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## Move Onward, Press Forward and Take a Deep Breath Can Lifestyle Interventions Improve Quality of Life of Women with Breast Cancer ...and How Can We Be Sure?

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“The quality of life is more important than life itself”

Few would argue with this statement. But the originating source might surprise you. Was it a renowned psychologist? A famous painter? Or perhaps an unrivaled hedonist? No, these words were first uttered by Alexis Carrell, a French surgeon and 1912 Nobel Prize laureate recognized for his work on vascular suture and organ transplantation.

In this issue, two papers report the results of randomized trials that targeted quality-of-life (QoL) as their primary outcome.<sup>1,2</sup> While both studies tested lifestyle interventions among women with breast cancer and share several similarities, they are distinctly different. The article by Courneya and colleagues reports the results of a trial (n=242) which compared aerobic or resistance exercise with usual care.<sup>1</sup> Although this group of investigators is renowned for delivering exercise interventions that are well-received and which improve QoL, the results of this trial are somewhat different from other reports from this group. While secondary endpoints such as self-esteem were significantly improved in both intervention arms, and other arm-specific differences were observed (such as increased aerobic fitness in the aerobic arm and increased muscular strength, lean body mass and chemotherapy completion rates in the resistance exercise arm), fatigue, depression, anxiety and -- most importantly--QoL did not differ among women assigned to the exercise interventions as compared to usual care. These findings are distinctly different from those that Courneya et al. reported in *JCO* in 2003.<sup>3</sup> The results of this smaller (n=52), two-armed trial found a significant increase in QoL with an aerobic exercise intervention as compared to usual care, with change scores of  $+9.1 \pm 14.1$  versus  $+0.3 \pm 8.5$  points, respectively ( $p < .001$ ). So, why are these findings so discrepant? Was it the intervention? Most likely not, since graduated thrice weekly aerobic regimens were used in both trials.<sup>1,3</sup> Was it the outcome measure? Perhaps, since there are differences between the Functional Assessment of Cancer Therapy (FACT) Breast and Anemia scales;<sup>4,5</sup> however, this still is unlikely. Instead, the most likely difference was that participants in the current study were actively receiving chemotherapy, as compared to those who had completed their primary treatment. Having conducted studies among patients who are in active treatment compared to those who have completed therapy, it is easy to recognize and fully appreciate the data offered by these two trials, including adherence and attrition rates of 98.5% and 1.9%, respectively, for the former trial and 68–72% and 7.9%, respectively, in the most recent study. These rates are still admirable, but they point to the challenges in developing effective interventions that must overcome the host of barriers in patients who are under active treatment. Behavioral interventions that are instituted in these patients come during a period when patients are saddled with competing time constraints and also when their emotional and physical energies are being

drained. However, such interventions also may demonstrate their greatest impact during this time of treatment. While QoL may not necessarily be an outcome that is responsive during this point in time, other endpoints, such as those observed by Courneya and colleagues, i.e., improved strength, fitness, lean body mass and chemotherapy completion rates are certainly very important outcomes.

The trial conducted by Moadel et al.<sup>2</sup> is helpful in discerning the time period when behavioral interventions might be most effective in improving QoL. This study is distinctly different from that of Courneya et al. in that it tested the efficacy of yoga, a mindfulness-based intervention as contrasted to an exercise intervention, for improving QoL among breast cancer survivors. The sample accrued for this study (n=128) was diverse, not only in terms of ethnic and racial minorities (42% African-American, 23% Hispanic, 23% Non-Hispanic White and 4% Other) and educational level (76% high school or less and 24% with at least some college). This is an admirable achievement, since two-thirds of lifestyle interventions conducted to date have relied on samples that are at least 90% white and 80% college-educated.<sup>6</sup> The study is also unique with respect to treatment completion, with roughly half of the sample in active treatment and the other half having completed their therapy. Like the findings of Courneya et al.,<sup>1</sup> no significant differences in QoL, fatigue or distress were observed between women randomized to yoga compared to usual care, though a significant difference was found for social wellbeing, with the yoga arm experiencing significantly lesser decreases than those in usual care (change scores were -0.51 vs. -2.78, respectively [p<.0001]). However, within the subset of women (n=71) who were not currently receiving chemotherapy, secondary analyses showed several differences between study arms, with the intervention group experiencing significantly improved QoL (p<.008), emotional well-being (p<.015), social well-being (p<.004), spiritual well-being (p<.009), and less distress (p<.031). These results suggest that the timing of lifestyle interventions may be key if QoL is the primary outcome. Certainly, if lessons are to be learned across lifestyle interventions, it is worthwhile to consider the recent systematic review and meta-analysis by Schmitz and colleagues who weighed the evidence on the impact physical activity interventions on improving QoL during treatment and found it to be “weak,” whereas the evidence for interventions that were timed post-treatment were judged as “strong.”<sup>7</sup>

In determining the strength of evidence for this review, Schmitz and colleagues took into consideration not only the findings of previous research, but also the design features of each trial. As in the reviews of Knols et al.<sup>8</sup> and Bower et al.,<sup>9</sup> they acknowledged the importance of a carefully constructed attention control group to assure rigorous control for factors such as group context, instructor attention, number of contacts, and other factors. Unfortunately, most previous studies that have tested physical activity or mindfulness-based interventions have employed usual care or wait list controls and thus lack optimal rigor. While the studies offered by Courneya et al.<sup>1</sup> and Moadel et al.<sup>2</sup> provide valuable information, they also exhibit this limitation. Thus, to move the science forward, lifestyle intervention trials must employ an appropriate attention control – a need which may be even greater if QoL or other self-reported data serve as primary endpoints.

In closing, let’s revisit Alexis Carrell, the originator of the statement that “quality of life is more important than life itself.” What became of this Nobel laureate and father of transplantation? Unfortunately, after a strong start, he got on the wrong track and became a vocal proponent of eugenics and the Fascist party. He died in relative obscurity and ironically lost the QoL that he enjoyed in his younger years. Thus, he serves as a tragic, yet appropriate example of the importance of science and its interpretation in determining QoL for this editorial on QoL, which reaffirms the importance of science and its interpretation.

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