

## Letters

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### **Comments on *Survival of Breast Cancer Patients in Lithuania and Norway, 1988–1992*, Kliukienė and Andersen, *Eur J Cancer* 1998, 34, pp. 372–377**

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KLIUKIENĖ AND Anderson report survival differences among breast cancer patients in Lithuania and Norway in an article recently published in the *European Journal of Cancer* [1]. The study is very interesting, but, since it is based on cancer registry data, it might have some limitations concerning the validity of the results. This should be properly discussed in order to avoid misinterpretation of the results.

Appropriately, the authors evaluated the influence of known prognostic factors on survival, such as tumour size, lymph node status and age at diagnosis, in order to control for confounding bias. However, I believe that some aspects, such as the influence of screening activities and treatment differences in survival rates, were not discussed properly, and need to be examined further.

According to the authors, the survival rate difference was more pronounced in stage II and stage III patients. This was probably related to the fact that the tumour size and lymph node status in these groups were much more favourable in the Norwegian dataset, perhaps as an effect of more intensive screening activities by breast self-examination campaigns in this country. The authors stated that breast self-examination has positive effects in reducing breast cancer mortality, which have not been established by prospective studies. The two most important ongoing prospective randomised trials, one in Russia and another in China, have not found, among patients performing breast self-examination, consistent evidence of a reduction in mortality so far [2, 3].

The authors also suggest that selection bias should be discussed in their study, since 80% of the patients in the Lithuanian dataset were from a geographical region where a single institution was responsible for breast cancer treatment. However, they discard such a possibility based on the fact that age and stage cancer distributions of the study population were similar to those observed in the rest of the country

(Lithuania). None the less, the possibility of selection bias regarding treatment differences was not considered in the analysis, and this factor accounts for considerable variations in survival rates, since it has been found to be a strong prognostic factor [4]. Moreover, the type of institution where a breast cancer patient receives treatment has been proved to influence survival, with patients treated at teaching and large community hospitals having the best prognosis [5].

Therefore, although the age and stage distribution of the Lithuanian dataset were similar to the whole country data, the treatment offered was possibly more favourable in the hospital abridging 80% of the Lithuanian dataset than would be observed in the rest of the country. Such selection bias could spuriously decrease the survival differences observed between Norway and Lithuania because of treatment differences.

Hence, the study results should be considered with some restrictions, since the differences found could be less accurate than expected.

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### **Response from J. Kliukienė and A. Andersen**

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WE THANK Dr de Souza for his interesting comments on our paper 'Survival of breast cancer patients in Lithuania and Norway, 1988–1992' [1].

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The cancer registries in both countries are nationwide and have been based on compulsory reporting of new cancer cases from 1953 in Norway and from 1964 in Lithuania. It is, therefore, possible to establish reliable databases over the years.

Regarding the effect of breast self-examination, we referred to the Finnish study with a long follow-up period (1973–1986) which found a lower breast cancer mortality than expected (a rate ratio of 0.75) in the cohort of 28 785 women who recorded their practice of breast self-examination over a 2-year period. The study in Shanghai, mentioned by Dr de Souza, is certainly of interest. The authors concluded that a longer follow-up of the participants is required before final assessment can be made of the efficacy of breast self-examination. The Russian study cited by Dr de Souza showed no significant difference in 5- and 9-year survival between breast cancer patients in the self-examination and control groups. We think that the duration of follow-up in that study was not long enough to evaluate the influence of breast self-examination on mortality from breast cancer.

The treatment of breast cancer is centralised in Lithuania, and in the period of our study, there were only three other hospitals in the country responsible for the treatment of breast cancer, and all of them followed guidelines for treatment of the disease determined by the Oncology Centre in Vilnius.

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## Second Primary Cancers Following Thyroid Cancer in Slovenia. A Population-based Cohort Study

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THERE ARE only a few reports on second primary cancers following thyroid cancer [1–3]. The present study was designed to evaluate our clinical impression that there might be an increased risk of cancer in hormone-dependent organs (i.e. breast, ovaries) in thyroid cancer patients.

The data of the Cancer Registry of Slovenia (CRS), covering a population almost 2 000 000, and medical records of patients treated at the Institute of Oncology in Ljubljana were used. The completeness of cancer registration in Slovenia is approximately 95% [4, 5]. To obtain standardised incidence ratios (SIRs), the observed number of second primary cancers was divided by the expected number. For statistical evaluation, 95% confidence intervals (CI) were calculated assuming a Poisson distribution of the observed number of second primary cancers using Fisher's method. SIRs for all and selected cancer sites were analysed for the following periods of follow-up: less than 1 year, 1–4, 5–9, 10–14, 15–19, and 20 years and more.

Between January 1971 and December 1993, 1,009 patients with thyroid cancer were reported to the CRS. Of these, 95 had multiple primary cancers. In 38 patients the thyroid gland was the first tumour site. We excluded patients who had any carcinoma before the thyroid cancer (57 patients, 5.6%), patients with thyroid cancer diagnosed at the time of death or synchronous carcinoma which was defined as carcinoma diagnosed within 1 month (26 patients, 2.6%), malignant lymphomas or carcinoma of unknown origin as the second primary (32 patients, 3.2%). In total, 894 patients (241 males, 653 females) were included in the study, of whom 30 developed second primary cancer after the thyroid cancer.

The mean age at thyroid cancer diagnosis was 54.9 years. The mean follow-up time was 5.17 years (range 0–23.57 years, median 2.83) and the mean period between diagnosis of the first and the second cancer was 5.65 years (range 0–17.7 years, median 3.46).

A significantly elevated SIR in second primary cancer(s) was observed only in males for all tumour sites taken together (SIR = 1.90; 95% CI = 1.02–3.25), but not for specific tumour sites. In females, however, the SIR was not significantly elevated, neither in all nor in the specified tumour sites (Table 1).

Analysing the time distribution, 15 cases of second primary cancer were diagnosed during the first 5 years, 13 between 5 and 14 years, and 2 between 15 and 19 years after the first primary cancer. A statistically significant increase in the SIR for all tumour sites together was observed only for males within the span of 10–14 years after the first primary cancer (SIR = 4.72, 95% CI = 1.28–12.05).

A higher than expected incidence of other cancers following thyroid cancer has been observed in some previous studies [1, 6, 7]. The data on second primary cancers following thyroid cancer differ considerably [1–3, 6–10]. The reason could be attributed to the difference in the incidence of cancer and in the methodology for calculating the risk of second primary cancers. Other factors, such as environmental conditions, genetic and socioeconomic factors could also be involved. An elevated risk for breast cancer after thyroid cancer has been reported by some authors [2, 8, 10]. In contrast, Akslen and Glatre [3] and Teppo and colleagues [9] found no increase in the risk for breast cancer after thyroid cancer.

Our study showed an increased risk for a second primary cancer only in males for all tumour sites together. However, as it is known that male patients with thyroid cancer have a worse prognosis, this might be the reason for the 'increased surveillance' of these patients and a possible *ascertainment bias*.