Empowering readers in the interpretation of findings

In reference to ***'Tan S, Abdullah MS, Telisinghe PU, Ramasamy R. Breast cancer in Brunei Darussalam - Incidence and the role of evaluation of molecular markers. Brunei Int Med J. 2011;7:250-9.'***

To the Editor,

I read with interest the recent article by Tan *et al*., who reported on an analysis of breast cancer molecular markers and survival in the population of Brunei Darussalam.[1] Congratulations to the authors for their effort in generating research relevant to breast cancer management in Brunei Darussalam both at an individual and population level. However, it is just as important to ensure that sound epidemiology is used in the interpretation of findings including clear discussion of key limitations. I am concerned that a number of important limitations in the methodology employed in the study were not highlighted to readers.

The authors used univariate analysis only to look for association between markers and outcome. The absence of multivariate analysis means that interactions between markers or the role of other confounding variables were not accounted for. Furthermore, running multiple univariate analysis will result in an increase in type 1 error where one will wrongly reject the null hypothesis H0 (no real association) in favour of H1 (a finding of association). In the survival analysis, differences in important variables between the groups such as stage of disease, age, co-morbidities could easily lead to differences in survival rather than the presence or absence of a molecular marker. Therefore, it would be wrong to conclude that prognosis in the study population is related to a marker when the authors have not incorporated other epidemiological methods in their analysis to identify and adjust for possible confounders.

Locally generated answers on cancer prognostic markers and survival are keenly sought after by patients, their family, medical profession and policy makers. In view of the significance of such information, it is essential that key limitations which can easily change the conclusion of a study are clearly highlighted in the discussion to empower readers in helping them interpret the findings.

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1: Tan S, Abdullah MS, Telisinghe PU, Ramasamy R. Breast cancer in Brunei Darussalam - Incidence and the role of evaluation of molecular markers. Brunei Int Med J. 2011;7:250-9.

Response:

The article Breast Cancer in Brunei Darussalam – Incidence and the role of evaluation of molecular markers states the limitations of the study due to the small number of samples and incompleteness of the available data. [1] The possible relationships between independent causal variables and the outcome are generally understood in epidemiological studies. This is not always the case with the common immunohistochemical markers investigated in breast cancer and the process of carcinogenesis. Type 1 errors are minimal when probability values of <0.001 are considered with ten analyses e.g. in Table 4 and multivariate analysis may not change this. Multivariate analysis is also less useful in situations where there are known relationships between some markers (e.g. between OR and pS2), and when there are insufficient data and numbers to study the effects of different treatments. Therefore classical epidemiological approaches may not be simply applied to examining the prognostic value of immunohistochemically determined molecular markers. Furthermore, the findings reported in the survival analysis are fully consistent with those reported for other populations as discussed in the article, and therefore the conclusions are most

likely valid also for Brunei Darussalam. The work reported in the article is however only a beginning and it is appreciated that much more remains to be investigated, as pointed out by Dr Yung.

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Increasing testing versus increasing burden of disease

*In reference to '**Chong VH, Telisinghe PU. Rising incidence of breast cancer in Brunei Darussalam. Brunei Int Med J. 2011;7:260-8**.'*

To the Editor,

I would like to applaud Drs Chong and Telisinghe for their effort in publishing important epidemiological data on breast cancer in Brunei Darussalam.[1] I read with interest their report that breast cancer incidence in Brunei Darussalam is increasing based on an analysis of data available from the State Department of Pathology from 1984 to 2010. However, I am concerned that one key bias was not addressed in the paper before coming to this conclusion which has important implications.

It is plausible that the increase in breast cancer incidence may be a result of increased testing and hence diagnosis! Such an inherent bias resulting from improved access to healthcare in terms of staff, services and availability of technology combined with improving awareness of breast cancer both in the population and medical profession over the 27 years of the study must be adjusted for or acknowledged as a key limitation. Increased testing over the period can easily lead to a false finding of increased incidence of a disease when in actual fact the true burden of disease in the population has not changed! The more one looks the more one finds.

An increase in the identification of the disease, one could argue is a good thing if it is not due to an increase in the burden of the disease. If data is not available to differentiate the two then one must take extra care before concluding that breast cancer incidence is increasing in Brunei Darussalam.

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1: Chong VH, Telisinghe PU. Rising incidence of breast cancer in Brunei Darussalam. Brunei Int Med J. 2011;7:260-8.

Response:

We thank Dr Yung for his interest in our article. [1] We agree that improvement of the health care services coupled with increasing awareness of medical disorders and in this case breast cancer, may well have contributed to the increase in the number of breast cancer diagnosed. However, this still account for only a very small proportion of the total diagnosed cases. The increase in the adjusted standardised rate is too high to be accounted by increase in detection as suggested by Dr Yung.

Data from the same registry indicated that the proportion of early disease (stage one) still only accounted for a very small proportion of the total number of cases, less than five percent. With better awareness and increased detection one would expect this proportion to increase with time. Despite improvement in health care provision in our setting, there is currently no screening programme for breast cancer, except for those at high risk i.e. family members of those diagnosed with breast cancer. Currently, the annual number of mammogram done is still very low and is very selective; patient with breast cancer surveillance of the re-

maining breast, family members and those who wanted screening. Unfortunately, the numbers who want screening is still very small.

As discussed in the discussion section of the article, similar to what have been reported by other countries, the reasons for the increase in breast cancer incidence in Brunei Darussalam are probably the same. This includes aging population, change in life style (fewer and delayed pregnancies, shorter time spent breast feeding) and increasing incidence of weight disorders and obesity. Similar trends have also been reported for other cancers such as colorectal which share similar risk factors. Therefore, the rising incidence of breast cancer as reported in our article is real and is not just due to increased in case detections.

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