Is there evidence for sex differences in the association between diabetes and cancer?

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To the Editor: In a recent issue of *Diabetologia*, Ohkuma et al conducted a meta-analysis of a large number of studies with significant heterogeneity, and reported an association between diabetes and cancer, which varied according to sex [1]. They concluded that the diabetes-associated excess risk of cancer is greater in women than men. The authors included a study performed by our team in their analysis; in this study we analysed a population of 2.3 million men and women [2]. Indeed, we reported hazard ratios for all-site and for site-specific cancers for men and women separately. Ohkuma et al discussed the inclusion of sex-specific cancers as a possible explanation for their findings [1]. However, we suggest that the inclusion of such cancers raises questions as to the very meaning of their findings. In our study, of a total of 64,921 cancer events in women, 24,452 (38%) were female-specific

cancers (corpus uteri, ovarian and female breast cancer), while, of 63,799 cancer events in men, 14,099 (22%) were male-specific cancers (prostate cancer). While diabetes was positively associated with all female cancers examined, except for breast cancer in premenopausal women (4083 events), it was negatively associated with prostate cancer. In all other site-specific cancers, the hazard ratios in our study were quite similar between men and women. We therefore encourage the investigators to further explore the association between diabetes and cancer within cancer sites that are not sex-specific.

Another potential caveat, which may have contributed to the findings of Ohkuma et al's meta-analysis, is the different age distribution between men and women. Life expectancy in women is about 4 years longer than in men; and in our study, age was separately adjusted for each sex. If the hazard ratio for cancer among men and women with diabetes varies with age (i.e. there is a diabetes–age interaction) then this could contribute to an observation that the age-adjusted hazard ratio is higher among women with diabetes than men with the disease. To the best of our knowledge, the existence of a diabetes–age interaction has not been addressed in the literature.

In conclusion, the inclusion of sex-specific cancers and/or a diabetes–age interaction may explain the differences observed by Ohkuma et al [1] in hazard ratios for all-site cancers between men and women.

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