

APPENDIX 1

Results of the literature review

Potential relevant self-management behaviours identified from literature are presented in table 1-5 and substantiated by summaries of evidence. When evidence was available from COPD guidelines/statements, no additional (systematic) reviews or longitudinal studies are presented. By a lack of evidence from guidelines, available (systematic) reviews are presented. Longitudinal studies are presented when (systematic) reviews were lacking. Exceptions were made when relevant longitudinal studies were published after reviews or when relevant (systematic) reviews were not listed in guidelines.

Table 1 Phase 1: Stable phase (low risk)

Self-management behavior	Guideline/statement	(Systematic) Review	Longitudinal study	Summary of evidence regarding behavior
Adherence to pharmacotherapy (LABA/LAMA and/or ICS)	<ul style="list-style-type: none"> GOLD, 2016¹ Criner, 2015² 	NA	NA	Treatment with long-acting inhaled bronchodilators (long-acting β_2 -agonist <i>LABA</i> , long-acting muscarinic antagonist <i>LAMA</i> , or a combination of), with or without inhaled corticosteroids <i>ICS</i> , are therapies that reduce the number of exacerbations and hospitalizations. ^{1,2}
Influenza vaccination uptake	<ul style="list-style-type: none"> GOLD, 2016¹ Criner, 2015² 	NA	NA	Influenza vaccines is a therapy that reduces the number of exacerbations and hospitalizations and is recommended to prevent acute exacerbations. ^{1,2}
Daily physical activity	<ul style="list-style-type: none"> GOLD, 2016¹ Spruit, 2013³ 	NA	NA	<ul style="list-style-type: none"> Patients should be encouraged to maintain physical activity to prevent COPD exacerbations.¹ Physical activity levels predict important outcomes in COPD. Lower physical activity levels are associated with a higher risk of an exacerbation-related hospitalization and re-hospitalizations.³
Avoiding viral or bacterial stimuli (hand hygiene and/or avoiding contact with people with a cold)	NA	NA	<ul style="list-style-type: none"> Gandhi, 2012⁴ Donaldson, 2012⁵ Jenkins, 2012⁶ Rabe, 2013⁷ 	<ul style="list-style-type: none"> The cohort study of Ghandi (2012) shows that Human rhinoviruses (HRV) can be detected in a large proportion of acute exacerbations of COPD. Contact with school aged children is considered to be a risk factor for both infection and symptomatic HRV illness. This study states that good hand hygiene, and avoidance of direct contact with ill children, may avoid HRV related illness in COPD patients.⁴ The cohort study of Donaldson (2012) showed that patients experienced 1,052 exacerbations in the cold season compared to 676 in the warm season: an excess of 56.6%. This study concludes that exacerbation severity is worse in the winter and recovery times are longer, which may

				<p>be influenced by increased prevalence of viral infections during winter.⁵</p> <ul style="list-style-type: none"> • The RCT of Jenkins (2012) showed that exacerbations in the northern and southern regions of the world almost had a two-fold increase in the winter months. This study states that factors potentially contributing to this include: increased exposure to viral infections, increased host susceptibility, greater time spent indoors, reduced physical activity and temperature-related reduction in lung function. These patterns also relate to lower weekly mean temperatures, influenza activity and personal cold exposure factors.⁶ • The study of Rabe (2013), based on POET-COPD trial, shows as well that mean monthly exacerbation rates during winter were higher than during summer. This study highlights a marked impact of season on exacerbation outcomes, antibiotic treatment, timing of second exacerbations, and all-cause mortality.⁷
<p>Managing exposure to air quality (air pollution/temperature/humidity)*</p>	NA	<ul style="list-style-type: none"> • Song, 2014⁸ • Hansel, 2015⁹ • Ni, 2015¹⁰ 	NA	<ul style="list-style-type: none"> • The systematic review of Song (2014) focused on the effect of outdoor air pollution on COPD in China, United States and European Union. Outdoor air pollution contributes to the increased burden of COPD. Increase of air pollution was significantly associated with death and exacerbations. This study states that controlling air pollution will have substantial benefit to COPD morbidity and mortality.⁸ • The review of Hansel (2015) focused on both air pollution and temperature in COPD. <p>Air pollution: Several studies relate outdoor air pollution to increased risk of COPD exacerbations. The APHEA project (data from 6 European cities) found increased risk of COPD hospital admissions with several air pollutants.</p> <p>Hot temperature: A study in New York City found an increased risk of 7,6% of COPD hospitalization for every 1°C increase above a threshold temperature of 29°C.</p> <p>Humid air: Studies in asthma suggest that breathing hot humid air may result in bronchoconstriction that is mediated via cholinergic pathways.</p> <p>Cold temperature: Studies demonstrated an impact of cold temperatures on lung function and risk of exacerbations among COPD patients. A large study in Taiwan</p>

				<p>detected a 0.8% increase in COPD exacerbations for every 1°C decrease in mean daily temperature.⁹</p> <ul style="list-style-type: none"> The review of Ni (2015) focused on recent studies of the role of fine Particulate Matter (PM) in acute exacerbations of COPD (AECOPD). Fine PM leads to AECOPD via inflammation, oxidative stress, immune dysfunction, and altered airway epithelial structure and microbiome. This study shows that reducing fine PM levels is a suitable approach to lower AECOPD incidence and reduce COPD progression.¹⁰
Quitting smoking or cutting down smoking	<ul style="list-style-type: none"> GOLD, 2016¹ Criner, 2015² 	NA	NA	<p>Smoking cessation reduces the number of exacerbations and hospitalizations.¹ Smoking cessation counselling and treatment using best practices is advised to prevent exacerbations. Although, the evidence for smoking cessation in the prevention of acute exacerbations of COPD is low, Criner et al (2015) state that evidence supports smoking cessation for many reasons.²</p>

Notes: Italic indicates the self-management behaviours that are considered to be relevant in more than one phase and therefore return in several phases.

*Self-management behaviour added based on expert opinion in face validity round. **Abbreviations:** LABA, long-acting β 2-agonist; LAMA, long-acting muscarinic antagonist; ICS, inhaled corticosteroids; NA, not applicable.

Table 2 Phase 2: Mild deterioration of symptoms phase

Self-management behavior	Guideline/ statement	(Systematic) Review	Longitudinal study	Summary of evidence regarding behavior
Early detection of symptom deterioration*	NA	NA	Wilkinson, 2004 ¹¹	Recognition of exacerbation symptoms and prompt treatment is a required self-management skill to prevent exacerbations as it is associated with faster recovery, lower risk for hospitalization and increased quality of life. ¹¹
<i>Correct increase of short-acting bronchodilators (SABA)</i>	<ul style="list-style-type: none"> • GOLD, 2016¹ • Criner, 2015² 	NA	NA	<ul style="list-style-type: none"> • SABA (with or without short-acting anticholinergics) are usually the preferred bronchodilators for treatment of exacerbations (although this is not based on RCT's).¹ • In patients with moderate to severe COPD, the guideline of Criner et al (2015) suggests the use of short-acting bronchodilators (short-acting muscarinic antagonist plus short-acting b2 - agonist) to prevent acute moderate exacerbations of COPD.²
<i>Performing breathing exercises (i.e. dyspnea regulation and/or mucus clearance techniques)</i>	NA	<ul style="list-style-type: none"> • Facchiano, 2011¹² • Hill, 2010¹³ • Aaron, 2014¹⁴ 	NA	<ul style="list-style-type: none"> • The literature review of Facchiano (2011) concluded that regularly practiced pursed lip breathing is an effective self-management strategy for individuals with COPD to improve their dyspnea.¹² • Both the systematic review of Hill (2010) and the review of Aaron (2014) provided no evidence that breathing exercises improves lung function or symptoms, or reduces admission to hospital, length of hospital stay or exacerbation rates.^{13,14}
<i>Performing energy conservation techniques (prioritizing activities /managing energy conservation for physical activity)</i>	NA	<ul style="list-style-type: none"> • Bourbeau, 2007^{15**} • Disler, 2012¹⁶ 	NA	<ul style="list-style-type: none"> • The article of Bourbeau (2007) concludes that energy conservation is important for COPD patients. The self-management skills needed from the patient is to prioritize activities, plan schedules and pace yourself.¹⁵ • According to Disler (2012) pacing physical activity has a positive impact on patients' ability to physically self-manage their COPD, as completing physical activity at one's own speed enables patients to conserve energy and achieve physical goals while avoiding exertional dyspnea and the emotional distress that comes with breathlessness.¹⁶

Notes: *Italic*: indicates the self-management behaviours that are considered to be relevant in more than one phase and therefore return in several phases.

*Self-management behaviour added based on expert opinion in face validity round.** Article included based on relevance, no (systematic) review. **Abbreviation:** NA, not applicable.

Table 3 Phase 3: Exacerbation (including onset)

Self-management behavior	Guideline/statement	(Systematic) Review	Longitudinal study	Summary of evidence regarding behavior
Early detection of an exacerbation	NA	NA	<ul style="list-style-type: none"> • Trappenburg, 2011¹⁷ • Wilkinson, 2004¹¹ 	The RCT of Trappenburg (2011) and the cohort study of Wilkinson (2004) underlined the importance of improving self-management skills to enhance early detection and to take early and appropriate actions by patients in exacerbation episodes. Recognition of exacerbation symptoms and prompt treatment was associated with accelerated recovery, lower risk for hospitalization, increased quality of life and lesser impact on health status. ^{11,17}
Prompt treatment with a course of corticosteroids and/or antibiotics (Contacting health care provider)	GOLD, 2016 ¹	NA	NA	Systemic corticosteroids shorten recovery times of exacerbations, improve lung function (FEV1) and arterial hypoxemia. In addition, reduces the risk of early relapse. Use of antibiotics remain controversial. There is evidence for antibiotic use in case of clinical signs of bacterial infection (e.g. increased sputum purulence). Advice of GOLD report is to subscribe antibiotics based on symptoms or if mechanic ventilation is required. In addition, prompt treatment is vital to reduce the burden of COPD. ¹
Prompt treatment with a course of corticosteroids and/or antibiotics (Self-treatment)	NA	NA	Zwerink, 2016 ¹⁸	The study of Zwerink (2016) concludes that self-treatment of exacerbations is beneficial in COPD patients without significant comorbidities because it reduces exacerbation duration, exacerbation severity and health-care utilization leading to considerable cost savings. ¹⁸
Manage stress and anxiety (by using relaxation techniques)	NA	Hurst & Wedzicha, 2009 ¹⁹	Eisner, 2010 ²⁰	<ul style="list-style-type: none"> • Depression and anxiety are common in COPD, and likely to affect symptom perception and therefore exacerbation presentation. It is important to detect and treat comorbid psychological conditions, though a specific effect on exacerbation reduction has not been documented.¹⁹ • The cohort study of Eisner (2010) showed that in patients with COPD, anxiety was related to poorer health outcomes including worse submaximal exercise performance and a greater risk of self-reported functional limitations. COPD patients with anxiety had a higher longitudinal risk of COPD exacerbation. This study states that further research is needed to determine whether systematic screening and treatment of anxiety in COPD will improve health outcomes and prevent functional decline and disability.²⁰

Abbreviation: NA, not applicable.

Table 4 Phase 4: Recovery

Self-management behavior	Guideline/ statement	(Systematic) Review	Longitudinal study	Summary of evidence regarding behavior
Completing treatment of antibiotics and/or corticosteroids*	GOLD, 2016 ¹	NA	NA	The recommended length of antibiotic therapy is usually 5-10 days according to the GOLD guideline. ¹
Manage stress and anxiety (concerning current event)	NA	<ul style="list-style-type: none"> Harrison, 2014²¹ Hurst & Wedzicha, 2009¹⁹ 	NA	<ul style="list-style-type: none"> The review of Harrison (2014) suggested that psychological assessment should be routinely conducted as part of patient management, since exacerbations have a profound emotional impact on patients. Although symptoms of anxiety and depression are common in COPD patients, patients rarely present with psychological symptoms severe enough to warrant a clinical diagnosis.²¹ Depression and anxiety are common in COPD, and likely to affect symptom perception and therefore exacerbation presentation. It is important to detect and treat comorbid psychological conditions, though a specific effect on exacerbation reduction has not been documented.¹⁹
Adjusted exercise- and resistance training	<ul style="list-style-type: none"> GOLD, 2016¹ Spruit, 2013³ 	NA	NA	<ul style="list-style-type: none"> Lack of routine physical activity was found to be predictive of readmission in a hospital.¹ Physical inactivity after AECOPD is associated with readmission with subsequent exacerbation.³

Notes: Italic: indicates the self-management behaviours that are considered to be relevant in more than one phase and therefore return in several phases. *Self-management behaviour added based on expert opinion in face validity round. **Abbreviation:** NA, not applicable.

Table 5 Phase 5: Stable phase (at risk)

Self-management behavior	Guideline/statement	(Systematic) Review	Longitudinal study	Summary of evidence regarding behavior
Increased awareness for recurring exacerbation	NA	Hurst & Wedzicha, 2009 ¹⁹	NA	It is now recognized that exacerbations are not random events, but rather cluster together in time such that in the period immediately following a first exacerbation there is increased risk of a second. ¹⁹ This review refers to a study of Hurst et al (2009) that shows that exacerbations cluster in time and that there is a high risk period for recurrent exacerbations in the 8-week period after an initial exacerbation. ²²
Early (re)start of pulmonary rehabilitation*	Criner, 2015 ²	<ul style="list-style-type: none"> Spruit, 2015²³ Puhan, 2011²⁴ 	NA	<ul style="list-style-type: none"> In patients with moderate, severe, or very severe COPD who experienced a recent exacerbation (i.e., < 4 weeks) pulmonary rehabilitation is recommended to prevent acute exacerbations of COPD.² The review of Spruit (2015) found that although pulmonary rehabilitation has no direct effect on the physiologic derangements in lung function, it provides the greatest improvements in dyspnea, exercise tolerance, and health-related quality of life of any intervention available for patients with chronic respiratory disease. It also decreases subsequent healthcare use, especially when provided following an exacerbation of COPD.²³ A review of Puhan (2011) on the evidence from nine trials suggests that pulmonary rehabilitation is effective in COPD patients after acute exacerbations to reduce hospital admissions and mortality and improves quality of life.²⁴

Notes: *Self-management behaviour added based on expert opinion in face validity round. **Abbreviation:** NA, not applicable.

References

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APPENDIX 2

Topic list face validity round

Reflection on conceptual model (without potential relevant self-management behaviors)
<ul style="list-style-type: none">○ Do you recognize this pattern in the COPD course and subdivision in phases?○ For each phase:<ul style="list-style-type: none">▪ What are relevant behaviors to reduce the impact of exacerbations in your opinion (for each phase of the conceptual model)?▪ What is the association between these behaviors and reduction of impact of exacerbations?▪ Which behaviors are most important to reduce the impact of exacerbations in your opinion?
Reflection on conceptual model with potential relevant self-management behaviors
<ul style="list-style-type: none">○ Do you recognize these self-management behaviors as being relevant to reduce the impact of exacerbations (for each phase of the conceptual model)?○ Which behaviors are most important in your opinion (to reduce the impact of exacerbations)?○ Are there any self-management behaviors missing in your opinion?

APPENDIX 3

Example question Delphi survey 1

2. Influenza vaccination uptake

	Strongly disagree				Uncertain or equivocal				Strongly agree
	1	2	3	4	5	6	7	8	9
Influenza vaccination is relevant to prevent the occurrence of exacerbations and/or reduce exacerbation frequency.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
There is substantial room for improvement in influenza vaccination uptake given current vaccination rates in COPD patients.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I am confident that influencing influenza vaccination uptake is feasible*.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* Feasible: Potentially successful by balancing efforts/barriers versus benefits.

Example question Delphi survey 2

2) Performing breathing exercises (i.e. dyspnea regulation and/or mucus clearance techniques)

Statement 1: Breathing exercises are relevant to reduce symptoms and/or prevent further deterioration.

Panel feedback:

'I am unimpressed by strength of evidence'

'Little is known about the individual need for breathing exercises. It is certainly not for all patients'

'Whereas the use of breathing exercises will lead to symptom relieve, it will not (directly) influence further deterioration of the exacerbation.'

Group score round 1:

Median = 5.5 / IQR = 2.25



Please rate your level of agreement on the statement:

Strongly disagree				Uncertain				Strongly agree
1	2	3	4	5	6	7	8	9
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

If your score is other than 5 or 6, could you explain why?

Specification of self-management behaviors assessed in Delphi rounds

- Adherence (fixed dose & proper technique) to pharmacotherapy (Long-acting bronchodilators LABA/LAMA and/or inhaled corticosteroids ICS)
- Influenza vaccination uptake
- Daily physical activity
- Avoiding viral or bacterial stimuli (hand hygiene and/or avoiding contact with people with a cold)
- Managing exposure to air quality (air pollution/temperature/humidity)
- Quitting smoking or cutting down smoking
- Early detection of symptom deterioration
- Correct increase of short-acting bronchodilators (SABA)
- Performing breathing exercises (e.g. dyspnea regulation and/or mucus clearance techniques)
- Performing energy conservation techniques (e.g. prioritizing activities and managing energy conservation for physical activity)
- Early detection of an exacerbation
- Prompt treatment with a course of corticosteroids and/or antibiotics
 - *Self-treatment*
 - *Contact with a healthcare provider for treatment*
- Manage stress and anxiety (by using relaxation techniques)
- Completing treatment of antibiotics and/or corticosteroids
- Manage stress and anxiety (concerning current event)
- Adjusted exercise- and resistance training
- Increased awareness for a recurrent exacerbation
- Early (re)start of pulmonary rehabilitation
- New behavior that was added after round 1: Managing exposure to indoor air quality