

## Letters to the Editor

### DIAZEPAM AND BREAST CANCER

SIR,—Recent correspondence<sup>1-4</sup> has questioned whether diazepam promotes the growth of breast cancer. Although suspicions were raised by both animal<sup>1,3</sup> and human observations,<sup>5</sup> it has been suggested that "human studies have resolved the issue",<sup>4</sup> since the two latest studies have failed to find a relationship between prior diazepam use and risk of breast cancer. However, one of these studies<sup>6</sup> included only a preliminary screening of diazepam and many other drugs, and the other<sup>7</sup> was limited by having few subjects who reported extensive exposure.

We had the opportunity to evaluate diazepam from data previously collected during a multicentre breast cancer screening programme, the Breast Cancer Detection Demonstration Project. This programme, sponsored by the National Cancer Institute and the American Cancer Society, involved over 280 000 participants at twenty-nine screening locales. Eligible cases were all women detected with breast cancer during screening between July, 1973 and May, 1977, at twenty-eight of the centres. Controls were participants who were never recommended for biopsy during the course of screening. Controls were matched to cases on centre, age, race, time of entry to the project, and length of continuation as screening subjects. Completed home interviews were obtained from 86% of eligible breast cancer patients and 74% of controls.

The results are summarised in the table. Prior use of diazepam was reported by 20% of the 1227 cases and 23% of the 1213 controls, resulting in an age-adjusted relative risk of 0.87 (95% confidence interval 0.7-1.1). Univariate adjustments for menopausal status, parity, age at first live birth, age at menarche, family history of breast cancer, previous breast biopsies, use of oral contraceptives or menopausal oestrogens, education, and income did not alter this

estimate. The risk of breast cancer did not increase with increasing years of use or years since initial use, nor was the risk affected by age at first use. To determine whether diazepam use may have a promoting effect on late stages of carcinogenesis, we examined the risks according to the recency of diazepam use and searched for interactions of use with known risk factors—e.g., family history of breast cancer. No excess of breast cancer was found in any of these subgroups.

Our results thus fail to demonstrate a relation between diazepam use and risk of breast cancer. We were unable fully to assess the influence of diazepam use on growth promotion. However, if diazepam does accelerate the growth and spread of existing lesions, as has been suggested,<sup>1,3</sup> we would expect that users would be diagnosed earlier than non-users. Examination of age-specific risks associated with diazepam use provided no support for this notion. The issue of growth promotion is being further evaluated by examining the relation between diazepam and various clinical and pathological indices, including size of lesion and stage of disease.

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RELATIVE RISKS\* OF BREAST CANCER

	Cases	Controls	Relative risk (and 95% confidence interval)
<b>Ever use of tranquilisers</b>			
No	652	639	1.00
Yes, diazepam	249	280	0.87 (0.7-1.1)
Yes, other	226	204	1.09 (0.9-1.4)
Unknown	100	90	1.08 (0.8-1.5)
<b>Years of use of diazepam†</b>			
1-4	194	198	0.97 (0.8-1.2)
5-9	32	62	0.51 (0.3-0.8)
10+	17	13	1.28 (0.6-2.7)
Unknown	6	7	0.83 (0.3-2.5)
$\chi^2$ for linear trend = -1.50 (p=0.07)			
<b>Years since first use of diazepam‡</b>			
<5	133	129	1.01 (0.8-1.3)
5-9	58	89	0.64 (0.4-0.9)
10-14	30	29	1.01 (0.6-1.7)
15+	12	11	1.07 (0.5-2.4)
Unknown	16	22	0.71 (0.4-1.4)
$\chi^2$ for linear trend = -1.20 (p=0.12)			
<b>Years since last use of diazepam</b>			
Current	108	135	0.78 (0.6-1.0)
1-2	44	37	1.17 (0.7-1.3)
3+	80	83	0.94 (0.7-1.3)
Unknown	17	25	0.67 (0.4-1.2)

\*Age-adjusted: reference group for all risks are women unexposed to any tranquiliser.

Unknowns excluded from linear trends. † $\chi^2$  for linear trend = -1.50 (p=0.07). ‡ $\chi^2$  for linear trend = -1.20 (p=0.12).

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