Cost-Effectiveness of Intensive versus Standard Blood-Pressure Control

TO THE EDITOR: Bress et al. (Aug. 24 issue)[1] report on the Systolic Blood Pressure Intervention Trial (SPRINT) cost-effectiveness analysis of intensive blood-pressure lowering. However, the generalizability of such simulations is dependent on the external validity of the risks of adverse events attributed to the intervention. In our community-based, prospective cohort study that was representative of the community-dwelling population of Ireland,[2] among participants who were 75 years of age or older and who met the inclusion criteria for SPRINT, the rates of injurious falls and syncope were approximately five times the rates among participants who were 75 years of age or older in the standard-blood-pressure target group of SPRINT-Senior.[3]

Injurious falls were excluded from the projections in the analysis by Bress et al. because of a lack of a significant difference between the groups. SPRINT-Senior,[3] and thus SPRINT overall, may have been underpowered for injurious falls, since SPRINT was powered for cardiovascular events rather than for injurious falls. Given the costs of accidental falls and syncope in the United States,[4] if the number of injurious falls at baseline in the eligible population[2] is higher than the number of these falls in SPRINT, the validity and interpretation of such simulations may be undermined.

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THE AUTHORS REPLY: With regard to the comments by Sexton and colleagues: the risks of serious adverse events in SPRINT may not reflect risks among older patients who are treated in the community. In the community-based study by Sexton et al., the risks of injurious falls or syncope among Irish adults who were 75 years of age or older and who met the criteria for SPRINT were approximately five times those among adults who were 75 years of age or older at baseline in SPRINT.[1] However, this difference may be due to different methods of ascertainment of injurious falls and syncope between the studies: ascertainment was based on self-report or proxy in the study by Sexton et al., whereas it was based on the number of participants who required a visit to the emergency department in SPRINT.[1,2]

In our analysis, we excluded injurious falls on the basis of the results of SPRINT[2] and the SPRINT-Senior subgroup analysis.[3] However, we examined cost-effectiveness over a range of baseline and intensive treatment–related risks of serious adverse events. We estimated that the risk of serious adverse events would need to be seven times the risk in SPRINT to make intensive systolic blood-pressure control a lower value (i.e., an incremental cost-effectiveness ratio that was >$100,000 per quality-adjusted life-year). Nonetheless, the risk of serious adverse events is important to consider when deciding on the intensity of blood-pressure control in older patients. Health systems and providers need an objective means to identify patients who are most likely to benefit from intensive blood-pressure control with a low risk of serious harms.

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Since publication of their article, the authors report no further potential conflict of interest.

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Recent Developments in Radiotherapy

TO THE EDITOR: Citrin (Sept. 14 issue)[1] provides a comprehensive review of developments in radiotherapy. However, I think that advances in personalized radiotherapy should also have been discussed. Emerging evidence suggests that cancer is a very heterogeneous disease necessitating individualized treatment protocols.[2] Radiosensitivity-predictive assays based on genotypic signatures of tumors have been shown to distinguish between certain radiosensitive tumors and radioresistant tumors.[3] This model has implications for the selection of patients for various doses of radiotherapy and radiosensitizing combination treatment.

Furthermore, cancers can be classified according to "radiomics," a temporal set of radiologic data characterized by the underlying pathophysiological features and heterogeneity of the tumor.[4] Various degrees of radiosensitivity among subclones can therefore be exploited by adaptive doses of radiation on the basis of genotypically driven radiomic signatures. This approach complements biopsies and allows for the noninvasive tracking of radiomic changes without intratumor sampling errors.

Finally, mathematical models have been developed that take into account tumor heterogeneity, dynamically acquired radioresistance, and normal tissue damage. These models have been used to inform dose fractionation, leading to prolonged survival among mice.[5] Therefore, personalized radiotherapy offers great hope in the era of precision medicine.

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5. Leder K, Pitter K, LaPlant Q, et al. Mathematical modeling of PDGF-driven glioblastoma reveals optimized radiation dosing schedules. Cell 2014;156:603-16.
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THE AUTHOR REPLIES: The omission of a discussion of advances in personalized radiotherapy was not based on a perceived lack of importance, but instead on the need to prioritize concepts to be addressed in the allotted space. Personalized approaches to radiotherapy have been explored for many years. These approaches focus on tailoring treatment to the characteristics of the tumor and to the patient's anatomical features, the underlying susceptibility of normal tissue to injury, and response of the tumor to therapy. Growth in the capacity to create and analyze genomic data and information from other advanced molecular techniques has further enhanced the opportunities in this arena.

Several recently published, comprehensive review articles and position papers on this topic summarize the challenges and opportunities of integrating personalized approaches into clinical radiotherapy.[1-3] Perhaps the most clinically advanced example of tumor biomarker–based personalization of radiotherapy is the ongoing evaluation of deintensified treatment regimens for human papillomavirus–associated tumors of the head and neck.[4] Even this approach remains investigational and has yet to be integrated into consensus treatment guidelines.

The evaluation of personalized approaches extends to surveillance after treatment as well. It has been hypothesized that early detection of minimal residual disease through analysis of circulating tumor cells, circulating nucleic acids, or