

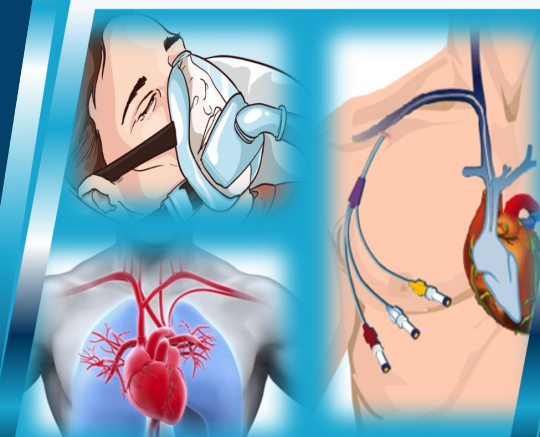
LAGASIO CHIARA
Medicina Interna 1-UTIM
Ospedale San Paolo Savona

BPCO
RIACUTIZZATA:UPDATE
TERAPIA 2024

2° Edizione

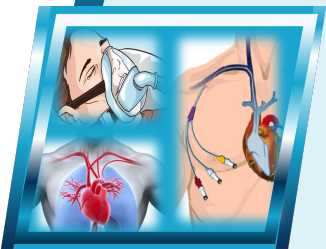
Area Critica in
Medicina Interna

13 Aprile 2024
Savona



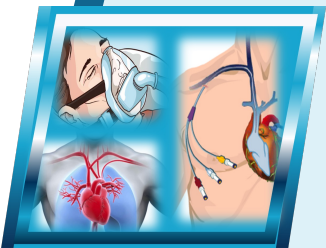
BPCO

Patologia polmonare eterogenea caratterizzata da sintomi respiratori cronici (dispnea, tosse, produzione di espettorato, esacerbazioni) dovuti ad anomalie delle vie aeree (bronchite, bronchiolite) e/o degli alveoli (enfisema) che causano ostruzione persistente, spesso progressiva, delle vie aeree



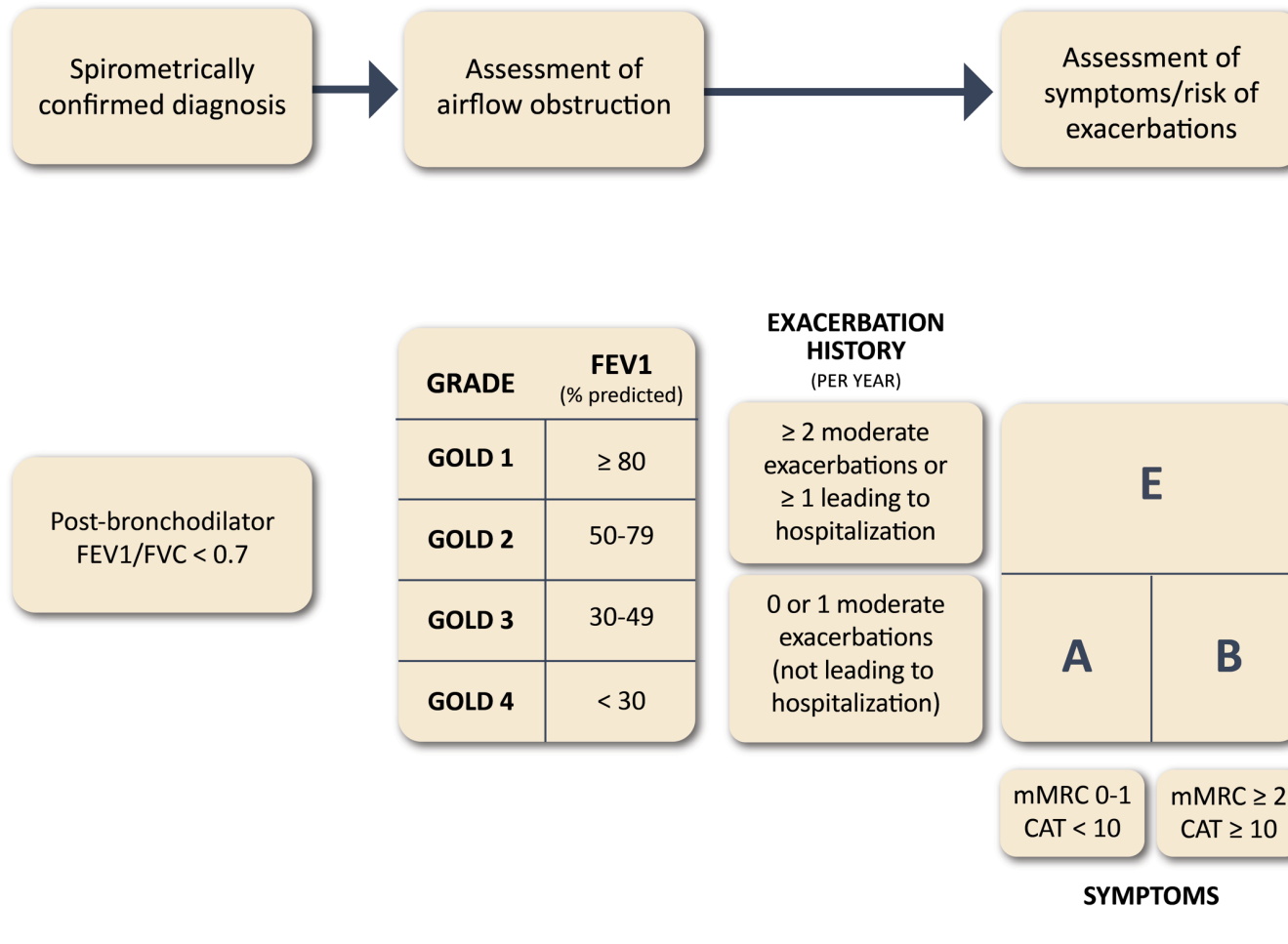
DIAGNOSI

- Presentazione clinica compatibile con BPCO
- Spirometria: limitazione flusso aereo non reversibile $FEV_1/FVC < 0.7$ dopo broncodilatazione



GOLD ABE Assessment Tool

Figure 2.10



RIACUTIZZAZIONE

Peggioramento acuto dei sintomi respiratori che richiede una terapia aggiuntiva



RIACUTIZZAZIONE

Evento complesso:

- aumento infiammazione vie aeree
- aumentata produzione di secrezioni
- intrappolamento d'aria



DISPNEA



Exacerbation of COPD

Airway and lung inflammation

Exacerbations of respiratory symptoms in patients with COPD

Exacerbation of coexistent non-respiratory diseases

- Arterial hypertension
- Decompensated heart failure
- Ischemic heart disease
- Arrhythmias
- Pulmonary embolism
- Stroke
- Anemia
- Depression

Exacerbation of coexistent respiratory diseases

- Pneumonia
- Chronic bronchitis
- Asthma
- Bronchiectasis
- Interstitial lung diseases
- Foreign bodies/Atelectasis
- Pneumothorax/Pleurisy
- Cancer

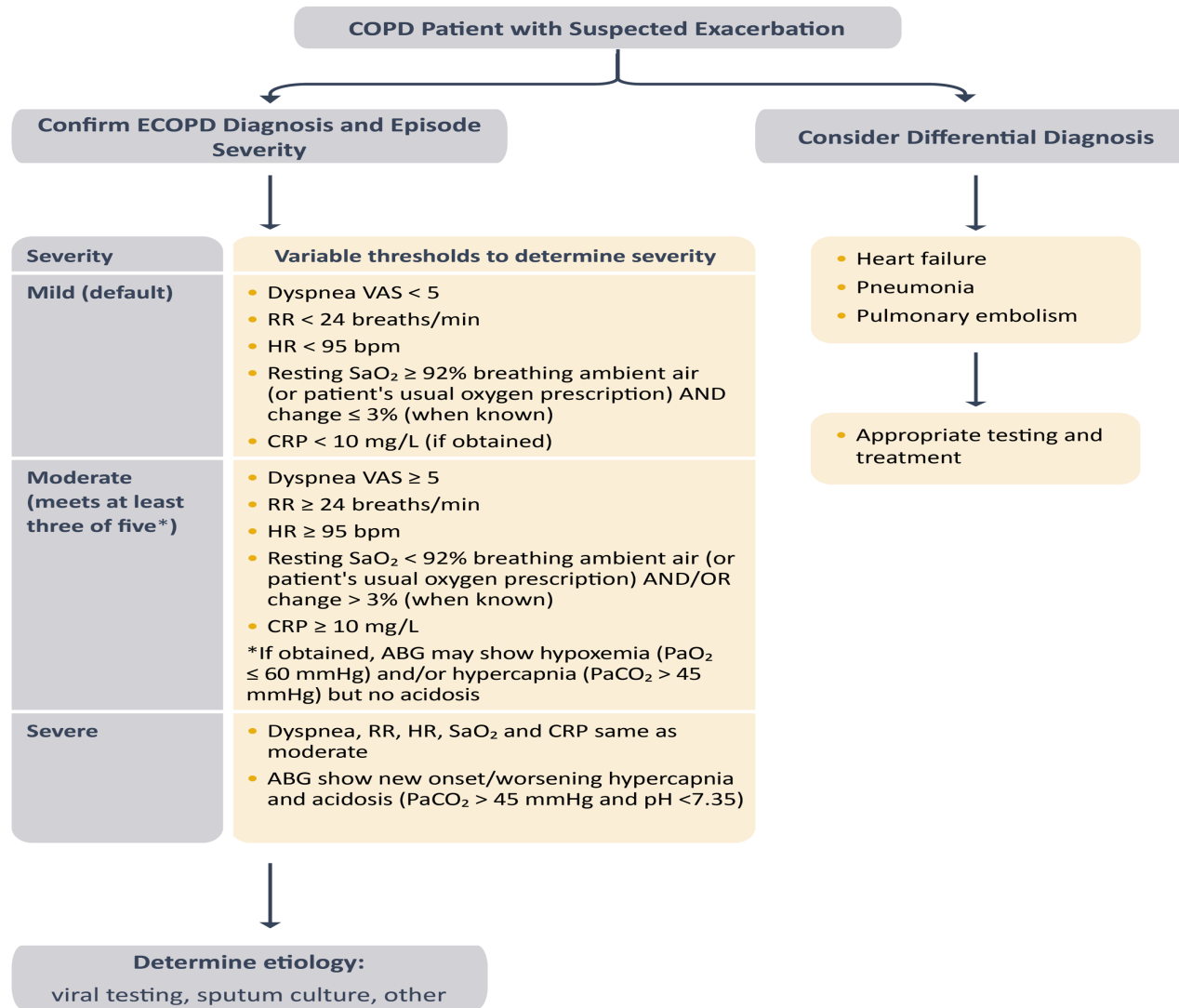
Respirology-2021-MacLeod et al.

Chronic obstructive pulmonary disease exacerbation fundamentals: Diagnosis, treatment, prevention and disease impact



Classification of the Severity of COPD Exacerbations

Figure 4.3



Adapted from: The ROME Proposal, Celli et al. (2021) Am J Respir Crit Care Med. 204(11): 1251-8.

Abbreviations: VAS visual analog dyspnea scale; RR respiratory rate; HR heart rate; SaO₂ oxygen saturation; CRP C-reactive protein; ABG arterial blood gases; PaO₂ Arterial pressure of oxygen.



Potential Indications for Hospitalization Assessment*

Figure 4.4

- Severe symptoms such as sudden worsening of resting dyspnea, high respiratory rate, decreased oxygen saturation, confusion, drowsiness
- Acute respiratory failure
- Onset of new physical signs (e.g., cyanosis, peripheral edema)
- Failure of an exacerbation to respond to initial medical management
- Presence of serious comorbidities (e.g., heart failure, newly occurring arrhythmias, etc.)
- Insufficient home support

*Local resources need to be considered



Management of Severe but not Life-threatening Exacerbations*

Figure 4.5

Assess severity of symptoms, blood gases, chest radiograph

Administer supplemental oxygen therapy, obtain serial arterial blood gas, venous blood gas and pulse oximetry measurements

Bronchodilators:

- Increase doses and/or frequency of short-acting bronchodilators
 - Combine short-acting beta 2-agonists and anticholinergics
 - Consider use of long-acting bronchodilators when patient becomes stable
 - Use spacers or air-driven nebulizers when appropriate
-

Consider oral corticosteroids

Consider antibiotics (oral) when signs of bacterial infection are present

Consider noninvasive mechanical ventilation (NIV)

At all times:

- Monitor fluid balance
- Consider subcutaneous heparin or low molecular weight heparin for thromboembolism prophylaxis
- Identify and treat associated conditions (e.g., heart failure, arrhythmias, pulmonary embolism etc.)

*Local resources need to be considered



BRONCODILATATORI

- INALATORI:
 - broncodilatatori a breve durata di azione associati ad anticolinergici se possibile con distanziatori
 - ➔ basso livello evidenza
- SISTEMICI:
 - metilxantine endovenose sconsigliate per gli effetti collaterali



GLUCOCORTICOIDI

- Migliorano la funzionalità polmonare
- Riducono tempi di recupero
- Migliorano ossigenazione
- Riducono rischio ricadute e di fallimento terapeutico
- Riducono la durata dell'ospedalizzazione



prednisolone 40 mg/die per 5 giorni



ANTIBIOTICI

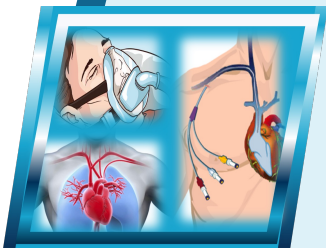
Secondo le linee guida GOLD:

SOLO in pazienti con:

- aumento della dispnea
- aumento del volume dell'espettorato
- presenza di espettorato purulento

Oppure

se necessitano di ventilazione meccanica (invasiva o non invasiva)



ANTIBIOTICI



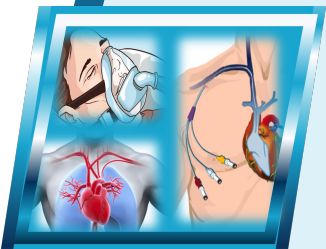
- riducono del 77% rischio di mortalità a breve termine
- riducono del 53% il rischio di fallimento terapeutico



ANTIBIOTICI

QUALE?

Secondo le resistenze locali



OSSIGENOTERAPIA

Target:

sat O₂ 88%-92%



VENTILAZIONE NON INVASIVA

Indications for Noninvasive Mechanical Ventilation (NIV)

Figure 4.8

At least one of the following:

- Respiratory acidosis ($\text{PaCO}_2 \geq 6.0$ kPa or 45 mmHg and arterial $\text{pH} \leq 7.35$)
- Severe dyspnea with clinical signs suggestive of respiratory muscle fatigue, increased work of breathing, or both, such as use of respiratory accessory muscles, paradoxical motion of the abdomen, or retraction of the intercostal spaces
- Persistent hypoxemia despite supplemental oxygen therapy

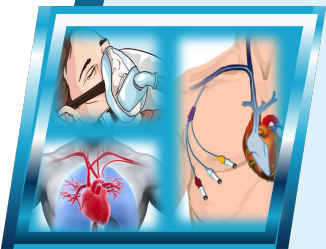


OSSIGENOTERAPIA AD ALTI FLUSSI

- Riduce la frequenza respiratoria,
- riduce l'impegno dei muscoli respiratori
- migliora gli scambi respiratori



Migliora l'ossigenazione e la ventilazione
e riduce ipercapnia



High flow nasal therapy versus noninvasive ventilation as initial ventilatory strategy in COPD exacerbation: a multicenter non-inferiority randomized trial

Cortegiani *et al. Crit Care* (2020) 24:692

Conclusion:

HFNT was statistically non-inferior to NIV as initial ventilatory support in decreasing PaCO₂ after 2 h of treatment in patients with mild-to-moderate AECOPD, considering a non-inferiority margin of 10 mmHg. However, 32% of patients receiving HFNT required NIV by 6 h. Further trials with superiority design should evaluate efficacy toward stronger patient-related outcomes and safety of HFNT in AECOPD.



Management of Severe but not Life-threatening Exacerbations*

Figure 4.5

Assess severity of symptoms, blood gases, chest radiograph

Administer supplemental oxygen therapy, obtain serial arterial blood gas, venous blood gas and pulse oximetry measurements

Bronchodilators:

- Increase doses and/or frequency of short-acting bronchodilators
 - Combine short-acting beta 2-agonists and anticholinergics
 - Consider use of long-acting bronchodilators when patient becomes stable
 - Use spacers or air-driven nebulizers when appropriate
-

Consider oral corticosteroids

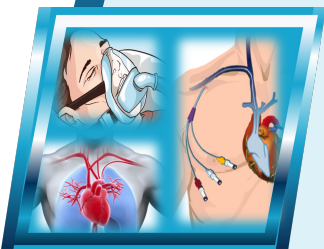
Consider antibiotics (oral) when signs of bacterial infection are present

Consider noninvasive mechanical ventilation (NIV)

At all times:

- Monitor fluid balance
- Consider subcutaneous heparin or low molecular weight heparin for thromboembolism prophylaxis
- Identify and treat associated conditions (e.g., heart failure, arrhythmias, pulmonary embolism etc.)

*Local resources need to be considered



Key Points for the Management of Exacerbations

Figure 4.6

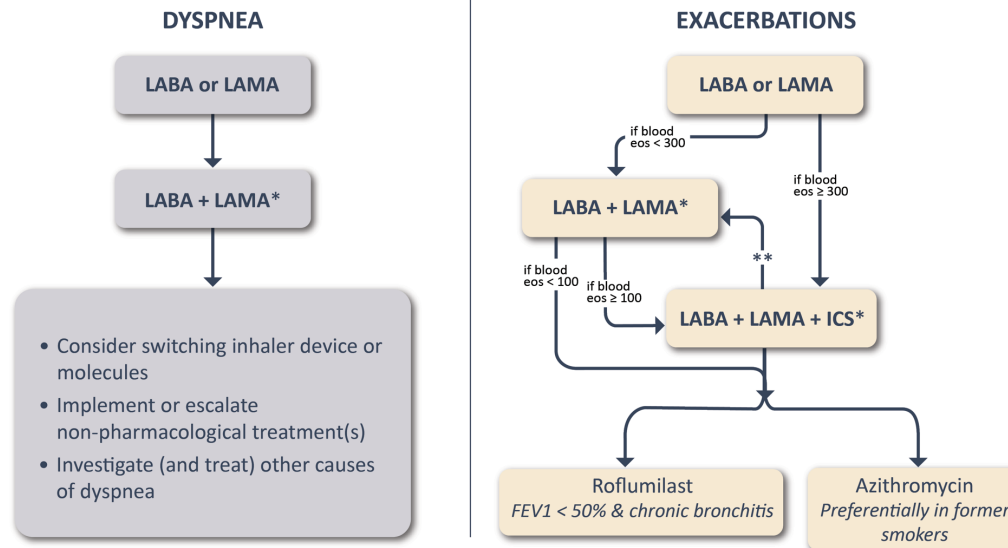
- Short-acting inhaled beta₂-agonists, with or without short-acting anticholinergics, are recommended as the initial bronchodilators to treat an acute exacerbation **(Evidence C)**
- Systemic corticosteroids can improve lung function (FEV₁), oxygenation and shorten recovery time and hospitalization duration. Duration of therapy should not normally be more than 5 days **(Evidence A)**
- Antibiotics, when indicated, can shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration. Duration of therapy should normally be 5 days **(Evidence B)**
- Methylxanthines are not recommended due to increased side effect profiles **(Evidence B)**
- Non-invasive mechanical ventilation should be the first mode of ventilation used in COPD patients with acute respiratory failure who have no absolute contraindication because it improves gas exchange, reduces work of breathing and the need for intubation, decreases hospitalization duration and improves survival **(Evidence A)**



Follow-up Pharmacological Treatment

Figure 3.9

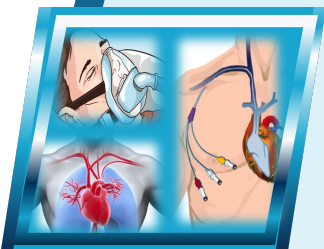
- 1 IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.
- 2 IF NOT:
 - Check adherence, inhaler technique and possible interfering comorbidities
 - Consider the predominant treatable trait to target (dyspnea or exacerbations)
 - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
 - Place patient in box corresponding to current treatment & follow indications
 - Assess response, adjust and review
 - These recommendations do not depend on the ABE assessment at diagnosis



*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment

**Consider de-escalation of ICS if pneumonia or other considerable side-effects. In case of blood eos ≥ 300 cells/μl de-escalation is more likely to be associated with the development of exacerbations

Exacerbations refers to the number of exacerbations per year



Interventions that Reduce the Frequency of COPD Exacerbations

Figure 4.11

Intervention Class	Intervention
Bronchodilators	LABAs LAMAs LABA + LAMA
Corticosteroid-containing regimens	LABA + ICS LABA + LAMA + ICS
Anti-inflammatory (non-steroid)	Roflumilast
Anti-infectives	Vaccines Long Term Macrolides
Mucoregulators	N-acetylcysteine Carbocysteine Erdosteine
Various others	Smoking Cessation Rehabilitation Lung Volume Reduction Vitamin D Shielding measures (e.g., mask wearing, minimizing social contact, frequent hand washing)



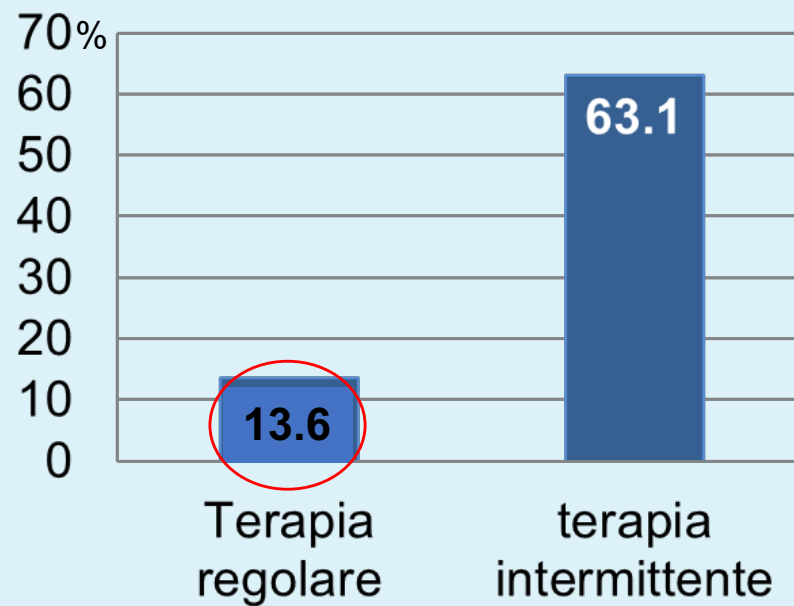
Prevalenza di pazienti che assumono la terapia inalatoria in modo regolare o intermittente (Rapporto OsMed gennaio 2015)

Ipert.5
5,5

DM2
62,5

Stat.
44,0

Terapia
regolare



Aderenza > 80% della
terapia prescritta

Aderenza < 20% della
terapia prescritta



Rapporto OSMed

<http://www.agenziafarmaco.gov.it/it/content/rapporti-osmed-luso-dei-farmaci-italia>



L'evoluzione dell'aderenza: Rapporto OsMed gennaio 2021

	Totale N=117.143			
	2019	2020	2021	Δ % 21-20
Bassa aderenza*^				
45-54 anni	55,0	49,7	48,6	-2
55-64 anni	51,8	44,7	44,8	0
65-74 anni	48,8	42,8	42,3	-1
75-84 anni	46,1	41,1	39,8	-3
≥85 anni	48,9	43,2	42,5	-2

Donne	51,9	45,4	46,1	2
Uomini	47,2	42,2	40,2	-5
Totale	49,9	44,0	43,5	-1
Alta aderenza*^				
45-54 anni	15,8	18,0	20,4	13
55-64 anni	18,6	22,1	23,1	5
65-74 anni	20,9	24,2	25,2	4
75-84 anni	22,3	25,9	27,0	4
≥85 anni	21,4	25,3	25,2	0

Donne	18,6	22,0	22,2	1
Uomini	21,7	24,7	26,8	8
Totale	19,9	23,2	24,2	4

L'uso dei Farmaci in Italia

Rapporto Nazionale
Anno 2021



Il trattamento è stata definita come copertura terapeutica (valutata in base alle DDD) < 40 % del periodo di osservazione mentre l'alta aderenza è stata definita terapeutica ≥ 80% del periodo di osservazione (per ulteriori dettagli consultare i metodi statistici).



Evidence Supporting a Reduction in Mortality with Pharmacotherapy and Non-pharmacotherapy in COPD Patients

Figure 3.17

Therapy	RCT*	Treatment effect on mortality	Patient characteristics
Pharmacotherapy			
LABA+LAMA+ICS ¹	Yes	Single inhaler triple therapy compared to dual LABD therapy relative risk reduction: IMPACT: HR 0.72 (95% CI: 0.53, 0.99) ^{1a} ETHOS: HR 0.51 (95% CI: 0.33, 0.80) ^{1b}	Symptomatic people with a history of frequent and/or severe exacerbations
Non-pharmacological Therapy			
Smoking cessation ²	Yes	HR for usual care group compared to intervention group (smoking cessation) HR 1.18 (95% CI: 1.02, 1.37) ²	Asymptomatic or mildly symptomatic
Pulmonary rehabilitation ^{3#}	Yes	Old trials: RR 0.28 (95% CI 0.10, 0.84) ^{3a} New trials: RR 0.68 (95% CI 0.28, 1.67) ^{3b}	Hospitalized for exacerbations of COPD (during or ≤ 4 weeks after discharge)
Long-term oxygen therapy ⁴	Yes	NOTT: ≥ 19 hours of continuous oxygen vs ≤ 13 hours: 50% reduction ^{4a} MRC: ≥ 15 hours vs no oxygen: 50% reduction ^{4b}	PaO ₂ ≤ 55 mmHg or < 60 mmHg with <i>cor pulmonale</i> or secondary polycythemia
Noninvasive positive pressure ventilation ⁵	Yes	12% in NPPV (high IPAP level) and 33% in control HR 0.24 (95% CI 0.11, 0.49) ⁵	Stable COPD with marked hypercapnia
Lung volume reduction surgery ⁶	Yes	0.07 deaths/person-year (LVRS) vs 0.15 deaths/person-year (UC) RR for death 0.47 (p = 0.005) ⁶	Upper lobe emphysema and low exercise capacity

*RCT with pre-specified analysis of the mortality outcome (primary or secondary outcome); #Inconclusive results likely due to differences in pulmonary rehabilitation across a wide range of participants and settings.

1. a) IMPACT trial (Lipson et al. 2020) and b) ETHOS trials (Martinez et al. 2021); 2. Lung Health Study (Anthonisen et al. 2005); 3. a) Puhan et al. (2011) and b) Puhan et al. 2016; 4. a) NOTT (NOTT, 1980) and b) MRC (MRC, 1981); 5. Kohlein trial (Kohlein et al. 2014); 6. NETT trial (Fishman et al. 2003)

ICS: inhaled corticosteroid; IPAP: inspiratory positive airway pressure; LABA: long-acting beta₂-agonist; LABD: long-acting bronchodilator; LAMA: long-acting anti-muscarinic; LTOT: long-term oxygen therapy; NPPV: noninvasive positive pressure ventilation; LVRS: lung volume reduction surgery; UC: usual treatment control group.

