Competing risk of death in Kaplan-Meier curves when analyzing subsequent keratinocyte cancer

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To the Editor

We have read with great interest the article by Wehner et al[1] about the timing of subsequent new keratinocyte carcinomas in patients who present with basal cell carcinoma (BCC) or cutaneous squamous cell carcinoma (SCC).[1] The authors estimated the probability of developing a subsequent KC by calculating 1 minus the Kaplan-Meier (KM) survival probability. The use of the KM method for other end points than overall mortality can lead to a violation of a key assumption, which is the independent censoring assumption. In a KM curve with subsequent KC as the event of interest, patients who die are censored. The independent censoring assumption means that we assume that patients who are censored at time *t* have the same risk of developing the event of interest as those patients who are still in follow-up at time *t*. It is impossible to develop a KC after death, and not adjusting for this will lead to an overestimation of the probability of developing a new KC.

One possibility to take the competing risk of death into account, is to compute a cumulative incidence curve (CIC). Other methods are also available and described elsewhere.[2-4] A CIC is calculated by the sum of the multiplication of the overall survival probability with the hazard of a subsequent KC at each time point.

To show the difference between both methods (KM and CIC), we used data from the Rotterdam Study.[5] We calculated 1 minus the KM survival probability and the CIC of the second metachronous KC (BCC or SCC, including keratoacanthoma but no in situ SCC) between January 1, 1990, and December 31, 2013, among 1644 patients with a first KC. After 10 years of follow-up the probability of a subsequent KC was 40% using the KM method (Figure 1). This probability was an overestimation—the actual probability was 34% using the CIC. Twenty years after diagnosis, the difference was even larger (74% for KM vs 52% for CIC) because the problem of competing risk due to death became larger.

In conclusion, the problem of competing risk can occur for all end points other than overall mortality when using the KM method (eg, melanoma-specific death—patients cannot first die due to other causes and then due to melanoma). It especially occurs in older populations (ie, higher probability of other competing events such as death) and when the follow-up time is long.

We would like to ask if Wehner et al[1] could re-analyze their data using the CIC method.

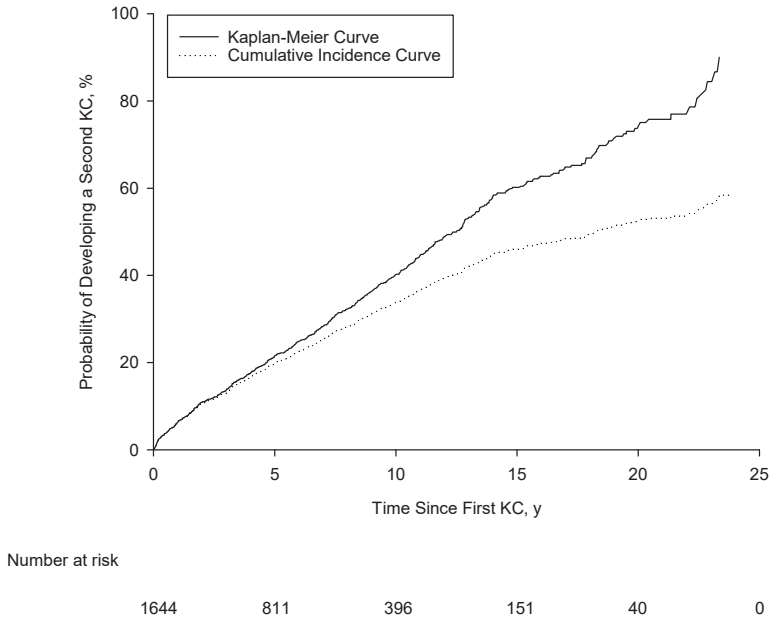

Figure 1. Kaplan-Meier Curve vs Cumulative Incidence Curve of the Probability of Developing a Second Keratinocyte Cancer (KC)

The solid line represents the biased Kaplan-Meier estimate of the probability of a subsequent KC due to the competing risk of death. The dotted line represents the correct probability of a subsequent KC using a cumulative incidence curve, taking the competing risk of death into account.

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