

## Editorial

### **Systematic reviews of pain and online interventions for cancer patients show evidence of mixed efficacy and highlight need for more rigorously designed research**

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Two systematic reviews are highlighted in this month's PEC, one exploring educational interventions to reduce cancer-related pain, the other focusing on online interventions for cancer patients. Pain is a common and feared experience of patients living with cancer, particularly at the end of life, and can have a major impact on quality of life, limiting the activities in which people can participate and causing suffering and distress. It has long been reported that cancer-related pain is inadequately treated in routine clinical practice, and there is little evidence of improvement over time [1]. The literature suggests that both patient and health professional barriers contribute to these poor outcomes, with education of both groups recommended to overcome these barriers. Thus the current systematic review of reviews of educational interventions to improve cancer pain outcomes by Adam, Bond, and Murchie [2] is both timely and important.

Adam, Bond, and Murchie [2] identified eight systematic reviews summarizing the results of 34 randomised controlled trials, of which two were pilot studies. Thus there is a considerable body of research in this area. Most studies targeted patient and caregiver education, and those that did target health professional education rarely measured patient outcomes. Thus the evidence for impact on patient outcomes of health professional interventions is still very preliminary, and this was identified by the review authors as a major methodological problem that should be addressed in future studies.

This review-of-reviews concluded that there is evidence of a small, statistically significant impact of patient/caregiver education intervention on pain intensity, in the order of 1 point on a 10 point scale. The authors rightly question the clinical significance of such a small improvement. Where measured, quality of life and functional outcomes were not impacted by the interventions. As other outcomes that might reflect real benefit, such as reduced emergency visits, were measured in none of the cited studies, it is not clear whether these were impacted. Thus the review highlights the need for our community to pause and reflect on why interventions are not having greater impact, and which factors may be contributing to successful and less successful outcomes [2].

Unfortunately the studies included in this review-of-reviews did not provide any answers to these questions. No factors were consistently identified as leading to better outcomes, although some reviews did conclude that factors such as high dose and intensity of intervention [3], and patient characteristics such as having a better prognosis, being an inpatient and having higher baseline pain [4], may increase chances of intervention benefit. A similar summary of eight systematic reviews,

which overlapped with but did not exactly replicate the set of included studies in Adam, Bond, and Murchie's review [2], reached the same conclusion that attempts to understand the reasons for heterogeneity between results have so far been unsuccessful [5].

Adam, Bond, and Murchie [2] propose that inconsistent and negative results are the result of a piecemeal approach to intervention without use of an overarching framework to ensure that all relevant factors are addressed. The authors provide a useful diagram summarizing such a framework that may assist future studies to test this proposal. The authors also suggest taking into account factors that may influence or moderate intervention effects, and particularly propose (on the basis of the literature cited above) intervention setting and dose, and patient prognosis and baseline pain, as relevant factors. However, evidence suggests that other factors, such as patient education levels [6] and health literacy [7], may influence pain behaviour and receptiveness to intervention, and should also be considered.

As in the online intervention area, the methodological quality of included studies, as well as of systematic reviews, varied. Jho et al [4] noted that poorer quality trials, and those that used usual care control groups, reported larger effect sizes. It remains an important consideration when we conduct trials and review the evidence, to use optimal designs where possible so that effect sizes are not over-estimated and the field is not left with the perennial cry that "more high quality studies are needed!"

Online resources have considerable potential to provide information and support to large numbers of cancer patients in a widely accessible and cost-effective manner. Recently there has been an explosion in the number of these online resources, but their impact on patient outcomes has been evaluated in just a handful of studies; only 14 publications provided sufficient outcome data for inclusion in the systematic review by McAlpine, Martin-Sanchez, Joubert, Merolli, and Drummond [8] featured in this issue.

The online resources reviewed by McAlpine et al [8] are very heterogeneous; their designs varied greatly, along with their efficacy. Some had positive (albeit often transitory) effects; many were ineffective, while a couple had adverse effects. No firm conclusions about the efficacy of online interventions for cancer patients can be drawn from the review, but it does highlight some of the methodological issues needing to be addressed in further research in this area.

Numerous studies were excluded from the review by McAlpine et al [8] due to measurement of outcomes with no clinical relevance, e.g. patient acceptability and satisfaction. Establishing the acceptability and feasibility of online interventions is an important initial step, but it should be noted that high satisfaction is not necessarily associated with improvements in clinically meaningful outcomes and is sometimes accompanied by poor clinical outcomes, as in Salzer et al [9]. Consequently, a clinically relevant primary outcome assessed using a validated measure is recommended when evaluating online interventions.

Many of the interventions reviewed by McAlpine et al [8] lacked any theoretical foundation. Hypothesizing a mechanism by which an online intervention impacts the primary outcome may focus intervention design, and assessing that mechanism may

further our limited understanding of how online interventions work. It is also important to consider what dose of an online intervention may be required to derive a clinically meaningful benefit. Traditionally, number of logins and time spent online have been used to calculate dose, but recently other usage metrics such as number of activities completed have been proposed [10].

Choice of comparison condition is another important issue to consider when evaluating online interventions. The majority of the studies reviewed by McAlpine et al [8] were randomized controlled trials, but many compared the active intervention with a waitlist control, which is likely to bias results due to some participants using the Internet for non-directed self-help while on the wait-list. Conversely, others may not use the Internet for this purpose when they otherwise would have, because of anticipated future benefit from the active intervention.

Carefully selected comparators may also help determine which aspects of multifaceted online interventions are effective and identify synergistic components. It would be beneficial if studies of multidimensional interventions compared different versions of the intervention with each other as well as a control condition. For example, Wootten et al [11] compared access to: a) an online self-guided intervention for prostate cancer survivors (My Road Ahead) alone, b) My Road Ahead plus a moderated online forum, c) the moderated online forum alone. Participants with combined access to My Road Ahead and the moderated forum showed significantly superior improvements in psychological distress compared to those with access to either intervention alone. These comparisons may necessitate more participants, but the ability to recruit to online interventions from Internet-users worldwide should ameliorate this issue to some degree.

Comparisons with pre-existing offline interventions are also needed to determine the added value of online interventions compared with more traditional interventions and may produce unexpected results. For example, in one study reviewed by McAlpine et al [8] it was found that those given information online had marginally worse QOL than those given paper information booklets two months post-intervention [12].

Contrary to common assumptions; a couple of the studies reviewed by McAlpine reported adverse effects of online interventions. In addition to the abovementioned study by Salzer [9], another study found that 6 months after participating in a rehabilitation course, those who also participated in an Internet support reported less reduction in anxious pre-occupation, helplessness, confusion, and depression [13]. The limited efficacy of online interventions to date and the potential for adverse effects reinforces the need for their rigorous evaluation. Hopefully the review by McAlpine et al [8] will provide some useful pointers for researchers working in this burgeoning area and the great promise of online interventions to cost-effectively deliver information and support to a large number of cancer patients will be realized.

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