

# Current and future best practice for the management of non-cystic fibrosis bronchiectasis

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# Expert panel



**Dr Charles Daley**

National Jewish Health and University of Colorado  
Denver, CO, USA  
Icahn School of Medicine at Mount Sinai  
New York, NY, USA



**Dr Anne O'Donnell**

Georgetown University  
Washington, DC, USA



**Prof. Stefano Aliberti**

Humanitas University  
Humanitas Research Hospital  
Milan, Italy



# Agenda

**Disease prevalence and risk factors for acute exacerbations**

**Management of chronic infection**

**Available and emerging pharmacotherapeutic strategies**

# Disease prevalence and risk factors for acute exacerbations

## Dr Charles Daley

National Jewish Health and University of Colorado  
Denver, CO, USA  
Icahn School of Medicine at Mount Sinai  
New York, NY, USA



# Incidence and prevalence of non-CF bronchiectasis

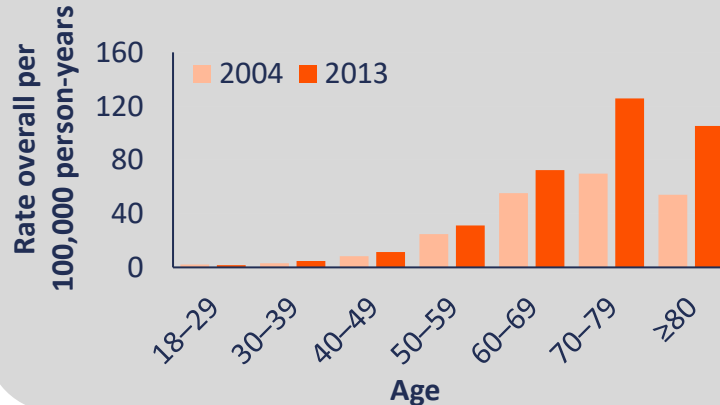
- **Prevalence** and **incidence** increase with age and are increasing over time, although recent data are lacking<sup>1-4</sup>



- **Incidence:** 29 cases/100,000 adults aged  $\geq 18$  years in 2013<sup>2</sup>
- **Prevalence:** 139 cases/100,000 adults aged  $\geq 18$  years in 2013<sup>2</sup>
  - 8.7% per year increase in US Medicare outpatient claims database from 2000–2007<sup>3\*</sup>



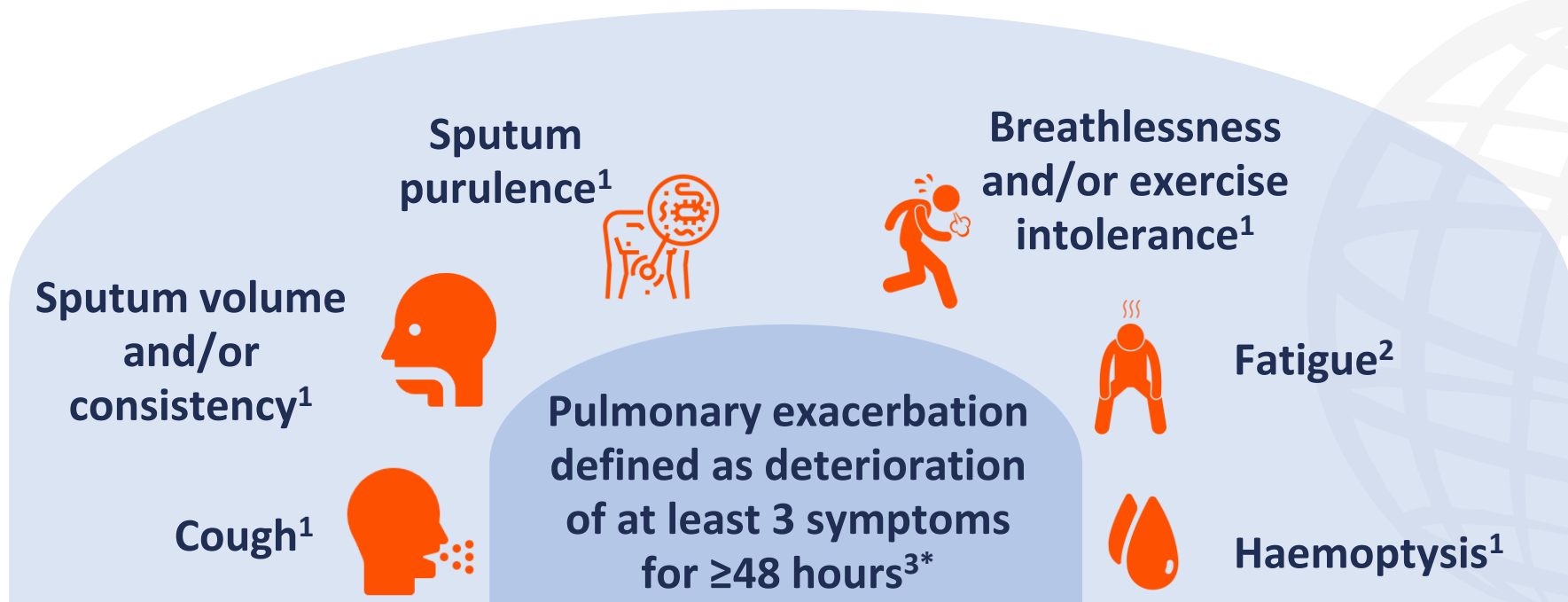
## UK incidence of non-CF bronchiectasis<sup>4</sup>



\*Analysis of Medicare outpatient claims database of patients with non-CF bronchiectasis. CF, cystic fibrosis.

1. Eralp EE, et al. *BMC Pulm Med.* 2020;20:172; 2. Weycker D, et al. *Chron Respir Dis.* 2017;14:377–84; 3. Seitz AE, et al. *Chest.* 2012;142:432–9; 4. Quint JK, et al. *Eur Respir J.* 2016;47:186–93.

# Acute exacerbations in non-CF bronchiectasis



\*Definition from European Multicentre Bronchiectasis Research Collaboration (EMBARC) and US Bronchiectasis Research Registry (BRR) definitions working group. CF, cystic fibrosis.

1. Macfarlane L, et al. *Clin Med (Lond)*. 2021;21:e571–7; 2. Delestre-Levai I, et al. *ERJ Open Res*. 2021;7:00096–2021; 3. Hill AT, et al. *Eur Respir J*. 2017;49:1700051.

# Management of chronic infection

## Dr Charles Daley

National Jewish Health and University of Colorado  
Denver, CO, USA  
Icahn School of Medicine at Mount Sinai  
New York, NY, USA





# Chronic infection in patients with non-CF bronchiectasis



- Most studies report up to 60% of patients with non-CF bronchiectasis have a chronic infection<sup>1</sup>
- No current standardized definition for chronic infection<sup>1</sup>
- **General definition: Two or more consecutive positive cultures or >50% of cultures positive for the same pathogen within 6–12 months, in samples taken at least 1 month apart<sup>1–3</sup>**

CF, cystic fibrosis.

1. Di Pasquale M, et al. *Expert Opin Pharmacother*. 2020;21:1975–90; 2. Martínez-García MÁ, et al. *Arch Bronconeumol (Engl Ed)*. 2018;54:88–98; 3. Pressler T, et al. *J Cyst Fibros*. 2011;10(Suppl. 2):S75–8.

# Treatments for chronic infection in patients with non-CF bronchiectasis



- **Mechanical airway clearance**<sup>1</sup>
- **Mucolytic agents** (nebulized saline solution)<sup>2</sup>
- **Oral/IV antibiotics** (macrolides)<sup>2</sup>



- **Long-term inhaled antibiotics** (gentamicin, tobramycin, colistin, ciprofloxacin, aztreonam)<sup>2,3</sup>
- **Mucolytic agents** (bromhexine)<sup>4</sup>



- **Long-term bronchodilators and corticosteroids**<sup>2</sup>
- **Mucolytic agents** (rhDNase, acetylcysteine)<sup>2</sup>

CF, cystic fibrosis; IV, intravenous; rhDNase, recombinant human deoxyribonuclease.

1. Severiche-Bueno D, et al. *Breathe*. 2019;15:286–95; 2. Imam JS, Duarte AG. *Respir Med*. 2020;166:105940;

3. Martínez-García M-G, et al. *Arch Bronconeumol*. 2018;54:88–98; 4. Hill AT, et al. *Thorax*. 2019;74(Suppl. 1):1–69.

# Eradication protocol guidance for the management of non-CF bronchiectasis



- Some clinical guidelines recommend **inhaled antibiotics** for the treatment of early infection with *Pseudomonas aeruginosa*<sup>1–3</sup>
- ERS guidelines suggest not to use eradication protocols for other organisms<sup>3</sup>

# Available and emerging pharmacotherapeutic strategies

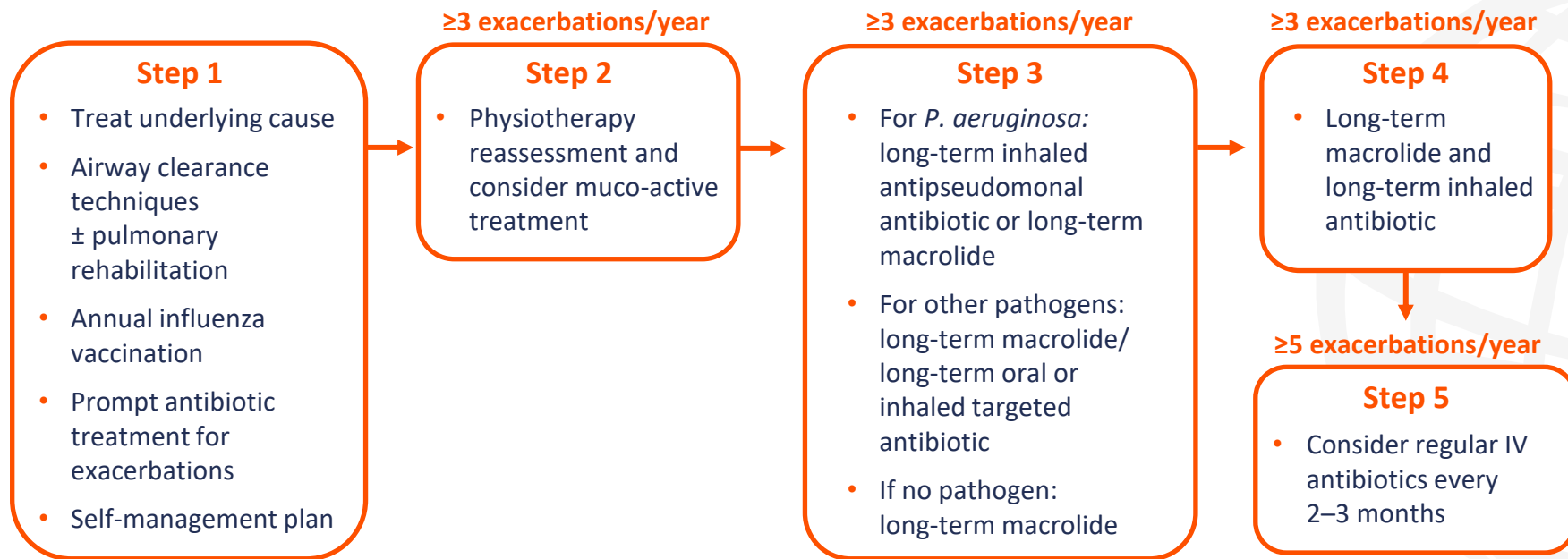
## Dr Charles Daley

National Jewish Health and University of Colorado  
Denver, CO, USA  
Icahn School of Medicine at Mount Sinai  
New York, NY, USA



# Stepwise management of stable non-CF bronchiectasis

British Thoracic Society Guidelines



The next step in the management pathway should be considered if significant symptoms persist, even if patients do not meet exacerbation criteria

# Key clinical trials in non-CF bronchiectasis

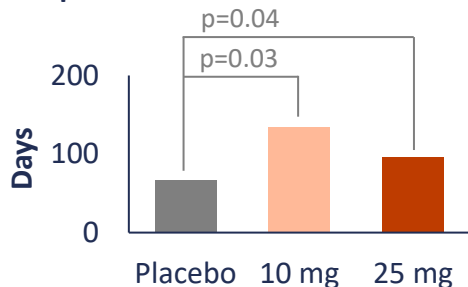
## Brensocatic (WILLOW)<sup>1</sup>



N=256

Phase II study of adult patients with  $\geq 2$  exacerbations in past 12 months

### 25th percentile of time to first exacerbation



Higher incidence of dental and skin AEs for 10 mg and 25 mg brensocatic doses, respectively, vs placebo

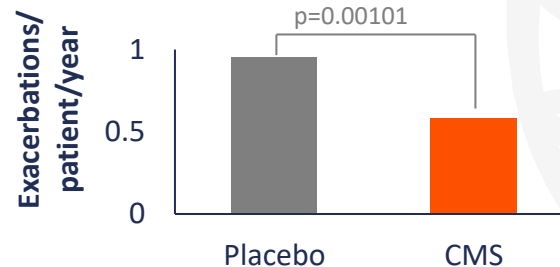
## Colistimethate sodium (PROMIS-I)<sup>2,3</sup>



N=377

Phase III study of adult patients with *P. aeruginosa* in sputum and  $\geq 2$  exacerbations or 1 requiring IV antibiotics in past 12 months

### Annual exacerbation rate



Similar proportion of patients with AEs between treatment arms

AE, adverse event; AESI, AE of special interest; CF, cystic fibrosis; CMS, colistimethate sodium; IV, intravenous.

1. Chalmers J, et al. *N Engl J Med.* 2020;383:2127–37; 2. Haworth CS, et al. *Eur Respir J.* 2021;58:RCT4267;

3. NCT03093974. Available at: <https://clinicaltrials.gov/ct2/show/NCT03093974> (accessed 5 April 2022).

# Clinical trials in non-CF bronchiectasis in progress

## **Brensocatib** (oral DPP-1 inhibitor)<sup>1</sup>

- ASPEN phase III trial
  - Estimated completion: March 2024

## **Benralizumab** (subcutaneous anti-IL-5R)<sup>4</sup>

- MAHALE phase III trial
  - Estimated completion: January 2026

## **Colistimethate sodium** (inhaled antibiotic)<sup>2</sup>

- PROMIS II phase III trial
  - Estimated completion: February 2022

## **Roflumilast** (oral anti-inflammatory)<sup>5</sup>

- NCT04322929 phase II trial
  - Estimated completion: February 2022

## **Melphalan** (inhaled alkylating agent)<sup>3</sup>

- SEADIB1 phase II trial
  - Estimated completion: December 2021

## **CSL787** (inhaled immunoglobulin)<sup>6</sup>

- NCT04643587 phase I trial
  - Estimated completion: May 2022

CF, cystic fibrosis; DPP, dipeptidyl peptidase; IL-5R, interleukin 5 receptor.

1. NCT04594369. Available at: <https://clinicaltrials.gov/ct2/show/NCT04594369> (accessed 23 March 2022); 2. NCT03460704. Available at: <https://clinicaltrials.gov/ct2/show/record/NCT03460704> (accessed 23 March 2022); 3. NCT04278040. Available at: <https://clinicaltrials.gov/ct2/show/NCT04278040> (accessed 23 March 2022); 4. NCT04278040. Available at: <https://clinicaltrials.gov/ct2/show/NCT05006573> (accessed 23 March 2022); 5. NCT04322929. Available at: <https://clinicaltrials.gov/ct2/show/record/NCT04322929> (accessed 23 March 2022); 6. NCT04643587. Available at: <https://clinicaltrials.gov/ct2/show/NCT04643587> (accessed 23 March 2022).