Appendix 8: Placebo effect?

We suggest that the following supports clinical efficacy rather than a major placebo effect.

(i) The finding that 61% of our cohort reported benefit is twice the accepted potential placebo effect of most interventions (30%).

(ii) If dyspnea, as a symptom, responds to doses of opioids lower than those used for pain (our experience and that of other clinicians outside this trial), then perhaps the effect is genuine, and if adverse effects are dose related, they would not be expected or occur at the low doses we used in the first two weeks.

(iii) For HRQoL and dyspnea scores, an effect at 2 weeks is maintained to 4–6 months (this would seem a long duration for a placebo effect).

(iv) A low study non-completion rate of only 20%, especially given the disease severity in our participants, speaks to the likely efficacy and acceptability of the treatment.

(v) The sustained longer-term benefits occurred in the absence of any follow-up from the study team beyond the 4–6 months interval. In Halifax, we sought and received responses from 18/23 (78%) patients taking opioids beyond our initial study timelines. After a mean duration of opioid treatment of 16 months (range 10–21 months), the earlier significant improvement in dyspnea intensity (NRS) observed at 4–6 months was maintained, and again all patients chose to continue with opioids based on significant and maintained improvements in dyspnea and/or HRQoL (data not shown). This, we suggest, refutes arguments suggesting a potential placebo effect attributable to "therapeutic interviews" and other team interventions.

Note: HRQoL = health-related quality of life; NRS = numerical rating scale.

Appendix to: 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. DOI:10.9788/cmajo.20120031. Copyright © 2013 Canadian Medical Association or its licensors