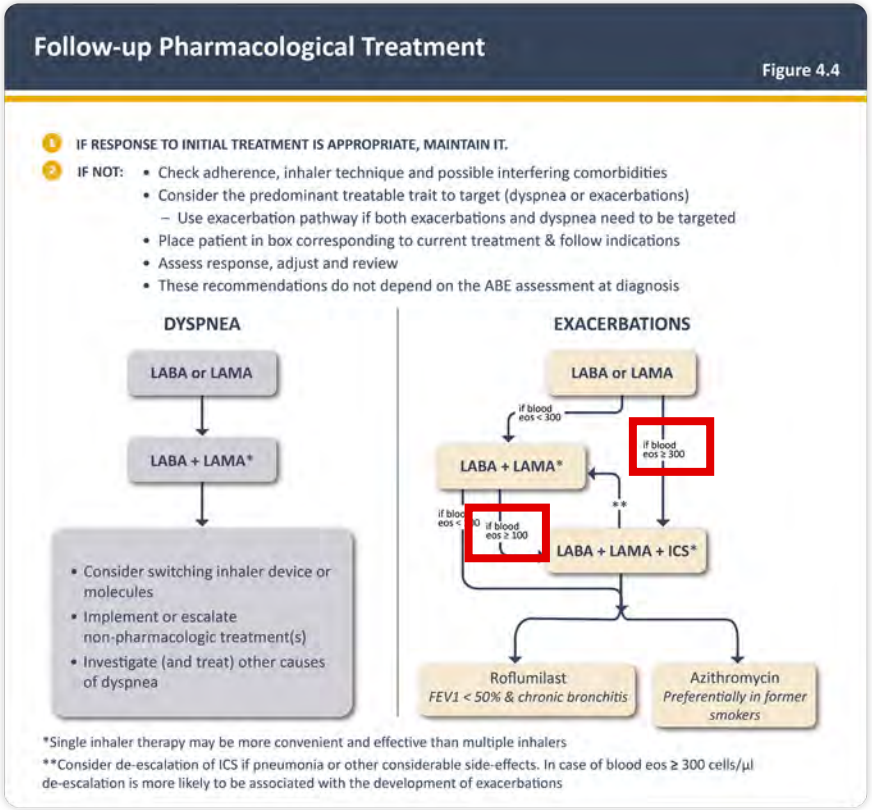
# Initial Pharmacotherapy



# Follow-up Pharmacotherapy



# Endotyping in COPD:
## Blood Eosinophils and Inhaled Corticosteroids

- Improved Exacerbation Prevention in Post-Hoc analyses of blood eos in ICS/LABA trials:
  - FORWARD→ AECOPD rate reduction, Δ FEV1,SGRQ
  - INSPIRE→ AECOPD rate reduction
  - TRISTAN→ AECOPD rate reduction
  - 3 RCTs of Budesonide/Formoterol → AECOPD rate reduction, Δ FEV1,SGRQ
  - 2 RCTs of Fluticasone/Vilanterol → AECOPD rate reduction
  - WISDOM → Increased Moderate/Severe Exacerbations after ICS withdrawal

*Siddiqui SH, AJRCCM. 2015* *Pascoe, Lancet Respir Med. 2015* *Bafadhel M, Lancet Respir Med. 2018*
*Pavord ID, Thorax 2016* *Watz H, et al. Lancet Respir Med 2016*

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# Endotyping in COPD:
## Blood Eosinophils and Inhaled Corticosteroids

**Equipoise in Inhaled Therapy Trials:**

### LABA/LAMA vs ICS/LABA

- **FLAME (2016):** indacaterol/glycopyrronium superior/similar to salmeterol/fluticasone regardless of blood eosinophil levels

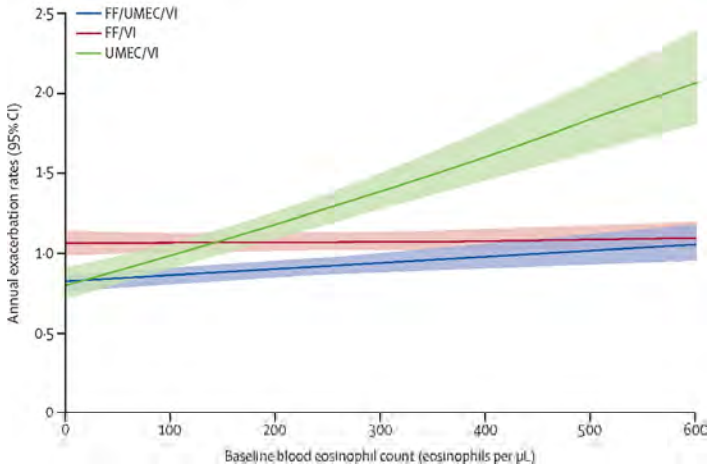
### Triple Therapies (ICS/LABA/LAMA)

- **IMPACT (2018):** fluticasone/umeclidium/vilanterol decreased exacerbations more than LAMA/LABA (umeclidium/vilanterol) or ICS/LABA (fluticasone/vilanterol) regardless of eosinophil counts
- **ETHOS (2020):** budesonide/glycopyrrolate/formoterol decreased exacerbations more than LAMA/LABA (glycopyrrolate/formoterol) or ICS/LABA (fluticasone/vilanterol) regardless of eosinophil counts

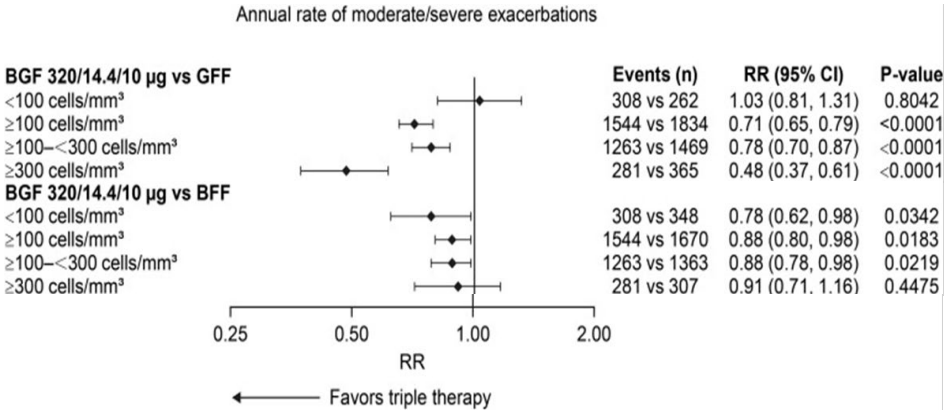
*Wedzicha JA, et al NEJM 2016* *Lipson D, et al NEJM 2018* *Rabe KF, et al NEJM 2020*

# Endotyping in COPD:
## Triple Therapy Post-Hoc Analyses of Eosinophils

### IMPACT




### ETHOS






*Pascoe S et al, Lancet Respir Med* 2020

*Bafhadel M et al, Int J Chron Obstruct Pulmon Dis 2022*

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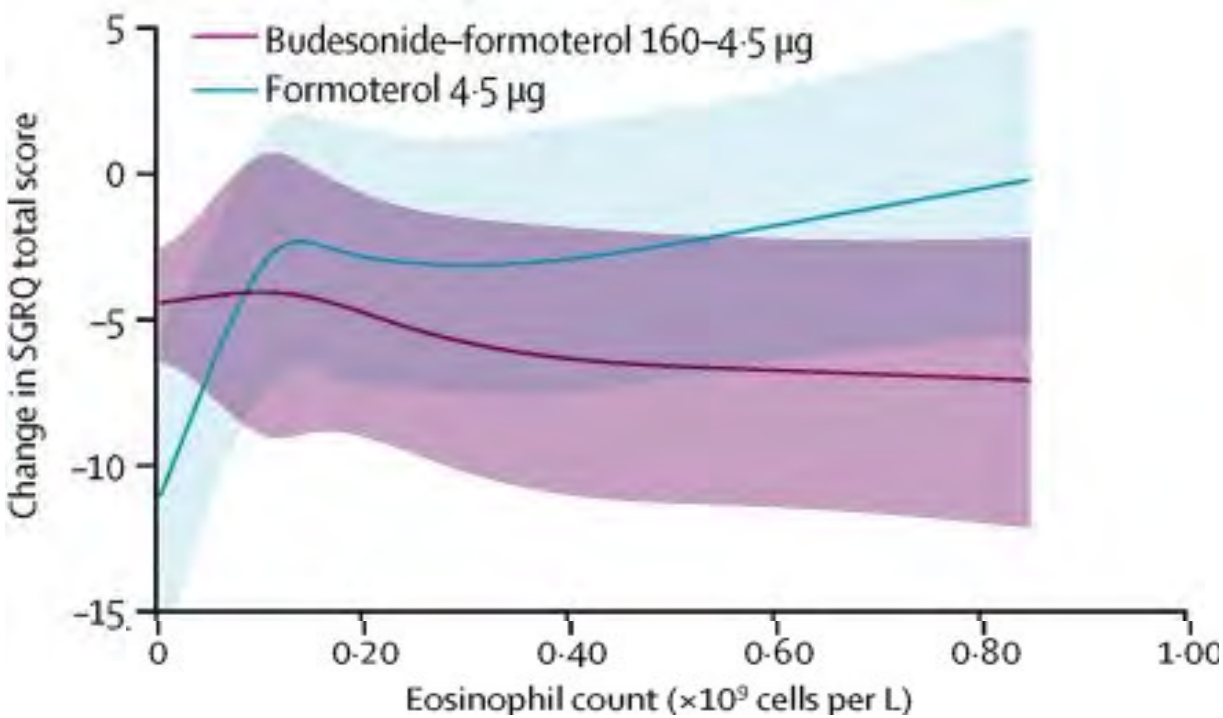
# ICS containing regimens may not have an effect with Blood Eos <100






*Bafhadel et al, Lancet Respir Med* 2018

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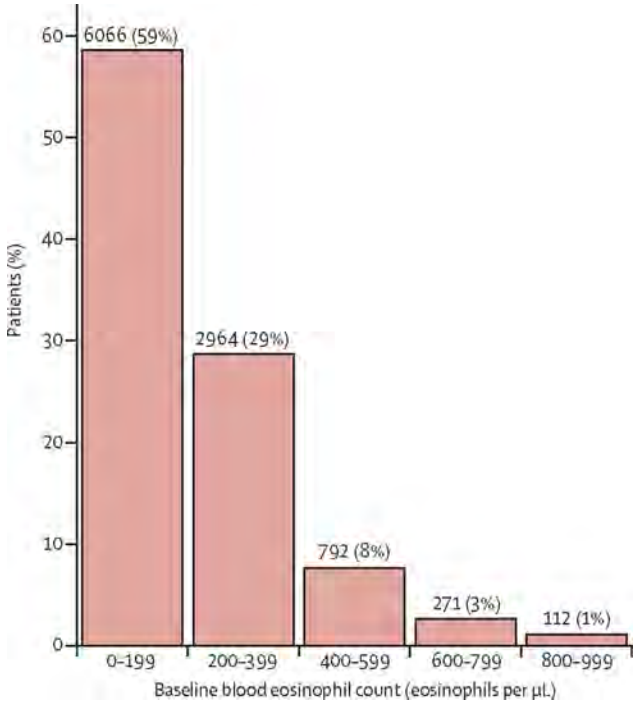
# Blood Eosinophil counts in IMPACT




*Pascoe S et al, Lancet Respir Med* 2020

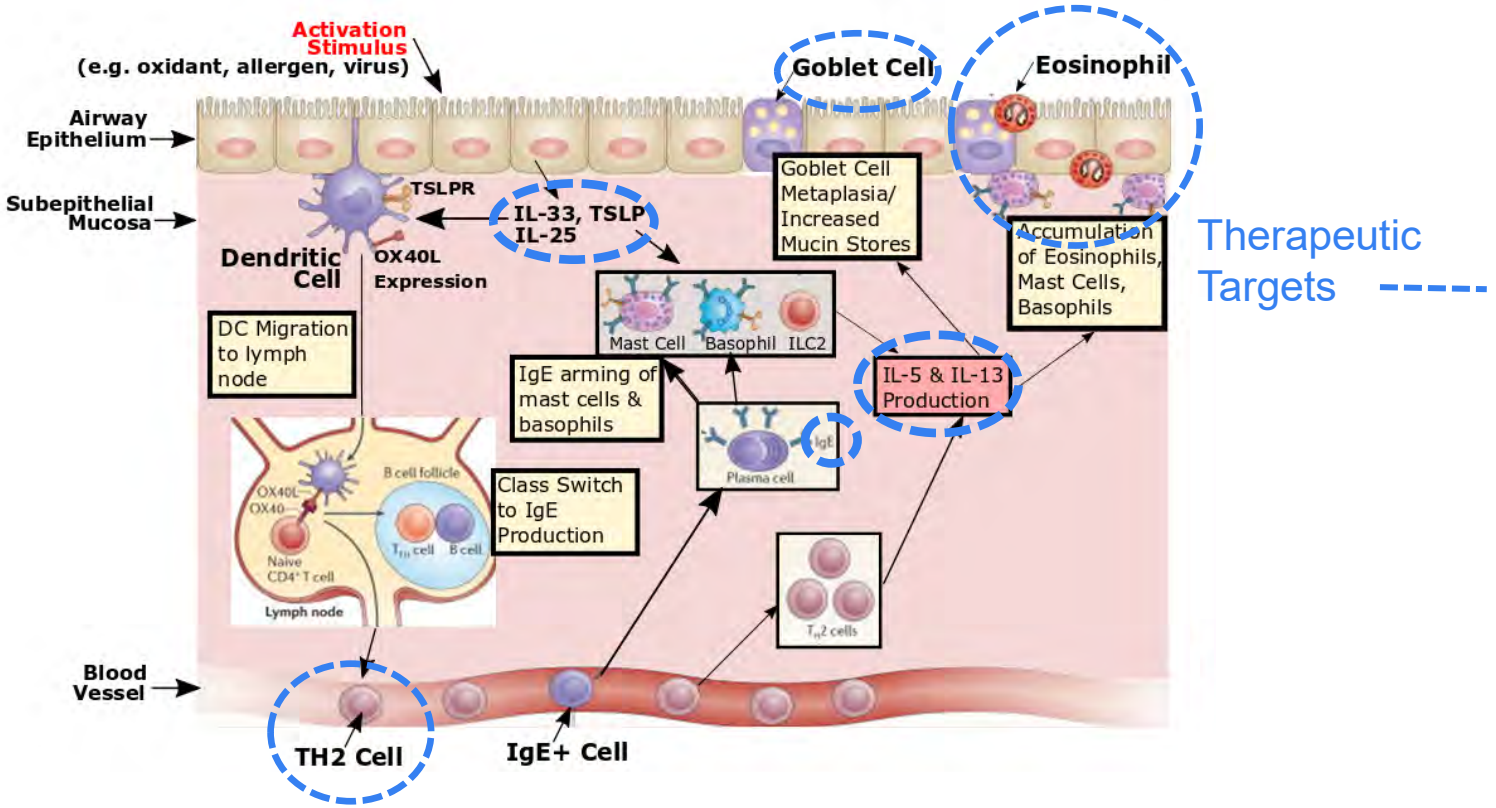
# Biologics in COPD

# Biologics in Development in COPD

***None of these are FDA approved*

| Biologic | Target | Trial |
|---|---|---|
| **Mepolizumab** | IL-5 | **METREX & METREO** *(Pavord ID, et al NEJM 2017)*<br>MATINEE *(Ongoing, Est Completion: 8/24)* |
| **Benralizumab** | IL-5R | **GALATHEA & TERRANOVA** (*Lipson D, et al NEJM 2018*)<br>RESOLUTE *(Ongoing, Est Completion: 6/25)* |
| **Dupilumab** | IL4R<br>(IL-4 & IL-13) | **BOREAS** *(Rabe KF, et al NEJM 2023)*<br>**NOTUS** *(not yet reported)* |
| **Tezepelumab** | TSLP | COURSE *(Phase 2a, Ongoing, Completed: 1/24)* |
| **Itepekimab** | IL-33 | AERIFY-1 & 2 *(Ongoing, Est Completion: 11/25)* |
| **Tozorakimab** | IL-33 | OBERON & TITANIA *(Ongoing, Est Completion: 8/25)* |
| **Astegolimab** | ST2 | ARNASA *(Ongoing, Est Completion: 6/25)* |

# Type 2 Inflammation in the Airway






*Fahy, Nat Rev Immun. 2015*

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# Eosinophils as a therapeutic target: Anti-IL-5 Biologics

## *Mixed Results to Date*

### Mepolizumab (anti-IL-5)

**Eligibility**
- 10 pack year smoking history
- Triple therapy x3 months
- ≥ 2 moderate or ≥ 1 severe exacerbation
- Current diagnosis of asthma excluded
- Blood Eos:
  ≥150/µL at screening **OR**
  ≥300/µL during previous year

**METREX**
- *Statistically significant 18% reduction in exacerbations*
- No difference in symptom scores

**METREO**
- Did not reach significance for exacerbations
- No difference in symptom scores

### Benralizumab (anti-IL-5Rα)

**Eligibility**
- 10 pack year smoking history
- Dual or Triple Therapy
- ≥ 2 moderate or ≥ 1 severe exacerbation
- Symptomatic: MMRC ≥ 1
- Current diagnosis of asthma excluded
- Blood Eos:
  ≥220/µL at baseline

**GALATHEA** **Terranova**
- Neither reached significance for exacerbations
- *Both showed improvement in lung function*

*Lipson D, NEJM 2018* *Pavord ID, NEJM 2017*

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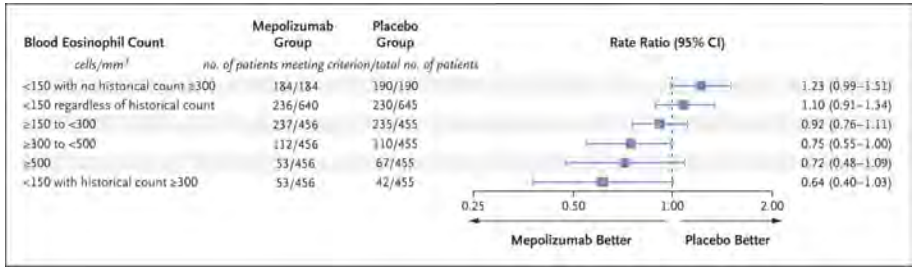
# Eosinophils as a therapeutic target: Anti-IL-5 Biologics

## *Post-Hoc Analyses: Potential efficacy with higher eos?*

### Mepolizumab (anti-IL-5)

**METREX**

**METREO**



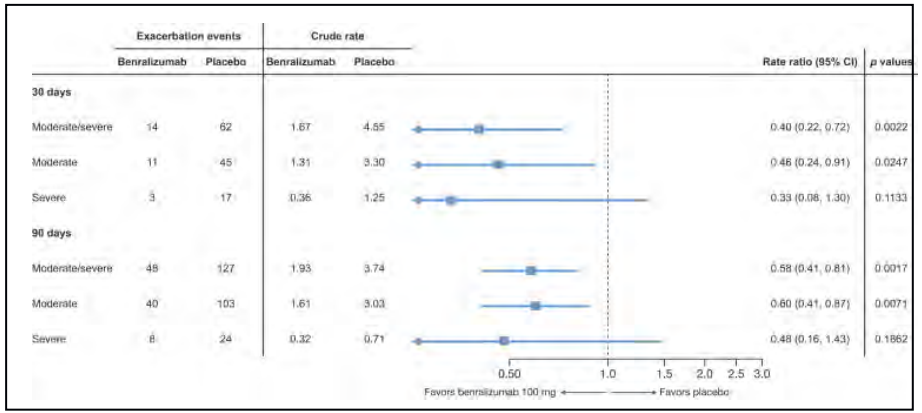
| Blood Eosinophil Count (cells/mm³) | Mepolizumab Group (no. of patients meeting criterion/total no. of patients) | Placebo Group | Rate Ratio (95% CI) |
|---|---|---|---|
| <150 with no historical count ≥300 | 184/184 | 190/190 | 1.23 (0.99–1.51) |
| <150 regardless of historical count | 236/640 | 230/645 | 1.10 (0.91–1.34) |
| ≥150 to <300 | 237/456 | 235/455 | 0.92 (0.76–1.11) |
| ≥300 to <500 | 112/456 | 110/455 | 0.75 (0.55–1.00) |
| ≥500 | 53/456 | 67/455 | 0.72 (0.48–1.09) |
| <150 with historical count ≥300 | 53/456 | 42/455 | 0.64 (0.40–1.03) |



### Benralizumab (anti-IL-5Rα)

**GALATHEA**

**Terranova**



| | Exacerbation events | | Crude rate | | Rate ratio (95% CI) | p values |
|---|---|---|---|---|---|---|
| | Benralizumab | Placebo | Benralizumab | Placebo | | |
| 30 days | | | | | | |
| Moderate/severe | 14 | 62 | 1.67 | 4.55 | 0.40 (0.22, 0.72) | 0.0022 |
| Moderate | 11 | 45 | 1.31 | 3.30 | 0.48 (0.24, 0.91) | 0.0247 |
| Severe | 3 | 17 | 0.36 | 1.25 | 0.33 (0.08, 1.30) | 0.1133 |
| 90 days | | | | | | |
| Moderate/severe | 48 | 127 | 1.93 | 3.74 | 0.58 (0.41, 0.81) | 0.0017 |
| Moderate | 40 | 103 | 1.61 | 3.03 | 0.60 (0.41, 0.87) | 0.0071 |
| Severe | 8 | 24 | 0.32 | 0.71 | 0.48 (0.16, 1.43) | 0.1862 |



*Lipson D, NEJM 2018* *Pavord ID, NEJM 2017*

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# IL-4 and IL-13 as a therapeutic target: Dupilumab

## *BOREAS Trial*

**Eligibility**

- 10 pack year smoking history
- triple therapy for ≥ 3 months
- ≥ 2 moderate or ≥ 1 severe exacerbation
- Chronic bronchitis
- No history of asthma
- Blood Eos:
  ≥300/µL at screening

Table 1. Selected Demographic and Disease Characteristics of the Patients at Baseline (Intention-to-Treat Population).*

| Characteristic | Placebo (N=471) | Dupilumab (N=468) | Total (N=939) |
|---|---|---|---|
| Age — yr | 65.2±8.1 | 65.0±8.0 | 65.1±8.1 |
| Male sex — no. (%) | 322 (68.4) | 298 (63.7) | 620 (66.0) |
| Race or ethnic group — no. (%)† | | | |
| White | 397 (84.3) | 393 (84.0) | 790 (84.1) |
| Black | 2 (0.4) | 3 (0.6) | 5 (0.5) |
| Asian | 67 (14.2) | 67 (14.3) | 134 (14.3) |
| American Indian or Alaska Native | 4 (0.8) | 3 (0.6) | 7 (0.7) |
| Native Hawaiian or other Pacific Islander | 1 (0.2) | 0 | 1 (0.1) |
| Multiple | 0 | 2 (0.4) | 2 (0.2) |
| Hispanic or Latino ethnic group — no. (%)† | | | |
| Hispanic or Latino | 129 (27.4) | 132 (28.2) | 261 (27.8) |
| Non-Hispanic or non-Latino | 342 (72.6) | 335 (71.6) | 677 (72.1) |
| Unknown | 0 | 1 (0.2) | 1 (0.1) |
| Smoking status — no. (%) | | | |
| Former smoker | 323 (68.6) | 334 (71.4) | 657 (70.0) |
| Current smoker | 148 (31.4) | 134 (28.6) | 282 (30.0) |
| Smoking history — pack-yr‡ | 41.4±24.4 | 39.6±22.3 | 40.5±23.4 |
| Body-mass index§ | 27.6±5.7 | 27.5±5.4 | 27.6±5.6 |
| Background medication — no. (%)¶ | | | |
| Triple therapy‖ | 461 (97.9) | 455 (97.2) | 916 (97.6) |
| Inhaled high-dose glucocorticoid | 126 (26.8) | 131 (28.0) | 257 (27.4) |
| Biomarkers of type 2 inflammation | | | |
| Blood eosinophil count at randomization | | | |
| Mean — per µl | 408±331 | 394±261 | 401±298 |
| Median (interquartile range) — per µl | 330 (230–460) | 340 (250–460) | 340 (240–460) |
| Postbronchodilator FeNO — ppb** | 23.51±22.00 | 25.18±22.79 | 24.33±22.40 |
| Distribution — no./total no. (%) | | | |
| ≥20 ppb | 188/442 (42.5) | 195/433 (45.0) | 383/875 (43.8) |
| <20 ppb | 254/442 (57.5) | 238/433 (55.0) | 492/875 (56.2) |
| No. of moderate or severe COPD exacerbations in previous yr | 2.3±1.0 | 2.2±1.1 | 2.3±1.0 |
| Lung function | | | |
| Prebronchodilator $FEV_1$ — liters | 1.32±0.46 | 1.28±0.45 | 1.30±0.46 |
| Postbronchodilator $FEV_1$ | | | |
| Volume — liters | 1.41±0.47 | 1.39±0.47 | 1.40±0.47 |
| Percent of predicted value | 50.6±13.0 | 50.6±13.3 | 50.6±13.1 |
| Postbronchodilator ratio of $FEV_1$ to FVC | 0.5±0.1 | 0.5±0.1 | 0.5±0.1 |
| SGRQ total score†† | 48.4±17.8 | 48.4±17.0 | 48.4±17.4 |
| E-RS–COPD total score‡‡ | 13.0±6.9 | 12.9±7.2 | 12.9±7.1 |



Bhatt, et al. NEJM 2023

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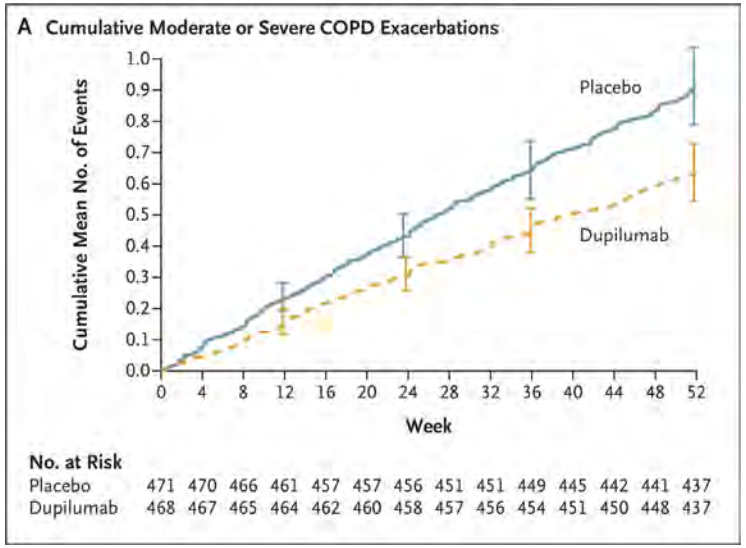
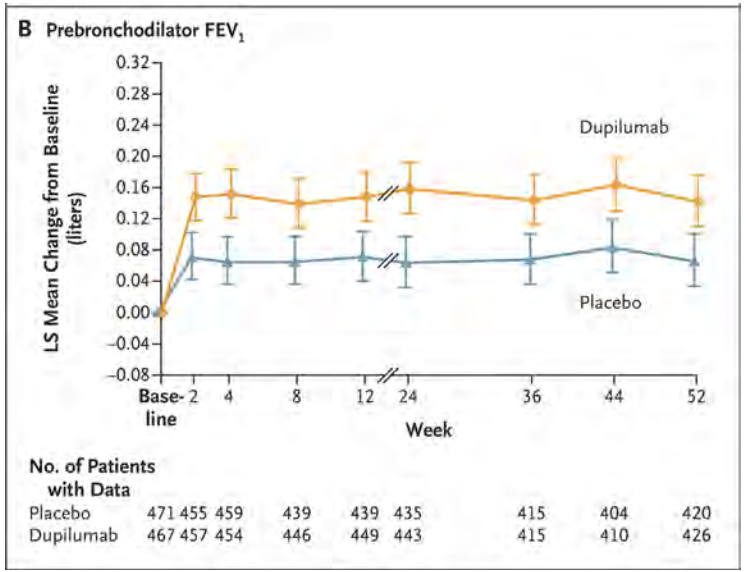
# IL-4 and IL-13 as a therapeutic target: Dupilumab
# *BOREAS Trial*

**Exacerbations: 30% reduction**




**Pre-Bronchodilator FEV1**






*Bhatt, et al. NEJM 2023*

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# BOREAS

## Additional Outcomes

**Table 2. End Points Corrected for Multiplicity (Intention-to-Treat Population).***

| End Point | Placebo (N=471) | Dupilumab (N=468) | P Value |
|---|---|---|---|
| **Primary end point** | | | |
| Annualized rate of moderate or severe exacerbations of COPD | | | |
| Adjusted annualized rate of moderate or severe exacerbations — events per yr (95% CI) | 1.10 (0.93 to 1.30) | 0.78 (0.64 to 0.93) | |
| Rate ratio vs. placebo (95% CI) | — | 0.70 (0.58 to 0.86) | <0.001 |
| **Secondary and other end points** | | | |
| Change in prebronchodilator $FEV_1$ from baseline to wk 12 | | | |
| Least-squares mean change (95% CI) — liters | 0.077 (0.042 to 0.112) | 0.160 (0.126 to 0.195) | |
| Least-squares mean difference vs. placebo (95% CI) — liters | — | 0.083 (0.042 to 0.125) | <0.001 |
| Change in prebronchodilator $FEV_1$ from baseline to wk 52 | | | |
| Least-squares mean change (95% CI) — liters | 0.070 (0.033 to 0.107) | 0.153 (0.116 to 0.189) | |
| Least-squares mean difference vs. placebo (95% CI) — liters | — | 0.083 (0.038 to 0.128) | <0.001 |
| Change in prebronchodilator $FEV_1$ from baseline to wk 12 among patients with a baseline $F_ENO$ ≥20 ppb | | | |
| Least-squares mean change (95% CI) — liters | 0.108 (0.038 to 0.177) | 0.232 (0.164 to 0.299) | |
| Least-squares mean difference vs. placebo (95% CI) — liters | — | 0.124 (0.045 to 0.203) | 0.002 |
| Change in prebronchodilator $FEV_1$ from baseline to wk 52 among patients with a baseline $F_ENO$ ≥20 ppb | | | |
| Least-squares mean change (95% CI) — liters | 0.120 (0.047 to 0.192) | 0.247 (0.176 to 0.318) | |
| Least-squares mean difference vs. placebo (95% CI) — liters | — | 0.127 (0.042 to 0.212) | 0.003 |
| Change in SGRQ total score from baseline to wk 52 | | | |
| Least-squares mean change (95% CI) | −6.4 (−8.0 to −4.8) | −9.7 (−11.3 to −8.1) | |
| Least-squares mean difference vs. placebo (95% CI) | — | −3.4 (−5.5 to −1.3) | 0.002 |
| SGRQ total score improvement ≥4 points at wk 52 | | | |
| Percentage of patients (95% CI) | 43.1 (38.6 to 47.7) | 51.5 (46.9 to 56.1) | |
| Odds ratio vs. placebo (95% CI) | — | 1.4 (1.1 to 1.9) | 0.009 |
| Change in E-RS–COPD total score from baseline to wk 52 | | | |
| Least-squares mean (95% CI) | −1.6 (−2.1 to −1.1) | −2.7 (−3.2 to −2.2) | |
| Least-squares mean difference vs. placebo (95% CI) | — | −1.1 (−1.8 to −0.4) | 0.001 |
| Annualized rate of moderate or severe exacerbations of COPD among patients with a baseline $F_ENO$ ≥20 ppb | | | |
| Adjusted annualized rate of moderate or severe exacerbations — events per yr (95% CI) | 1.12 (0.83 to 1.50) | 0.70 (0.51 to 0.96) | |
| Rate ratio vs. placebo (95% CI) | — | 0.62 (0.45 to 0.87) | 0.005 |



*Bhatt, et al. NEJM 2023*

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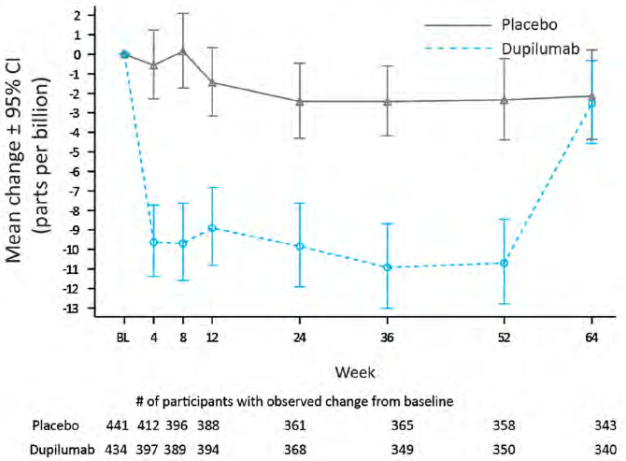
# Biomarker Responses in BOREAS

| | Placebo (N=470) | Dupilumab 300 (N=469) |
|---|---|---|
| **Blood eosinophils,** cells/μL | | |
| Percent change from baseline at week 52 | | |
| N | 376 | 372 |
| Median | -9.45 | -11.95 |
| **Fibrinogen, mg/dL** | | |
| Percent change from baseline at week 52 | | |
| N | 391 | 399 |
| Median | -1.3 | -2.6 |
| **$FE_{NO}$, ppb** | | |
| Percent change from baseline at week 52 | | |
| N | 358 | 350 |
| Median | -6.9 | -28.6 |

**FIGURE S8. FRACTIONAL EXHALED NITRIC OXIDE FROM BASELINE TO END OF 52-WEEK TREATMENT PERIOD AND FOLLOW-UP 12-WEEK OFF-TREATMENT PERIOD IN THE SAFETY POPULATION**




BL baseline, CI confidence interval. Error bars represent 95% confidence intervals. 95% CIs have not been adjusted for multiplicity and should not be used for hypothesis testing.



*Bhatt, et al. NEJM 2023*

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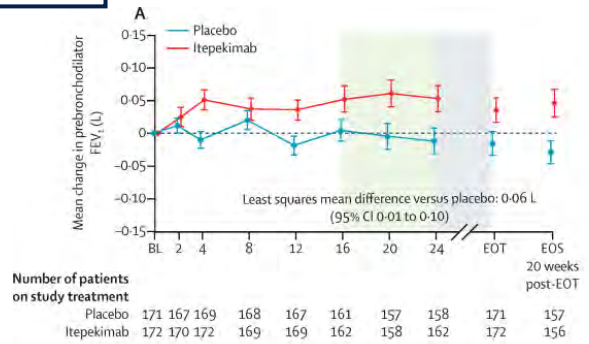
# IL-33 as a therapeutic target in COPD:

## Itepikimab phase 2 trial

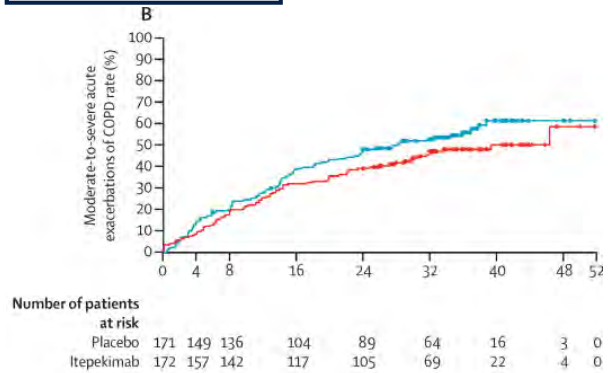
**Eligibility**

- 10 pack year smoking history
- Dual or triple therapy
- ≥ 2 moderate or ≥ 1 severe exacerbation
- Chronic bronchitis
- Symptomatic: CAT >10
- Blood Eos: any

**FEV1**




**Exacerbations**




***No Significant Differences*



*Rabe KF, et al. Lancet Resp Med 2021*

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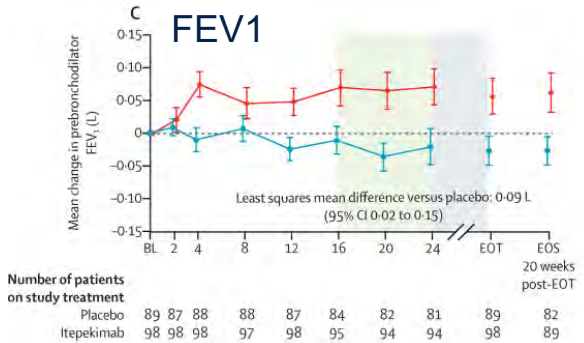
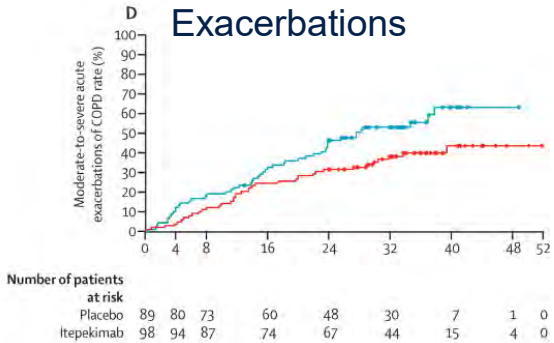
# IL-33 as a therapeutic target in COPD:

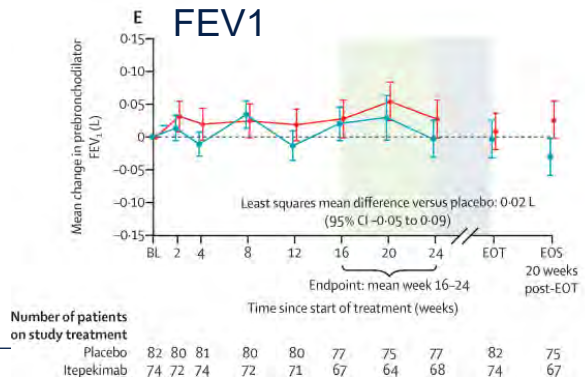
## Itepikimab phase 2 trial

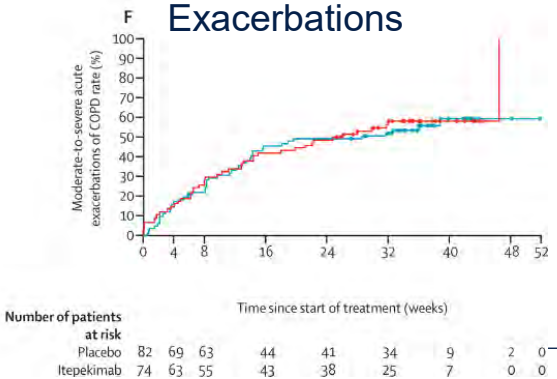
### Former Smokers




### Current Smokers




*Rabe KF, et al. Lancet Resp Med 2021*



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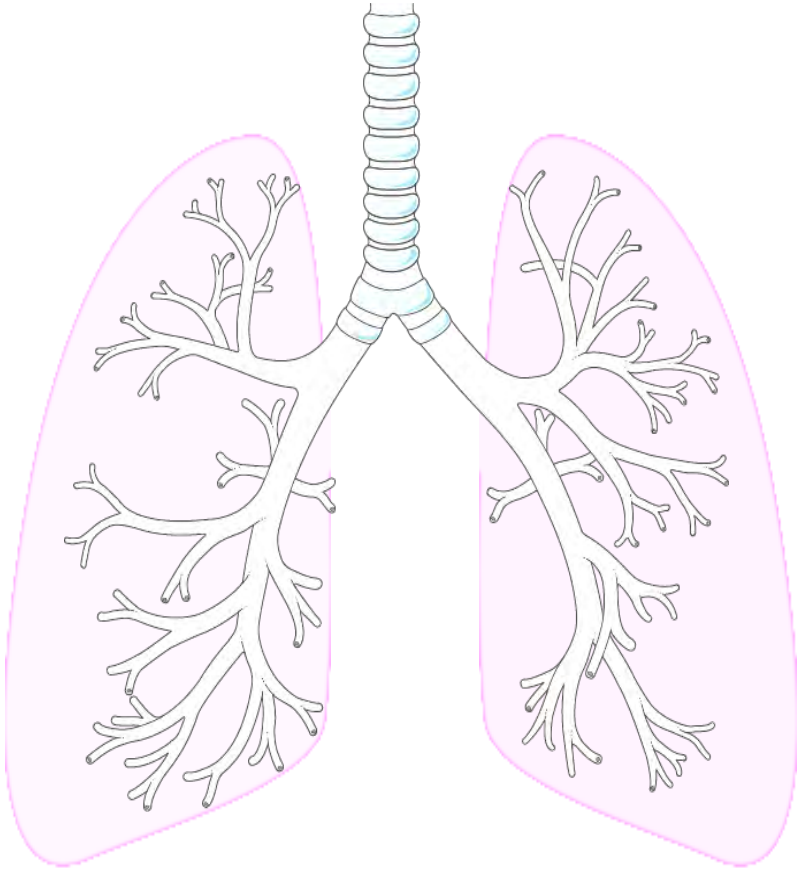
# Biologics in Development in COPD

***None of these are FDA approved*

| Biologic | Target | Trial |
|---|---|---|
| **Mepolizumab** | IL-5 | **METREX & METREO** *(Pavord ID, et al NEJM 2017)*<br>MATINEE *(Ongoing, Est Completion: 8/24)* |
| **Benralizumab** | IL-5R | **GALATHEA & TERRANOVA** (*Lipson D, et al NEJM 2018*)<br>RESOLUTE *(Ongoing, Est Completion: 6/25)* |
| **Dupilumab** | IL4R<br>(IL-4 & IL-13) | **BOREAS** *(Rabe KF, et al NEJM 2023)*<br>**NOTUS** *(not yet reported)* |
| **Tezepelumab** | TSLP | COURSE *(Phase 2a, Ongoing, Completed: 1/24)* |
| **Itepekimab** | IL-33 | AERIFY-1 & 2 *(Ongoing, Est Completion: 11/25)* |
| **Tozorakimab** | IL-33 | OBERON & TITANIA *(Ongoing, Est Completion: 8/25)* |
| **Astegolimab** | ST2 | ARNASA *(Ongoing, Est Completion: 6/25)* |

# Conclusions

- There is evidence that T2 inflammation plays a major role in a subset of patients with COPD
- Patients with T2 inflammation, as measured by blood eos, appear to respond better to inhaled corticosteroids than those without T2 inflammation
- There are multiple T2 biologics in the pipeline for COPD with clinical trials ending in 2024 and 2025
- Dupilumab is currently the only biologics with strongly positive results in COPD, but there is promise that others will work in COPD subgroups with blood eosinophils >300.
- Alarmin-based therapy, targeting IL-33 or TSLP, is being studied in both T2 low and T2 high individuals.



# Bronchoscopic Management of Airways Diseases

**Brian Shaller, MD**
**Assistant Professor**
**Stanford**

Brian Shaller is a Clinical Assistant Professor in the Division of Pulmonary, Allergy & Critical Care Medicine at Stanford University. He trained in Interventional Pulmonology at the Cleveland Clinic and helped establish Stanford's Interventional Pulmonology fellowship program in 2022, for which he currently serves as Associate Program Director. Dr. Shaller's clinical and academic interests include advanced diagnostics for lung nodules, endoscopic management of central airway diseases, and procedural education.

# BRONCHOSCOPIC MANAGEMENT OF ~~AIRWAY~~ BENIGN obstructive lung DISEASES

FOR ALL PULMONOLOGISTS!

Brian Shaller, MD

Clinical Assistant Professor of Medicine

Associate Program Director, Interventional Pulmonology Fellowship

Stanford University School of Medicine

California Thoracic Society

# RELEVANT DISCLOSURES

- I have the following relationships with ACCME defined ineligible companies:
  - None pertinent to this topic

- I WILL discuss off-label use and/or investigational use of any drugs or devices
  - Bronchial rheoplasty, cryospray, and targeted lung denervation have breakthrough device designation from the FDA and are approved for use in clinical trials only

# OBJECTIVES

- Identify benign airway diseases for which there are bronchoscopic interventions
- Describe general mechanisms of action of different interventions
- Discuss clinical evidence and eligibility criteria for different interventions
- Assess the role of bronchoscopic interventions in broader context of patient care

# LIMITATIONS OF THERAPEUTIC BRONCHOSCOPY

| | Generation | | Diameter, cm | Length, cm | Number | Total cross sectional area, $cm^2$ |
|---|---|---|---|---|---|---|
| Conducting zone | Trachea | 0 | 1.80 | 12.0 | 1 | 2.54 |
| | Bronchi | 1 | 1.22 | 4.8 | 2 | 2.33 |
| | | 2 | 0.83 | 1.9 | 4 | 2.13 |
| | | 3 | 0.56 | 0.8 | 8 | 2.00 |
| | Bronchioles | 4 | 0.45 | 1.3 | 16 | 2.48 |
| | Terminal bronchioles | 5 ↓ 16 | 0.35 ↓ 0.06 | 1.07 ↓ 0.17 | 32 ↓ $6\times10^4$ | 3.11 ↓ 180.0 |
| Transitional and respiratory zones | Respiratory bronchioles | 17 | ↓ | ↓ | ↓ | ↓ |
| | | 18 | | | | |
| | | 19 | 0.05 | 0.10 | $5\times10^5$ | $10^3$ |
| | Alveolar ducts | $T_3$ 20 | ↓ | ↓ | ↓ | ↓ |
| | | $T_2$ 21 | | | | |
| | | $T_1$ 22 | | | | |
| | Alveolar sacs | T 23 | 0.04 | 0.05 | $8\times10^6$ | $10^4$ |

| Do I have a bronchoscopic intervention? |
|---|
| Definitely |
| Possibly |
| I guess I can take a look . . . |
| Wait, what?<br><br>Isn't there an inhaler for that? |

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# LIMITATIONS OF THERAPEUTIC BRONCHOSCOPY

| RANK | ICD-10 CODE | ICD-10 DESCRIPTION | PERCENT OF PULMONOLOGIST VISITS |
|---|---|---|---|
| 1 | J449 | Chronic obstructive pulmonary disease, unspecified | 8.90% |
| 2 | J069 | Acute upper respiratory infection, unspecified | 7.00% |
| 3 | J301 | Allergic rhinitis due to pollen | 5.90% |
| 4 | J9601 | Acute respiratory failure with hypoxia | 5.40% |
| 5 | J029 | Acute pharyngitis, unspecified | 5.10% |
| 6 | J45909 | Unspecified asthma, uncomplicated | 4.80% |

https://www.definitivehc.com/resources/healthcare-insights/top-conditions-pulmonologist-visits

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# EVOLUTION OF BRONCHOSCOPIC THERAPEUTICS

- **First 100+ years:** therapeutics limited to central-lobar-segmental airways

- **Last 10-15 years:** multiple new treatment options for peripheral obstructive lung diseases

  - **2010:** bronchial thermoplasty for asthma
  - **2018:** endobronchial valves for emphysema
  - **2019:** bronchial rheoplasty and cryospray for chronic bronchitis
  - **2020:** targeted lung denervation for COPD

# APPROVED INTERVENTIONS

**Bronchial thermoplasty (asthma)**

**Bronchoscopic lung volume reduction (emphysema)**

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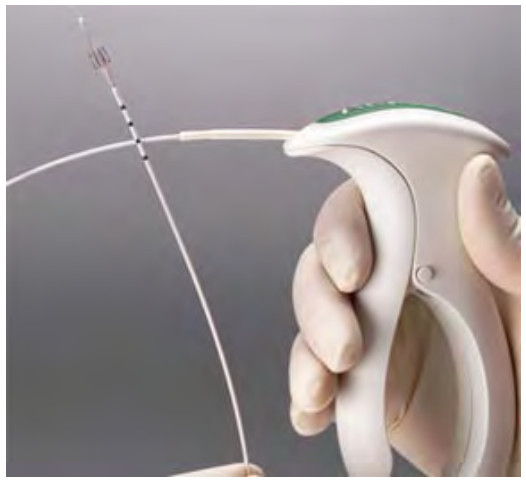
# BRONCHIAL THERMOPLASTY (BT)

- Delivery of radiofrequency (RF) energy to intermediate-size airways for the treatment of severe asthma

- Alair system (Boston Scientific) FDA-approved since 2010


Foot pedal

Grounding pad



Catheter (1.5 mm OD)

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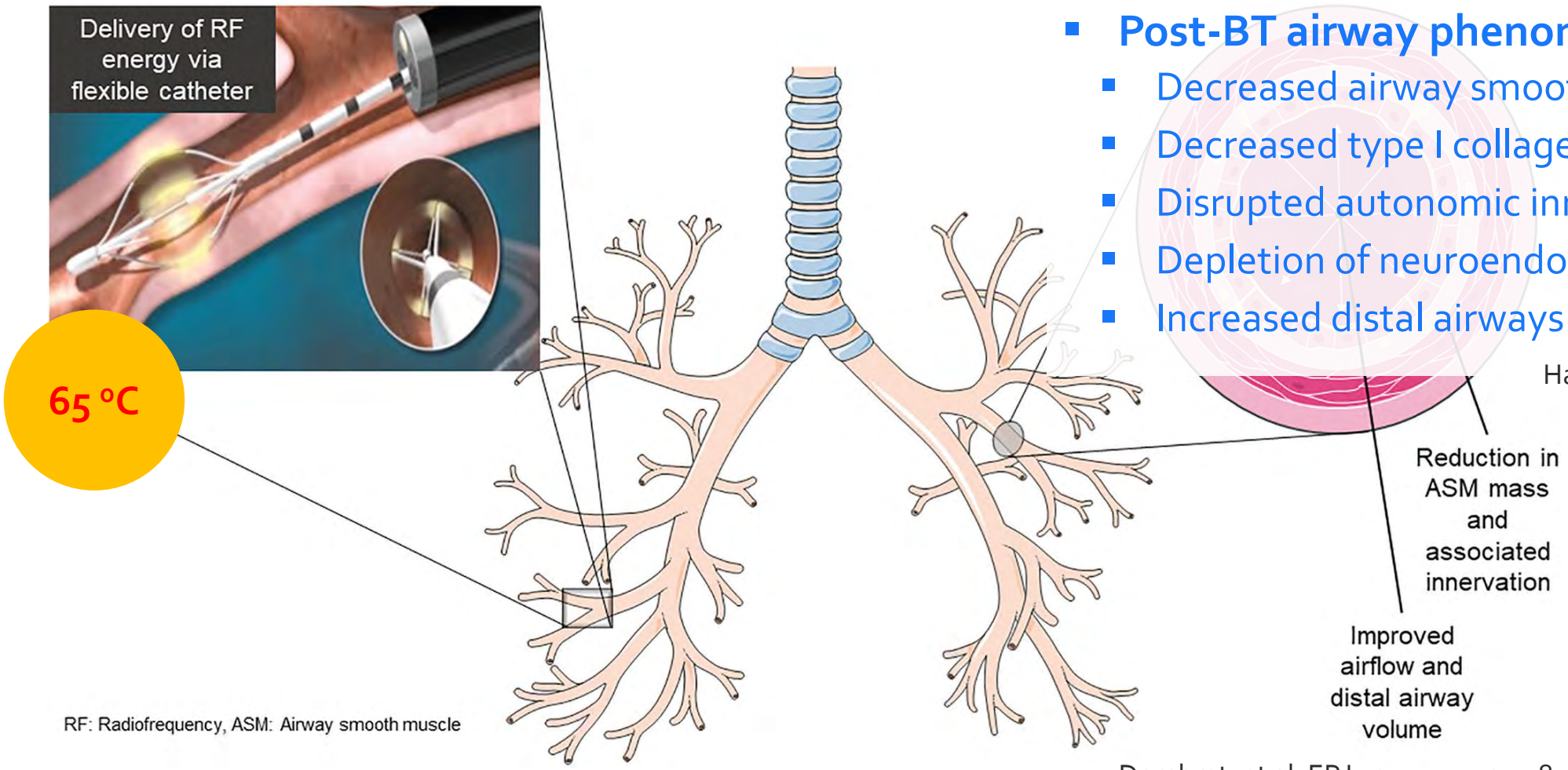
# BRONCHIAL THERMOPLASTY (BT)




- **Post-BT airway phenomena:**
  - Decreased airway smooth muscle mass
  - Decreased type I collagen deposition
  - Disrupted autonomic innervation
  - Depletion of neuroendocrine cells
  - Increased distal airways volume on HRCT

Hashmi, et al. Respirology 2022.

Dombret, et al. ERJ 2014;23:510-518.

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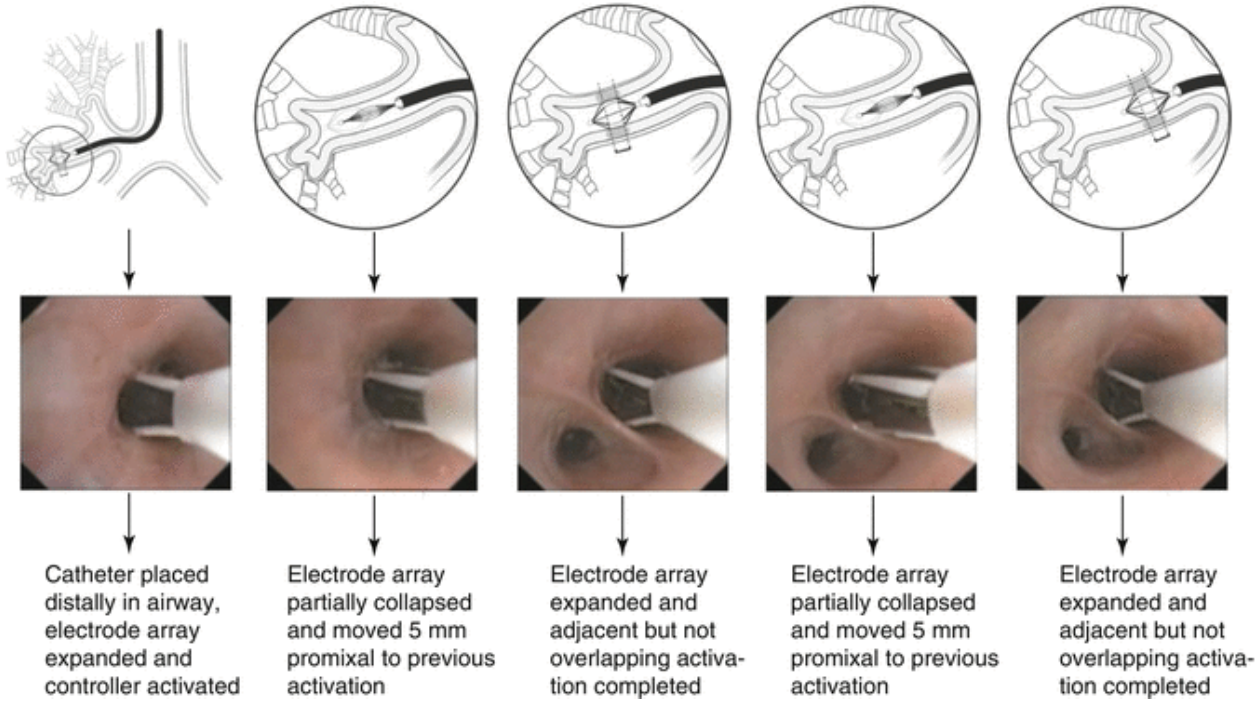
# BRONCHIAL THERMOPLASTY (BT)

- **Course of treatment:**
  - 3 sessions (RLL, LLL, both upper lobes)
  - 3 weeks apart
  - Treat all airways from 3 → 10 mm in diameter

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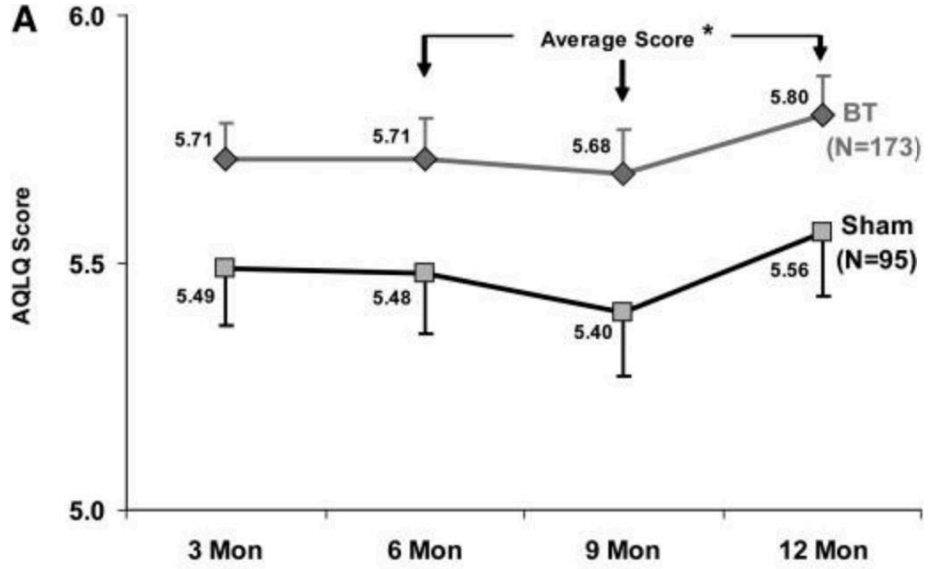
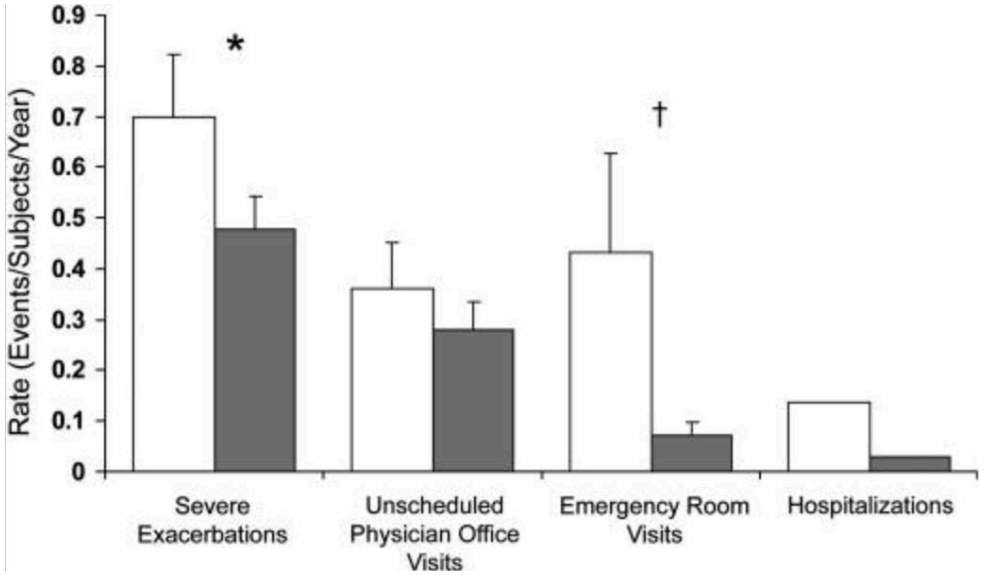
# BRONCHIAL THERMOPLASTY (BT)

- **AIR2 (2010)** – multicenter, double-masked, sham-controlled randomized trial
  - Pre-BD $FEV_1$ ~78%p, Asthma QoL Questionnaire score ~4.4
  - Small but statistically significant improvements in AQLQ, severe exacerbations, ED visits @ 12 mo
  - Sustained improvements over median 12 yrs (BT10+, 2021)




**AIR2:** Castro, et al. AJRCCM 2010.
**BT10+:** Chaudhuri, et al. Lancet Respir Med 2021.

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# BRONCHIAL THERMOPLASTY (BT)

- **Risks/complications:**
  - Asthma exacerbation *(increased* x 3 mo post-tx), upper respiratory tract infection
  - Lower respiratory tract infection, atelectasis, hemoptysis (*uncommon*)

- **AIR2 (2010):**
  - 85% experienced an adverse event (~1 event/session)
  - 8.4% required hospitalization

Castro, et al. AJRCCM 2010.

# BRONCHIAL THERMOPLASTY (BT)

- **Eligibility criteria:**
  - ≥ 18 years old
  - Severe asthma
  - GINA step ≥ 4 treatment
  - $T_H2$-low phenotype
  - ACT score ≤ 19

- **Exclusion criteria:**
  - Smoker
  - Life-threatening exacerbations/24 mo
  - ≥ 3 LRTIs/12 mo
  - $FEV_1$ < 50%p
  - Implanted electronic device

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# BRONCHIAL THERMOPLASTY (BT)

- **Criticisms of BT:**
  - Study patient characteristics not clearly representative of severe asthma
  - Racial/ethnic homogeneity (80% white in AIR2)
  - High rate of AEs, increased exacerbations over 3 months
  - Magnitude of benefit may not be clinically meaningful
  - Degree of benefit in sham arm (placebo effect)
  - Lack of long-term follow-up for sham controls

Thomson NC. J Asthma Allergy 2019.

# BRONCHIAL THERMOPLASTY (BT)

- **Role of BT in asthma treatment:**
  - Uncontrolled at Step 5, referred to specialty center, no access/eligibility for biologics (GINA 2023)

https://ginasthma.org/2023-gina-main-report/

- **Biased opinion:**
  - Consultation with asthma specialist and consideration of clinical trials should come first
  - Failure of advanced medical management should prompt reevaluation of diagnosis
  - BT is becoming treatment of last resort

# BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- Bronchoscopic procedure to treat hyperinflation in patients with emphysema

- Various modalities have been/are being studied
  - Endobronchial coils
  - Airway bypass stents
  - Thermal vapor ablation
  - One-way endobronchial valves

**Zephyr**

**Spiration**

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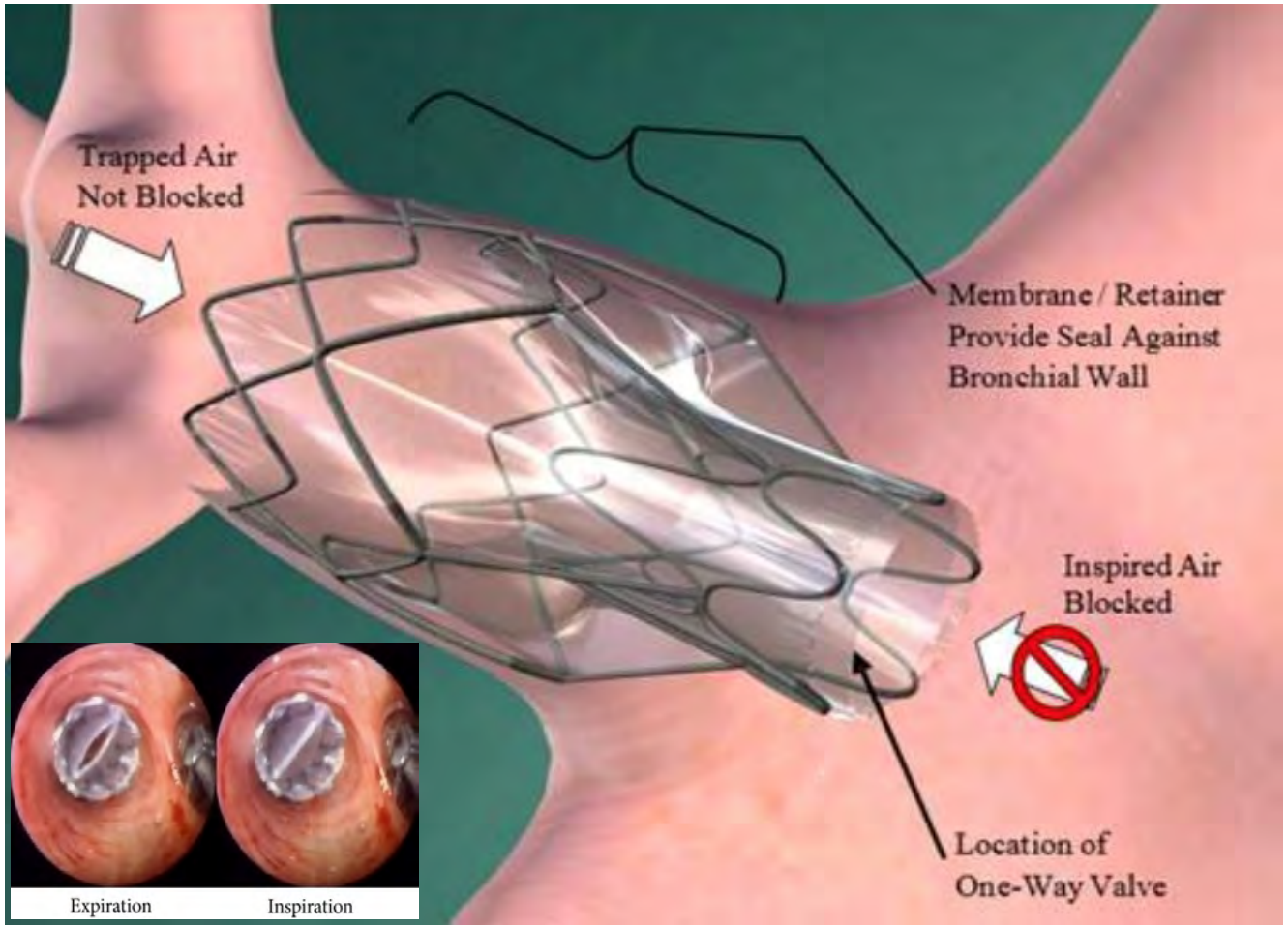
# BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)




https://www.accessdata.fda.gov/cdrh_docs/pdf18/P180002B.pdf

- One-way valves placed in airways let air out but not in
- Gradual collapse of lobe(s)
- Reduced hyperinflation

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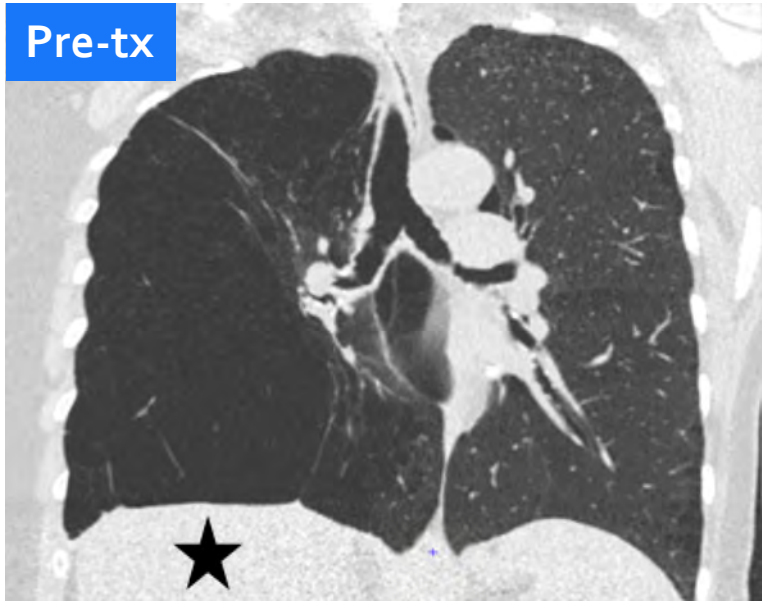
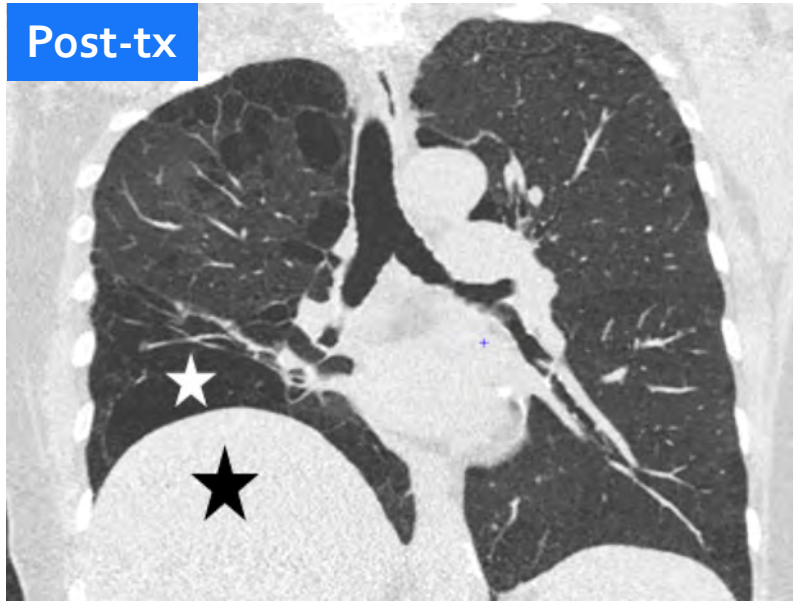
# BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- **Physiologic outcomes of BLVR:**
  - Improved diaphragm length-tension relationship → better muscle mechanics
  - Less V/Q mismatch
  - Improved $FEV_1$

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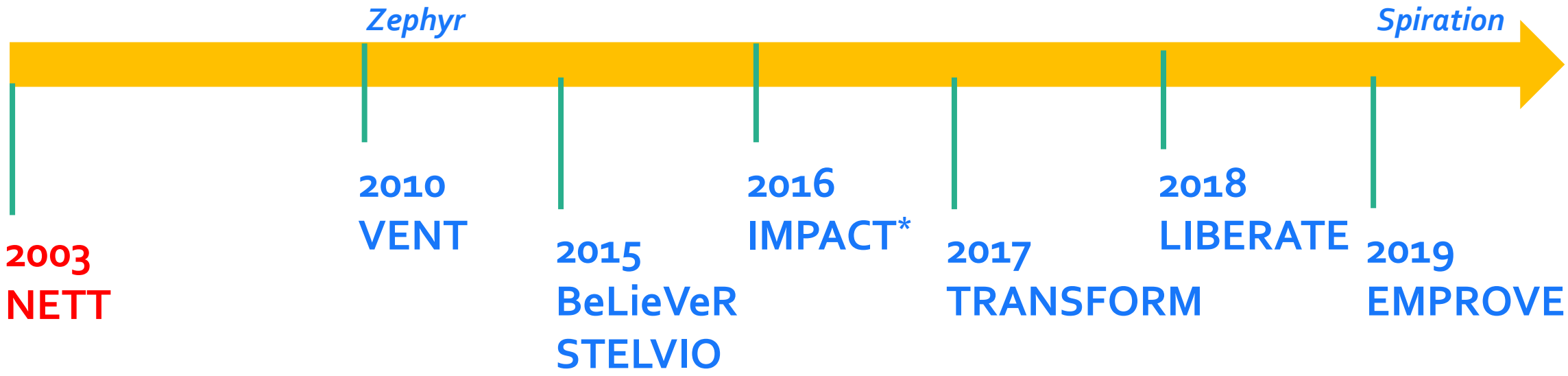
# BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- **Clinical trial data:**




**Homogeneous emphysema*

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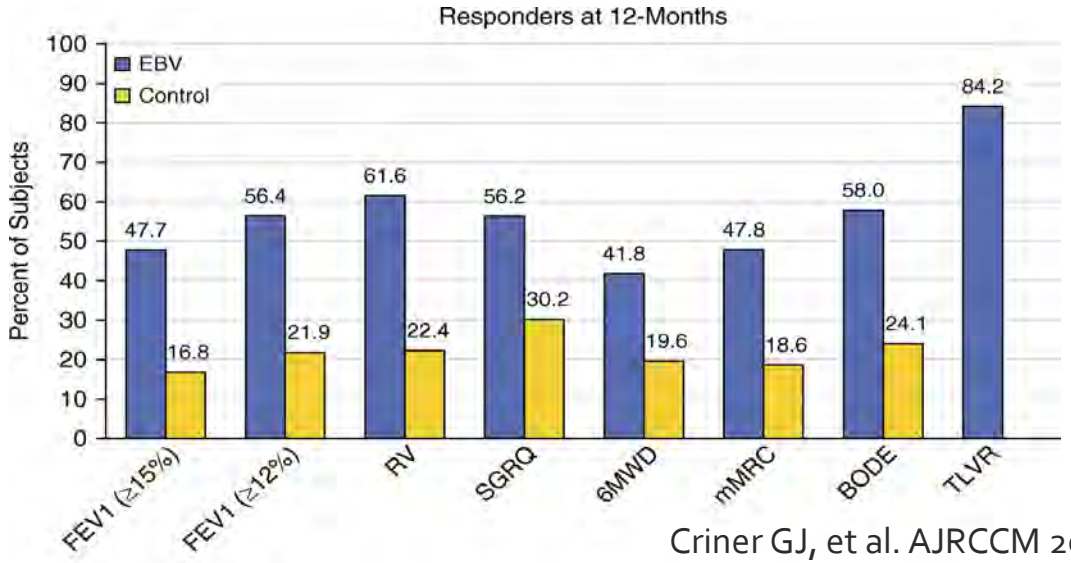
# BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- **LIBERATE (Zephyr, 2018)**
  - $FEV_1$ 28%p
  - RV 224.5%p
  - 6MWD 311 m
  - Emphysema destruction 70.9%
  - Heterogeneity 25.5%




Criner GJ, et al. AJRCCM 2018.

- **EMPROVE (Spiration, 2019)**
  - $FEV_1$ 30.8%p
  - RV 207.5%p
  - 6MWD 303.5 m
  - Emphysema destruction 63.6%
  - Heterogeneity 25.3%

| 12-month outcomes | Valves | Control |
|---|---|---|
| $FEV_1$ improvement ≥ 15% | 37.2 | 5.1 |
| SGRQ reduction ≥ 4 pts | 50.5 | 22.0 |
| mMRC reduction ≥ 1 pt | 48.9 | 7.3 |

Criner GJ, et al. AJRCCM 2019.

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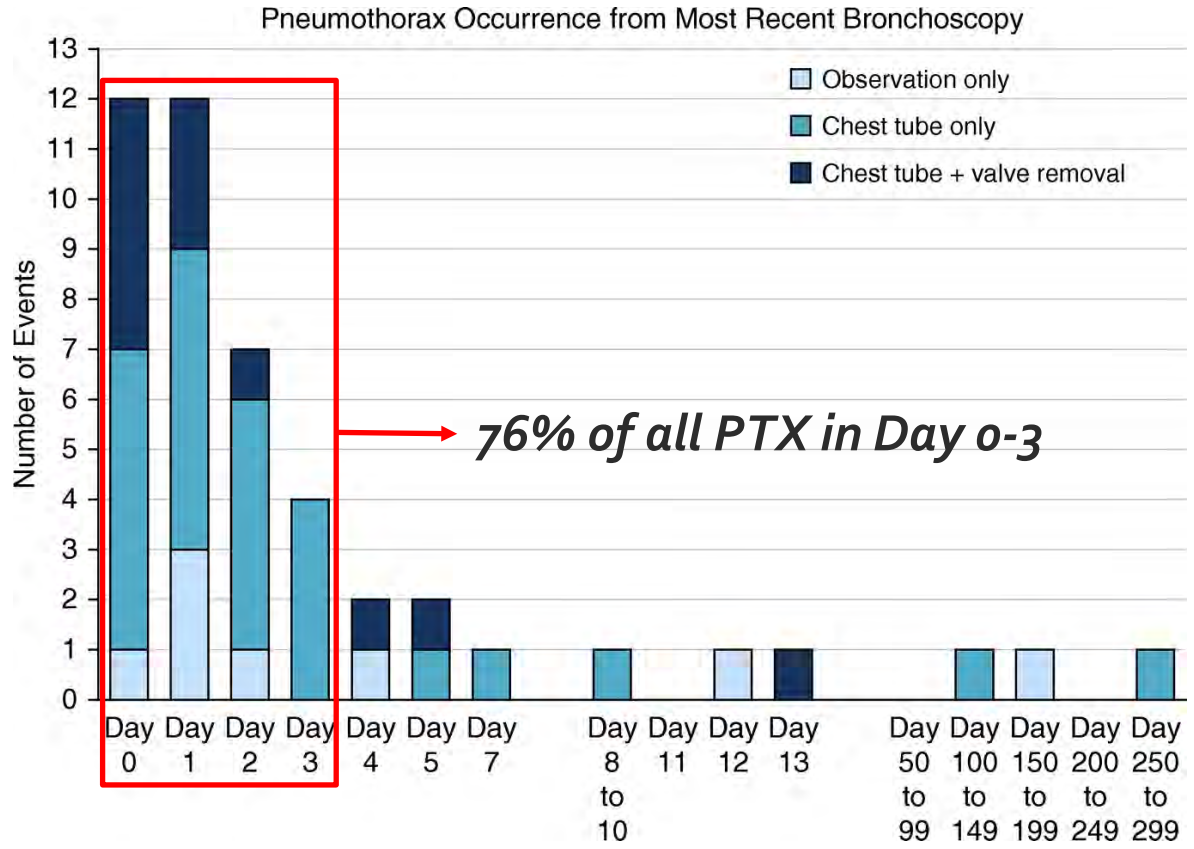
# BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- **Risks/complications:**
  - Pneumothorax (26.6% in LIBERATE)
  - No significant differences in other adverse events




Criner GJ, et al. AJRCCM 2018.

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# BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- **Eligibility criteria:**
  - ≥ 18 years old
  - Emphysema with hyperinflation
    - RV ≥ 150-175%p (heterogeneous)
    - RV ≥ 200%p (homogeneous)
  - $FEV_1$ 15-50%
  - 6MWD 100-500 m
  - Quit smoking ≥ 4 months ago
  - Completed pulmonary rehab

- **Exclusion criteria:**
  - ≥ 2 AECOPD hospitalizations in past year
  - ≥ 2 PNA in past year
  - Recent MI or LVEF < 45%
  - Bullae > 30% of hemithorax
  - Prior major chest surgery (LVRS, transplant, bullectomy, lobectomy, pleurodesis)
  - Significant sputum production
  - $DL_{CO}$ < 20%p
  - PASP > 45-50 mm Hg
  - $PaCO_2$ ≥ 50 mm Hg
  - $PaO_2$ ≤ 45 mm Hg

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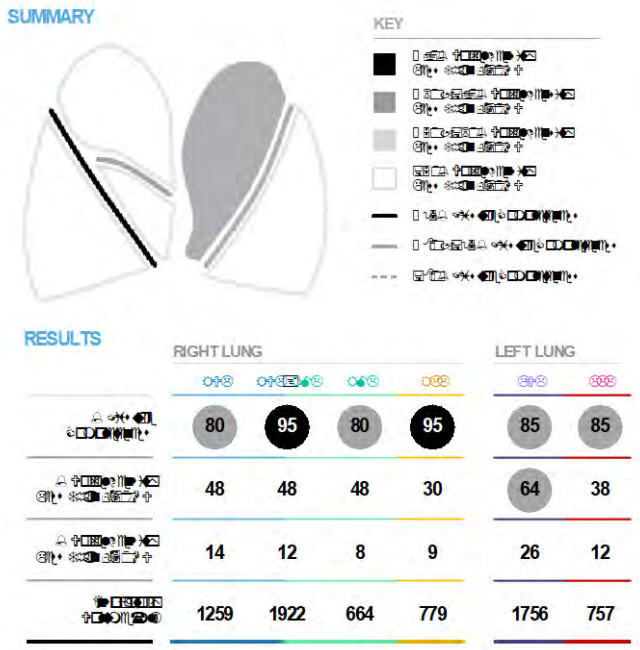
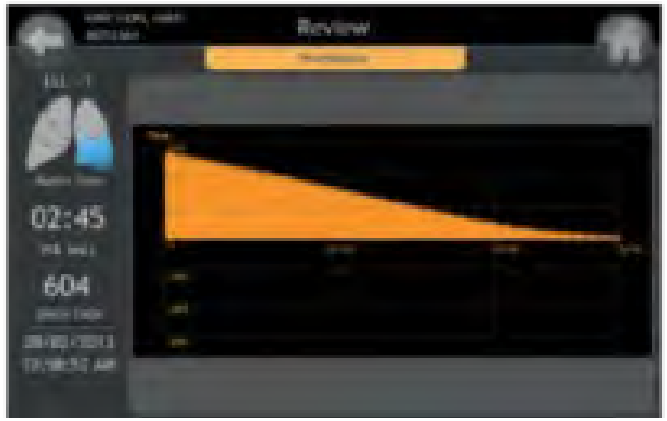
# BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- **Additional testing:**
  - CT analysis to assess lobe volumes, % destruction, heterogeneity and fissure-integrity
  - Balloon occlusion test during bronchoscopy to confirm fissure-integrity (*Zephyr only*)

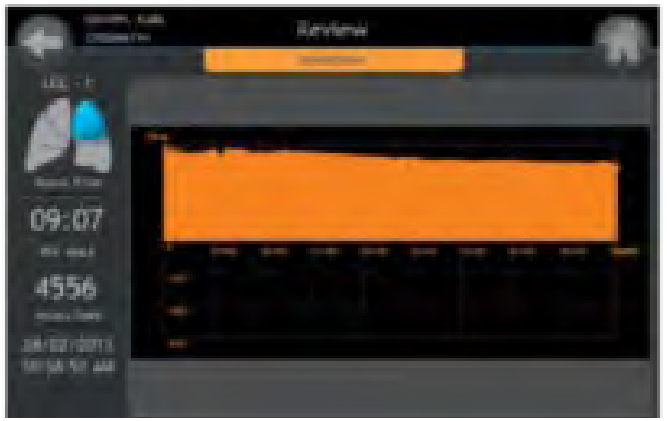



StratX Report (Zephyr)

Chartis assessment for fissure-integrity (Zephyr)




No collateral ventilation (CV-)
Complete fissure




Collateral ventilation (CV+)
Incomplete fissure

Luzzi V, et al. Eur Respir J 2018.

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# BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- **Emerging long-term data:**
  - Sustained improvements in RV, $FEV_1$, and SGRQ at 3 years
  - Improved median survival in 1 study (+1.7 years *vs* "controls")

Hartman, et al. ERJ Open Res 2022.
Hartman, et al. Respir Med 2022.

- **BLVR *vs* LVRS:**
  - Nonsurgical
  - Similar efficacy (CELEB, 2023) → Buttery, et al. ERJ 2023 – *early view*.
  - Does not complicate future chest surgery
  - Not limited to upper lobes*

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# BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- **When to consider BLVR in treatment of severe emphysema:**
  - Symptomatic despite maximal medical therapy + pulmonary rehab
  - Avoid LVRS
  - Delay time-to-transplantation
  - Potential future chest surgery (e.g., transplantation)

- **Biased opinion:**
  - Few interventions address hyperinflation or poor muscle mechanics
  - Pulmonary rehab, NIV, and BLVR should be considered *early* for emphysema patients

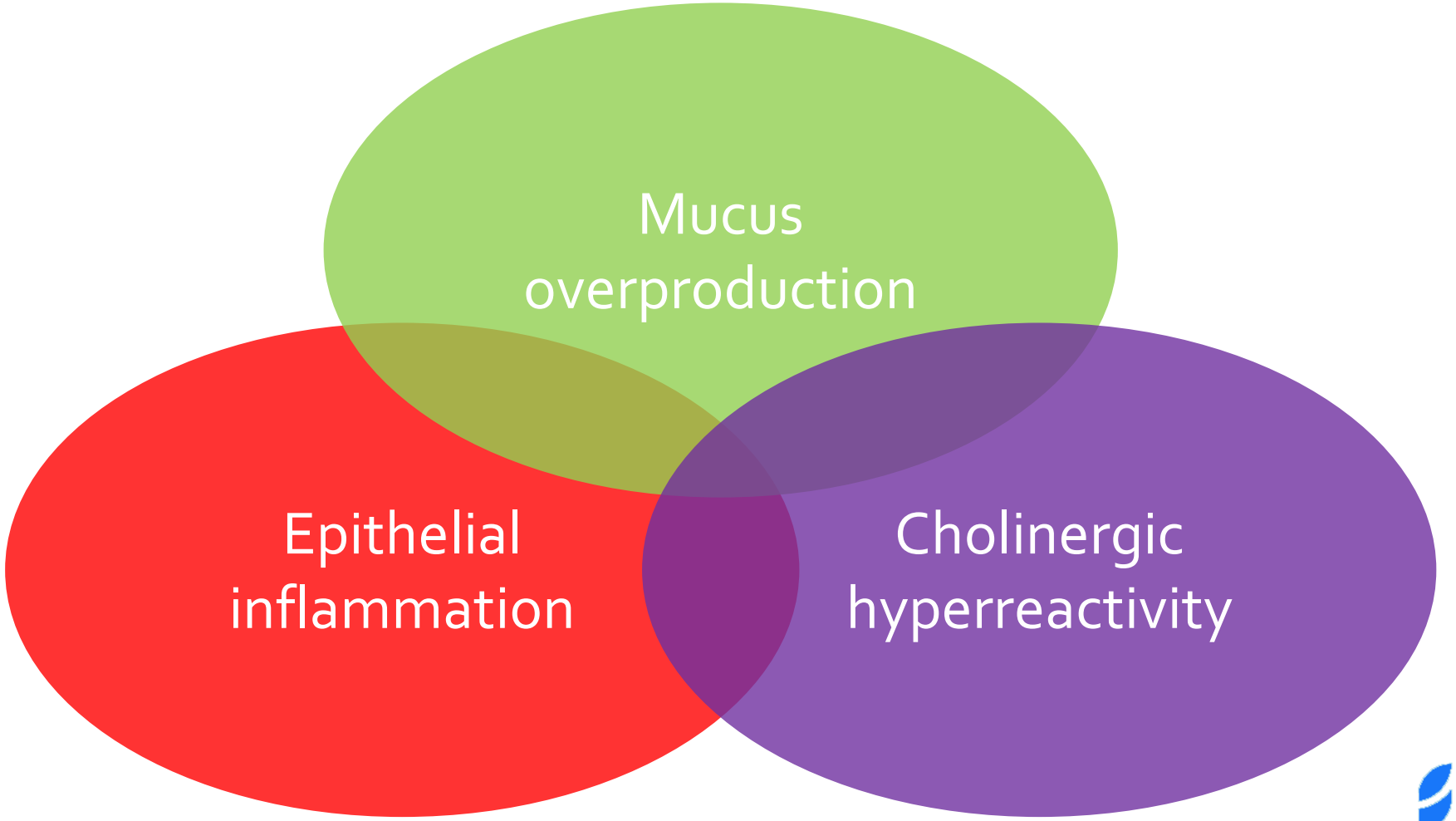
# FUTURE INTERVENTIONS

**Bronchial rheoplasty (chronic bronchitis)**

**Cryospray (chronic bronchitis)**

**Targeted lung denervation (COPD)**

# COPD WITHOUT SIGNIFICANT EMPHYSEMA

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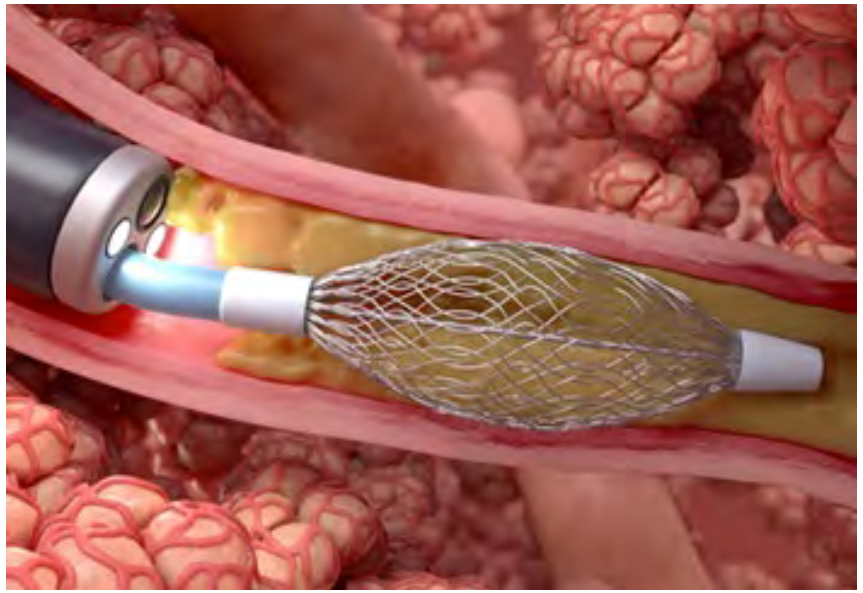
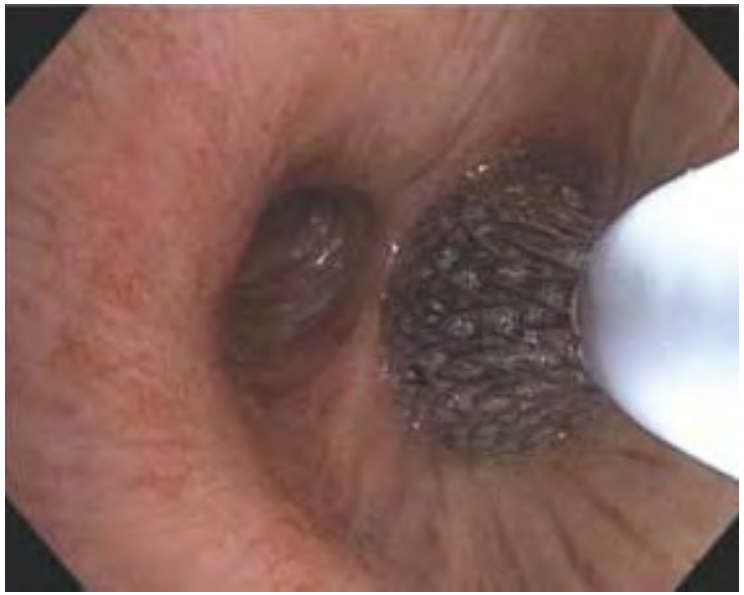
# BRONCHIAL RHEOPLASTY

- Pulsed electric field (PEF) energy to ablate goblet cells

- RheOx system (Gala Therapeutics) granted breakthrough device status in 2019



galatherapeutics.com



Sciurba FC, et al. BMJ Open Respir Res 2023.

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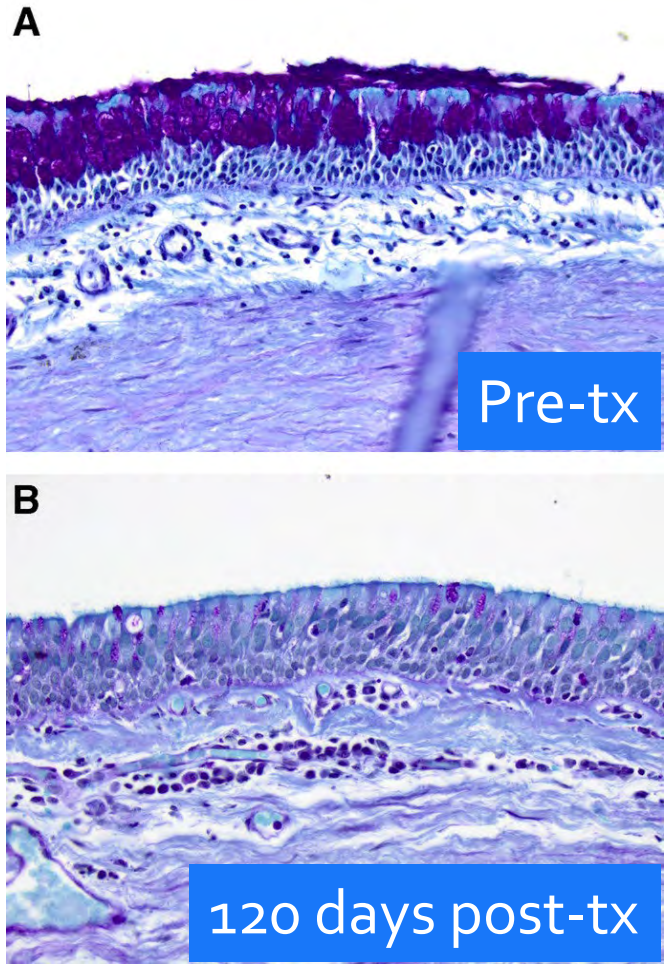
# BRONCHIAL RHEOPLASTY




- High-frequency, short-duration nonthermal, pulsed energy field
- Disrupts cellular homeostasis → apoptosis
- Preserves tissue architecture → mucosal regeneration, but with fewer goblet cells

Valipour A, et al. AJRCCM 2020.

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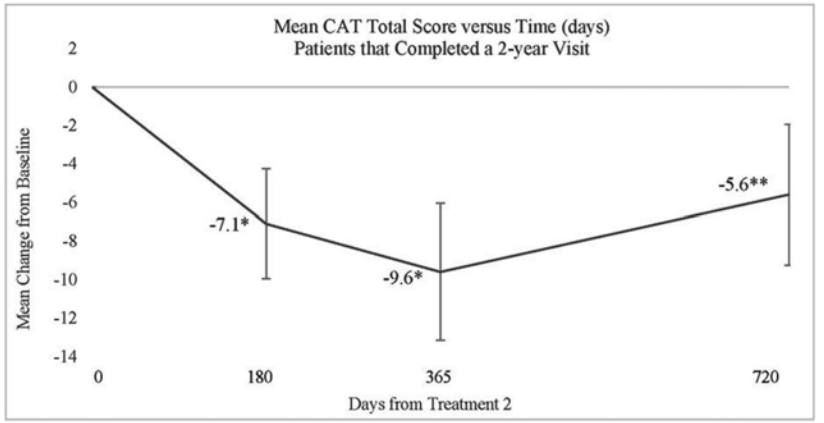
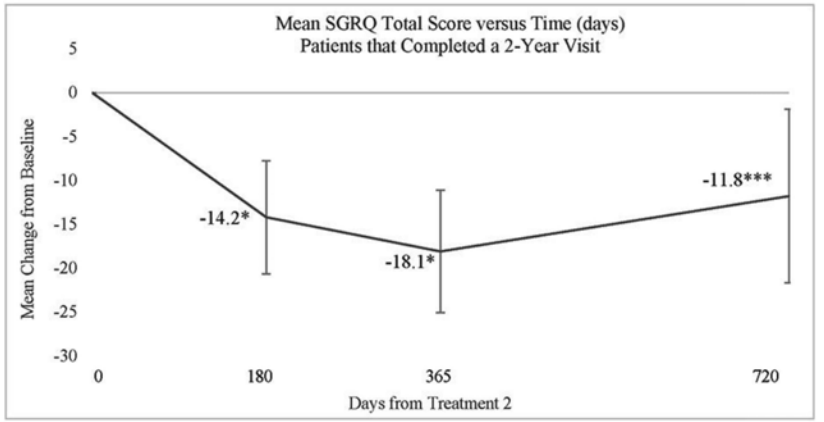
# BRONCHIAL RHEOPLASTY

- **Target patient population:**
  - FEV1 30-80%p
  - Chronic productive cough ≥ 3 mo/yr x 2 consecutive years
  - ≥ 10 pack-year smoking history
- **Observational data:**
  - Sustained improvements in CAT, SGRQ, sputum production
- **Adverse events:**
  - Moderate AECOPD, hemoptysis (self-limited)
- ***RheSolve:*** *multi-center, double-masked RCT (completed June 2023)*




Sciurba FC, et al. BMJ Open Respir Res 2023.

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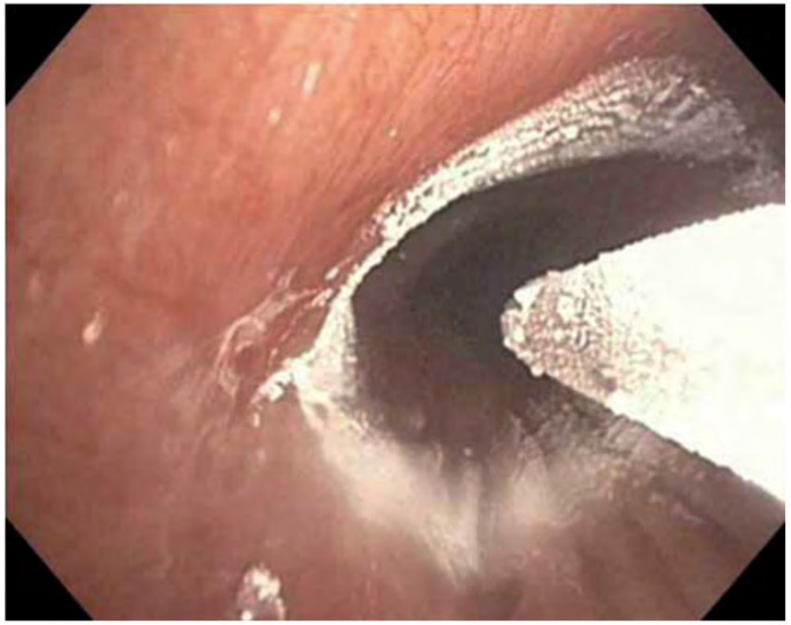
# CRYOSPRAY

- Metered-dose $LN_2$ sprayed in airways to denude bronchial epithelium

- RejuvenAir system (CSA Medical) granted breakthrough device status in 2019



Hartman JE, et al. Eur Respir Rev 2021.

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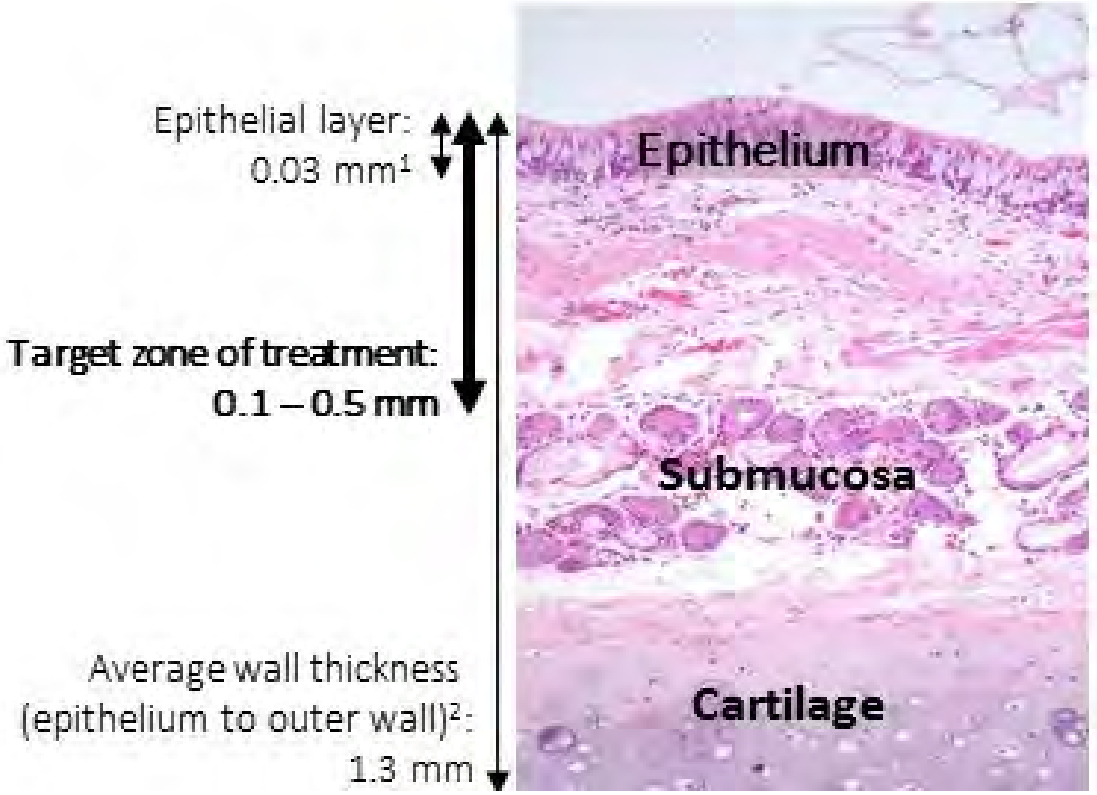
# CRYOSPRAY

- Temperature-drop (-196 °C) penetrates intosubmuco
- Entire epithelium is ablated
- Repopulation with healthy/normal epithelium




csamedical.com

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# CRYOSPRAY

- **Target patient population:**
  - Same as rheoplasty

- **Clinical data:**
  - Improved symptoms and sputum production relative to baseline at 9 mo
  - Mean SGRQ -9.6 points relative to sham arm in study of 31 patients at 6 mo

Garner JL, et al. ERJ 2020.
Orton CM, et al. ERJ 2022 (abstract).

- **Adverse events:**
  - AECOPD, PNA, worsening cough

- ***SPRAY-CB:*** *multi-center, sham-controlled RCT (underway)*

# TARGETED LUNG DENERVATION

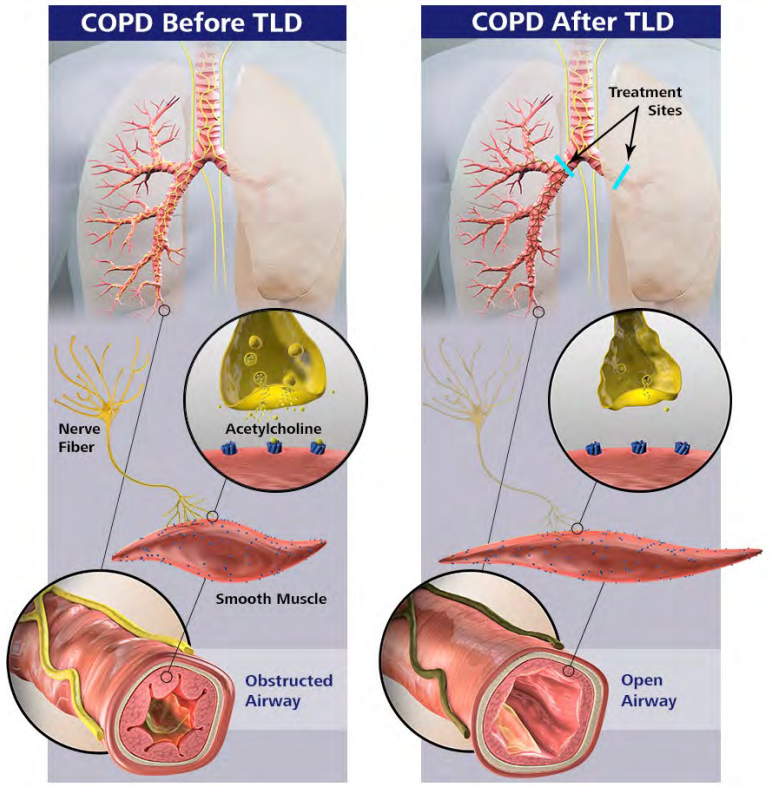
- Radiofrequency ablation (RFA) of vagal branches to the mainstem bronchi

- dNerva system (Nuvaira, Inc.) granted breakthrough device status in 2020

https://nuvaira.com/technology/

# TARGETED LUNG DENERVATION

- RFA disrupts peribronchial branches of vagus nerve
- Disruption of parasympathetic reflex in the airways
- Decreased smooth muscle tone and airway resistance




Neuvaira.com
Hummel JP, et al. J Appl Physiol 2018.

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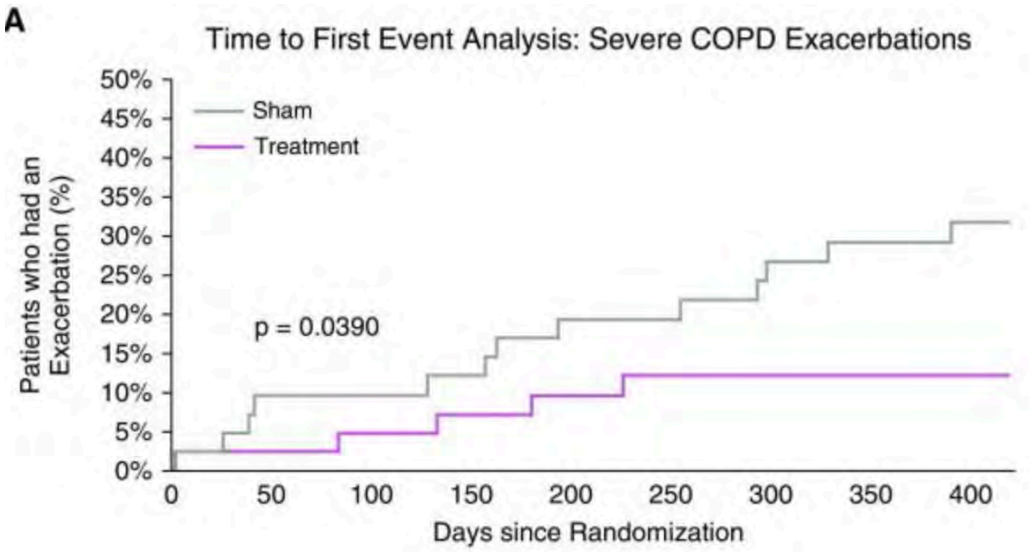
# TARGETED LUNG DENERVATION

- **Target patient population:**
  - FEV1 30-60%p
  - ≥ 2 moderate AECOPD or ≥ 1 severe AECOPD/12 mo

- **Clinical data:**
  - Improved symptom-control, fewer overall respiratory events, greater time-to-severe AECOPD *vs* sham controls
  - Benefit sustained up to 3 yrs

- **Adverse events:**
  - Esophageal complications

- ***AIRFLOW-3:*** *multi-center, sham-controlled RCT (underway)*




Slebos DJ, et al. AJRCCM 2019.

Valipour, et al. Int J Chron Obstruct Pulm Dis 2020.
Christophe P, et al. Respir Res 2021.
Conway F, et al. Respiration 2022.

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# SUMMARY

- Interventional bronchoscopy no longer limited to the central airways
  - Several interventions for clinical use or under investigation for treatment of benign small airway obstructive disease
- BT somewhat fraught with uncertainty, losing ground to biologics
- Robust data in support of BLVR for advanced emphysema
- New bronchoscopic treatments for non-emphysematous COPD under investigation

# THANK YOU!

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