Letter by Fu et al. regarding the article, “Polymorphisms in the vitamin D receptor gene and the lung cancer risk”

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To the Editor,

Fu et al. [1] present an interesting and comprehensive meta-analysis evaluating the polymorphisms of the vitamin D receptor (VDR) and lung cancer risk. We have read the article with great interest and appreciate its contribution to our current understanding of the associations between VDR polymorphisms and the susceptibility to lung cancer. However, we feel that some aspects of the study merit further discussion.

1. Three electronic databases (PubMed, Embase, and Wanfang database) for studies were systematically searched by the authors. However, the authors had not focused specifically or in any details on the issue of the completeness of the search strategy report for databases. Search strategy report plays an important role in systematic reviews.
2. We suggest that the authors should evaluate the methodological quality of the selected studies, which could avoid the potential bias and ensure maintenance of the quality of the meta-analysis. Each included paper could be independently assessed by two reviewers using a standardized electronic form of predefined criteria, and the authors could describe how to assess the quality of all studies in the meta-analysis and there were detailed scores for each trial. For instance, the Newcastle Ottawa scale as

recommended by the Cochrane Nonrandomized Studies Methods Working Group was developed to assess the quality of nonrandomized studies, specifically cohort and case-control studies. Studies with a score equal to or higher than 5 were considered “high quality,” whereas those scored less than 4 were considered “low quality.”

3. The departure of frequencies of VDR polymorphism from expectation under Hardy-Weinberg equilibrium in the control population should be assessed using the goodness-of-fit chi-square test and a $P < 0.05$ is considered significant disequilibrium. A significant difference between the observed and expected genotype frequencies under Hardy-Weinberg equilibrium (HWE) may indicate genotyping error [2]. Departure from HWE can be caused by factors such as inbreeding caused by consanguinity, assortative mating, i.e., non-random mating, selection, or migration [3]. Although exceptions to the conditions of HWE may explain deviation, it is critical that investigators recognize the need to perform a test of HWE and then evaluate the reason(s) for any observed deviation.
4. It is very important that a detailed description of “statistical analysis” should be provided systemically, such as heterogeneity across studies was tested by using the Cochrane Q or I^2 statistic, a random-effects model was used regardless of heterogeneity, a $P < 0.05$, or $I^2 > 50\%$ was judged as statistically significant.

Moreover, more carefully and scientifically designed studies with large samples are still needed.

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