

Opioids and adverse outcomes in elderly chronic obstructive pulmonary disease patients

To the Editor:

We read with interest the study by VOZORIS *et al.* [1] describing the risk of adverse outcomes associated with opioid use in elderly chronic obstructive pulmonary disease (COPD) patients. There is currently a strong debate on the prescription of opioids in patients with COPD. While several studies seemed to demonstrate the harmlessness of opioids in this population [2–4], two recent studies including the one by VOZORIS *et al.* [1] challenge this result [5]. The large number of included patients and the excellent method used in these two studies strongly support the idea of an excess morbidity or mortality associated with the opioid use in COPD patients. There is, however, one limitation that needs to be taken into consideration.

VOZORIS *et al.* [1] explain that patients receiving palliative care in the year prior to the index date were excluded. This seems appropriate since the use of morphine is recommended in the treatment of end-of-life dyspnoea. Nevertheless, we believe that this exclusion criterion is not strict enough to avoid a bias in the analysis and interpretation of mortality risk. Indeed, discussion of palliative care in COPD patients often arises in the context of acute respiratory failure [6]. Over half of pulmonologists claimed that end-of-life decisions in COPD patients occur during/after a major exacerbation [7, 8]. It is unlikely that patients receiving opioid drugs following a recent end-of-life decision were excluded from the study by VOZORIS *et al.* [1]. This potential bias may explain why no significant association was observed between opioid use and intensive care unit admissions in both the primary analysis and the sensitive analysis. Thus, the mortality results should be interpreted with caution.

In conclusion, the debate on the safety of morphine in COPD patients will remain open until further prospective studies refute or confirm the results published by VOZORIS *et al.* [1]. Based on table 3 in their article [1], a randomised placebo controlled study would require the inclusion of 17 664 patients to detect a significant difference ($\alpha=0.05$ and $\text{power}=0.8$) in COPD or pneumonia-related mortality, while 7746 patients would be necessary to detect a difference in all-cause mortality.



@ERSpublications

Opioids in patients with COPD: results of mortality should be interpreted with caution regarding exclusion criteria <http://ow.ly/IJbd304nC36>

Damien Viglino^{1,2} and Maxime Maignan^{1,2}

¹University Hospital Grenoble Alps – Emergency Dept and Mobile Intensive Care Unit, Grenoble, France. ²INSERM U1042, HP2 Laboratory, University Grenoble Alps, Grenoble, France.

Correspondence: Damien Viglino, Service des Urgences, CHU Grenoble Alpes, CS 10217, 38043 Grenoble cedex 9, France. E-mail: dviglino@chu-grenoble.fr

Received: Aug 12 2016 | Accepted: Aug 14 2016

Conflict of interest: None declared.

References

- 1 Vozoris NT, Wang X, Fischer HD, *et al.* Incident opioid drug use and adverse respiratory outcomes among older adults with COPD. *Eur Respir J* 2016; 48: 683–693.
- 2 Jennings A-L, Davies AN, Higgins JPT, *et al.* A systematic review of the use of opioids in the management of dyspnoea. *Thorax* 2002; 57: 939–944.
- 3 Currow DC, McDonald C, Oaten S, *et al.* Once-daily opioids for chronic dyspnea: a dose increment and pharmacovigilance study. *J Pain Symptom Manage* 2011; 42: 388–399.
- 4 Rocker GM, Simpson AC, Young J, *et al.* Opioid therapy for refractory dyspnea in patients with advanced chronic obstructive pulmonary disease: patients' experiences and outcomes. *CMAJ Open* 2013; 1: E27–E36.
- 5 Ekström MP, Bornefalk-Hermansson A, Abernethy AP, *et al.* Safety of benzodiazepines and opioids in very severe respiratory disease: national prospective study. *BMJ* 2014; 348: g445.
- 6 Carlucci A, Guerrieri A, Nava S. Palliative care in COPD patients: is it only an end-of-life issue? *Eur Respir Rev* 2012; 21: 347–354.
- 7 McNeely PD, Hébert PC, Dales RE, *et al.* Deciding about mechanical ventilation in end-stage chronic obstructive pulmonary disease: how respirologists perceive their role. *CMAJ* 1997; 156: 177–183.
- 8 Gaspar C, Alfarroba S, Telo L, *et al.* End-of-life care in COPD: a survey carried out with Portuguese pulmonologists. *Rev Port Pneumol* 2014; 20: 123–130.