Comment on “Age Conditional Probability of Ocular and Ocular Adnexal Malignancies”

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Age-conditional probability is defined as the probability of developing a disease in a given age range, conditional on never having developed the disease prior to the beginning of that age range. In a recent article, Nittmann and Margo [1] provided estimates of the age-conditional and lifetime probabilities of various ocular malignancies using data from the Surveillance, Epidemiology, and End Results (SEER) database. Despite the availability of this information in SEER since the 1990s, the authors note that this is the first time such estimates have been reported for ocular and ocular adnexal malignancies [1]. They found that the lifetime risk of all ocular and ocular adnexal cancers was 1 in 1,020 for males and 1 in 1,330 for females.

Age-conditional probabilities have several distinct benefits. First, age-conditional probabilities are more relevant for most people than lifetime risks, which represent the average risk of developing the disease over a lifetime for the infant population. Few infants are concerned about their risk of developing a given disease, however, and more frequently an adult individual is interested in their immediate risk of developing a given disease in their remaining lifetime, an estimate of which would have to condition on their current age. For example, a 40-year-old woman may be more interested in knowing that her

risk of developing conjunctival melanoma in the next 20 years, given that she has not yet had a conjunctival melanoma, is 1 in 153,000, as opposed to knowing that her lifetime risk of developing conjunctival melanoma from birth is 1 in 25,600. In that way age-conditional probabilities are dynamic rather than static estimates, similar to conditional survival estimates [2].

Additionally, age-conditional probabilities are particularly well-suited to identifying what age range carries the highest burden of disease. Nittmann and Margo [1] reported a large increase in the age-conditional probabilities of most ocular and ocular adnexal malignancies from age-group 20–39 to age-group 40–59. For example, the probability of getting uveal melanoma between the ages of 20 and 39, conditional on being alive and disease free at the age of 20, was 1 in 39,600 for males and 1 in 39,200 for females, and this increased to a probability of getting uveal melanoma between the ages of 40 and 59, conditional on being alive and disease free at the age of 40, of 1 in 6,640 for males and 1 in 7,970 for females. Conversely, the age-conditional probability of getting retinoblastoma decreased dramatically after age 3 years, with an age-conditional probability of getting retinoblastoma by age 3 conditional on being alive and disease free at age 2 of 1 in 74,000 and an age-conditional probability of getting retinoblastoma by age 4 conditional on being alive and disease free at age 3 of 1 in 226,000, representing a >3-fold decrease.

Finally, lifetime risk and age-conditional risk estimates account for competing causes of death. This is especially important in the study of rare diseases. The National Cancer Institute defines any cancer with an incidence of <15 cases per 100,000 people per year as rare [3]. Ocular and ocular adnexal malignancies are quite rare malignancies by this definition. For example, uveal melanoma, the most common ocular malignancy, had an age-adjusted incidence of 5.2 (95% CI 5.0–5.4) per million based on SEER data from 1973 to 2013 [4]. When a disease is this rare, the population at risk is much more likely to die from competing causes than to get the disease of interest in any given time period. Using a method that accounts for the competing causes of death is essential in obtaining accurate and interpretable estimates of risk over a given period of time.

Despite these benefits, age-conditional probabilities represent population-average risk, and do not account for individual-level factors that contribute to risk such as family history or genetic predisposition. A growing interest in personalized medicine has pushed many to favor the development of risk prediction models that can gen-

erate individual-level predictions based on combinations of covariates. However, population-average risks remain important for understanding the public health burden of cancers [1, 5] and age-conditional probabilities are an important complement to lifetime and cumulative risks in understanding the average risk of disease among the disease-free at specific ages.

Conflict of Interest Statement

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Author Contributions

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