COPD PHENOTYPES

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Dr. Benzo is the founding director of the Breathing and Behavior Laboratory, which develops and tests interventions that promote a participatory model of care; fosters self awareness and consciousness of human behavior; and studies the impact of these interventions on biologic markers and health outcomes.

The beneficial effect of conscious breathing and awareness of the breath has been proposed for centuries. Bridging the ancient knowledge with new science is at the core of Dr. Benzo's research and the Breathing and Behavior laboratory.

Chronic Obstructive Pulmonary Disease and lung cancer are the main chronic conditions studied; however, interventions in other chronic diseases processes (heart failure, chronic pain syndromes) are also being considered.

Dr. Benzo is part of the Dan Abraham Healthy Living Center, where some of his work on mindfulness and meditation is utilized.

Current research projects include:

- Effect of Motivational Interviewing based counseling for self care and Pulmonary Rehabilitation in patients with Chronic Obstructive Pulmonary Disease (COPD) after being hospitalized for an acute exacerbation. (Dr. Benzo PI: RO1 National Institutes of Health, National Heart Lung and Blood Institute).

- Preoperative Rehabilitation (Breathing Awareness Practice- Self Efficacy based training-inspiratory muscle training) before Lung Cancer Resection in patient with COPD and high risk of post operative Complications (Dr. Benzo PI: RO1 National Institutes of Health, National Cancer Institute).

- Cell phone-based activity monitoring plus Motivational Interviewing Counseling to maintain Physical Activity in COPD (Dr. Benzo PI at Mayo Clinic: R44 National Institutes of Health, National Institute of Aging).

- Motivational Interviewing counseling to maintain Physical Activity in COPD

- Mindfulness-based intervention (modified Mindfulness Based Stress Reduction-MBSR-)in COPD.

- Mindfulness-based Stress Reduction-MBSR- for Mayo Clinic employees.
• Effect of a Meditation Based Program on telomere length and function (in planning phase).
• Determining the relationships between self-efficacy for walking, actual walking performance and physical activity in patients with chronic lung disease.
• Device-guided slow breathing in COPD patients with clinically significant dyspnea.

Dr. Benzo’s educational background includes: Master of Science - Epidemiology Harvard University School of Public Health; Fellow - Pulmonary and Critical Care Medicine Medical University of South Carolina; Resident - Internal Medicine Medical University of South Carolina; Internship - Internal Medicine West Virginia University; Research Fellowship - Pulmonary and Critical Care Medicine West Virginia University; Resident - Internal Medicine Instituto de Investigaciones Medicas, University de Buenos Aires, Argentina; MD Universidad Nacional de Rosario, Argentina.

OBJECTIVES:
Participants should be better able to:

1. Identify clinically relevant COPD phenotypes;
2. Identify proper treatments for each type;
3. Personalize COPD care based on phenotype characterization.
COPD Phenotypes

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COPD in 2020

- third leading cause of death
- fifth cause in number of years lost due to ill-health, disability, or early death
Why Phenotype?

• ‘COPD phenotypes’ to classify patients into distinct subgroups, provide prognostic information, and ultimately alter clinically meaningful outcomes

• A phenotype is any observable characteristic that results from gene–environment interactions.
The bottom line:
one size (treatment) *does not* fit all COPD patients

**Phenotypes**

- No consensus on the number of them: from 2 to 328 millions
Proposed Phenotypes

- Frequent/Infrequent Exacerbator
- COPD-Asthma
- Frailty
- Comorbid
- Predominantly Emphysema

COPD-Asthma

- diagnosis of COPD in a patient with a history of previously diagnosed asthma before the age of 40 years

COPD-asthma overlap

Why matters

• more respiratory symptoms
• worse lung function
• more respiratory medication (x4)
• more hospitalization (x4) and exacerbations (x2-4)
• worse quality of Life
  • Menezes Chest. 2014 Feb;145(2):297-304

Treatment

• Characterized by higher response to inhaled corticosteroids.
• Rx of nasal and reflux symptoms can make a big difference
• Patients with neutrophil predominant BAL when treated with macrolides show a decline in exacerbation rate, improved peak expiratory flows, and improved quality of life. J Allergy Clin Immunol Pract. 2014 Sep-Oct;
• Results of the WISDOM study does not apply here. Magnussen N Engl J Med 2014; 371:1285-1294

• Bronchodilator reversibility status varies temporally and does not distinguish clinically relevant outcomes, making it an unreliable phenotype. Thorax 2012;67:701-708

The Asthma-COPD Phenotype has been characterized except

1. higher response to inhaled corticosteroids
2. poorer quality of life
3. response to macrolides if BAL is eosinophilic predominant
4. Higher hospitalization rate
The Asthma-COPD Phenotype has been characterized by?

1. higher response to inhaled corticosteroids
2. poorer outcomes
3. response to macrolides if BAL is neutrophil predominant
4. 1 and 2 only
5. all of the above

Exacerbator Phenotype (or the lack of)

- Exacerbations: worsening which necessitate a change in medication.
The ‘frequent exacerbator’ phenotype

• subjects who experience two or more exacerbations per year.
• This phenotype is relatively stable over time

Exacerbation Phenotype Prevention and Treatment

- Macrolides and quinolones
- Inhaled corticosteroids
- Mucolytics
- PDE4 inhibitors.
- Written Action Plan

From: Reduction of Hospital Utilization in Patients With Chronic Obstructive Pulmonary Disease: A Disease-Specific Self-management Intervention

the emergency action plan

My Plan when “My breathing is not doing well”

New symptoms:
- More shortness of breath than usual
- Sputum has changed color, consistency or volume

My Immediate Actions:
1. I take control of the situation (avoid panic and practice slow breathing while you figure your next step).
2. Use the rescue inhaler (usually albuterol, or corticosteroids) or a nebulizer treatment (usually albuterol or dornase) as frequent as needed (every two hours).

Actions if symptoms don’t improve in the initial 12 hours or before going to bed:
1. I start prednisone 1 tablet a day for 5 days.
2. I start my antibiotics if my sputum significantly changed:
   - Thick or Increased amount
   - Color (turned green or yellow)
3. I continue my bronchodilator (rescue inhaler) if I am more short of breath than usual.
4. I call the study counselor if I need any reassurance or help.

Follow Up:
- If symptoms get worse or do not improve after 48 hrs, Contact my doctor. If after 5pm or on the weekend, I go to my local emergency department. Always be safe.
Current evidence-based approaches to the Exacerbator Phenotype in COPD

1. Macrolide Therapy
2. A written action Plan for antibiotic and Prednisone
3. Acetylcysteine
4. Roflumilast
5. Inhaled corticosteroids
6. All of the above
Current evidence-based approaches to the Exacerbator Phenotype in COPD?

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Phenotypes by Imaging

the optimal method: sampling of the middle lung region [20].
Emphysema

- LVRS
- Coil Therapy
Frailty Phenotype

Frailty

- Decreased resistance to disability and illness.
- Constellation of three or more signs and symptoms
  1. wasting (weight loss or cachexia)
  2. exhaustion (self-reported)
  3. Decreased physical activity, slowness (often measured by gait speed),
  4. Weakness (often measured by grip strength).
Frailty is associated with worsened survival and increased hospitalization

- 902 patients
- Frail patients had a worse survival with an adjusted Hazard Ratio (a HR) of 1.57
- Decreased time to hospitalization a HR of 1.70
- Increased hospital days (+8 days)

Survival by Frail Phenotype

AHR= 1.57
95% CI 1.08-2.29; p=0.018
Time to First hospitalization by Frail Phenotype

- AHR = HR 1.70; 95% CI 1.11-2.59; p=0.014

Self-perceived Frailty

- Adjusted risk of increased hospital days (est ↑2.17 days; p=0.032)
Gait Speed < 0.8 meters/sec is associated with frailty
Frailty Phenotype is defined which of the following characteristics?

1. wasting (weight loss or cachexia)
2. exhaustion (self-reported)
3. slowness (often measured by gait speed),
4. weakness (often measured by grip strength
5. 2 of the above
6. 3 of the above

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Rehabilitation is the answer

Home Rehab

• Pulmonary Rehabilitation is not available to all
• There growing evidence on home PR
• Remote monitoring is the frontier to explore
Emotional Frailty Phenotype

- More hospitalization
- More ER
- Lower QoL
- Lower Physical Activity

Identifying Emotional Frailty

- Anxiety (screen GAD2> 2)
- Depression (screen PHQ2>2)
- Fear of Breathlessness (1 question)
Active Anxiety and Depression Symptoms in COPD

• NETT cohort
• Single item responses from questionnaires
  • Quality of Well-being Scale,
  • St. George’s Respiratory questionnaire,
  • SF-36

Anxiety and outcomes

**Decreased survival**
• Antianxiety medication  HR 1.43; p=0.036
• Nervous and shaky HR 1.65; p<0.001

**Increased days in the hospital**
• Antianxiety medication 3.7 days; p<0.001
• Nervous and shaky 4.3; p<0.001
• Excessive worry 3.9; p<0.001

**Decreased time to first hospitalization**
• Nervous and shaky HR 1.67; p<0.001
Depression symptoms and outcomes

Decreased survival
• Tiredness  p<0.001

Increased days in hospital
• Lonely 3.8 days; p=0.001
• Irritability 1.7 days; p=0.049

Most effective method for treating depression-anxiety in patients with COPD

1. Pharmacological therapy
2. Cognitive Behavioral Therapy
3. Pulmonary Rehabilitation
4. None of the above
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Rehabilitation
Health Coaching
Health Coaching

• Mindful Communication through Motivational Interviewing
Mindful Communications
Key Principles of motivational interviewing

- R—Resist the righting reflex (resist fixing)
- U—Understand patient’s motivation (ambivalence)
- L—Listen to your patient (reflect)
- E—Empower your patient (engage)

Rollnick (2008)
MC is NOT about a technique or set of techniques that are applied to or (worse) "used on" people

Exploring Data for Phenotypes

• Cluster analysis is a technique for data exploration that groups subjects without an a priori hypothesis.
three groups using cluster analysis

- ‘mild respiratory COPD’
- ‘severe respiratory COPD’ group had increased hospitalizations due to COPD and increased all-cause mortality,
- ‘systemic COPD’ group had an increased incidence of cardiovascular disease
Practical points

- Defining Phenotypes translate not only in prognostic but actionable information
- Exacerbator, the lack of and Asthma-COPD
- Systemic phenotype (CHF, OSA, DM)
- Frailty (gait speed less than 0.8ms)
- Difficult Emotions (anxiety, depression fear of breathlessness)