Eligible and not eligible studies in the recent meta-analysis about p53 polymorphism and breast cancer risk

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LETTER TO THE EDITOR

Eligible and not eligible studies in the recent meta-analysis about p53 polymorphism and breast cancer risk

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Dear Editor,

We read with great interest the recent meta-analysis by Zhang et al. [1], which has reached important conclusions about the association between p53 codon 72 polymorphism and breast cancer risk.

Nevertheless, close inspection of the studies analyzed by the authors revealed some methodological issues that are worth mentioning and clarifying. Adopting the same search strings as Zhang et al. [1], we have located two relevant case/control studies in MEDLINE [2, 3] with a total number of 186 breast cancer cases and 266 controls, which have not been included in the meta-analysis. We believe that these two studies would be eligible for inclusion in the meta-analysis, as the exclusion criteria do not seem to apply on either of them.

Moreover, two pairs of overlapping studies may be worth commenting:

1. The study by Baynes et al. [4] and the study by Pharoah et al. [5] essentially represent the same SEARCH EPIC-Norfolk study. This is reflected upon the frequencies of GG-GC-CC in cases/controls, respectively, which are as follows: 1107-768-148/1177-854-166 for the study by Baynes et al. [4] and 1108-770-148/1177-854-166 for the study by Pharoah et al. [5] This seems of particular importance, as this study is of considerable sample size.
2. Two studies by Buyru et al. [6, 7] have been included in the meta-analysis; however, careful inspection of both studies reveals that the same cases have been included in them. The sole difference between the two studies emerges at the level of controls, as different control numbers have been included. As a result, incorporating one of the two studies by Buyru et al. might seem more appropriate.

Taking all the above into account, it would be valuable if the authors could provide a corrected estimation of the pooled odds ratio on a better defined set of eligible studies. We believe that these remarks will contribute to further, more accurate elaboration and substantiation of the original results presented by Zhang et al. [1].

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Rebuttal

We would like to thank Sergentanis and Economopoulos for their thoughtful comments. We have performed the core of the meta-analysis [1] taking into account their methodological comments. Specifically, we have included the two additional studies [2, 3], and we did not incorporate the studies by Pharoah et al. [5] and Buyru et al. [7], so as to eliminate the possibility of overlapping populations (n = 39 studies).

We are happy to report that the results persisted after the above-mentioned modifications. The pooled odds ratios (ORs) in the total of 39 studies were as follows: for GC versus GG genotypes, pooled OR = 0.908, 95% CI: 0.824–1.000, random effects; for CC versus GG genotypes, pooled OR = 0.915, 95% CI: 0.807–1.037, random effects. The dominant model (CC/GC vs. GG) retained its statistical significance, since the pooled OR was equal to 0.898 (95% CI: 0.818–0.987, random effects, cf. also the Fig. 1).

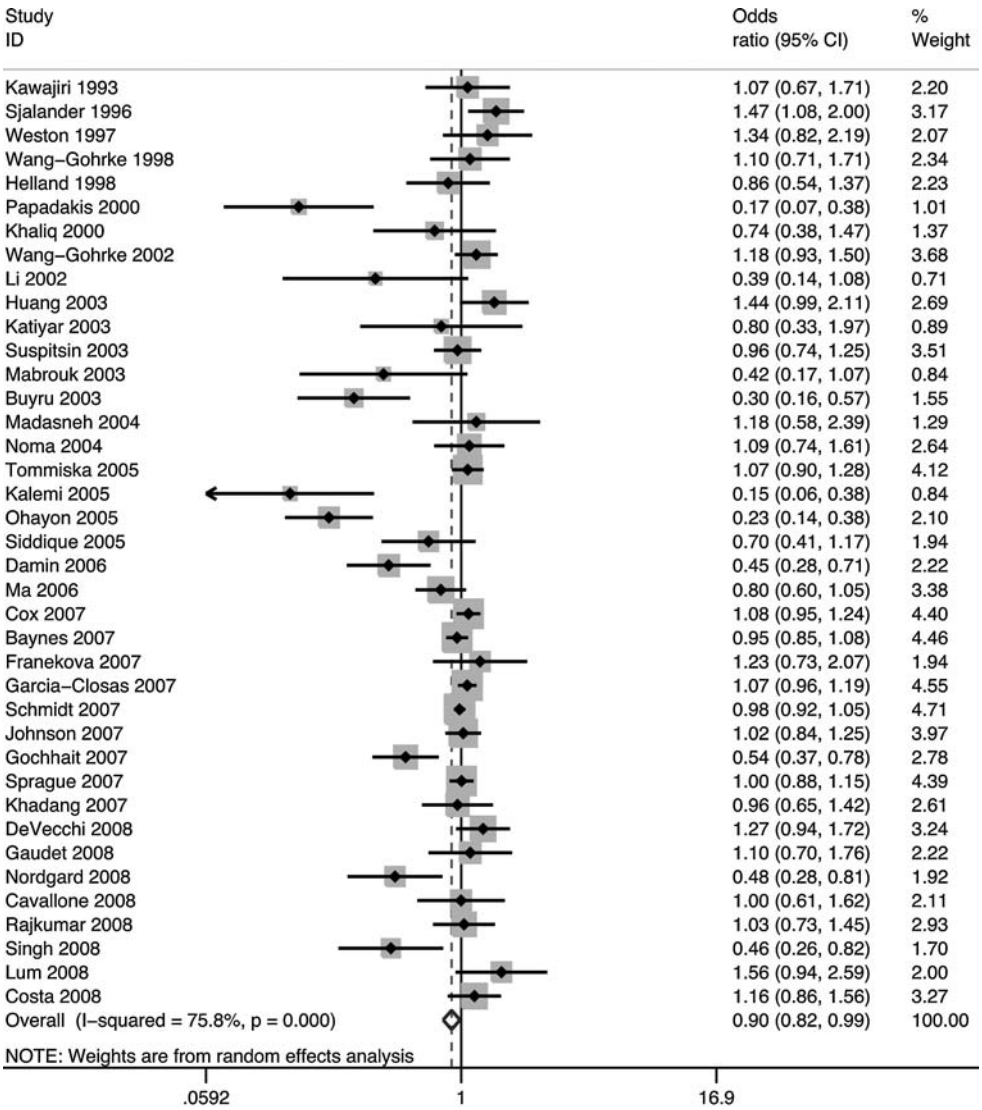

Fig. 1 Forest plot for the overall association (dominant model) between p53 codon 72 polymorphism status and breast cancer risk

The above may point to the validity and the robustness of the findings initially presented [1]. Indeed, given that the overall numbers at the initial analysis (26,041 breast cancer cases and 29,679 controls) are fairly large, the core of data has not been modified. As a result, we are happy to report that after elaborating our analysis under the light of the comments by Sergentanis and Economopoulos, the association between p53 codon 72 polymorphism and breast cancer risk remains well established.

References

1. Zhang Z, Wang M, Wu D, Wang M, Tong N, Tian Y, Zhang Z (2009) *P53* codon 72 polymorphism contributes to breast cancer risk: a meta-analysis based on 39 case-control studies. Breast Cancer Res Treat. doi:10.1007/s10549-009-0480-4
2. Helland A, Langerod A, Johnsen H, Olsen AO, Skovlund E, Borresen-Dale AL (1998) p53 polymorphism and risk of cervical cancer. Nature 396:530–531
3. Katiyar S, Thelma BK, Murthy NS, Hedau S, Jain N, Gopalkrishna V, Husain SA, Das BC (2003) Polymorphism of the p53 codon 72 Arg/Pro and the risk of HPV type 16/18-associated cervical and oral cancer in India. Mol Cell Biochem 252:117–124
4. Baynes C, Healey CS, Pooley KA, Scollen S, Luben RN, Thompson DJ, Pharoah PD, Easton DF, Ponder BA, Dunning AM (2007) Common variants in the ATM, BRCA1, BRCA2, CHEK2 and TP53 cancer susceptibility genes are unlikely to increase breast cancer risk. Breast Cancer Res 9:R27
5. Pharoah PD, Tyrer J, Dunning AM, Easton DF, Ponder BA (2007) Association between common variation in 120 candidate genes and breast cancer risk. PLoS Genet 3:e42
6. Buyru N, Tigli H, Dalay N (2003) P53 codon 72 polymorphism in breast cancer. Oncol Rep 10:711–714
7. Buyru N, Altinisik J, Demokan S, Dalay N (2007) p53 genotypes and haplotypes associated with risk of breast cancer. Cancer Detect Prev 31:207–213