Reviewer's report

Title: Incidence, Mortality Patterns and 5-year Relative Survival Ratio of Prostate Cancer among Residents in Singapore from 1968 to 2002

Version: 3 Date: 25 June 2008

Reviewer: Francesco La Rosa

Reviewer's report:

My comment
5. “The completeness of reporting is high with about 96% in the 1970s and close to 100% in the 1990s” Reporting of DCO and percentage of cases with MV would be more informative here. [Minor Essential Revision]

Author’s reply
We suspect MV means microscopic verification. From Appendix B of the Singapore Cancer Registry, it contains detailed break down of notification and basis of diagnosis. From 1993-97, 88.9% of the cases are microscopic verification, while from 1998-2002, 90.6%

New comment
Sorry for not specifying the meaning of MV; it is however a classic indicator of data quality for cancer registries. Thus I asked to report the MV% for prostate cancer included in the paper and not to the reviewer. Reporting by period as in your answer would be appropriate. [Minor Essential Revision]

My comment
6. Please explain why you tested for a linear trend in log rates over the study period.

Author’s reply
In general, the ASR for incidence and mortality are increasing exponentially. The log rates would improve the linear relation between the log rates and time.

New comment
No, definitely incidence and mortality are not increasing exponentially and, indeed, there is no general obvious trend for prostate cancer as for the other cancers. The question here was on the assumption of the (log-)linear shape over the whole study period. Since data for a rather long period are considered in this study, a linear constant trend is not warranted and in any case it cannot be safely assumed without testing. For instance, to this very end the joinpoint regression
method was recently proposed but, of course, there are other suitable modeling strategies. The question was to produce evidence that the model fitted well to mortality and incidence data or to change the model accordingly. Use joinpoint regression or other strategies to prove that trends are linear. [Major Compulsory Revisions]

My comment

8. Metastatic compared to cases without distant disease is a simplified staging information. This classification excludes also the locally advanced category that is used in the simplified stage coding adopted by cancer registries. However, this simple stage is useless here because of the 39% of cases without information. With this level of missingness that is likely to change by age class and time (Will Roger phenomenon) relative survival data are difficult to interpret. An improvement in reporting and an increasing diagnostic accuracy in assessing the presence of metastases is compatible with the steep increase in relative survival rates for cases with unknown metastatic status. [Major Compulsory Revisions]

Author’s reply

Missingness is unlikely to have a Will Roger phenomenon on the RSRs of nonmetastatic and metastatic cases because the cases in missing group (i.e. Metastasis status not known), are a mixture of two prostate cancer sub-type: non-metastatic and metastatic cases, and not a biologically meaningful sub-type, unlike stage migration. Therefore, it is difficult to predict the trend of RSRs with improvement in reporting and increasing diagnostic accuracy because RSRs will be affected by the composition of non-metastatic and metastatic cases which may change over time. In view of this difficulty, we did not use this group to infer prostate cancer trend in Singapore.

New comment

In the literature it is often stated that variables with >5% missing data should not be analyzed as such and that a variable with >15% missing is almost useless. Multiple imputation may be used in cases with non-negligible percentages of missing data. In this case the Authors state that there are two sources of missingness in the data, i.e. unreporting of metastases to the registry and incomplete prognostic evaluation. The composition of the missing category in terms of process originating missing values is not available and thus it is not possible to assess the relative contribution of the two missing sources. The first process, however, causes unpredictable bias. The second process, incomplete prognostic evaluation is subject to variation over time (e.g. when improved diagnostic technologies becomes available or when an existing test gains wider diffusion in the population) and is likely to cause a Will Roger phenomenon. Thus
I confirm that the analysis of relative survival by stage is unreliable and should not be reported in the paper or estimates on multiple imputed datasets should be reported. [Major Compulsory Revisions]

Moreover in the plot of metastatic to non-metastatic ratios by year, an increasing ratio is evident in more recent period (see reply to reviewer three). This would be an unexpected finding in the presence of increasing opportunistic screening with PSA, unless the percentage of missing is decreasing correspondingly as a consequence of more thorough investigation of cases.

New comment
A standardized incidence rate for the whole study period was added in the results (i.e. a standardized incidence rate for a 34 years period ); please report ASR for the more recent three or five years period.

New comment
“There have not been many reports on prostate cancer among the ethnic groups in Singapore.”
If appropriate change the statement into “There have not been many reports on prostate cancer by ethnic groups in Asian countries” or similar.

Changing diagnostic accuracy is denied by the Authors as an explanation for observed trend but proposed as an explanation for increasing mortality rates in a reply to a reviewer’s comment. Prostate cancer incidence increases steeply with age and more than other cancers it is a cancer of the elderly, thus access to care and diagnostic accuracy are likely to change over time and very likely to change over such a long study period as that considered in this paper (truncated rates at 65 or 75 years may be useful here). Cancer registries rely on the quality and completeness of existing health archives and completeness of registration in the oldest old is a common and acknowledged problem. Thus changing diagnostic accuracy and consequently of reporting to the registry are a likely explanation for study findings that should be properly considered and discussed. A true incidence increase without diffusion of opportunistic screening could be an alternative explanation. Thus it seems to me that the depth of analysis and discussion should be improved.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests