

Letter to the Editor

Opioids in chronic obstructive pulmonary disease: the whole picture using all available evidence

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Vozoris *et al.* are to be commended for their continued work on population patterns of prescribing in people with chronic obstructive pulmonary disease (COPD) [1, 2].

The burden of pain and breathlessness in people with COPD is clearly quantified [3]. More than 90% of people with advanced COPD have breathlessness at rest or on minimal exertion and between one third and two thirds have pain [3]. Symptom control is necessary in order to avoid a range of morbidities. Having long term, uncontrolled pain or breathlessness is a cause of significant suffering, and is intolerable when, for example, evidence supports the effective and safe use of regular low dose sustained release morphine for chronic refractory breathlessness [4, 5].

Vozoris *et al.* imply in this paper that disasters await clinicians who prescribe opioids in people with COPD for symptom relief [1]. The paper refers to 'significant risks' when the data presented and references cited are non-randomized studies that describe observed 'associations' only. Neither paper [1, 2] can demonstrate a causal relationship between prescribing and any subsequent outcomes. Neither study controls for potential confounders and, even were this to be done, causality still cannot be assigned [6].

The data presented by Vozoris *et al.* do not support the authors' conclusion that 'potential safety concerns are raised by the degree and pattern of new opioid use' in people with COPD [1]. Of particular interest in the current paper is what is *not* reported. Using an identical methodology and a similar cohort, the same authors reported the associations between recent prescriptions of benzodiazepines and increased exacerbations of COPD and increased presentations to the Emergency Department (ED) [2]. However, the current paper is silent about any associations with worsening of COPD or ED presentations [1].

Sicker people have a greater symptom burden, are prescribed more medications for symptom control, have more frequent exacerbations and more frequent presentations to the ED. If clinicians are reluctant to use a treatment, then often its use is delayed until there is a crisis. Such under-treatment might result in an even stronger, but still spurious, association between the treatment and any adverse outcome.

Data from adequately powered randomized controlled trials are required to inform the net effects of opioids in the setting of people with COPD such as benefits and harms collected using standardized assessments [7]. Such studies need to be complemented with detailed prospective pharmacovigilance studies in real world clinical settings quantifying adverse events and benefits [8].

Ultimately, the judicious use of opioids in people with COPD is justified and to preclude their use would continue to condemn a large population internationally to poor symptom control [9]. Work needs to continue urgently to define the population who will most benefit from opioids safely in COPD [10] and ensure that it becomes a registered indication for the treatment of chronic refractory breathlessness (at rest or on minimal exertion) so that clinicians can reduce avoidable suffering. The myths that have arisen around the use of regular low dose morphine in severe COPD need to be dispelled urgently.

Competing Interests

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare no

support from any organization for the submitted work, DC was a consultant to Mayne Pharma in the previous last 3 years and there are no other relationships or activities that could appear to have influenced the submitted work.

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RECEIVED

22 October 2015

ACCEPTED

16 November 2015

ACCEPTED ARTICLE PUBLISHED ONLINE

26 November 2015

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