BJC

British Journal of Cancer (2014) 111, 2201 | doi:10.1038/bjc.2014.186

Reply: Comment on 'The NQO1 polymorphism C609T (Pro187Ser) and cancer susceptibility: a comprehensive meta-analysis'

B Lajin*[,1] and A Alachkar[2]

[1]Department of Analytical Chemistry, Faculty of Pharmacy, University of Aleppo, Aleppo, Syria and [2]Department of Pharmacology, School of Medicine, University of California, Irvine, Irvine, CA, USA

Sir,

The aim of the performed meta-analysis was mainly to investigate the association between the overall cancer risk and the *NQO1* C609T polymorphism in the worldwide population as well as in individual ethnic groups, given the biological plausibility of combining several different cancer sites in the light of the common background implied by the known functions of the investigated enzyme. Most notably, our meta-analysis demonstrated a statistically significant association in the worldwide and Caucasian populations, as indicated by the resulting *P*-values. Power analysis was not published for most of the individual studies, and therefore it was not reported in our meta-analysis for each individual study. The main purpose of conducting the present meta-analysis was to overcome the expected low power in most of the individual studies due to the small sample sizes, and at least improve the power of detecting association by combining the large number of studies. The calculated power for our present meta-analysis was 97% for the worldwide population analysis and 98% for the Caucasian subgroup analysis ($\alpha = 0.05$). Calculations were performed using the genetic power calculator developed by Purcell *et al* (2003). Therefore, the conclusions of the meta-analysis are further supported by the obtained high power, which was not unexpected given the large total number of samples, the significant resulting odds ratios, and the low *P*-values. The power obtained far exceeds the standard, and rather arbitrary, value of 80% with respect to the worldwide and Caucasian population, which leaves no possibility of a false-positive association. Concerning the tumour site analysis, we had noted in the article that the results should be approached with caution due to the small sample sizes available, and we highlighted the need for more studies investigating individual cancer sites and involving less common ethnic groups in the conclusion. The main conclusion from the meta-analysis performed involved the total cancer risk combining all tumour sites.

It is noteworthy that *post hoc* power analysis is controversial and often misinterpreted (Hoenig and Heisey, 2001). The common well-accepted usage for power is in prospectively estimating a sufficient sample size to detect an association when it is present in order to avoid type II error and false-negative associations.

Finally, we believe that it is unlikely that the inadvertently missed single case sample had an impact on the results and conclusions of the meta-analysis that included 21 178 case samples.

REFERENCES

Hoenig JM, Heisey DM (2001) The abuse of power: the pervasive fallacy of power calculations in data analysis. *Am Stat* **55**: 19–24.

Purcell S, Cherny SS, Sham PC (2003) Genetic Power Calculator: design of linkage and association genetic mapping studies of complex traits. *Bioinformatics* **19**(1): 149–150.

*Correspondence: Dr B Lajin; E-mail: BassamL7@yahoo.co.uk

Published online 15 April 2014

BJC

British Journal of Cancer (2014) 111, 2201–2202 | doi:10.1038/bjc.2014.212

Need for clarification of data in a recent meta-analysis on the association of *NQO1* C609T polymorphism with cancer risk

X Cao[1] and W Shen*[,1]

[1]Department of Oncology, The Affiliated Jiangyin Hospital of Southeast University Medical College, Wuxi 214400, PR China

We read with great interest the recent paper by Lajin and Alachkar (2013). The authors performed a comprehensive meta-analysis of 92 case–control studies involving 21 178 cancer cases and 25 157 controls to examine the association between *NQO1* C609T polymorphism and cancer susceptibility. Their comprehensive meta-analysis results suggest that *NQO1* C609T polymorphism is an important genetic factor in the overall risk for developing cancer, especially in Caucasian populations. It is an interesting study. Nevertheless, we would like to raise several concerns related to this article.

First, sensitivity analysis may need to be routinely performed by excluding and including the Hardy–Weinberg equilibrium (HWE)-violating studies in meta-analyses of genetic association studies, which is a good approach to heterogeneity (Mao *et al*, 2010). We also assessed deviation from HWE in controls for all the included studies, and the results demonstrated that most genotype distributions for the control group were well goodness-of-fit except for five studies. However, the authors only performed the meta-regression analysis to identify three possible sources of heterogeneity including ethnicity, tumour site, and minor allele frequency (MAF). We would recommend that in their meta-analyses, the authors should conduct the meta-regression analysis including HWE, not only excluded these five studies deviated from HWE. Therefore, we believe that the bias would be introduced into the results of the meta-analysis due to this shortage.

Second, in the meta-analysis, the authors have retrieved data on the source of control groups (hospital- or population-based controls), but the definitions for the population-based study and hospital-based study were not clear in this meta-analysis. This point greatly influenced the results of this meta-analysis. For example, if the authors defined the population-based study as controls from healthy population, and the hospital-based study as controls from patients, we could clearly ascertain that at least the report by Zhang *et al* (2003) was not a population-based study. Furthermore, the authors should perform a stratified analysis by source of control groups.

Finally, the data reported by Lajin and Alachkar (2013) do not seem in line with the data provided by Malik *et al* (2011) in their original publication. The numbers reported by Lajin and Alachkar (2013) for CC, CT, and TT, in cases and controls, respectively, are 51–38–18 and 112–68–15. Interestingly enough, after carefully studying the data presented by Malik *et al* (2011), the frequencies that we have retrieved on the 108 cases and 195 controls were 51–39–18 and 112–68–15, respectively. Therefore, this similar error may exist in other included studies in the meta-analysis. It would be valuable if the authors could provide a more careful checking for genotype data in previously published studies.

In conclusion, the above comments may reveal that the association between the *NQO1* C609T polymorphism and cancer susceptibility was conflicting. We believe that this remark will contribute to further, more accurate elaboration and substantiation of the original results presented by Lajin and Alachkar (2013).

REFERENCES

Lajin B, Alachkar A (2013) The NQO1 polymorphism C609T (Pro187Ser) and cancer susceptibility: a comprehensive meta-analysis. *Br J Cancer* **109**(5): 1325–1337.

Malik MA, Zargar SA, Mittal B (2011) Role of NQO1 609C > T and NQO2-3423G > A polymorphisms in susceptibility to gastric cancer in Kashmir valley. *DNA Cell Biol* **30**(5): 297–303.

Mao C, Liao RY, Chen Q (2010) Sensitivity analyses including and excluding the HWE-violating studies are required for meta-analyses of genetic association studies. *Breast Cancer Res Treat* **121**(1): 245–246.