after surgery alone.[3] In addition, there may be decreased toxicity with reduction in chemotherapy dosage. Toxicity associated with cisplatin chemotherapy has prevented as many as 35% of patients from completing the full recommended 3 cycles, even in trials.[4] Haughey et al[5] found that the addition of postoperative chemotherapy did not improve survival in patients with OP SCCA with human papillomavirus-mediated tumors, and this presents a possible opportunity to decrease toxicity without jeopardizing control rates.

2. Which treatment is most cost-effective? This also is an excellent question. Analysis of cost of treatment is complicated and difficult because many factors contribute to cost: the expense of drugs, hospitalization, equipment, personnel, time off from work, and time to travel for treatment. The list is long and complex, and the cost-analysis models become complex; however, cost is going to be essential in the analysis of superiority of treatments as we wrestle with the escalating expense of health care. In a cost analysis of surgery vs radiation therapy vs chemoradiation therapy for esophageal cancer, Kuppusamy et al[6] found that surgical therapy alone was the least costly and that the expense increased with each additional method of treatment. In a similar study of OP SCCA, we found that surgery and surgery plus radiation therapy are cost-effective compared with a model in which every patient received primary chemoradiation therapy.[7]

I agree with Dr Foote and his colleagues emphatically that these questions of morbidity, quality of life, and cost are paramount in deciding which treatment to offer patients with OP SCCA. We at the Mayo Clinic Department of Otolaryngology/Head and Neck Surgery are enthusiastic and excited about the opportunity to test these treatments in clinical trials in an effort to determine the superior individualized treatment for our patients.

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Potential, but Unobserved, Adverse Cardiovascular Effects From Endurance Exercise

To the Editor: The review by O'Keefe et al[1] in the June 2012 issue of *Mayo Clinic Proceedings* discusses the hypothesis that excessive strenuous exercise may result in adverse cardiovascular effects. Data from Wen et al[2] are cited as supportive evidence that the mortality benefits of exercise "peak at 50 to 60 minutes of vigorous exercise per day." The reproduced figure, however, does not show a peak; rather, it possibly shows a plateau in the benefit of exercise at the highest level observed, and even the case for a plateau is unconvincing. Turning to the primary data, O'Keefe et al wrote a letter to the journal of publication[3] and received a response that proved their interpretation to be incorrect. Wen et al[4] responded to their letter with a description of data that show not only the absence of peak but also no evidence of a plateau, with a continuing trend to improved all-cause mortality and even better hazard ratios for cardiovascular disease at the highest level of exercise. Wen et al wrote, "We were not able to identify an upper limit of physical activity, either moderate or vigorous, above which more harm than good will occur. . . ." The interpretation of the data provided in the review by O'Keefe et al is misleading, particularly given the response of the authors of the original data.

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In reply: Dr Bubb correctly points out that Wen et al[1,2] found that the exercise-induced reductions in the risk of all-cause mortality continued to accrue with longer efforts. Yet, a 140% increase in one's time investment (from 50-120 min/d) would be expected to yield only an additional 5% risk reduction, from 40% to 45%.[2] Furthermore, the definition of vigorous exercise is open to interpretation.[3] Among the 416,000 Taiwanese adults in that study, those who did *any* activity at or above 6.5 metabolic equivalents (eg, jogging slowly, hiking, or doubles tennis, which most would not consider "vigorous exercise") during a typical week were placed in the group of vigorous exercisers. Multiple studies have shown that light- or moderate-intensity exercise does not pose the dose-dependent risk that appears to be associated with prolonged high-intensity exercise. Indeed, we often tell our patients that they can, for example, walk or garden all day long without concern about cardiovascular damage.[4,5]

Lee et al[6] recently reported that among 52,000 adults monitored for a mean of 15 years, the 14,000 runners had