

outcome, overall survival, has not yet been reported for this study. As the authors note, those results will be forthcoming. We certainly hope that this randomized controlled trial is as successful as their earlier pilot study.<sup>2</sup>

Second, although this is a dietician-initiated intervention, we do not glean a greater understanding of what dietary choices, in particular, are most important during cancer treatment. Instead, the confounding in this study secondary to multiple interventions and increased involvement by the care team obscures the effect of dietary changes. For example, although the screening for and treatment of depression is an important component of treatment for any highly morbid disease such as head and neck cancer, the incorporation of this additional intervention confounds the effects of the nutritional intervention.

Last, in this trial, the dieticians' goal appears to be to encourage patients to consume as many calories as possible without regard for macromolecule composition. As a result, this study puts the cart before the horse: To our knowledge, there is no evidence in humans regarding which dietary composition effectively improves patient-important outcomes in head and neck cancer. Studies of fasting, in both mice and humans, show the expected temporary weight loss with drastically improved overall survival and/or treatment toxicity profiles.<sup>3,4</sup> Additionally, varying carbohydrate composition in the diet can alter human metabolism and may have a role as a cancer treatment adjuvant.<sup>5,6</sup> Before we spend too much time exploring how best to encourage our patients to follow our dietary advice, we should make sure that we are encouraging them to choose the dietary intervention most likely to improve their outcome.

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## In Regard to Britton et al



*To the Editor:* We read the article by Britton et al<sup>1</sup> with interest. In their report of the *Eating as Treatment* trial, they randomized patients with head and neck cancer undergoing radiation therapy to motivational interviewing and cognitive behavioral therapy to improve nutritional status.<sup>1</sup> Patients randomized to this arm experienced less weight loss and fewer treatment interruptions. However, no report was given on local control and survival outcomes in the groups. Furthermore, it is unclear what nutritional recommendations were made to these patients.

The missing outcome data are of importance because similar patients who received pretreatment nutritional support in Radiation Therapy Oncology Group trial 90-03 experienced less weight loss as well, along with decreased grade 3 to 4 mucositis, than patients who did not receive baseline nutritional support. However, these patients also experienced a statistically significant decrease in locoregional control and survival at 5 years.<sup>2</sup> Although these patients had higher risk disease at presentation, after adjusting for prognostic factors, multivariable analysis revealed that nutritional support was a highly significant independent prognostic factor for increased locoregional failure. It would be interesting to see how the patients in this reported study fared with aggressive nutritional support.

Moreover, this raises an important point with nutritional studies; weight loss is not necessarily the result of a caloric deficit, but rather a combination of caloric deficit, inflammation, insulin resistance, and inadequate nutrient and vitamin intake.<sup>3</sup> Simply providing calories is unlikely to improve this situation and may feed the tumor instead of the patient if macronutrient composition is inadequate. No study to date has attempted to provide specific macronutrient support that considers both tumor and patient metabolism, but many attempts at nutritional support include supplements high in simple sugar such as Boost and Ensure, both of which contain a majority of glucose and high-fructose corn syrup. Such products may worsen insulin resistance and fuel both tumor glycolysis and tumor pentose phosphate pathway, which cancer cells use to offset free-radical damage from ionizing radiation.<sup>4</sup> Unfortunately, current research suggests that the opposite approach—limiting carbohydrates and increasing fat consumption—may combat muscle loss during treatment and

Conflict of interest: C.E.C. receives compensation for nutrition books.

support weight maintenance<sup>5</sup> while potentially increasing tumor radiosensitivity.<sup>6</sup>

Without consideration of macronutrient composition, nutritional support for cancer patients may continue to be suboptimal. Although we applaud the efforts of Britton et al, the lack of consideration of macronutrient composition and of the potential detrimental effects of aggressive nutritional support with improper macronutrient composition illustrates the lack of attention given to evidence-backed nutritional support for patients with cancer.

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## In Reply to Lee and Douthit, and Champ and Klement



We thank the authors for their interest in our trial.<sup>1,2</sup> Eating As Treatment (EAT) was a multidisciplinary, multilevel, and multicomponent trial of a behavioral intervention. It aimed to change not just patient self-care behaviors but also the clinical interaction style of the dietitians. It was not a trial of a nutritional intervention.

We acknowledge the secondary analysis of the Radiation Therapy Oncology Group 09-03<sup>3</sup> trial, suggesting that patients who received nutritional support before radiation therapy had inferior outcomes compared with those who received nutritional support while on treatment. However, it should be noted that the EAT intervention was provided while patients were receiving radiation therapy, not prior as was the case in Radiation Therapy Oncology Group 09-03. Furthermore, nutritional support delivered at this timepoint was supported by systematic review<sup>4</sup> and European<sup>5</sup> and Australian<sup>6</sup> best practice guidelines. More broadly, malnutrition during head and neck cancer treatment has been associated with mortality,<sup>7,8</sup> and the EAT trial aimed to assist dietitians to ameliorate this.

The clinical advice provided by dietitians in the study was unchanged between control and intervention phases, and the trial included no specific macronutrient prescription. We agree that this does not provide insight into what is the most beneficial dietary advice for patients with head and neck cancer, only that adherence with that advice can be improved.

Patients in the trial were blinded to treatment allocation. Both groups received a form of care that differed only in the way the dietitians interacted with them, not in the advice they were given. It would not have been possible for the patients to correctly deduce their allocation on the basis of increased involvement of the treating team, as suggested, because there were no differences in the average number of sessions or session duration between control and intervention patients.

Finally, it is important to understand that complex behavior change interventions are by necessity multifactorial.<sup>9</sup> Although there were multiple components to the EAT intervention, each component was well established, had been shown to be effective in other settings, and was clearly detailed in the published study protocol.<sup>10</sup> We do not conceptualize these as multiple interventions but simply components of the larger complex intervention that was EAT.

We look forward to reporting on the survival outcomes of the trial and contributing further to this area.

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