Letters to the Editor

Skin cancer as a marker of sun exposure: a case of serious immortality bias

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Brendum-Jacobsen et al. recently published in this journal\textsuperscript{1} analyses of Danish register data concerning myocardial infarction, hip fracture and death from any cause, using incidence of skin cancer as indicator of high exposure to sunlight. The basic idea in the paper is that those who get a skin cancer diagnosis at any age are supposed to have been more exposed to the sun during their life than those who do not, and apparently the authors find it relevant to use ordinary prospective survival analysis to compare incidence of myocardial infarction, hip fracture and death from any cause between the two groups: those who (at some point) get a skin cancer diagnosis and those who do not.

Unfortunately, such an analysis is seriously flawed, because the definition of one of the two groups to be compared conditions on the future: in order to get a skin cancer diagnosis, and thus become a member of the skin cancer group, it is at least necessary to survive until age of diagnosis, but the authors’ analysis does not take this conditioning into account. Put another way: for those in the skin cancer group it is impossible to die until the age of diagnosis of the cancer, the so-called immortal person-time.\textsuperscript{2}

For ease of exposition we focus on the endpoint ‘death from any cause’. It is seen in the lower left panel of Figure 2\textsuperscript{1} that those who get non-melanoma skin cancer at some age have a hazard ratio of dying from any cause in the age interval 40–49 years of about 0.2 vs those who never get a non-melanoma skin cancer diagnosis. A main reason for this is probably that very few of those with non-melanoma skin cancer are at all at risk for dying—most of the members of this group get their skin cancer diagnosis at ages >50 years and are therefore by design immortal in the age interval 40–49.

Methodology aside, we find it very surprising that neither the authors nor the editorial process have questioned the strange results at many places in the paper. For example: the upper right corner of Table 2\textsuperscript{1} shows that persons who sooner or later get a diagnosis of malignant melanoma have a significantly reduced risk of dying from any cause: a hazard ratio of 0.89. Did no alarm bells sound? That the authors cautiously write ‘causal conclusions cannot be made’ in the abstract does not justify publishing a methodologically flawed analysis.

As a more comic point, we noted that \textit{IJE} now quotes \textit{P}-values with 308-digit precision—we hope that the chi-square approximation to the distribution of the log-rank statistic is justified!

References
