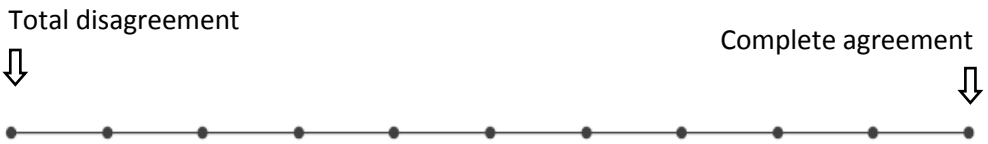
Supplementary materials

Figure S1. Delphi questionnaire

1. COPD patients with FEV1> 50%, not symptomatic

1.1 Do you think it is useful to start therapy with long-acting bronchodilators in COPD patients, in the absence of symptoms?



What is your rationale for this choice?

Do you have other comments?

2. COPD patients with FEV1>50% , symptomatic

2.1 If a symptomatic COPD patient with FEV1>50% is treated with one long-acting bronchodilator, what should be the first choice?

LABA ⇩ LAMA ⇩

What is your rationale for this choice?

Do you have other comments?

2.2 What should be the first choice when treating a symptomatic COPD patient with FEV1>50%? Single or dual bronchodilation?

LABA or LAMA ⇩ LABA/LAMA ⇩

What is your rationale for this choice?

Do you have other comments?

2.3 When a COPD patient with FEV1>50% remains symptomatic despite treatment with a single bronchodilator, a treatment with a combination of LABA/LAMA is the best choice.

Total disagreement ⇩ Complete agreement ⇩

What is your rationale for this choice?

Do you have other comments?

2.4 When a COPD patient with FEV1>50% had one exacerbation (requiring treatment with oral corticosteroids and/or antibiotics, but no hospitalization) in the previous 12 months *despite treatment with a LAMA*, a combination of LABA/LAMA is the best choice.

What is your rationale for this choice?

Do you have other comments?

2.5 When a COPD patient with FEV1>50% had one exacerbation (requiring treatment with oral corticosteroids and/or antibiotics, but no hospitalization)in the previous 12 months *despite treatment with a LABA*, a combination of LABA/LAMA is the best choice.

What is your rationale for this choice?

Do you have other comments?

2.6 When a COPD patient with FEV1>50% had one exacerbation (requiring treatment with oral corticosteroids and/or antibiotics, but no hospitalization) in the previous 12 months, an ICS should be added.

What is your rationale for this choice?

Do you have other comments?

3. COPD Patient with FEV1< 50% but not symptomatic

3.1 What should be the first choice when treating this patient?

	Not appropriate ⇩									Entirely appropriate ⇩
a) SABA/SAMA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
b) LABA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
c) LAMA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
d) LABA/ICS	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
e) LABA/LAMA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
f) LABA/LAMA/ICS	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**

What is the rationale for this choice?

Do you have other comments?

4. Symptomatic COPD patients with either FEV1< 50% and/or 2 exacerbations and/or 1 hospitalization for an exacerbation in the previous 12 months

4.1 What should be the first choice when treating a symptomatic COPD patient, with FEV1≤50%, but no exacerbations in the previous 12 months?

Not appropriate ⇩ Entirely appropriate ⇩

a) LAMA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
b) LABA/ICS	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
c) LABA/LAMA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
d) LABA/LAMA/ICS	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**

What is the rationale for this choice?

Do you have other comments?

4.2 If the same patient, with FEV1≤50%, but no exacerbations in the previous 12 months remains symptomatic *after initial treatment with a LAMA*, what should be the most appropriate treatment?

Not appropriate ⇩ Entirely appropriate ⇩

a) LABA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
b) LABA/ICS	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
c) LABA/LAMA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
d) LABA/LAMA/ICS	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**

What is the rationale for this choice?

Do you have other comments?

4.3 If the same patient, with <u>FEV1≤50%, but no exacerbations in the previous 12 months</u> remains symptomatic *<u>after initial treatment with a LABA</u>*, what should be the most appropriate treatment?

	Not appropriate ⇩									Entirely appropriate ⇩
a) LAMA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
b) LABA/ICS	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
c) LABA/LAMA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
d) LABA/LAMA/ICS	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**

What is the rationale for this choice?

Do you have other comments?

4.4 If a symptomatic COPD patient has an FEV1≤50% but only 1 exacerbation (requiring treatment with oral corticosteroids and/or antibiotics, but no hospitalization) in the previous 12 months, what should be the first choice treatment?

	Not appropriate ⇩									Entirely appropriate ⇩
e) LAMA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
f) LABA/ICS	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
g) LABA/LAMA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
h) LABA/LAMA/ICS	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**

What is the rationale for this choice?

Do you have other comments?

4.5 If a COPD patient has an FEV1≤50% and 2 exacerbations (requiring treatment with oral corticosteroids and/or antibiotics) or 1 hospitalization for an exacerbation in the previous 12 months, what should be the first choice treatment?

Not appropriate ⇩ Entirely appropriate ⇩

a) LAMA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
b) LABA/ICS	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
c) LABA/LAMA	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
d) LABA/LAMA/ICS	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**

What is the rationale for this choice?

Do you have other comments?

4.6 An ICS should always be added to the treatment if a COPD patient had 2 or more exacerbations (requiring treatment with oral corticosteroids and/or antibiotics, but no hospitalization) in the previous 12 months.

Total disagreement ⇩ Complete agreement ⇩

What is the rationale for this choice?

Do you have other comments?

4.7 An ICS should always be added to the treatment if a COPD patient had an exacerbation requiring a hospitalization in the previous 12 months.

Total disagreement ⇩ Complete agreement ⇩

What is the rationale for this choice?

Do you have other comments?

Table S1. Rationales that were within the consensus range and were given by at least two participants in the first round

1.1 Do you think it is useful to start therapy with long-acting bronchodilators in COPD patients with bronchial obstruction, in the absence of symptoms? YES/NO	
BE	- Symptoms are very often un(der) recognized/ underestimated - UPLIFT sub analysis results for GOLD II FEV1 decline
EU	- UPLIFT shows that this may have an impact on the FEV1 decline - Patients with such a low lung function will have reduced physical capacity even if not declaring symptoms
2.1 If a symptomatic COPD patient with FEV1>50% is treated with one long-acting bronchodilator, what should be the first choice?	
BE	- No evidence that one is better than the other for symptoms but LAMA better than LABA regarding exacerbations - No evidence of superiority - Depending on the patient (glaucoma? prostate?)
EU	- A variety of studies suggest that LAMAs and LABAs have similar efficacy regarding lung function and symptoms - Studies showed that LAMAs are better than LABAs regarding prevention of exacerbations
2.2 What should be the first choice when treating a symptomatic COPD patient with FEV1>50%? Single or dual bronchodilation?	
BE	- This depends on the symptoms - Follow-up and adjustment to dual if necessary - The effect of adding a second long acting bronchodilator on symptoms is modest
EU	- Single may be sufficient - After LABA or LAMA step-up is possible
2.3 When a COPD patient with FEV1>50% remains symptomatic despite treatment with a single bronchodilator, a treatment with a combination of LABA/LAMA is the best choice.	
BE	- Studies on dual bronchodilation - The additive effect of the two bronchodilators on FEV1 and dyspnea - Logical step up
EU	- Most LABA/LAMA studies showed some superiority regarding patient reported outcomes compared to single bronchodilators
2.4. When a COPD patient with FEV1>50% had one exacerbation (requiring treatment with oral corticosteroids and/or antibiotics, but no hospitalisation) in the previous 12 months *despite treatment with a LAMA*, a combination of LABA/LAMA is the best choice.	
BE	- Only one moderate exacerbation is not the sign of an uncontrolled COPD - More evidence is needed of low doses of steroids in these cases
EU	- Improving bronchodilation - There is no sufficient evidence that adding ICS to LAMA will be effective
2.5. When a COPD patient with FEV1>50% had one exacerbation (requiring treatment with oral corticosteroids and/or antibiotics, but no hospitalisation)in the previous 12 months *despite treatment with a LABA*, a combination of LABA/LAMA is the best choice.	
BE	- Dual bronchodilation will be more effective in preventing exacerbations
EU	/
2.6 When a COPD patient with FEV1>50% had one exacerbation (requiring treatment with oral corticosteroids and/or antibiotics, but no hospitalisation) in the previous 12 months, an ICS should be	

added.	
BE	- A frequent exacerbator is >1/year - There is evidence of additive effect of ICS in patients with frequent exacerbations - Only if suspicious of asthma associated
EU	/
3.1. COPD patients with FEV1> 50%, not symptomatic. What should be the first choice when treating this patient?	
BE	- The risk of exacerbations is high in this group, so optimizing bronchodilation can be important in the prevention of these exacerbations - LAMA can reduce the risk of exacerbations, which is higher in this group of patients - Therapeutic test on dyspnea perception
EU	- This (small) group has never been analyzed - just an extrapolation of existing data
4.1. What should be the first choice when treating a symptomatic COPD patient, with FEV1≤50%, but no exacerbations in the previous 12 months?	
BE	- Maximal bronchodilation - Better symptom control - The goal is to relieve dyspnoea in this setting. No ICS
EU	- Maximal bronchodilation should be ensured - LABA/LAMA combination has more impact on the symptoms - ICS would not be useful if no exacerbations
4.2. If the same patient, with FEV1≤50%, but no exacerbations in the previous 12 months remains symptomatic *after initial treatment with a LAMA*, what should be the most appropriate treatment?	
BE	- Step up - ICS are not indicated without exacerbations - Maximal bronchodilation - Adverse events of corticoids
EU	- Maximal bronchodilation should be ensured
4.3. If the same patient, with FEV1≤50%, but no exacerbations in the previous 12 months remains symptomatic *after initial treatment with a LABA*, what should be the most appropriate treatment?	
BE	- Step up - Maximal bronchodilation - Adverse events of corticoids concerning pneumonias, no indication if no frequent exacerbations
EU	- Symptom control may be improved by LABA/LAMA
4.4 If a symptomatic COPD patient has an FEV1≤50% but only 1 exacerbation (requiring treatment with oral corticosteroids and/or antibiotics, but no hospitalisation) in the previous 12 months, what should be the first choice treatment?	
BE	- Only one exacerbation and so no ICS are indicated
EU	/
4.5 If a COPD patient has an FEV1≤50% and 2 exacerbations (requiring treatment with oral corticosteroids and/or antibiotics) or 1 hospitalisation for an exacerbation in the previous 12 months, what should be the first choice?	
BE	- Additive effect of ICS in COPD patients with frequent exacerbations
EU	- Basic bronchodilator therapy (LABA/LAMA) + ICS to reduce number of exacerbations
4.6. An ICS should always be added to the treatment if a COPD patient had 2 or more exacerbations (requiring treatment with oral corticosteroids and/or antibiotics, but no hospitalisation) in the previous 12 months.	

BE	- Answer depends on the potential risk of adverse events - Because of Studies like "Wisdom ", the absolute need of ICS is questioned
EU	- Answer depends on individual patient - Yes if the patient is already on LABA or LAMA (at least awaiting FLAME) - ICS has an essential role for prevention after BDs therapy
4.7. An ICS should always be added to the treatment if a COPD patient had an exacerbation requiring a hospitalisation in the previous 12 months.	
BE	- Not always true anymore, depends on the patient - ICS are required in frequent exacerbations but not for one severe exacerbation alone
EU	- There is no sufficient evidence that adding ICS to BD will be always effective in preventing exacerbations, requiring a hospitalization