The prevalence of chronic obstructive pulmonary disease (COPD) in Canada is high and rising. Dyspnea is the predominant symptom and, for patients with advanced COPD, conventional optimized treatments often fail to provide relief. Control of dyspnea can be an ongoing struggle. Many patients experience severe and unpredictable “dyspnea crises” that, when superimposed on relentless background dyspnea, often trigger additional fear, panic, feelings of helplessness and further erosion of quality of life among patients and their family caregivers. For those living with advanced COPD, symptom relief is important, and responding to their needs should be a priority.

Opioids have long been used to relieve dyspnea in patients with malignant disease. However, many clinicians are uncomfortable with this approach for COPD, where opioids remain underused and barriers to opioid prescribing have been identified. The Canadian Thoracic Society recently released a clinical practice guideline that recommends the use of opioids for refractory dyspnea in patients with advanced COPD. Nevertheless, uptake of these recommendations may be limited unless long-held biases are overcome.

To increase the understanding of these issues, we built on earlier survey work and a preliminary qualitative inquiry by conducting two studies: one to explore the experiences of patients and family caregivers when opioids are prescribed to treat refractory dyspnea, and one to explore physicians’ perspectives and attitudes toward opioid use for dyspnea in advanced COPD.

Methods

Approach

Both studies were approved by the research ethics board at Capital Health in Halifax, Nova Scotia. The physician study was approved by five other research ethics boards of the district.
health authorities in Nova Scotia. Given the dearth of evidence about patient and family caregiver experiences with opioids for dyspnea, it was appropriate to use a qualitative approach. We supplemented this approach with quantitative measures to further describe participants and maximize comprehensiveness,19 an approach consistent with current calls for mixed-methods approaches to evaluate dyspnea in advanced disease11–13 and the benefit of palliative care interventions.15 To identify physicians’ attitudes about and experience with prescribing opioids in this context, we used a single qualitative approach and collected basic demographic information.

Setting
The studies were conducted in both urban and rural settings. Most interviews with patients and family caregivers were conducted in their homes. (Most patients were housebound as a result of their advanced disease.) Physicians were interviewed in their offices or at a location of their choice.

Sampling
For both studies, we used purposive sampling14 to maximize the likelihood of recruiting participants with sufficient experience with the phenomenon of interest. For the study involving patients and family caregivers, the phenomenon of interest was their experiences of living with opioid therapy.

We recruited potential participants for the patient and family caregiver study from among patients with severe, stable COPD (as defined by the Canadian Thoracic Society) who had been previously prescribed and were already taking opioids for dyspnea and who were followed (currently or previously) by the Division of Respirology or by the home outreach service of the Division of Palliative Medicine at Capital Health in Halifax. We also recruited from among the family caregivers living with these decedents using opioids for refractory dyspnea. Clinicians in the immediate circle of care made potential participants aware of the study. Interested patients and/or family caregivers were sent study information. Consent forms were mailed to some participants in advance; most were willing to review documentation in person, and all agreed to participate at this stage. The full inclusion and exclusion criteria are listed in Appendix 1 (www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.111758/-/DC1).

Physicians in Nova Scotia were eligible to participate if they practised primarily in respirology, family medicine, internal medicine or palliative medicine. Within a purposive sampling framework, we used a convenience sample approach to contact potential physicians (via their office secretaries) who were likely to care for patients with COPD. Study information was sent to interested physicians, who then chose an interview time and location.

Data collection and analysis
After obtaining informed consent, we collected demographic data from patients, family caregivers and physicians (Appendix 2 and 3, www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.111758/-/DC1). Two of the authors (J.Y. and C.S.) then conducted semistructured one-on-one interviews with patients, family caregivers and physicians separately until theoretical saturation was achieved. Theoretical saturation was determined by a consensus decision by the interviewers (J.Y. and C.S.) to interview no more participants at the point at which they were hearing no new information, with confirmation by the study analyst (M.D.) that no new concepts were emerging and that further interviews would not add substantively to the content.

We explored the experience of living with COPD and dyspnea (patients and family caregivers), treating patients with COPD and managing dyspnea (physicians) and attitudes about opioid use (all participants). We developed interview guides (Appendix 4 and 5, www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.111758/-/DC1) through an iterative process based on themes identified in our previous research, literature reviews conducted in preparation for these studies, and testing of the interview guide in a pilot study.9 Prompts were rarely needed because the patients and family caregivers were eager to discuss their experiences and concerns. Interviews with physicians proceeded similarly.

Patients and family caregivers completed validated quantitative assessments for the severity of dyspnea,11,15 functional status (palliative performance scale),4 anxiety and depression17 and quality of life.18,19 Additionally, they indicated the “helpfulness” of opioids on a 5-point Likert scale (1 = not helpful at all; 5 = very helpful) and whether, when balancing the benefits and adverse effects, they wanted to continue opioid therapy (yes or no), and the reason(s) for their choice in terms of changes in dyspnea, quality of life and adverse effects.20 Quantitative tools were completed by patients and family caregivers following their qualitative interviews. If the participants were fatigued, they completed the tools within a few days and returned the documents to the study coordinator.
The digitally audiorecorded interviews were transcribed verbatim. The study analyst (M.D.) used an interpretive description approach to analyze the data from each study separately. The first step in the analysis process was to describe the phenomenon of interest (the experiences of patients and family caregivers with opioid treatment for dyspnea in advanced COPD, and the perspectives of physicians caring for such patients and their attitudes about the use of low-dose opioids for the treatment of dyspnea). This was followed by an interpretive step involving all members of the team, which involved grappling with possible meanings of the described observations from a clinical perspective. The value of this methodology lies in its capacity to capture practice-relevant particularities of individual experiences as well as broader commonalities across those experiences. In addition, M.F. independently listened to early audio files (to ensure unbiased conduct of interviews), read subsequent transcriptions and reviewed the derived themes.

Results

Patients’ perspectives

Of the 10 patients invited to participate, one provided consent but died before data collection. Another patient chose not to participate but her caregivers were enrolled. Eight patients were enrolled in the study (five men and three women, mean age 71 [standard deviation 9] years, range 52–79 years). Six of the eight patients lived in an urban area. Scores on the palliative performance scale ranged from 50%–70%. All patients had a score of 5 on the Medical Research Council dyspnea scale (i.e., they were too short of breath to leave their homes or were breathless when dressing or undressing), varied in scores for dyspnea intensity, anxiety and depression, were on optimal conventional inhaled COPD therapies as per Canadian Thoracic Society guidelines, were taking a combination of a sustained-released product (dose range 20–30 mg morphine equivalent, twice a day) with additional immediate-release morphine sulfate for breakthrough dyspnea, and one patient was taking sublingual fentanyl. Commonly reported adverse effects included constipation and dry mouth. These adverse effects were usually mild, although four patients reported severe individual symptoms including dry mouth, itching, sweating and decreased libido.

All patients reported that opioids provided significant improvements to their quality of life, relief of their dyspnea, or both, and cited this as their main reason to continue taking opioids over the longer term (Box 1). Patient responses to the quality-of-life questionnaire supported this finding, with five of seven patients who responded recording scores of 5 or higher (out of 10). Patients reported that opioids were either “very” or “somewhat” helpful and, balancing the benefits and adverse effects, all wished to continue taking opioids.

Family caregivers’ perspectives

Family caregivers (age range 34–75 years, five men, seven women) perceived the benefits of opioids to be meaningful and substantial, and they felt that the adverse effects were not a major concern. Of the 11 caregivers who responded to our questionnaire, all supported continued opioid use, and 9 rated opioids as “very” helpful. Caregivers described opioids as helping patients to breathe more “normally”; most observed improvements in their family members’ symptoms of anxiety and depression. Some described patients as looking younger, and we heard frequent comments about increased activities and ability to do more. During the interviews, many caregivers reported reductions in their own stress levels and improvements in their own quality of life (Box 2).

Relationships (according to patients and family caregivers)

We have previously described the burdens that advanced COPD imposes on relationships between spouses and/or between patients and their children. In the current study, we again heard repeated descriptions of guilt (e.g., if caregivers left patients on their own for any length of time). We also heard of resilience and a determination to “see things through” (Box 3). When

**Box 1: Patients’ perspectives on relief of symptoms with the use of opioids**

**Interviewer:** How would you say the morphine has changed your breathing?

- “Ah, it takes away a lot of the struggle, you know. You’re not struggling to catch your next breath. You’re more relaxed … I still lose my breath mind you if I overexert, and it doesn’t take much to overexert you know, just, but ah, it’s made my life more comfortable, yeah.” — Patient 9
- “Well it [opioid treatment] seemed to give me a whole new outlook. Even though I didn’t do much walking around and that kind of stuff, I could still do more because I felt better, oh just all over felt better … I think it relaxes me, and I don’t know how but it helps with the breathing so, if that’s just because I’m relaxed or if it actually does something I don’t know, which in turn makes everything go better, smoother.” — Patient 1
- “If I [the patient demonstrated heavy breathing] like that, I know my oxygen and my puffer don’t work so I take that [opioid] then, as soon as I take that then, three, four minutes, she’s cleared right up.” — Patient 5
exploring with patients and family caregivers whether or how opioids (for dyspnea) had changed their relationships, some caregivers described how the patients’ use of opioids had imposed a new routine, depending on the medication used and the setting, and that it did so within a sense of teamwork. We also heard concern that stopping morphine would shorten life (Box 3).

**Fears and communication**
Both patients and family caregivers expressed some concern about addiction, respiratory suppression and imminent death, but they indicated that these fears were easily and quickly alleviated by honest and open communication with their health care professionals (Box 4).

**Physicians’ perspectives**
Twenty-eight physicians (17 men, 11 women) from urban (n = 17) and rural (n = 11) settings were enrolled from five of nine district health authorities in Nova Scotia. Upon initial contact, one physician declined participation and another declined audiorecording but agreed to note-taking (citing concerns about a tendency to some profanity at times). Physicians practised family medicine (n = 10), respiratory medicine (n = 6), internal medicine (n = 6) and palliative medicine (n = 6). Of the 25 physicians who reported their age, the median age was 52 (range 29–70) years, with a median practice experience of 20 (range 3–45) years. Many physicians expressed frustration with suboptimal control of dyspnea in patients with advancing COPD, and they expressed a desire to learn about new potential treatments. They expressed various levels of comfort with prescribing and administering opioids in hospital settings; most were uncomfortable with prescribing opioids in home or community settings. While most physicians were reluctant to prescribe opioids for patients with advanced COPD, those with experience prescribing opioids for dyspnea found them to be effective for providing some relief for some patients (Box 5). Of those who had not prescribed opioids in this context, some felt that opioids might be of value and that palliative interventions such as opioids might not be used often enough for these patients (Box 5).

The risk of respiratory depression was a concern for many physicians, including those from palliative care, although this group was more likely to prescribe opioids for COPD for patients whose symptom burden was high and poorly relieved by other conventional measures (Box 6).

Physicians from all disciplines suggested that lack of education and knowledge about opioids were the greatest barriers to opioid use in advanced COPD. They also worried about possible censure for prescribing opioids for COPD for patients whose symptom burden was high and poorly relieved by other conventional measures (Box 6).

**Box 2: Experiences and perceptions of family caregivers about the effects of opioids**

- “This is a miracle, I mean for me it’s … the grey hair I’ve created before fentanyl. I haven’t had any more since.” — Family Caregiver 2
- “Well she’s not worried. She’s not breaking down and crying. She’s happier. She watches her game show. The look on her face is much, much better and I see her in the mornings when she comes out here to have her tea she looks great to me in comparison to what it was. Yeah, it’s unreal. And if I miss, if I’m not on the ball like to get her a drink, she’ll say I need my morphine and I just go in and give her that little 0.5.” — Family Caregiver 9
- “… You know it’s given Mom a better quality of life. It’s given us so we’re not so worried, watching her struggle right.” — Family Caregiver 10
- “Even for when he’s just like you know going out to come upstairs to go for a drive with us, you know, he knows that he has to take the liquid stuff [opioid] about 15–20 minutes before he’s coming up and it makes a difference. The days that … he doesn’t take it, he’s winded. So, it makes a difference. You can see it.” — Family Caregiver 7

**Box 3: Perspectives of patients and family caregivers on relationships, resilience and routines after opioids were started**

- “I never done much cooking or anything like that but she helps me. You learn. Wash the clothes and stuff like that, I never had to. She done all that. I mixed some clothes up when I first did it and I got yelled at for that. Then I figured it out … Yeah, you’ve got to do what you’ve got to do. Yeah, you can’t be down about it. You’ve got to be up as high as you can. I don’t dwell a lot on the end and stuff, I don’t sit around.” — Family Caregiver 1
- “I used to worry and worry and worry and now I just take one day at a time. Most of the time, there are some days when you think about it and then you say well look that’s enough thinking. Just go and do something else. That’s what I have to do, and with the grandchildren they don’t give you time to think about anything anyway. Yeah, come on grammy, come on, come now and they’re just so cute.” — Patient 1
- “As soon as he wakes up I give him his morphine, the short-acting before he has his shower because it helps; and then as soon as he’s out here, he gets his, he takes 40 mg in 24 hours, yeah 24 hours of morphine. But I mean I think he’s doing real good. I would never stop the morphine though. No. Because I don’t think he’d last.” — Family Caregiver 3

**Interpretation**
Patients reported that the benefits of opioid therapy outweighed the burdens and chose to continue to take opioids when they balanced the benefits with the adverse effects. All found opioids helpful with improvements to their quality...
of life or dyspnea or both. Concerns about safety or stigma regarding opioid treatment were rare. Family caregivers echoed this view, and some felt that opioids had actually helped to extend patients’ lives. Both patients and family caregivers described the burden of living with severe, persistent dyspnea and how opioids had improved the quality of their lives. Conversely, many physicians indicated uncertainty and discomfort about prescribing opioids to patients with COPD. Lack of guidance, confidence and experience, a fear of respiratory suppression, and concern about censure were key factors limiting their willingness to prescribe opioids in this context. However, most acknowledged that dyspnea is difficult and frustrating to manage and thus were willing to consider opioids for this purpose. These findings suggest a substantial gap between patients’ and caregivers’ experiences and physicians’ current practices related to opioid therapy for refractory dyspnea in advanced COPD.

Despite the trend toward more explicit recommendations and clinical practice guidelines from professional societies for the use of opioids to treat refractory dyspnea in patients with advanced COPD,27,28 many physicians remain hesitant to do so. From a medical perspective, a shroud of uncertainty and disquiet continues to surround the use and prescription of opioids for patients with COPD. Arguably, disproportionate emphasis has been placed on the risk of respiratory depression that is not supported by currently available evidence. Deep-rooted fears that militate against the use of opioids are likely based on innumerable factors, but our findings suggest that, while physicians report prognostic uncertainty, fear of hastening death via respiratory suppression, and fears of recrimination, their patients, for the most part, appear to be open to whatever will relieve their dyspnea.

We are unaware of similar studies specifically dealing with attitudes about the use of opioids for dyspnea in patients with COPD, other than our preliminary work. Our initial surveys at continuing medical education events highlighted clinicians’ discomfort with prescribing opioids as a treatment for dyspnea in patients with advanced COPD.4 We followed this survey with a pilot study of respiratory therapists’ and family physicians’ experiences and attitudes in New Brunswick.7 In the present study, we extend this pilot work by providing insights into patients’ and family caregivers’ experiences with opioids, and contrasting this with physicians’ perspectives and current practices.

Our interpretation of data from our two studies was inevitably influenced by the investigators’ professional backgrounds (medical: G.R.;...
In my generation of physicians when you were in med school that was •
I must admit, I would be leery even at this point, on this date in 
CO PD

Box 7: Perspectives of physicians about regulatory bodies and pre-
Note: CME = continuing medical education, COPD = chronic obstructive pulmonary disease.

Box 6: Physicians’ concerns about prescribing opioids for refractory dyspnea in patients with advanced COPD
• “I mean when I went to medical school, we were taught to never consider opioids in people with COPD. We were going to kill them. It was like if you gave them one dose of morphine, they would be dead and it would be your fault. That was the teaching. So it was a revelation to me, I don’t know, five, seven years ago to go to a CME thing and have people talking about using opioids and starting to use it, and certainly in terms of dealing with anxiety and breathlessness.” — Physician 13, Family Medicine

• “In my generation of physicians when you were in med school that was hammered in, ‘Well you can’t do this. You’re going to have respiratory depression.’ I’m sure there is a 10-year generation where that was hammered into you, just like, ‘Don’t use a beta-blocker in heart failure.’ So you have to relearn. I think it’s just a matter of re-learning and being comfortable using it.” — Physician 21, Family Medicine

• “So, I’m not concerned with respiratory depression if a patient is started on an appropriate low dose, titrated appropriately, and monitored appropriately.” — Physician 3, Palliative Medicine

• “I worry about it all the time. People overdose, old and frail people really easily, when they [other health professionals] are not used to giving opioids. So they hear about giving opioids for shortness of breath and they lay it on to them and even the people who have pain, that scares me if they’re people that don’t understand that 5 mg of morphine is not the same as 5 mg of Dilaudid or, you know, they don’t know how to convert to the fentanyl patch. So I worry about it all the time when other people are doing it. I don’t worry about when I do it, no.” — Physician 11, Palliative Medicine

Note: 

Recent qualitative work involving physicians from the United States that focused on attitudes surrounding opioid prescribing for pain at the end of life or for noncancer pain among elderly adults also reported fear of censure (via drug enforcement agencies) and the need to improve knowledge, as well as overcome barriers to and fears surrounding opioid prescribing. There is little data on real-time prescribing of opioids for COPD-related dyspnea. Retrospective data from a Saskatchewan database indicate a far lower prevalence of opioid prescribing toward the end of life among patients with COPD who have dyspnea than among patients with lung cancer. The strongest evidence available at this time from clinical trials (a systematic review favouring the use of opioids and a short-term randomized crossover trial) supports the experiences of the patients and family caregivers interviewed in our study (i.e., effective relief of dyspnea without evidence of respiratory depression). More recently, in a dose-increment and pharmacovigilance study involving 65 patients in Australia in which opioids were used for refractory dyspnea (mostly due to COPD), there were no cases of respiratory depression during a mean follow up of three months, and 51% of patients reported a benefit sufficient for them to continue taking opioids. Preliminary data from an ongoing Canadian clinical trial (clinical.trials.gov, trial no. NCT00982891) indicate even higher levels of
self-reported efficacy and acceptability over a period of two to six months.16

Limitations
The aim of qualitative studies is not generalizability, and our study is no exception. However, by conducting our study in both urban and rural settings, we hoped to generate new insight applicable to both. We accept that our quantitative data from the included patients and family caregivers (collected once and a small sample) was too limited to be generalizable; we have thus not reported all of the details here. Although we recruited physicians from several disciplines and from urban and rural settings, the views of the participating physicians may not represent the views of all those who care for patients with advanced COPD in Nova Scotia or elsewhere in Canada.

We recognize a potential bias in that we interviewed only patients who were taking opioids, and so we cannot report the views or concerns of patients or family caregivers who had been offered and declined or who had discontinued the use of opioids; however, we were primarily interested in those who had used opioids. We chose to enrol family caregivers who were living with patients who used opioids; the experiences of family caregivers who live elsewhere may be different. We are unable to comment on whether anxiety or depression had improved substantially for patients after opioids were started, but caregivers often mentioned that their loved one appeared “more relaxed.” We did not collect spirometric measures of airflow obstruction (i.e., FEV1 or FEV1/FVC ratio); most of the included patients were housebound, living with high dyspnea burden and had not undergone recent pulmonary function testing.

Conclusion
If the perspectives of the physicians interviewed represent those of physicians who practise elsewhere in Canada, patients living with advanced COPD and refractory dyspnea are unlikely to experience treatment benefits comparable to those of our study participants. Family members may also be denied potential relief of associated stress that can burden them for years.24 Discrepancies between the positive experiences of patients and family caregivers and the reluctance of physicians to prescribe opioids for refractory dyspnea constitute an important gap in care. Bridging this gap will likely require innovative educational initiatives to improve the uptake of guidelines and confidence in prescribing opioids for refractory dyspnea. At professional society conferences in both Canada and the United States, we have used, to good effect, film footage of patients and their caregivers discussing the effects of opioids for refractory dyspnea. Others have recently promoted the concept of a rapid learning model, similar to the “plan, do, study, act” cycle promoted by the Institute for Healthcare Improvement,17 to disseminate new information from clinical trials and consensus statements from professional societies about palliation of dyspnea.18

To address the many knowledge gaps regarding patient and caregiver perspectives, we are collecting, in an ongoing clinical trial, both quantitative and qualitative assessments of patient and caregiver experiences before and for six months after opioids are initiated for refractory dyspnea in advanced COPD.

Our patients and caregivers have taught us much about effective palliation; we have a duty to act on their insights. The Canadian Medical Association’s code of ethics reminds us of our responsibility to “first consider the wellbeing of the patient” and that doing so requires our engagement in “lifelong learning to maintain and improve … professional knowledge, skills, and attitudes.”19 Evidence is accumulating to suggest that soon the appropriate question will no longer be if we should prescribe opioids to help palliate refractory dyspnea in patients living with advanced COPD, but rather how to do this competently20 and when.

References

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Contributors: Graeme Rocker, Joanne Young and Cathy Simpson contributed to the conception and design of the study. Interviews were conducted by Joanne Young and Cathy Simpson, and verbatim transcriptions were analyzed by Margaret Donahue. All of the authors contributed to the interpretation of data, drafting and revising the article, and gave final approval of the version submitted for publication.

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