Appendix 7: Clinical implications and lessons learned

1. **Gaining trust**. Many patients assume that morphine is used when people are dying. When patients understood instead that our intent was to use opioids to potentially help them to *live* better, they were more willing to consider a trial of opioids. A simple strategy that worked for many was to discuss how our starting dose of morphine related to (and was much lower than) the dose equivalent in a tablet of Tylenol 3 (acetaminophen 300 mg / codeine phosphate 30 mg), a medication that was more familiar and less intimidating to many.
2. **Small gains matter.** Patients very much embody their own advice "try it — you have nothing to lose." Many do not have great or unrealistic hopes going into such trials and thus small gains become quite significant given the poor quality of life that often predates their opioid experience.
3. **Anticipate disappointment.** Despite, or perhaps because of, their rather meager hopes, disappointment looms larger and seems more devastating in these circumstances. Communication is key and requires ongoing monitoring of, listening for, and responding to questions, concerns, and change, both positive and negative.
4. **Each patient was in reality a case of N=1**. Each had a unique baseline situation; each had a unique response regarding dose effects initially and over time, adverse effects, development of tolerance, etc. There is no "one size fits all" approach when using opioids for refractory dyspnea.
5. **Inadequate treatment of constipation**. This was a source of significant suffering for some patients in the trial. Being willing to stay on top of adverse effects and work to find appropriate, timely answers is an important part of sustaining trust and achieving best care for these patients.
6. **Titrating doses based on symptom.** Assessing dyspnea “tolerability” turned out to be an imperfect metric for making titration decisions. Patients “tolerate” poor symptom control and have learned to do so over a long period of time. While some might rate a dyspnea intensity of 8/10 as tolerable, others could state 5/10 as intolerable. This speaks to the subjective nature of dyspnea and its perception.
7. **Opioid preparations/dosing.** Although most preferred the sustained-release pill, some patients could not tolerate a switch, preferring to remain on a lower dose of immediate-release morphine syrup. In addition, we had to accept that small changes in opioid doses, i.e. from 1–1.5 mg QID, particularly in elderly and frail patients, were often sufficient to achieve an acceptable level of dyspnea or avoid adverse effects, dose changes that are not possible with current sustained-release preparations. Nevertheless, most patients ultimately were pleased to move away from more frequent and less convenient dosing of a short-acting liquid. Ideally there would be a lower dose (5 mg) sustained-release product. This is not available currently.
8. **Assessments/measurements.** From previous experience in studies of advanced COPD, we anticipated a poor rate of completion of quantitative tools but found instead a remarkable willingness, both on the parts of patients and their caregivers, to complete our questionnaires. We heard from many that they viewed this research as highly important and wished to share their experiences with others.

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.
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