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REPLY

Reply to Sanguankeo and Upala on "Sleep disturbances increase the risk of dementia: A systematic review and meta-analysis"

Recently the putative role of sleep problems in the incidence and development of dementia attracted considerable attention [1]. We previously reported on this relationship in a systematic review and meta-analysis [2]. In a commentary on our work, Drs. Sanguankeo and Upala proposed two points that might strengthen our meta-analysis [3]. We thank them for these suggestions and appreciate their efforts in improving the quality of our work. However, we should point out that in our meta-analysis, we had already taken the comments they offered into consideration.

Sanguankeo and Upala first concerned that the high prevalence rates reported in two of the studies included in our meta-analysis "might cause inconsistency between studies and difficulty in interpretation of pooled relative risk (RR)." A number of authors have previously discussed the boundary conditions under which odds ratio (OR) and RR could be treated almost equally, and found that the low discrepancies of OR and RR are mainly related to two factors, the low prevalence or incidence of the outcome and the small magnitude of OR [4,5]. When the cut-off value of the prevalence or incidence of events is less than or equal to 10% [4], or as another study proposes when only the incidence of outcome in the unexposed group is no more than 10% [5], the OR and RR could be pooled together. The two original papers we included that concerned Sanguankeo and Upala both reported low incidences of dementia [6,7]. Morgan et al. found that after 4 years follow up, only about 4.0% participants were diagnosed with dementia [6], and Yaffe et al. used hazard ratio to estimate the effect of sleep disturbances on dementia and reported that 9.1% of veterans without sleep disturbances at baseline later developed dementia [7]. Moreover, the statistical calculations ranging from 0.7 to 1.3, which were estimated based on the case and matched control in Morgan study and the retrospective cohort study of Yaffe, were too small for a risk of overestimate. Consequently, we pooled these two papers with the other articles in our meta-analysis.

Sanguankeo and Upala also noted that conducting a subgroup analysis can be a way to determine the causes of heterogeneity. We conducted several such subgroup analyses. One such analysis according to each category of statistical calculations found that the heterogeneity of sleep disturbances on all-cause dementia was not influenced by the calculation types ($p = 0.689$). Other subgroup analyses investigated the role of various factors (e.g. depression and the assessment of sleep disturbances) on heterogeneity and found that the heterogeneity could be partially explained by the assessment methods of sleep disturbances and depression (both $p < 0.001$). Unfortunately, it is not easy to achieve low heterogeneity based on information extracted from a relatively limited number of studies [8]. In the future, to reduce the bias caused by aggregate study level data meta-analyses, individual participant data meta-analyses are needed to further clarify the relationship between sleep disturbances and dementia [9].

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