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### References

1. Anghelescu DL, Snaman JM, Trujillo L, et al. Patient-controlled analgesia at the end of life at a pediatric oncology institution. Pediatr Blood Cancer 2015;62:1237–1244.

2. Nijland L, Schmidt P, Frosch M, et al. Subcutaneous or intravenous opioid administration by patient-controlled analgesia in cancer pain: a systematic literature review. Support Care Cancer 2019;27:33–42.

3. Mherekumombe MF, Collins JJ. Patient-controlled analgesia for children at home. J pain symptom Manag 2015; 49:923–927.

4. von Baeyer CL, Spagrud LJ, McCormick JC, et al. Three new datasets supporting use of the Numerical Rating Scale (NRS-11) for children's self-reports of pain intensity. PAIN 2009;143:223–227.

5. Malviya S, Voepel-Lewis T, Burke C, Merkel S, Tait AR. The revised FLACC observational pain tool: improved reliability and validity for pain assessment in children with cognitive impairment. Pediatr Anesth 2006;16:258–265.

6. Mitchell S, Morris A, Bennett K, Sajid L, Dale J. Specialist paediatric palliative care services: what are the benefits? Arch Dis Child 2017;102:923–929.

7. Anghelescu DL, Zhang K, Faughnan LG, Pei D. The Safety and Effectiveness of patient-controlled analgesia in Outpatient children and young Adults with cancer: a Retrospective study. J Pediatr Hematol Oncol 2015;37:378–382.

8. Beecham E, Oostendorp L, Crocker J, et al. Keeping all options open: parents' approaches to advance care planning. Health Expect 2017;20:675–684.

9. Collins JJ, Berde CB, Frost JA. Pain assessment and management. In: Wolfe J, Hinds PS, Sourkes BM, eds. Textbook of interdisciplinary pediatric palliative care. Philadelphia: Elsevier Health Sciences, 2011:284–299.

10. von Baeyer CL. Children's self-report of pain intensity: what we know, where we are headed. Pain Research & Management. J Can Pain Soc 2009;14:39–45.

## *Acute-on-Chronic Breathlessness: Recognition and Response*

Lovell et al. are to be commended for their description of the widespread effects of breathlessness within the construct "total breathlessness".[1] Despite the large body of evidence on the experience of people living with chronic breathlessness, clinicians still struggle with its recognition and assessment. Even when recognized, the symptom is undertreated[2] and is experienced by people over many years[3–5] and is associated with repeated unplanned presentations to health services.[6]

In our prospective observational study of 1212 patients presenting to the emergency department by ambulance,[5] 20% presented due to acute-on-chronic breathlessness (acute worsening of chronic breathlessness). The concept of acute-on-chronic breathlessness builds on the definition of chronic breathlessness syndrome[7] and mirrors concepts of disease (acute-on-chronic renal failure) or symptoms (acute-on-chronic pain). Acute-on-chronic breathlessness is a construct beyond the "dyspnea crisis," which is limited in its definition to late-stage disease[8] and encompasses all forms of episodic breathlessness, triggered or untriggered.[9]

In our emergency department study, one-third of people with acute-on-chronic breathlessness were discharged home but without evidence of a plan to manage the ongoing chronic breathlessness. Unless clinicians (in any setting) recognize *both* the acute and chronic aspects of acute-on-chronic breathlessness, the life experience of chronic breathlessness remains invisible, which denies the patient access to evidence-based interventions[10,11] and misses opportunities to lessen the likelihood of representations.[6]

Community clinicians struggle with how to identify, assess, and manage chronic breathlessness. There are now useful frameworks to guide clinicians' assessment[12] and management.[13] As described in the Breathing Space concept,[14] the clinician plays a pivotal role in recognizing background chronic breathlessness—a step often overlooked.

Defining chronic breathlessness syndrome[7] has been an important first step. There is a new imperative: if a patient presents with acute breathlessness, there is now a responsibility for clinicians to determine whether this is an isolated episode of acute breathlessness or a presentation of acute-on-chronic breathlessness.

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### References

1. Abernethy AP, Wheeler JL. Total dyspnoea. Curr Opin Support Palliat Care 2008;2:110–113.

2. Ahmadi Z, Sandberg J, Shannon-Honson A, Vandersman Z, Currow DC, Ekström M. Is chronic breathlessness less recognised and treated compared with chronic pain? A case-based randomised controlled trial. Eur Respir J 2018;52:1800887.

3. Johnson MJ, Bowden JA, Abernethy AP, Currow DC. To what causes do people attribute their chronic breathlessness? A population survey. J Palliat Med 2012;15:744–750.

4. Currow DC, Dal Grande E, Ferreira D, Johnson MJ, McCaffrey N, Ekström M. Chronic breathlessness associated with poorer physical and mental health-related quality of life (SF-12) across all adult age groups. Thorax 2017;72:1151–1153.

5. Hutchinson A, Pickering A, Williams P, Bland JM, Johnson MJ. Breathlessness and presentation to the emergency department: a survey and clinical record review. BMC Pulm Med 2017;17:53.

6. Nunez S, Hexdall A, Aguirre-Jaime A. Unscheduled returns to the emergency department: an outcome of medical errors? Qual Saf Health Care 2006;15:102–108.

7. Johnson M, Yorke J, Hansen-Flaschen J. Towards an expert consensus to delineate a clinical syndrome of chronic breathlessness. Eur Respir J 2017;49.

8. Mularski RA, Reinke LF, Carrieri-Kohlman V, et al. An official American Thoracic Society workshop report: assessment and palliative management of dyspnea crisis. Ann Am Thorac Soc 2013;10:S98–S106.

9. Simon ST, Higginson IJ, Benalia H, et al. Episodes of breathlessness: Types and patterns—a qualitative study exploring experiences of patients with advanced diseases. Palliat Med 2013;27:524–532.

10. Ekström M, Bajwah S, Bland JM, Currow DC, Hussain J, Johnson MJ. One evidence base; three stories: do opioids relieve chronic breathlessness? Thorax 2018;73:88–90.

11. Bausewein C, Schunk M, Schumacher P, Dittmer J, Bolzani A, Booth S. Breathlessness services as a new model of support for patients with respiratory disease. Chronic Respir Dis 2018;15:48–59.

12. Hopkinson NS, Baxter N. Breathing SPACE—a practical approach to the breathless patient. NPJ Prim Care Respir Med 2017;27:5.

13. Spathis A, Booth S, Moffat C, et al. The Breathing, Thinking, Functioning clinical model: a proposal to facilitate evidence-based breathlessness management in chronic respiratory disease. NPJ Prim Care Respir Med 2017;27:27.

14. Hutchinson A, Barclay-Klingle N, Galvin K, Johnson MJ. Living with breathlessness: a systematic literature review and qualitative synthesis. Eur Respir J 2018;51:1701477.

## *Challenges in Recruiting Patients to a Controlled Feasibility Study of a Drug for Opioid-Induced Constipation: Lessons From the Population With Advanced Cancer*

To the Editor:

Clinical research is difficult in populations with advanced illness because patients have a high disease burden and short life expectancy, poor functional status and high distress, or an unpredictable course characterized by changing therapies and an increased risk of adverse events. This is reflected in the paucity of published trials; fewer than 1% are conducted in an advanced illness population. The lack of randomized trials means that high-quality evidence plays a small role in defining best clinical practices and standards for end-of-life care.[1]

We initiated a small multicenter trial of oral naloxegol (Movantik®) in patients with advanced cancer, cancer-related pain, and opioid-induced constipation (OIC) to determine the feasibility of a larger definitive study. Large controlled studies in populations with chronic noncancer pain recruited adequately and confirmed naloxegol's efficacy.[2,3] Two previous studies in patients with cancer-related pain were closed prematurely owing to poor patient enrollment.[4] Our study attempted to address the recruitment issues identified in previous efforts, but recruitment challenges again led to early study closure. This experience may provide insight into the problem of poor trial enrollment in populations with advanced illness.

### *Methods*

A multicenter randomized, placebo-controlled study was designed to assess the feasibility of a definitive trial of naloxegol for OIC in a population with advanced cancer. Secondary outcomes included tolerability, safety, and efficacy.

#### *Study Design and Sample Size*

To reduce patient burden, the design included fewer study visits and a shorter double-blind