

Letters

A Response to: Challenges in Recruiting Patients to a Controlled Feasibility Study of a Drug for Opioid-Induced Constipation: Lessons From the Population With Advanced Cancer



To the Editor:

We were most interested to read the letter by Bull et al.¹ As researchers, clinicians and academics in supportive and palliative care, the letter resonated with our own experiences when trying to recruit to studies exploring the problems of disordered bowel function in patients with advanced cancer. Although the authors of the published letter attribute this to the advanced cancer population, we would like to suggest an alternative opinion. In contrast, we submit that rather than this being an issue with the advanced illness stage of this patient cohort, the problems were related to the symptom they were investigating: constipation.

There are two issues that support our contention that the problems were related to constipation symptoms rather than cohort in question. The first is the track record of the Australian national Palliative Care Clinical Studies Collaborative.² This group based at the University of Technology Sydney (Australia) is multi-center palliative care research network with participating sites in each mainland state that conducts investigator-led clinical studies in palliative care. Established in 2006, Palliative Care Clinical Studies Collaborative is the first, largest, and most successful global palliative care trials group having successfully completed nine adequately powered Phase III controlled clinical trials, randomized more than 2000 participants; published more than 100 manuscripts; and secured \$AU25M in competitive funding. This group has completed randomized control trials in difficult palliative care problems including pain,³ inoperable malignant bowel obstruction,⁴ delirium at the end of life,⁵ chronic breathlessness,^{6,7} and nausea.⁸ This group has demonstrated by recruitment that such trials are acceptable to frail patients, their families, and other health professionals. Furthermore,

the group's track record summarized above confirms the feasibility of these trials.

The second point is that the Collaborative has also tried to complete studies in constipation symptoms. When examining our own difficulties with recruiting, we turned to Australian national data with the aim of understanding at a population level the issues more clearly. To achieve this, we interrogated national data sets pertaining to specialist palliative care as entered into the Australian Palliative Care Outcomes Collaboration records. This resource contains point-of-care details for more than 85% of all people seen by specialist palliative care services nationally,⁹ of whom 80% have cancer as the reason for referral to palliative care. An analysis of consecutive referrals to participating palliative care services who had died between January 1, 2013 and December 31, 2015 was undertaken. There were 50,319 patients included on the basis that they had at least one measurement of distress (mean 3.27) from bowel symptoms on a 0–10 numerical rating scale in the last 55 days of life. According to national prescribing data in 2014, laxatives were the most commonly dispensed palliative care-related prescription¹⁰ suggesting that many of this group were likely to receiving laxatives and, by extrapolation, constipated. However, at the same time, distress from bowel symptom scores highlighted that most were less bothered by these issues than expected. There was, however, a small group (3.6%) who rated their distress as severe. These observations are consistent as an earlier interrogation of the Palliative Care Outcomes Collaboration data highlighting that at time of referral to palliative care, less than 5% were bothered by severe constipation symptoms.¹¹

To conclude, this letter's aim is not to minimize the fact that for some people, bowel symptoms are severe and distressing, and this group requires attention. The challenge is identifying the sub-group who is at most risk and start focusing our research attention to better understanding their unmet needs.

Katherine Clark, MBBS, MMed, PhD, FRACP,
FACHPM
Cancer and Palliative Care Network
Northern Sydney Local Health District
NSW, Australia
E-mail: Katherine.Clark@health.nsw.gov.au

Northern Clinical School
The University of Sydney
NSW, Australia
Improving Palliative, Aged and Chronic Care
through Clinical Research and Translation
University of Technology Sydney
NSW, Australia

Samuel Allingham, BMath [Hons]
Palliative Care Outcomes Collaboration
Australian Health Services Research Institute
Innovation Campus
University of Wollongong
NSW, Australia

Jane L. Phillips, RN, BSN, PhD, FACN
Improving Palliative, Aged and Chronic Care
through Clinical Research and Translation
University of Technology Sydney
NSW, Australia

Linda Brown, MBus, BBus [Mgmt]
Improving Palliative, Aged and Chronic Care
through Clinical Research and Translation
University of Technology Sydney
NSW, Australia

David C. Currow, BMed, MPH, PhD, FRACP,
FAHMS
Improving Palliative, Aged and Chronic Care
through Clinical Research and Translation
University of Technology Sydney
NSW, Australia

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Authors' Response



To the Editors:

We appreciate the response of Clark et al. to our article, Challenges in Recruiting Patients to a Controlled Feasibility Study of a Drug for Opioid-Induced Constipation: Lessons From the Population With Advanced Cancer (*JPSM* 2019;57(5):e5–e8), and their extensive experience from the Australian Palliative Care Outcomes Collaboration. Although we agree that distress from constipation may be limited to a small percentage of the cancer population and contribute to recruitment challenges, other factors we encountered included late referrals, rapid trajectory of disease, limited opioid use, and disinterest because of dealing with multiple issues during advanced illness. Attributing the problem to one issue is a bit like looking for a needle in a haystack. Nonetheless, we agree: Although constipation has been reported in as many as 70%–90% of opioid-treated cancer patients, perhaps as Clark points out, it is a small subset that experiences significant distress.

Dr Janet Bull, MD, MBA
Four Seasons
Flat Rock, North Carolina, USA
E-mail: jbull@fourseasonscfl.org

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