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Appendix

Chronic obstructive pulmonary disease pathways as a tool to improve appropriateness in Internal Medicine Departments

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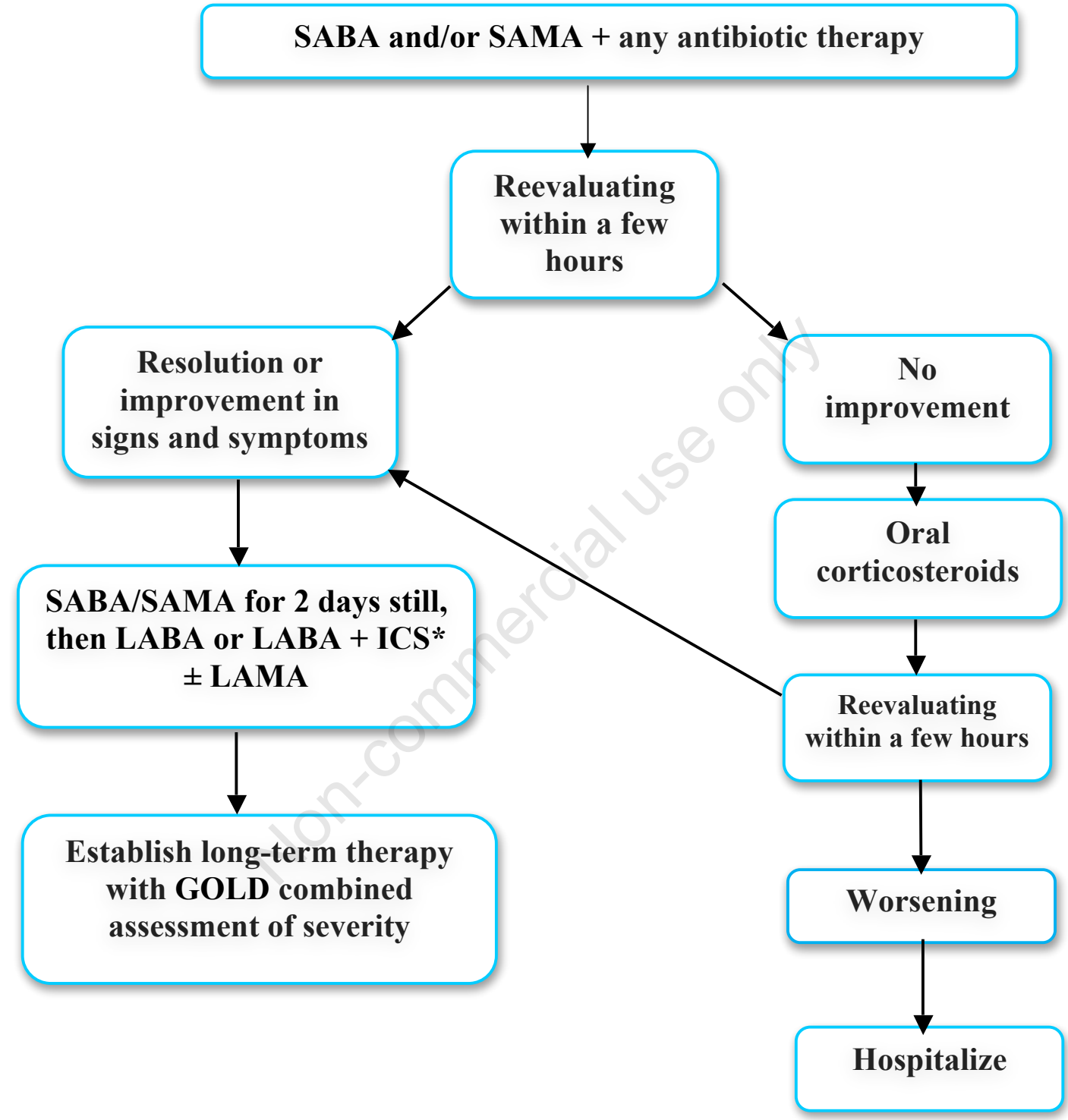
Appendix Figure 1. Algorithm for the home management of acute exacerbation of chronic obstructive pulmonary disease (AECOPD).[1]



*****In symptomatic patients with FEV1<60% pre-bronchodilator (EMEA and AIFA 2011) or with frequent exacerbations[2]*

Appendix Figure 2. Acute exacerbation of chronic obstructive pulmonary disease (AECOPD): managment of patient hospitalized in general ward.

Medical bronchodilator therapy

Suspend any home therapy for stable COPD, prescribing:

h 8 am-2 pm-8 pm: SABA 2-3 puff with spacer and/or **SAMA** spray 2 puff with spacer

h 11 pm: LABA+ICS 2 puff with spacer

Note: In non-cooperative pt use spacer with mask. If it is impossible to administer spray with spacer and the only propellant available is the O_2, should be administered the aerosol with bronchodilator for a maximum of 6 min[3]

Corticosteroid therapy: Several international guidelines[4-6] recommend prednisone equivalent doses of 30 to 40 mg day os/iv for 7-14 days. A recent study[7] showed equal efficacy of shorter cycles (5 days *versus* 14 days). GOLD 2014[2] recommended 40 mg/die for 5 days. Other authors recommend doubled doses, especially in the early days.[8]

Establish group of exacerbation for antibiotic therapy

☐A ☐B ☐C If present purulent sputum, it is required: sputum cultivation

Antibiotic therapy (blood cultures if exist fever)**:**

Group A or **B**: ***amoxicillin/clavulanate*** fl 1.2 g x 3/die *or* **clarithromycin** fl 500 mg x 2/die *or* ***ceftriaxone*** 2 g/die *or* ***cefotaxime*** 2 g x 3/die. If intolerance or ineffectiveness: ***levofloxacin*** 500 mg/die

Group C: ***levofloxacin*** 500 mg/die ev *or* ***piperacillin/tazobactam*** 2 o 4 g x 3/die *or* ***cefepime*** fl 2 g x 2/die.

Treatment time approximately 5-10 days.

When possible, the preferred route of administration is oral; iv administration will be prescribed in cases of difficulty in swallowing, malabsorption, incompatibility with other oral therapy, lack of oral formulations (*i.e.*, some cephalosporins, piperacillin/tazobactam).

Pt with respiratory failure: carry out titration of oxygen in the following way:

Place ventimask to FiO_2 24%; if not tolerated by pt → nasal cannulas: 1 L/min (however, with nasal cannulas the determination of the FiO_2 is very inaccurate, and the patient need for closer monitoring of O_2Sat and ABG)

Place pulse oximeter: check O_2Sat every 10' and increase FIO_2 according to target: 94-98% in hypoxemic-normocapnic pt; 88-92% in pt hypoxemic-hypercapnic. Within half an hour monitor ABG (see below)

Assessment of nutritional status: **NRI** (*nutrition risk index*) _____ **INA** (*instant nutritional assessment*) _____

NRI = [1.519 x Alb + 0.417 x (current weight/weight usual) x 100] borderline: >97.5; mild malnut: 83.5-97.5; severe malnut: ≤83.5
INA: normal: Alb≥3.5 and lymphocytes ≥1500; high risk: Alb< 3.5 and total lymphocytes <1500

Assessment of fluid and electrolyte balance

- Dehydration: tongue, hand, peripheral venous turgor, hypotension, tachycardia, urinary specific weight, 24-h urine output
- Edema
- Calculated plasma osmolarity =2xNa + glucose/18 + nitrogen/2.8
- Serum creatinine, nitrogen, serum electrolytes (Na, K, Cl, Ca, Mg)
- Calculation of water deficit =TBW x (285-Osm)/Osm

[**TBW**=total body water= 60% body weight in pt M <65 years; 50% in pt F <65 years and in pt M >65 years; 45% in pt F >65 years]

Risk assessment thrombo-embolic and hemorrhagic

List the **comorbidities** and determine **therapy**

After 30 min: clinical control + ABG (if pt in O_2 therapy)

Clinical control:

Bronchodilator response adequate/effective: continue therapy

Bronchodilator response insufficient/ineffective: + theophylline/aminophylline [*bolus 6-7 mg/kg in 50 cc saline in 30';* mainten. *1 fl in 500 cc saline in 24 h*]

Verify presence/absence of signs of *respiratory effort*

ABG: Target: to stabilize PO_2 ~60-65 mmHg, $SatO_2$ ~92%, PaO_2/FIO_2>300, **without** ↑ CO_2, **without** pH <7.35

Possible cases:

PaO_2>60 with $PaCO_2$<45 and pH≥7.35→ titration perfect, continue therapy

PaO_2>60 with $PaCO_2$>45 and pH ≥7.35→ too much FIO_2?→ ↓ to FiO_2 previous, clinical recheck and repeat ABG after 1 h

PaO_2<60 with $PaCO_2$<45 and pH≥7.35→ position FIO_2 at the next level, check clinically the pt and repeat ABG after 1 h

PaO_2<60 with $PaCO_2$>45 and pH<7.35 → the pt need for mechanical ventilation: working

In the cases 2 and 3, control ABG after an hour, we will have the same possibilities from 1 to 4

CONCLUSION

Clinical-instrumental controls OK → continue therapy and clinical controls + ABG every day

If signs of respiratory effort [dyspnea, neck/head protrusion with shoulders elevat/antepuls, use resp. accessories muscles, abdom paradox breath (back abdomen during inpiration), alternate breath (chest and abdomen desynchronization during respiration), Hoover's sign (back inspir intercost spaces), RR>25/min] and/or respiratory acidosis →NIV

3^{rd}-4^{th} DAY

Clinical improvement: replace initial **SABA** and/or **SAMA** with **LABA+ICS** 2 puff x2 ± **LAMA**

Begin to decrease every 2 days corticosteroid ev→ 20 mg+10 →10 mg+10 →per os 8 mg +8 →8 mg/die →4 mg/die→ STOP

No clinical improvement: continue therapy until then set and postpone the change of therapy

At any time, if signs of respiratory effort and/or respiratory acidosis → **NIV**

DAYS LATER

Clinical improvement: if not done in 3rd-4th day, replace the initial SABA and/or SAMA

Clinical controls and ABG (pt in O_2 therapy) daily or more frequent if the situation warrants

According to clinical improvement and regression of fever, consider shift of antibiotic therapy from intravenous to oral

Educate the patient/caregiver on the use of MDIs and the management of O_2 therapy (pt in O_2 therapy)

ORIENTATION TO DISCHARGE

Write in folder, daily, signs of clinical improvement: ↓cough, ↓ dyspnea, ↓ and sputum color changes, temperature, respiratory parameters, blood tests required (kidney function, liver function, blood counts, etc.), recovery of previous skills (walking, eating, dressing, etc.).

Continue, if necessary, with the training of the patient/caregiver on the use of inhaler device and oxygen (if O_2 therapy)

After the acute phase, evaluate whether to perform spirometry + mMRC dyspnea scale and CAT for combined rating of severity or if it is more appropriate to delay it by 1-2 months

DISCHARGE

Indicate in the discharge letter, home medications prescription and verify that the patient/caregiver has well understood

Provide/renew any prescription of home O_2. Specify in the letter of discharge mode of administration and ensure that the patient/caregiver has well understood the instructions

For patients who smoke, require permanent discontinuation of smoking (if necessary with the help of questionnaires smoke)

Clearly indicate the coordinates of the next ambulatory monitoring (date, time, place), carrying out, where possible, direct booking at PC, prescribing the request on regional prescription (reducing the commitments of the patient/caregiver)

Clearly indicate the exams to be checked and, if it has not been possible to do so at the end of hospitalization, require the spirometric evaluation within 1-2 months, then returning to the combined rating of gravity

Ensure that the home management is well organized

Appendix Figure 3A. Thromboembolic and hemorrhagic risk assessment sheet.

1 - Assessment of thromboembolic risk

[Padua prediction score[9]]

Risk factor	Score	In	Date	Date	Date	Date	Out
Active cancer*	**3**						
Previous VTE**	**3**						
Reduced mobility***	**3**						
Already known thrombophilic condition****	**3**						
Recent (≤1 month) trauma and/or surgery	**2**						
Elderly age (≥70 years)	**1**						
Heart and/or respiratory failure	**1**						
Acute myocardial infarction or ischemic stroke	**1**						
Acute infection and/or rheumatic disorder	**1**						
Obesity (BMI≥30)	**1**						
Ongoing hormonal treatment	**1**						
Total score →							

**local or distant metastases and/or chemotherapy or radiotherapy in the previous 6 months*
***excluding superficial venous thrombosis*
****bedrest with bathroom privileges (either due to patient's limitations or on physicians order) for at least 3 days*
*****defects ATIII, Prot C/S, Factor V Leiden, prothrombin variant 20210, LAC/APA*

***Score <4* = LOW VTE risk**	***Score ≥4* = HIGH VTE risk**

Recommended prophylaxis

LOW risk → No prophylaxis
HIGH risk → LMWH at prophylactic doses[#] or fondaparinux[#] 2.5 mg/die

[#]If CrCl <50 reduce the doses of 30-50%; if CrCl <30 → calcium heparin by monitoring aPTT
If BMI > 30 increase the dose of 25%; if ♀<45 kg or ♂ <57 kg half the dose
If you decide to use prophylaxis, dose the PLT at baseline and every 5 days until the 15th day (every day for 5 days if heparin in 100 days earlier). Suspect heparin-induced thrombocytopenia (HIT) if platelets drop by 50% from baseline

In patient with a history of previous HIT: prophylaxis with fondaparinux (evidence C)

Appendix Figure 3B

2 - *WARNING FOR BLEEDING RISK*

Assessment of bleeding risk

Bleeding risk scores assigned to each independent factor identified with the multiple logistic regression model[10]

Bleeding risk factors	Scores
Moderate renal failure, GFR 30-59 *vs* ≥60 mL/min/m^2	1
Male vs female	1
Age, 40-84 y *vs* < 40 y	1.5
Current cancer	2
Rheumatic disease	2
Central venous catheter	2
ICU (Intensive Care Unit)/CCU (Coronary Care Unit)	2.5
Severe renal failure, GFR <30 *vs* ≥60 mL/min/m^2	2.5
Hepatic failure (INR>1.5)	2.5
Age, ≥85 y *vs* <40 y	3.5
Platelet count <50,000/mmc	4
Bleeding in 3 months before admission	4
Active gastroduodenal ulcer	4.5

Physicians should use caution in prescribing anticoagulant prophylaxis to patients with an admission bleeding risk score of ≥7.0.

Also keep in mind the FOLLOWING CONTRAINDICATIONS:

- ABSOLUTE CONTRAINDICATIONS TO HEPARIN -
Untreated congenital bleeding diathesis*: hemophilia, severe von Willebrand
Neurosurgery, ophthalmic surgery
Bleeding in progress (brain/gastrointestinal/genitourinary)
Spinal or epidural anesthesia or lumbar puncture in the previous 4 h or 12 h after administration
Therapy with anticoagulants
Thrombocytopenia <30,000/mmc
Heparin-induced thrombocytopenia (HIT)
Native valve endocarditis
- RELATIVE CONTRAINDICATIONS TO HEPARIN -
Acquired haemorrhagic diathesis*: hepatic failure with INR> 1.5 + thrombocytopenia
Metastasis/cerebral angiomas with bleeding risk as a result of morphological examinations of Level II (angio-CT or MRI)
Gastric/genitourinary/eye bleeding in the 14 days preceding
SBP>230 and/or DBP>120 mmHg

*Evidenced by: hematoma formation or spontaneous bruising, prolonged bleeding tendency after accidental or surgical wounds, hypermenorrhea without organic changes

Memento: You need an interval of 10-12 h after the last dose of LMWH and invasive maneuver, the next dose should be administered 6-8 h after surgery, in the absence of major bleeding.
If spinal anesthesia is practiced, remove the catheter 10-12 h after.

Appendix Figure 4A

CLASSIFICATION OF PATIENTS WITH STABLE COPD

mMRC (modified Medical Research Council)[11]

(the patient must choose and mark one answer)

0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on the level or walking up a slight hill
2	I walk slower than people of the same age on the level, because of breathlessness, or I have to stop for breathing when walking on my own pace on the level
3	I stop for breathing after walking about 100 meters or after a few minutes on the level
4	I am too breathless to leave the house or I am breathless when dressing or undressing

CAT (COPD ASSESSMENT TEST)[12]

(calculation of the impact of COPD on patients' lives: mark the patient's response)

								Points
I never cough	**0**	**1**	**2**	**3**	**4**	**5**	I cough all the time	
I have no phlegm (mucus) in my chest at all	**0**	**1**	**2**	**3**	**4**	**5**	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	**0**	**1**	**2**	**3**	**4**	**5**	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	**0**	**1**	**2**	**3**	**4**	**5**	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	**0**	**1**	**2**	**3**	**4**	**5**	I am very limited doing activities at home	
I am confident to leave my house despite my lung condition	**0**	**1**	**2**	**3**	**4**	**5**	I am not confident at all to leave my house because of my lung condition	
I sleep soundly	**0**	**1**	**2**	**3**	**4**	**5**	I don't sleep soundly because of my lung condition	
I have lots of energy	**0**	**1**	**2**	**3**	**4**	**5**	I have no energy at all	
							Total score	

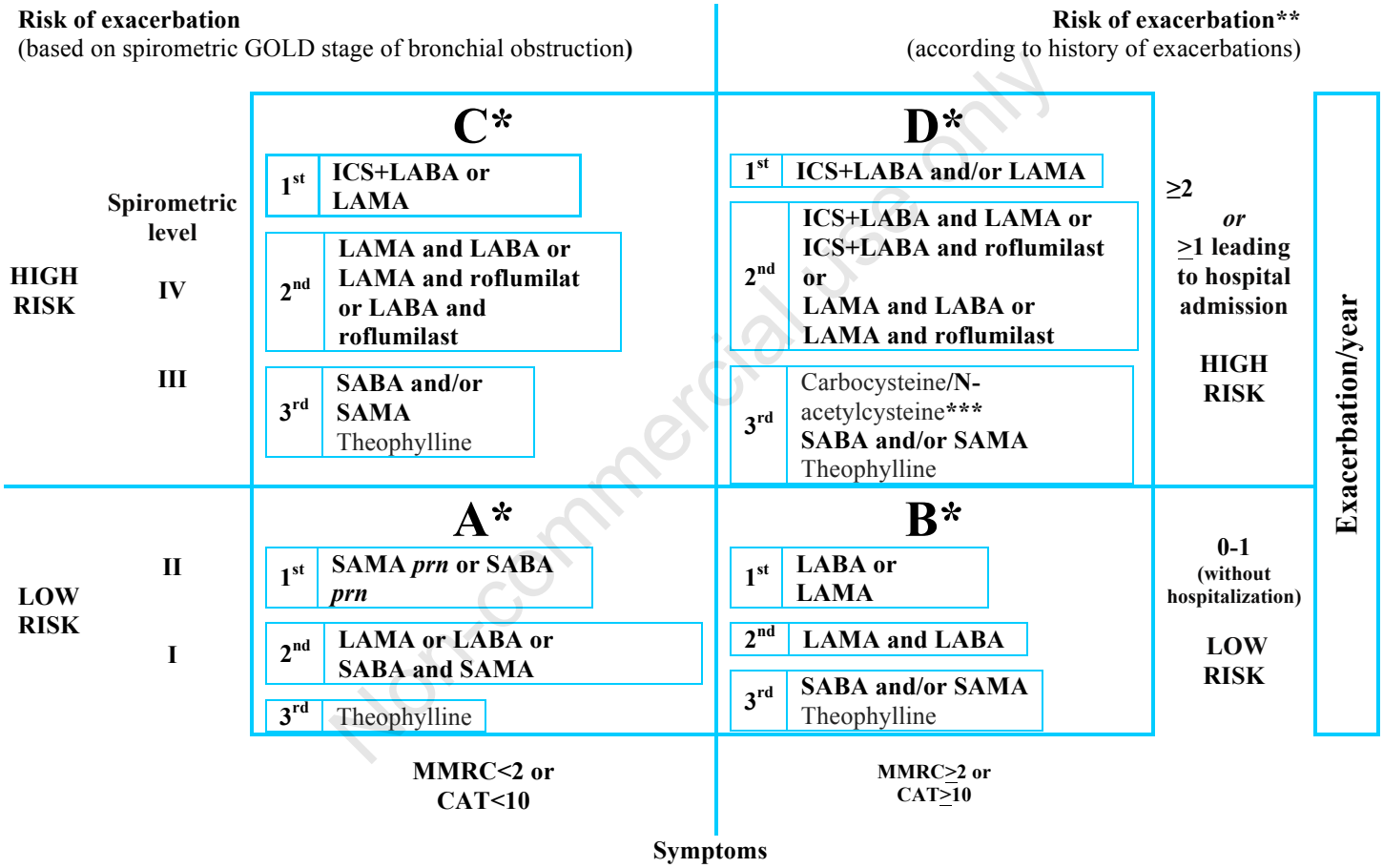
Appendix Figure 4B

Combined assessment of severity and subsequent treatment
Pharmacological management of stable COPD

[FEV1/FVC <0.7]

Spirometric level	FEV1 (%)
I	≥80
II	50-79
III	30-49
IV	<30

Combined assessment of severity and subsequent treatment
Pharmacological management of stable COPD



*1st = First choice of treatment; 2nd = alternative treatment; 3rd = other possible treatments
**One or more hospitalizations for acute exacerbations of COPD should be considered as high risk[9]
****Widespread use in pt COPD is not recommended. In those not treated with ICS therapy, carbocysteine and N-acetylcysteine appear to reduce the exacerbations*[2]

Diagnostic conclusion:

COPD GOLD spirometric level (I-II-III-IV) …….	**GOLD severity stage (A-B-C-D) ……**

Notes: The combined assessment of severity of COPD must be reported in the discharge letter.

Appendix Figure 5A

Anti-smoking questionnaires

Fagerstrom test (to 6 questions) **- Assesses the degree of nicotine dependence**

How soon after you wake up do you smoke your first cigarette?

within 5 min → 3
6 to 30 min → 2
31 to 60 min → 1
after 60 min → 0

Do you find it difficult to refrain from smoking in places where it is forbidden?

Yes → 1
No → 0

Which cigarette would you hate most to give up?

The first one in the morning → 1
Any other → 0

How many cigarettes a day do you smoke?

10 or less → 0
11 to 20 → 1
21 to 30 → 2
31 or more → 3

Do you smoke more frequently during the first hours after waking up than during the rest of the day?

Yes → 1
No → 0

Do you smoke if you are so ill that you are in bed most of the day?

Yes → 1
No → 0

Nicotine dependence score ☐☐

Interpretation of test based on numerical score:

0-2: low dependence
3-4: moderately dependent
5-6: highly dependent
7-10: very highly dependent

Appendix Figure 5B

Tests for the assessment of motivation to quit smoking

How important is it for you to stop smoking completely?

desperately important	→ 4
very important	→ 3
somewhat important	→ 2
not very important	→ 1

How determined are you to stop?

extremely determined	→ 4
very determined	→ 3
somewhat determined	→ 2
not entirely determined	→ 1

Why do you want to quit smoking? (more than one answer)

because my health is suffering	→ 5
not to get sick in the future	→ 4
because smoking is too expensive	→ 3
because prompted by other	→ 2
for the health of my family	→ 1

In your opinion, how high are the chances of being able to stop?

extremely high	→ 6
very high	→ 5
high enough	→ 4
not very high	→ 3
low	→ 2
very low	→ 1

Total score ☐☐

Interpretation of test based on numerical score:

4 to 6: low motivation: not yet seriously considered to quit smoking
7 to 10: average motivation: evaluating both the benefits of quitting and the risks of smoking
11 to 14: high motivation: there are times when you are more determined to quit
15 to 19: very high motivation: you are ready to quit smoking

Depending on the outcome of these tests, as well as on the basis of clinical evaluation of the patient, you program the type of action to be taken (and its timing) for the treatment of smoking.

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