REVIEWERS	AUTHOR RESPONSE
General Comments to the Author:	
Reviewer #3- Introduction: inclusion of CanCOLD data further emphasizes the importance of early diagnosis and prompt intervention.	Positive comment: No need for response
Figure 1: • Has utility in incorporating pharmacotherapy for optimizing stable COPD and prevention of AECOPD. This will improve ease of knowledge translation	Positive comment: No need for response
• Promotes personalized therapy for the COPD patient phenotypes	Positive comment: No need for response
Figure 2: • LVR (bronchoscopic and surgical interventions) are discussed in the introduction but not included in the continuum. Rationale?	LVR has been added as recommended.
• 'Assess for Features of Asthma' appear to have a fair amount of real estate' on the Comprehensive Management figure. In light of this Figure 1 (choice 1A) appears to complement this most; however, we do prefer Figure 1 (chose 1-A1) for COPD Management and Figure 1 (choice 1B) as a stand-alone figure.	The choice of the figure will be determined from a vote including the co-authors and the reviewers.
ACOS: document brings clarity to the health care providers on ACO (diagnosis and treatment).	Positive comment: No need for response
Clearly written, well referenced. Will be helpful in developing knowledge translation initiatives for health care professionals.	Positive comment: No need for response.
Reviewer #4 – Wording seems to be confusing sentences throughout. Need to see more ACO data? IMPACT trial results? The recommendations in Box 1, 2 and 3 were very well done.	The paper explains the literature research and review process; all papers were reviewed or opinion papers except 2 papers that were original research. The lack of data on ACO justifies why we proceeded with a Delphi Survey of almost 100 Canadian respirologists. Section PICO 3 describes it in much detail. The IMPACT trial is not published yet. The COPD position paper will be reviewed every three years in keeping with the CTS Living Guideline concept. However, given the new IMPACT findings an update is planned for April 2018 and to be presented at Canadian Respiratory Conference in Vancouver.
Reviewer #5 - Important update for intended audience. Clearly outlines literature summary and updated evidence based recommendations regarding the pharmacologic management of COPD in relation to the three questions.	Positive comment: No need for response.

Boxes 1-3 succinctly capture and outline the key messages for the three PICO questions.	
Major Comments	
Reviewer #5 – Although this position statement focuses on pharmacologic management the importance of smoking cessation could be strengthened on page 5 and possibly considered for ACO section.	More has been added to strengthen the topic of smoking cessation.
Reviewer #2 - The recommendation of SABD for patients with persistent symptoms, even if they are mild (MRC 2, CAT ˂10) is questionable. In fact, recommendation 1 (page 9) and this part of Figure 1 seem contradictory.	Fig 2 proposes SABD as PRN therapy (see change); it includes the possibility of prescribing LABD therapy in this group of patients when symptoms are present.
Reviewer #1 – Page 9. Recommendation 4. It describes step up from LABA to LABA/LAMA. Why only from LABA and not from either LABA or LAMA monotherapy? And why for persistently poor health status and not for persistent dyspnea or persistent exercise intolerance?	Recommendation 4 is based on existing data. Recommendations 2 and 3 are addressing the outcomes of dyspnea and exercise tolerance.
Reviewer #2 – Page 9, question 6 addresses 2 different situations: The first one is stepping down from triple therapy to dual therapy (ICS withdrawal) if persistence of symptoms. This can complement recommendation 2, as the indication of ICS for symptom relief in patients without an asthma component is not clear. However, the second situation refers to stepping down from dual therapy to one bronchodilator if symptoms persist. Taking into consideration that many COPD patients remain symptomatic despite optimal treatment, why recommend stepping down? Besides, this also contradicts question 5, which can be confusing (if a patient on LABA + LAMA still has symptoms, question 5 consider to add ICS while 6 consider stepping down to one LABD)	With respect to the outcomes dyspnea, exercise tolerance and HRQL, there is insufficient data for triple or dual step down. Regarding step down, we are not referring to persistence of symptoms but "no improvement" in response to the therapy.
Reviewer #1 Page 10. Key message 2. I would be more careful in this recommendation (despite the sentence "may be considered"), taking into account that the indication of ICS is neither symptom control nor improving exercise tolerance. The main indication of ICS is exacerbation prevention.	As suggested, we have added « the main indication is for exacerbation prevention » to be even more careful in making this recommendation;

Reviewer #1- Page 10. Key message 4. I would indicate that this recommendation refers to their efficacy in symptoms and exercise tolerance, because some of them can be useful for exacerbations prevention.	As suggested, we have added that it is for symptom, exercise tolerance, physical activity and health status.
Reviewer #2 – Page 11. The definition of what is considered frequent or severe exacerbations should be added to the text in addition to the Figures. In relation to this previous comment, two or more episodes during 2 years seem too wide. To consider a patient who has only 1 AECOPD per year as having frequent exacerbations is debatable.	
Reviewer #2 – Page 12, questions 1 to 4 are not reflected in the figures, where the treatment of choice for patients with AECOPD is start with a LABA/LAMA.	Agree these are not in the Box key messages and/or fig. The box and the fig don't incorporate all the recommendations but the most practical and important key messages.
Reviewer #1 - Page 12. Recommendation 10. Just a comment, I found very risky the recommendation of adding a macrolide in a patient with a history of ONE or more MODERATE to severe exacerbation despite inhaled therapy. Really a patient with only one moderate exacerbation deserves azithromycin continuously for a year (at least)? I am more in favour of the inclusion criteria of the Uzun paper in Lancet RM in which patients where included if they had at least 3 exacerbations while on optimal inhaled therapy. In fact, in page 19 it reads that "patients should be selected carefully (for macrolide therapy) considering the risk of bacterial resistance and side effects"	Recommendation is based on the evidence. However, we agree with the reviewer that we will not use azithromycin unless exacerbations are more recurrent. As suggested, we have made changes adding in Box 2- key message 4 « ≥3 ». We already have ref: Uzun (ref 137).
Reviewer #1- Page 13. Recommendation 12. Why given orally or intravenously? There is an abuse of the IV route with no more clinical benefits but increased side effects (see evaluation in recent ERS/ATS guidelines ERJ 2017). I would suggest to say "systemic corticosteroids" only, and even indicate that oral route is preferred whenever possible. Same for Key messages in page 14.	As suggested, we have kept the term systemic for Recommendation 12 and in Box 2- key message 5.
Reviewer #2 – The recommendation in Key message 2 (page 14) is clear. However, the recommendations or their order in page 12 is confusing. For example, section 4	Recommendations have no order. The recommendations are based on a complete lit review. The Box- key messages are what is recommended as being more practical.

recommends to step up to LABA+ LAMA from LABD, while 7 recommends triple therapy.	
Reviewer #2 – I would suggest moving theophylline to the end of the recommendations (page 12) as the evidence is weaker and it is not even included in the figures.	As suggested, theophylline has been removed to the end of the oral medication choice.
Reviewer #2 – Section 2 (page 14) and key message (page 13) do not seem appropriate here. This PICO question addresses maintenance treatment in stable patients to prevent AECOPD, while this section discusses treatment for an acute exacerbation. On the other hand, if the authors want to provide recommendations for AECOPD to prevent hospital admissions, this seems insufficient.	We removed recommendation 12. In Box 2- key messages, we kept the recommendation of not using systemic corticosteroids for maintenance therapy.
Reviewer #3- Page 14 PICO 2 Box 2 – Key messages: 3.3) key message: not sure if this brings enough clarity to the provider as to when and why triple therapy could be used in stable COPD experiencing exacerbations.	We have now separated the step up i) mono to duo therapy and ii) duo therapy to triple therapy. For duo to triple therapy, it is now Key message 4): In patients with stable COPD experiencing exacerbations despite the use of LAMA and LABA dual therapy, treatment *"step up"* with LAMA plus ICS/LABA triple therapy can be considered (unknown if triple therapy superior to LAMA plus LABA dual therapy: ongoing trials).
Reviewer #3 – Page 17 – PICO 3 Box 3 – Key messages: 2) of the three diagnostic criteria i. and iii. Appear redundant as spirometry is required for the diagnosis of COPD. What was the intention of repeating spirometry criteria (iii.)?	We have removed "in keeping with COPD". Because this is the way the questions were asked in the Delphi Survey, we have kept the rest of the information accepting that there will be some repetition.
Reviewer #1 – Figures: I prefer figure 1 (choice 1-A2). I think that inclusion of FEV1 is confusing. Does it mean that all criteria should be met? Symptoms plus FEV1? I would rather leave CAT and MRC alone. On the other hand, in mild COPD the first option as SABD prn is controversial. Would it be acceptable for a patient with MRC = 2? This is what is recommended here. In infrequent exacerbators, what does it mean the intermittent arrow from LAMA/LABA to triple? Is it suggested or not? Or only in some cases? Or only with caution? This is not clear.	This has been considered and changes made to fig 1 Fig 2 proposes SABD as PRN therapy (see changes); it includes the possibility of prescribing LABD therapy in this group of patients when symptoms are present. Additional information provided in the Fig legend

In frequent exacerbators, the arrow from triple to PDE4 is (in my opinion) inadequate, because this is only valid for patients with chronic bronchitis, which are only a subgroup of exacerbators. Similarly, it has been criticized that in GOLD D before PDE4, macrolides or mucolytics, all patients should be on triple, which is not supported by any evidence. The same here, it appears that before considering any oral therapy all patients should be on triple. There is still another issue with Fig 1 (choice 1-A2). What about patients with MRC 1-2 but frequent exacerbations? They exist, in fact in the NEJM paper even patients without COPD had respiratory exacerbations. Should they be on SABD prn (or LAMA or LABA only)? The figure is simple and easy, but inaccurate in these aspects. Probably a new approach to a decision algorithm including phenotypes could solve some of these issues.	Additional information provided in the Fig legend
Reviewer #2 – Figure 1: It seems that PDE4 is the oral treatment of choice and preferred over macrolides.	Because this is also aiming at a GP audience, we want to make sure that macrolide will not be used in every patient on triple therapy still having exacerbations
Reviewer #2 – Based on how Figure 1 is expressed, a mild COPD patient (CAT <10, MRC 1-2, (FEV1 >80%) but with frequent exacerbations (including hospital admissions) would be included in the left category and could be treated only with SABD.	Additional information provided in the Fig legend
Other Suggestions: Reviewer #1- Abstract: last line. "useful for clinician experts..", and what about the non-experts? In my opinion guidelines are even more useful for non-experts. Experts do not read guidelines, they write them. The same term appears in page 6 (Methodology)	Clinician experts changed for clinicians
Reviewer #1- Intro. The reference 1 is cited in the text after ref. 4.	We have made the correction
Reviewer #1- Page 3. It reads: "Improve assessment of dyspnea and activity limitation in stable COPD using evidence-based treatment algorithms". It does not make not much sense to me. Can we improve the assessment of dyspnea and activity by using treatment algorithms? Is it possible? How? I would say exactly the opposite that we can improve the treatment algorithms by incorporating accurate assessment of dyspnea and activity limitation.	Changes have been made for « we can improve the treatment algorithms by incorporating accurate assessment of dyspnea and activity limitation. »

Reviewer #1- Page 5. References in parenthesis should be moved to the reference list.	All refs have been reviewed and those not included, have now been added to the ref list
Reviewer #5 – On page 6 under Target Users: add in Certified Respiratory Educators (CRE) to list or replace COPD Educators with Certified Respiratory Educators	As suggested, we have added Certified Respiratory Educators (CRE)
Reviewer #1- Page 9. Please review numbers of references in the text. In recommendation 1, numbers jump from 43 to 60-71.	We have reviewed the ref numbers: …numbers jump from 43 to 60-71 ?
Reviewer #1- Page 31. Reference list. For the Spanish guideline I suggest to replace ref. 176 for the current document: Miravitlles M, Soler-Cataluña JJ, Calle M, et al Spanish COPD guidelines (GesEPOC) 2017. Pharmacological treatment of stable chronic obstructive pulmonary disease. Arch Bronconeumol 2017; 53: 324-335.	Ref list, ref 176 replaced for Spanish guideline by new ref: Miravitlles, Sloer-Cataluna JJ, Calle M et al Spanish COPD guidelines (GesEPOC) 2017. Pharmacological treatment of stable chronic obstructive pulmonary disease. Arch Bronconeumol 2017; 53: 324-335.
Reviewer # 2 – Figure 2. This figure suggests progression on treatment, but LTOT and NIV have different indications than oral therapies, they could be placed at the same level.	Changes made as suggested
Reviewer #3- CAT and MRC: will references/hyperlinks/figures be included for these tools?	Changes made as suggested
Reviewer # 2 – Section 1: page 8 says improving symptom, page 10 says improving symptom burden	Changes made page 8 improving symptoms and page 10 corrected for improving symptom.