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About the Cover

The graph featured on the cover depicts the receiver operating characteristics (ROC) curves of three multivariate models for predicting second primary tumors (SPTs) and/or recurrence of head-and-neck cancer. The patient cohort came from a randomized phase III trial in patients curatively treated for stage-I-or-II head and neck cancer. Model 1 incorporated established prognostic clinical variables (tumor site, stage, treatment) alone (green curve); model 2 combined these with epidemiologic variables (smoking pack-years; blue curve); and model 3 combined the clinical and epidemiologic with genetic variables (12 chromosomal single-nucleotide polymorphisms and one mitochondrial single-nucleotide polymorphism; red curve). The trend of one curve's improvement over another is depicted by a shift to the left. The measure of this improvement, however, is derived by comparing the models' areas under the curve (AUCs). Shown by AUCs of 0.61 (clinical variables alone) and 0.64 (clinical plus smoking variables), adding smoking data improved the clinical model very little. Adding both smoking and genetic variables in model 3, however, produced an AUC of 0.84, a significant increase over the model 2 AUC (bias-corrected 95% confidence interval, 0.15–0.27, based on 10,000 bootstrap samples) and thus a significantly improved ability to predict cancer. This work underscores the importance of incorporating germline genetic variation data with clinical and other risk-factor data into models for predicting clinical outcomes and cancer risk. See articles by Wu et al. (beginning on page 617) and Mayne and Gruber (beginning on page 605) for more information. Head and neck art credit: MedicalRF.com/Getty Images.

