



Breathlessness despite optimal pathophysiological treatment: on the relevance of being chronic

Capucine Morélot-Panzini, Dan Adler, Bernard Aguilaniu, Etienne Allard, Nathalie Bautin, Marc Beaumont, François-Xavier Blanc, Cécile Chenivesse, Laurence Dangers, Christophe Delclaux, et al.

► To cite this version:

Capucine Morélot-Panzini, Dan Adler, Bernard Aguilaniu, Etienne Allard, Nathalie Bautin, et al.. Breathlessness despite optimal pathophysiological treatment: on the relevance of being chronic. European Respiratory Journal, 2017, 50 (3), pp.1701159. 10.1183/13993003.01159-2017 . hal-04008553

HAL Id: hal-04008553

<https://hal.science/hal-04008553>

Submitted on 8 Mar 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Breathlessness despite optimal pathophysiological treatment: on the relevance or not of being chronic.

Journal:	<i>European Respiratory Journal</i>
Manuscript ID	ERJ-01159-2017
Manuscript Type:	Correspondence
Date Submitted by the Author:	09-Jun-2017
Complete List of Authors:	<p>Morelot-Panzini, Capucine; Pitié-Salpêtrière Hospital, Adler, Dan; HUG, Pneumology</p> <p>Aguilaniu, Bernard; Université Grenoble Alpes, France</p> <p>Allard, Etienne; Centre hospitalier universitaire Charles Nicolle, Département d'anesthésie-réanimation</p> <p>Bautin, Nathalie; CHRU de Lille, Service de Pneumologie et Immuno-Allergologie</p> <p>BEAUMONT, Marc; Centre Hospitalier Des Pays de Morlaix, Service de Réhabilitation Respiratoire</p> <p>Blanc, François-Xavier; CHU Nantes, Institut du Thorax, Pneumologie</p> <p>Chenivresse, Cecile; Centre Hospitalier Régional Universitaire de Lille, ; Université de Lille II,</p> <p>DANGERS, Laurence; Centre hospitalier universitaire Félix-Guyon, Réanimation Polyvalente</p> <p>DELCLAUX, Christophe; Assistance Publique-Hôpitaux de Paris (AP-HP), Hôpital Universitaire Robert Debré, , Service de Physiologie - Explorations Fonctionnelles</p> <p>Devillier, Philippe; Hôpital Foch, Laboratory of Pharmacology</p> <p>Didier, Alain; Hôpital Larrey,</p> <p>Georges, Marjolaine; CHU Bocage, Service de Pneumologie</p> <p>Housset, Bruno; Centre hospitalier intercommunal de Créteil,, Service de Pneumologie</p> <p>Janssens, Jean-Paul; Hôpitaux Universitaires de Genève, Pulmonary Diseases;</p> <p>Laveneziana, Pierantonio; Pitié-Salpêtrière Hospital, Service des Explorations Fonctionnelles de la Respiration, de l'Exercice et de la Dyspnée,</p> <p>Laviolette, Louis; Université Paris 6, Equipe de Recherche ER 10 UPMC, Laboratoire de Physio-Pathologie Respiratoire, Faculté de Médecine Pierre et Marie Curie (site Pitié-Salpêtrière)</p> <p>MUIR, Jean-François; Respiratory & Intensive Care Medicine, CHU de Rouen</p> <p>Ninot, Gregory; Université de Montpellier, , EA 4556</p> <p>Perez, Thierry; Hopital Calmette, CHRU Lille, Respiratory; Hôpital Calmette, CHRU Lille, Lung function</p> <p>Peiffer, Claudine; Hopital Universitaire Robert Debre, Physiologie Explorations Fonctionnelles</p> <p>Schmidt, Matthieu; Pitié-Salpêtrière Hospital, Service de Réanimation</p>

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

	Médicale Similowski, Thomas STRAUS, Christian; Pitié-Salpêtrière Hospital Taillé, Camille; Hôpital Bichat, service de pneumologie Van Den Broecke, Sandra; Centre Hospitalo-Universitaire St Pierre, Service de Pneumologie Roche, Nicolas
Key Words:	dyspnea, delphi, chronic respiratory insufficiency, acute respiratory failure

SCHOLARONE™
Manuscripts

Title

Breathlessness despite optimal pathophysiological treatment: on the relevance or not of being chronic.

Authors

Capucine MORÉLOT-PANZINI (1,2), Dan ADLER (3), Bernard AGUILANIU (4), Etienne ALLARD (5), BAUTIN Nathalie (6), Marc BEAUMONT(7, 8), François-Xavier BLANC (9), Cécile CHENIVESSE (6), Laurence DANGERS (10), Christophe DELCLAUX (11,12), Philippe DEVILLIER (13, 14), Alain DIDIER (15), Marjolaine GEORGES (16), Bruno HOUSSET (17, 18, 19), Jean-Paul JANSSENS (3), Pierantonio LAVENEZIANA (1, 20) , Louis LAVIOLETTE (21), Jean-François MUIR (22), Gregory NINOT (23), Thierry PEREZ (6), Claudine PEIFFER (24), Matthieu SCHMIDT (25, 26), Thomas SIMILOWSKI (1, 2, 19), Christian STRAUS (1, 20), Camille TAILLÉ (27, 28), Sandra Van Den BROECKE (29), Nicolas ROCHE, and the "dyspnea working group" of the *Société de Pneumologie de Langue Française*

Affiliations

(1) Sorbonne Universités, UPMC Université Paris 06, INSERM, UMRS_1158
Neurophysiologie respiratoire expérimentale et clinique, Paris, France

(2) Assistance Publique-Hôpitaux de Paris (AP-HP), Groupe Hospitalier Pitié-Salpêtrière Charles Foix, Service de Pneumologie et Réanimation Médicale, (Département "R3S"), Paris, France

(3) Hôpitaux Universitaires de Genève, Service de Pneumologie, Genève, Suisse

(4) Université Grenoble Alpes, France

(5) Centre hospitalier universitaire Charles Nicolle, Département d'anesthésie-réanimation Rouen, France.

(6) Centre Hospitalier Universitaire de Lille, Service de Pneumologie et Immuno-Allergologie, Lille, France

(7) Centre Hospitalier Des Pays de Morlaix, Service de réhabilitation respiratoire, Morlaix, France

(8) Université de Bretagne occidentale, EA3878, Brest, France

(9) Centre Hospitalier Universitaire de Nantes, Institut du Thorax, Service de Pneumologie, Nantes, France

(10) Centre hospitalier universitaire Félix-Guyon, Réanimation polyvalente, Saint-Denis, La Réunion, France

(11) Assistance Publique-Hôpitaux de Paris (AP-HP), Hôpital Universitaire Robert Debré, Service de Physiologie - Explorations Fonctionnelles Pédiatriques-CPPS - Pôle ESPPRII , Paris, France

(12) Université Paris Diderot, Sorbonne Paris Cité, INSERM U1141, Paris, France

(13) Université Versailles Saint-Quentin, UFR Sciences de la Santé Simone Veil, UPRES EA 220, Suresnes, France

- (14) Laboratoire de Recherche en Pharmacologie Respiratoire, Hôpital Foch, Suresnes, France
- (15) Centre Hospitalier Universitaire de Toulouse, Hôpital Larrey, Service de Pneumologie, Toulouse, France
- (16) Centre Hospitalier Dijon Bourgogne, Hôpital Francois Mitterrand, Service de Pneumologie et Soins Intensifs Respiratoires, Dijon, France
- (17) Service de pneumologie, Centre hospitalier intercommunal de Créteil, 94000 Créteil, France
- (18) Université Paris Est Créteil, Inserm UMRS 955, Créteil, France
- (19) Fondation du souffle, 66 Bd Saint-Michel, 75006Paris, France
- (20) Assistance Publique-Hôpitaux de Paris (AP-HP), Groupe Hospitalier Pitié-Salpêtrière Charles Foix, Service des Explorations Fonctionnelles de la Respiration, de l'Exercice et de la Dyspnée, (Département "R3S"), Paris, France
- (21) Centre de recherche, Institut Universitaire de cardiologie et de pneumologie de Québec, Université Laval, Québec, Canada.
- (22) Hôpital Charles Nicolle, Service de Pneumologie et Soins Intensifs, Rouen, France
- (23) Université de Montpellier, EA 4556, Montpellier, France
- (24) Assistance Publique-Hôpitaux de Paris (AP-HP), Hôpital Universitaire Robert Debré, Physiologie Explorations Fonctionnelles, Paris, France
- (25) Sorbonne Universités, UPMC Université Paris 06, iCAN (Institute of Cardiometabolism and Nutrition), Paris, France
- (26) Assistance Publique-Hôpitaux de Paris (AP-HP), Groupe Hospitalier Pitié-Salpêtrière Charles Foix, Service de Réanimation, Paris, France
- (27) Assistance Publique-Hôpitaux de Paris (AP-HP), Hôpital Bichat, Service de Pneumologie et Centre de Compétence des Maladies Pulmonaires Rares, Paris, France.
- (28) Université Paris Diderot, INSERM UMR 1152, Paris, France
- (29) Centre Hospitalo-Universitaire St Pierre, Université Libre de Bruxelles, Service de Pneumologie, Bruxelles, Belgique
- (30) Université Paris Descartes, EA 2511, Paris, France
- (31) Assistance Publique-Hôpitaux de Paris (AP-HP), Groupe Hospitalier Paris Centre site Cochin, Service de Pneumologie et Soins Intensifs Respiratoires, Paris, France

Correspondence :

Capucine Morélot-Panzini
Service de Pneumologie et Réanimation Médicale (*Département "R3S"*)
Groupe Hospitalier Pitié-Salpêtrière Charles Foix
47-83 Bd de l'Hôpital 75651 Paris Cedex 13
Phone: 33 1 42 16 77 71 Fax: 33 1 70 24 72 82
E-mail: capucine.morelot@psl.aphp.fr

In the May 2017 issue of the *European Respiratory Journal* (ERJ), Johnson et al. [1] propose the term "chronic breathlessness syndrome" to describe the clinical situation in which *"breathlessness persists despite optimal treatment of the underlying pathophysiology and results in disability of the patient"*. The term "disability" in this definition corresponds to *"physical limitations and/or a variety of adverse psychosocial, spiritual, or other consequences"*, which very closely matches the World Health Organisation definition of "disability" [2]. Of note, the relationship between breathlessness and disability has been well captured in the foreword of a document published in 2013 by the Forum of International Respiratory Societies [3], of which the first sentence reads: *"When we are healthy, we take our breathing for granted [...]. But when our lung health is impaired, nothing else but our breathing really matters"*. This sentence has become the "catch phrase" of the French lung health foundation ("Fondation du Souffle", <http://www.lesouffle.org>). Of note also, the explicit definition of "chronic breathlessness" as proposed by Johnson et al. is not very different from the implicit definition of "refractory breathlessness", the term previously used in many studies, and which has already been proposed as a distinct entity by some of the authors of the ERJ May perspective article [4]. Johnson et al. [1] submit that defining and naming this new syndrome will improve the visibility to a distressing and debilitating condition that is too often overlooked and neglected [5]. They postulate that this enhanced visibility will result in improved care and organisation of care, stronger research [6], and greater empowerment by patients and their caregivers. The editorial by Prof. Meting Basoglu published in the same issue of the ERJ [7] throws new light on this notion of empowerment. Making a daring but fascinating parallel between untreated dyspnoea and torture, Prof. Basoglu reminds us how and why addressing dyspnoea in general (and probably "chronic breathlessness" in particular) is a fundamental issue not only from the point of view of medicine *per se*, but also from the point of view of human rights [on this, see also 8]. He also makes a very convincing case for the importance of empowerment in the management of dyspnoea. Still in the same issue of the ERJ, Prof. Peter Calverley comments on the new syndrome [9] and, like all of us, concurs with Johnson et al. [1] about the relevance of making breathlessness a foremost concern of every clinician.

In order to contribute to the discussion called for in the article by Johnson et al. [1], we (a French speaking group of physicians with a special interest in dyspnoea) would like to make a few comments about this article and the accompanying editorial by Prof. Calverley [9]. These comments mostly pertain to the choice of words that has been made to name the new syndrome. In no way should they be interpreted as an expression of disagreement with the proposed approach and its aims: some of the authors of the present letter participated in the 2016 Dyspnea symposium during which the "chronic breathlessness" discussion was finalised (CMP, DA, EA, CC, PL, LL, CP, TS), and one of the authors of the article by Johnson et al. [1] is also a co-author of this letter (TS). Our letter should be taken as a mere illustration of the fact that differences of opinions always exist within consensus, and also as a substantiation of the dynamical nature of the syndrome naming process that is put forward by Johnson et al. [1].

The first of our comments concerns the choice of "breathlessness" rather than "dyspnoea" in the name of the syndrome. Since "dyspnoea" is widely used in the medical literature and in medical practice, it would be useful to clarify whether or not "chronic breathlessness syndrome" and "chronic dyspnoea syndrome" can be used interchangeably, and if not, to explain why. This is an important issue particularly for non-native English speakers. The answer to this question can have a significant impact on translations of the name of the new syndrome in other languages.

The second comment pertains to the use of the term "optimal treatment" in the definition of the syndrome, which can be ambiguous. We understand that, in this context, "optimal" means "maximal", or "state-of-the art", but this may not be exactly the same thing: in some conditions characterised by a marked irreversible component such as COPD or pulmonary fibrosis, maximal therapy can fail to provide optimal results both physiologically and, obviously, symptomatically. Beyond semantics, we feel that it is extremely important not to label a patient as suffering from "chronic breathlessness" before being sure that everything

has been done to correct the underlying pathophysiological condition, as failure to do so would be associated with a risk of depriving the patient of effective interventions in the present or in the future. For example, if "optimal" treatment of an underlying condition exists but is not available for a given patient at a given time, or if the patient refuses this treatment for any reason, the use of nonspecific symptomatic treatment to alleviate dyspnoea would be valid and in fact essential [as clearly reminded in the editorial of Prof. Basoglu, see 7]. Yet, the definition of "chronic breathlessness" would not be met, and placing such patients under the "chronic breathlessness" umbrella would carry the risk of "forgetting" that "optimal treatment" has not been applied and should be undertaken as soon as it becomes possible.

The third comment pertains to the choice of the term "syndrome" itself. In his editorial [9], Prof. Calverley challenges this choice and seems to suggest that "syndrome" should only be used to identify a *"consistent group of patients"* with *"a likely primary condition"*. Another reason to challenge the term "syndrome" is related to its very definition as *"a group of signs and symptoms that occur together and characterize a particular abnormality or condition"*. This definition is directly derived from the Greek etymology of the word, which means "running together" and thereby implies a combination of items. Since "chronic breathlessness syndrome" apparently comprises only one symptom, dyspnoea, use of the term "syndrome" may be deemed inappropriate. However, the clinical situations covered by "chronic breathlessness syndrome" actually share much more than dyspnoea, as they also have in common the multiple deleterious consequences of this symptom (e.g. psychological, social, etc.). The term "syndrome" may therefore be very appropriate, particularly to attribute a consistency to otherwise inconsistent groups of patients. This seems to be exactly what has been achieved with "chronic pain syndrome". "Chronic breathlessness syndrome" has the advantage of defining a common basis for the care of patients with a variety of diseases and disorders, but who are "unified" (as should their caregivers be) by breathlessness, or, more generally, "respiratory suffering". It suggests that all respiratory physicians (and beyond that all physicians caring for patients with dyspnoeic diseases, and there are many of them...) should be familiar with the principles of dyspnoea management in addition to the management of the underlying disease (of note, this notion is explicitly stated in the 2017 edition of the GOLD statement, indicating that *"all clinicians managing patients with COPD should be aware of the effectiveness of palliative approaches to symptom control and use these in their practice"*)[10]. Using "symptom" instead of "syndrome" (or omitting "syndrome"), as suggested by Prof. Calverley [9], would carry the risk of neglecting the multidimensional and pervasive nature of dyspnoea [11-15]. The process initiated by Johnson et al. [1] is designed to convince caregivers — and others — that the care of dyspnoea cannot be limited to the treatment of the symptom, but should address its behavioural and socio-psychological consequences. Consequently, we believe that "syndrome" is an appropriate term, as it gives a holistic dimension to the management of dyspnoea.

The fourth of our comments, and in fact the most important one, concerns the term "chronic" in the name of the new syndrome. This choice emerged from a Delphi process, which gives it validity. However, the study could have been biased by the composition of the group of experts, which did not include many physicians involved in acute care [1]. If one of the goals of creating the new syndrome is to "give consistency and visibility to inconsistent and invisible groups of patients" (see above), we believe that the word "chronic" could well be counterproductive in a number of cases, as it would deprive many patients of a significant conceptual progress. Indeed, all of the words used to describe "chronic breathlessness" in the article by Johnson et al. [1] can apply, word for word, to many clinical situations involving acute rather than chronic dyspnoea. For example, all patients hospitalised with severe acute exacerbations of COPD remain dyspnoeic at rest despite oxygen, bronchodilators and corticosteroids, with the corresponding lack of control emphasized by Prof. Basoglu [7], and shrunken lives. This description exactly fits the definition of the syndrome proposed by Johnson et al. [1] except regarding the time frame. Although this is not standard practice at the moment, these patients could, or more precisely should, be considered for dyspnoea-oriented treatments in addition to pathophysiology-oriented treatments. Even more striking in terms of the temporal dynamics of dyspnoea, critically ill patients receiving mechanical

ventilation often complain of breathlessness [16]. After dealing with the various technical aspects involved, including optimisation of inappropriate ventilator settings, many of these patients remain breathless [16], a situation strongly suspected to contribute to the development of post-traumatic stress syndrome [17]. It will be impossible to convince the intensivists in charge of such patients that they suffer from "chronic breathlessness", even though relief of dyspnoea in this setting is a fundamental clinical mission [18, 19]. We believe that persistence of dyspnoea despite maximal pathophysiological treatment of an acute condition is not a fatality and is not more acceptable than it is in the context of a chronic condition. We therefore also believe that the principles governing the therapeutic approach to acute breathlessness should be exactly the same as the those governing the therapeutic approach to chronic breathlessness. Following are examples of clinical questions that can be formulated to support this contention, such as *"should noninvasive ventilation be considered in COPD patients during severe acute exacerbations despite complete normalisation of blood gases in response to conventional treatment, in order to alleviate dyspnoea?"*; *"should we design trials of short-term low-dose opioids in addition to pathophysiological treatment in severe exacerbations of COPD?"*; *"should we re-think the management of opioids during mechanical ventilation with a dyspnoea paradigm in mind?"*; *"should the concept of 'integrated breathlessness service', as developed in supportive care [20, 21], be transposed to the ICU?"*; *"is there any reason to think that empathy, education, and cognitive therapies would not be effective if 'breathlessness that persists despite treatment' is acute rather than chronic?"* and so on.... With this in mind, we are afraid that "chronic breathlessness syndrome" could be a misnomer because it would "miss" many "non-chronic" but nonetheless clinically relevant situations. Johnson et al. [1] and Prof. Calverley in his editorial [9] briefly refer to this issue, but perhaps they do not attribute sufficient importance to what could possibly be seen as a major gap by many practitioners. The name "persistent breathlessness" would have avoided this problem, because it would have covered all acute and chronic situations. "Persistent breathlessness" (or "resistant" breathlessness", or any other "time neutral" term) would also have had the advantage of clarifying the discourse in certain cases, possibly with some added teaching value. Let's take an example: *"Dear Colleague, I am referring to you this patient with chronic obstructive pulmonary disease who has been treated with dual bronchodilation and inhaled corticosteroids since last year, and who presents with chronic breathlessness"*. It could take quite a long time for this sentence to be readily understood by a majority of practitioners. In contrast, *"Dear Colleague, I am referring to you this patient with COPD who has been treated with dual bronchodilation and inhaled corticosteroids since last year because she complains of persistent breathlessness"*? is probably more readily understandable and "teachable" (without the negative connotation of "refractory" that contributed to go from "refractory" to "chronic" during the Delphi process elaborated by Johnson et al. [1]).

All physicians dealing with dyspnoeic patients must have the same objective, namely to alleviate dyspnoea by all means, combining "pathophysiological" and "syndrome-based" strategies, irrespective of the time-frame involved. We suggest that this general goal would be more effectively promoted by the term "persistent breathlessness syndrome" than by "chronic breathlessness syndrome" and we therefore advocate an evolution in this direction. Polling the ERJ readership could perhaps provide useful information on this subject.

1. Johnson MJ, Yorke J, Hansen-Flaschen J, Lansing R, Ekström M, Similowski T, Currow DC. Towards an expert consensus to delineate a clinical syndrome of chronic breathlessness. *Eur Respir J* 2017: reference to be completed.
2. World Health Organization. World report on disability. www.who.int/disabilities/world_report/2011/en/ 2011.
3. Forum of International Respiratory Societies. Respiratory diseases in the world: realities of today, opportunities for tomorrow. Available from www.ersnet.org/images/firs-world-report.pdf. *European Respiratory Society publications* 2013.
4. Johnson MJ, Currow DC. Chronic refractory breathlessness is a distinct clinical syndrome. *Curr Opin Support Palliat Care* 2015; 9(3): 203-205.

5. Gysels M, Higginson IJ. Access to services for patients with chronic obstructive pulmonary disease: the invisibility of breathlessness. *J Pain Symptom Manage* 2008; 36(5): 451-460.

6. Currow DC, Abernethy AP, Allcroft P, Banzett RB, Bausewein C, Booth S, Carrieri-Kohlman V, Davidson P, Disler R, Donesky D, Dudgeon D, Ekstrom M, Farquhar M, Higginson I, Janssen D, Jensen D, Jolley C, Krajnik M, Laveneziana P, McDonald C, Maddocks M, Morelot-Panzini C, Moxham J, Mularski RA, Noble S, O'Donnell D, Parshall MB, Pattinson K, Phillips J, Ross J, Schwartzstein RM, Similowski T, Simon ST, Smith T, Wells A, Yates P, Yorke J, Johnson MJ. The need to research refractory breathlessness. *Eur Respir J* 2016; 47(1): 342-343.

7. Basoglu M. Effective management of breathlessness: A review of potential human rights issues. *Eur Respir J* 2017: reference to be completed.

8. Currow DC, Abernethy AP, Ko DN. The active identification and management of chronic refractory breathlessness is a human right. *Thorax* 2014; 69(4): 393-394.

9. Calverley PMA. Chronic breathlessness : syndrome or symptom ? . *Eur Respir J* 2017: reference to be completed.

10. Global Strategy for the Diagnosis MaPoC, Global Initiative for Chronic Obstructive Lung Disease (GOLD), . Available from: <http://goldcopd.org/>. 2017.

11. Laviolette L, Laveneziana P, Faculty ERSRS. Dyspnoea: a multidimensional and multidisciplinary approach. *Eur Respir J* 2014; 43(6): 1750-1762.

12. Parshall MB, Schwartzstein RM, Adams L, Banzett RB, Manning HL, Bourbeau J, Calverley PM, Gift AG, Harver A, Lareau SC, Mahler DA, Meek PM, O'Donnell DE, American Thoracic Society Committee on D. An official American Thoracic Society statement: update on the mechanisms, assessment, and management of dyspnea. *Am J Respir Crit Care Med* 2012; 185(4): 435-452.

13. Banzett RB, O'Donnell CR, Guilfoyle TE, Parshall MB, Schwartzstein RM, Meek PM, Gracely RH, Lansing RW. Multidimensional Dyspnea Profile: an instrument for clinical and laboratory research. *Eur Respir J* 2015; 45(6): 1681-1691.

14. Morelot-Panzini C, Gilet H, Aguilaniu B, Devillier P, Didier A, Perez T, Pignier C, Arnould B, Similowski T. Real-life assessment of the multidimensional nature of dyspnoea in COPD outpatients. *Eur Respir J* 2016; 47(6): 1668-1679.

15. Williams MT, John D, Frith P. Comparison of the Dyspnoea-12 and Multidimensional Dyspnoea Profile in people with COPD. *Eur Respir J* 2017; 49(3).

16. Schmidt M, Demoule A, Polito A, Porchet R, Aboab J, Siami S, Morelot-Panzini C, Similowski T, Sharshar T. Dyspnea in mechanically ventilated critically ill patients. *Crit Care Med* 2011; 39(9): 2059-2065.

17. de Miranda S, Pochard F, Chaize M, Megarbane B, Cuvelier A, Bele N, Gonzalez-Bermejo J, Aboab J, Lautrette A, Lemiale V, Roche N, Thirion M, Chevret S, Schlemmer B, Similowski T, Azoulay E. Postintensive care unit psychological burden in patients with chronic obstructive pulmonary disease and informal caregivers: A multicenter study. *Crit Care Med* 2011; 39(1): 112-118.

18. Chanques G, Nelson J, Puntillo K. Five patient symptoms that you should evaluate every day. *Intensive Care Med* 2015; 41(7): 1347-1350.

19. Schmidt M, Banzett RB, Raux M, Morelot-Panzini C, Dangers L, Similowski T, Demoule A. Unrecognized suffering in the ICU: addressing dyspnea in mechanically ventilated patients. *Intensive Care Med* 2014; 40(1): 1-10.

20. Booth S, Ryan R, Spathis A. Service delivery of complex interventions for refractory breathlessness. *Curr Opin Support Palliat Care* 2016; 10(3): 228-235.

21. Higginson IJ, Bausewein C, Reilly CC, Gao W, Gysels M, Dzingina M, McCrone P, Booth S, Jolley CJ, Moxham J. An integrated palliative and respiratory care service for patients with advanced disease and refractory breathlessness: a randomised controlled trial. *Lancet Respir Med* 2014; 2(12): 979-987.