



EDITORIAL

Watch out for sticky diagnosis bias in older men with prostate cancer *Editorial comment to “Evidence of overestimating prostate cancer mortality in Estonia: a population-based study by Innos K et al.”*

Ever heard of sticky diagnosis bias, when death from other causes is erroneously attributed to the target diagnosis, thus incorrectly increasing cause specific mortality estimates? The article by Innos et al. featured in the current issue of the Scandinavian Journal of Urology highlights this important topic [1]. In this article, the authors evaluated the validity in the official mortality statistics in Estonia for prostate cancer as the underlying cause of death. An expert panel performed a blinded review of medical records to assess if prostate cancer stated as the underlying cause of death in the death certificate was accurate.

The authors found a substantial 1.5-fold overestimation of prostate cancer mortality in Estonia. The overestimation was more than two-fold in men age ≥ 85 years but was also present and ranged from 1.3 to 1.4 in other age groups. Medical review verified less than half of prostate cancer deaths in men who had localized prostate cancer at diagnosis, while the verification rate was close to 90% in men who had distant metastases. Only a modest underreporting of prostate cancer deaths was observed among men previously recorded to have died of other causes. In other words, the authors found a strong sticky diagnosis bias.

The current study is in accordance with several previous studies that have assessed the validity of prostate cancer as the underlying cause of death in official mortality statistics in Nordic countries. Danish [2] and Norwegian [3] studies reported that the cause of death was misclassified in cause of death registers, resulting in an overestimation of the proportion of deaths from prostate cancer. For example, in the Norwegian study over-reporting of prostate cancer deaths was as high as 33% and misattribution of prostate cancer death increased significantly with increasing age and decreasing Gleason score.

However, it is important to point out that the absence of evidence is not evidence of absence [4] and it is close to impossible to prove that someone did not die from a particular cause. Therefore, it is challenging to evaluate the accuracy of reported prostate cancer death among men without any recorded signs of death by prostate cancer, in particular among older men with multiple comorbidities [3]. Older men with localized prostate cancer without signs of progression are often followed in primary care, with little use of PSA testing or imaging, resulting in absence of evidence. This may result in misclassification of death in a review of medical records, both among men for whom death was originally attributed to prostate cancer and to other causes. Without evidence of a specific cause of death, we argue that

an otherwise seemingly healthy man with a prior prostate cancer diagnosis is more likely to have his prostate cancer assigned as the cause of death, again due to a sticky diagnosis bias. His assigned cause of death to prostate cancer will be challenging to validate retrospectively but may be wrong.

Additional evidence of sticky diagnosis bias has been found in studies with other designs. Substantial differences were observed between cause-specific survival estimates and relative survival estimates. Both methods measure net-survival, i.e. survival where one can only die of prostate cancer. Cause-specific survival is based on the classification of the underlying cause of death whereas relative survival is obtained by comparing the survival of men with prostate cancer to a disease-free comparable background population. In a recent nationwide population-based Swedish study, substantially higher relative survival estimates compared to cause-specific mortality were found for men with low-and intermediate-risk prostate cancer and for men over 80 [5]. A Norwegian study of similar design also found that these estimates differed, in particular for men above age 85 [6]. It is important to note that both cause-specific and relative survival have limitations: cause-specific survival is sensitive to misclassification of the cause of death and relative survival requires comparability between the two populations, which is challenging to obtain.

What is evident in the current article by Innos et al. and other articles on the true cause of death in men with prostate cancer, is that there is a considerable overestimation in prostate cancer specific mortality in cause of death registers in the Nordic countries and Estonia, especially among older men and men with low-risk disease. These results are important as the findings suggest that cause-specific cancer mortality should be utilized with caution when used as outcome. In conclusion, to mitigate a sticky diagnosis bias, physicians need to be trained in issuing death certificates in order to increase the validity of cause of death registers.

Disclosure statement

Oskar Bergengren certifies that there are no conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

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