CORRESPONDENCE

Re: Diabetes Mellitus and Risk of Colorectal Cancer in the Singapore Chinese Health Study

I read with interest the recent study by Seow et al. (1) which used data from the Singapore Chinese Health Study to show that individuals with diabetes were more likely to develop colorectal cancer than those without diabetes. These data add to the current body of literature suggesting that impaired glucose tolerance and hyperinsulinaemia influence carcinogenesis via insulin pathways.

In that study, 61,320 Singapore Chinese men and women aged 45 to 74 were enrolled in a prospective cohort study between April 1993 and December 1998. Diagnosis of diabetes was based on self-reporting of physician-diagnosed disease. Cancer cases were ascertained through the population-based Singapore Cancer Registry. The authors showed that diabetes was statistically significantly associated with an increased risk of colorectal cancer risk in both men (relative risk \[RR = 1.5\], 95% confidence interval \[CI = 1.2 to 2.1\]) and women (\[RR = 1.4, 95\% CI = 1.0 to 1.9\]). This association was robust after adjustment for factors such as age, sex, body mass index, cigarette and alcohol use, physical activity, and family history of colorectal cancer.

Recent trends in diet and lifestyle are reflective of Singapore’s rapid industrial development and rising affluence. The prevalence of diabetes mellitus in Singapore has increased dramatically over the past few decades, from 1.9% of adults 18–69 years old in 1975 to 4.7% in 1984, 8.6% in 1992, and 9.0% in 1998, and some evidence exists to suggest that these rates may substantially underestimate the prevalence of diabetes, probably because of underdiagnosis (2). The incidence rate of colorectal cancer has also climbed steadily over the past few decades and is now similar to the rates seen in Western countries (3). Because diabetes rates are relatively high and because colorectal cancer is now the most common cause of cancer in Singapore, it would seem that preventing diabetes may help prevent colorectal cancer.

However, the potential impact of the findings of Seow et al. should be examined further. Their results suggest a relatively modest difference in the risk of colorectal cancer—0.66%—between those with diabetes and those without. On the basis of a calculated population attributable risk, I estimate that only 5.7% of colorectal cancer in the population is due to diabetes and could be prevented by eliminating diabetes.

Seow et al. (1) assert that underreporting of diabetes attenuates the true association between diabetes and the risk of colorectal cancer. However, all incident cases of colorectal cancer in their study were identified through the well-maintained national Singapore Cancer Registry. Given the quality of screening services and the incidence rate of colorectal cancer in Singapore, a substantial level of underreporting is unlikely. If, in fact, the actual prevalence of diabetes was underestimated in this study, we can only expect the modest population attributable risk, considered to be the best measure of impact on the population, to decrease further.

Both diabetes and colorectal cancer have become major challenges to the health of the Singapore population, making prevention efforts critical. However, future studies will be necessary to demonstrate whether reductions in the incidence of diabetes will lead to declines in colorectal cancer incidence.

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RESPONSE

We thank Dr. Wong for her comments about our study. She points out that preventing diabetes is likely to have a small impact on the incidence of colorectal cancer in Singapore, the population attributable risk (PAR) being about 5.7%. The size of this PAR is a result of both the modest size of the effect (an approximately 50% increase in risk of colorectal cancer associated with a history of diabetes) and the low prevalence of self-reported diabetes due to its underdiagnosis in the study population (1). This underreporting leads to an underestimate of the PAR (2) and not to an overestimate, as asserted.

The PAR provides an estimate of the proportion of cases that would be prevented if a causal exposure is removed from the population (3). In our study hypothesis and in the interpretation of our results, we considered diabetes mellitus to be a surrogate marker for insulin resistance and for hyperinsulinemia. We believe that high levels of insulin and insulin-like growth factors play an etiologic role in the development of colorectal cancer, a view that is gaining increasing support from experimental and epidemiologic data (4,5).

Insulin resistance, which is primarily due to energy imbalance, physical inactivity, and consequent visceral adiposity (as evidenced by a high waist-to-hip ratio), is a prevalent condition, and diabetes mellitus is the most overt clinical manifestation of this phenomenon. Whereas 8.2% of adult Singapore residents have diabetes mellitus, a further 12% have demonstrable impaired glucose tolerance (1). The metabolic syndrome, a cluster of coronary risk factors that are linked by insulin resistance (6), is present in 23% of U.S. men and women (7). The aim of prevention, then, lies not in targeting diabetes mellitus in particular but in targeting the potentially modifiable lifestyle factors that lead to insulin resistance. If our understanding of the causal pathways is correct, these efforts will impact the incidence of a wide range of conditions, including colorectal cancer and cardiovascular disease. Large-scale epidemiologic studies with more proximate measures of insulin resistance will be needed to better estimate the potential impact of these interventions.
REFERENCES


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DOI: 10.1093/jnci/djj278
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