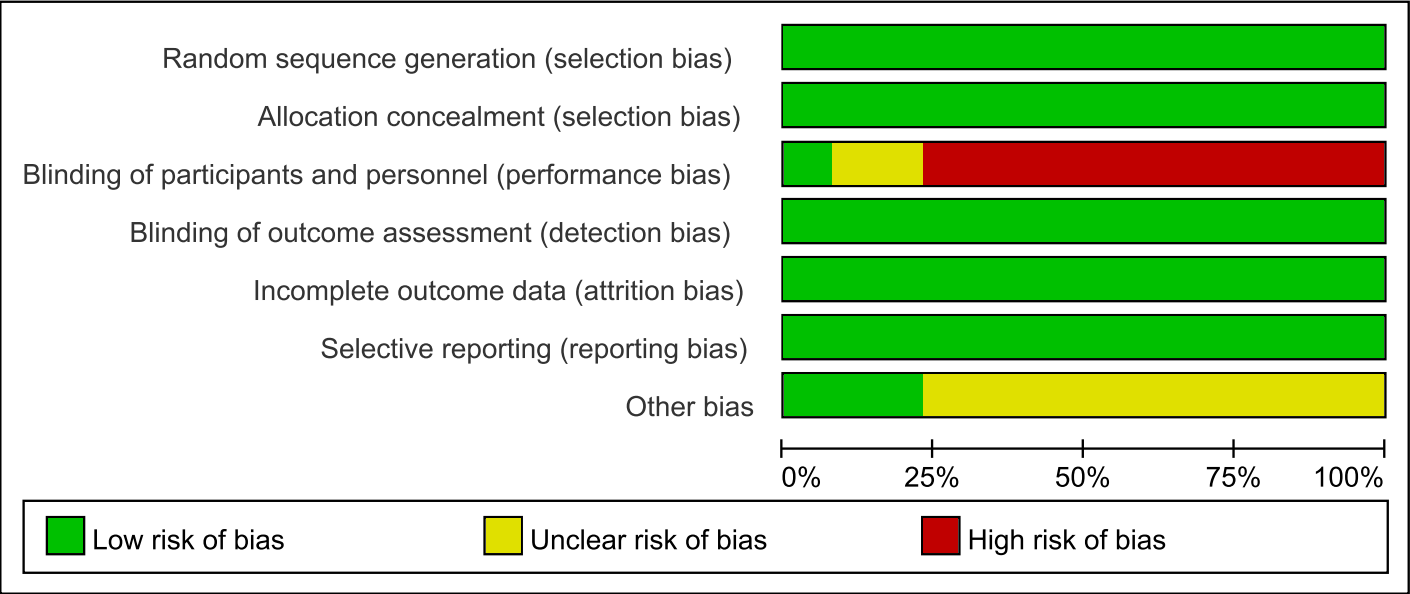


Figure S1: PRISMA flow diagram. 804 potentially relevant articles were identified by the search strategy, which were eventually restricted to 12 after independent evaluation of three authors.

A



B

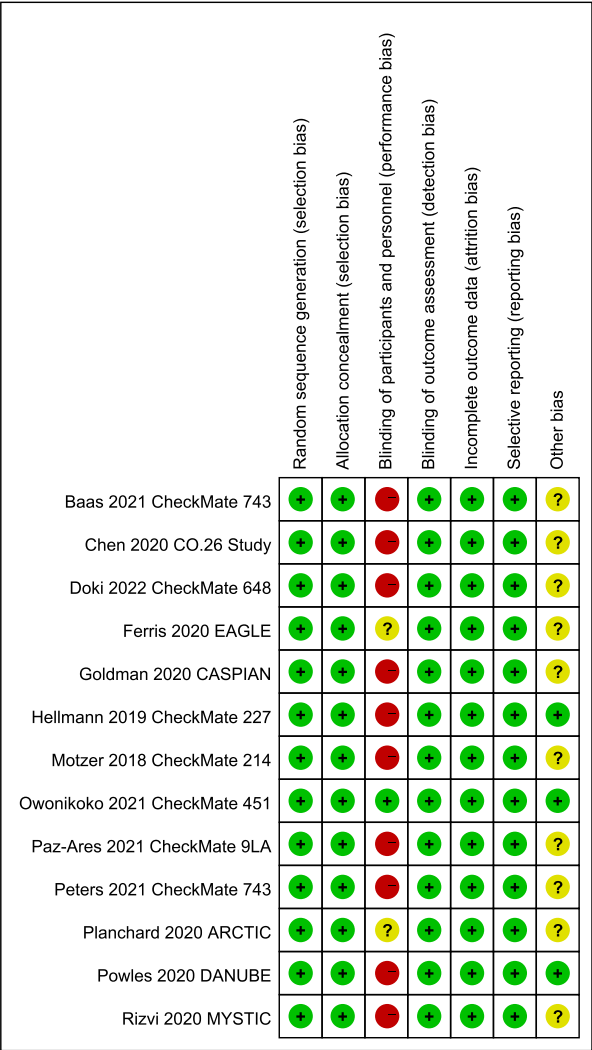


Figure S2: Risk of bias graph (A) and risk of bias summary (B). Cochrane Collaboration Tool was used in the assessment of risk of bias independently assessed by three different authors. RCTs included in the analysis were divided into "low risk", "high risk", or "unclear risk" of bias across predefined domains (selection, performance, attrition, and reporting bias).

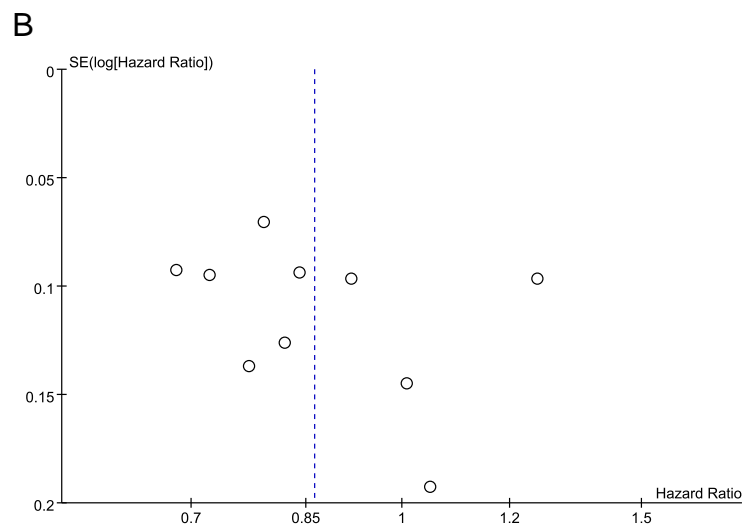
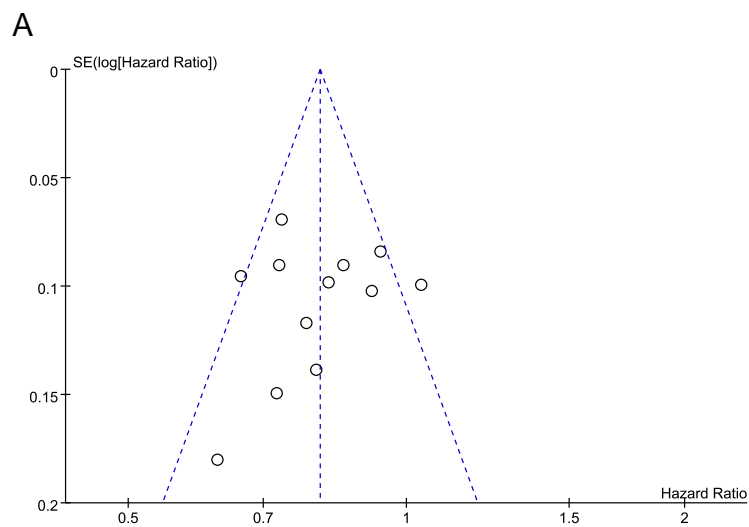
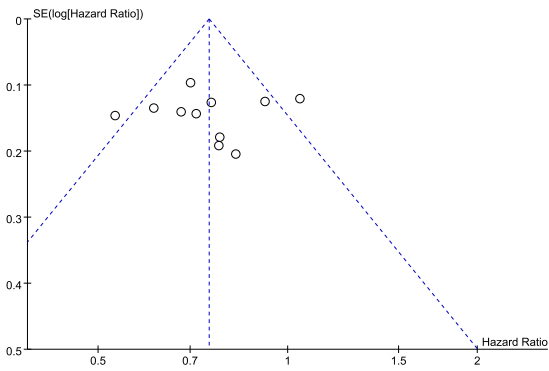
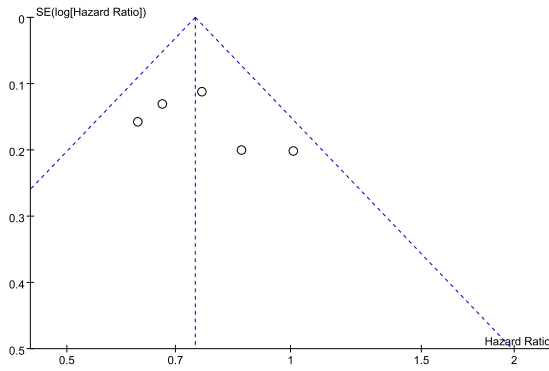


Figure S3: Funnel plots for (A) OS and (B) PFS between dual blockade of PD-1/PD-L1 and CTLA-4 versus SoC. Statistical analyses were performed by using Review Manager 5.3 software; funnel plots were used to assess publication bias.

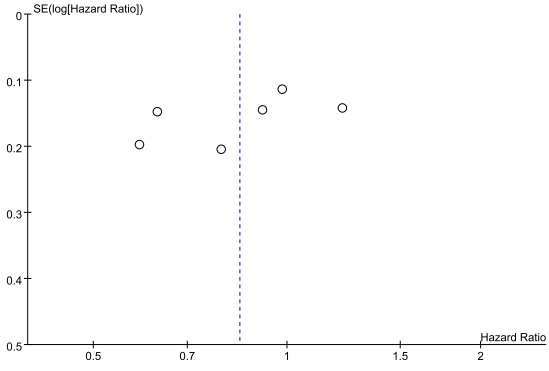
A Aged <65 years



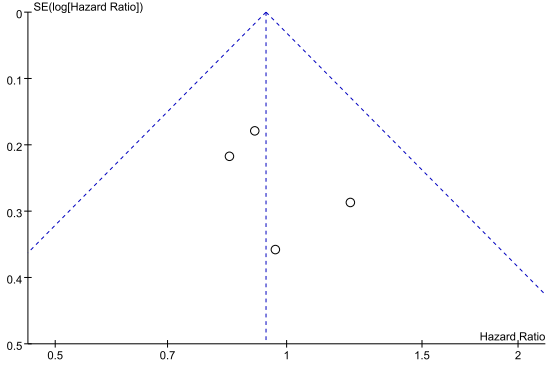
Aged 65-74 years



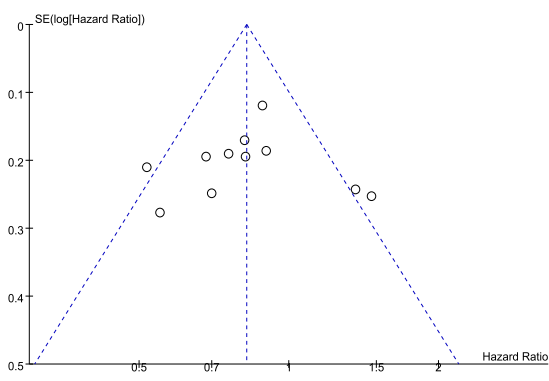
Aged ≥65 years



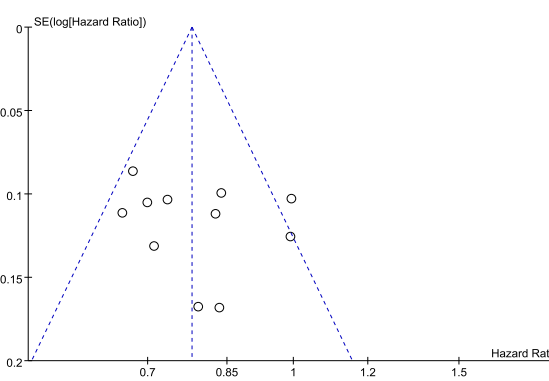
Aged ≥75 years



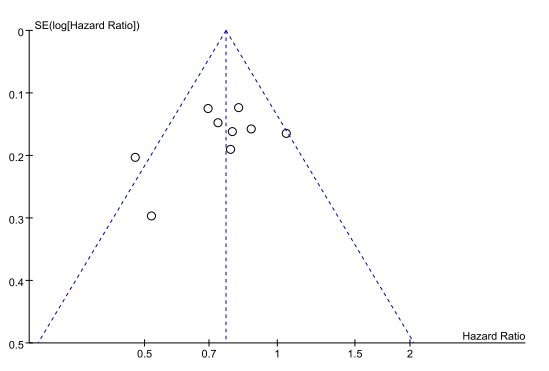
B Female



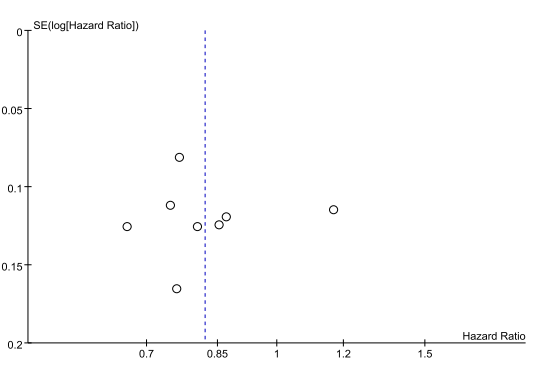
Male



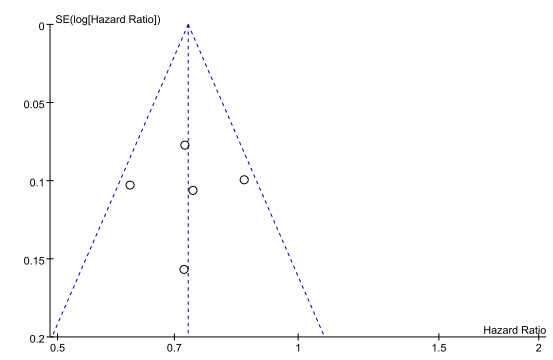
C PS 0



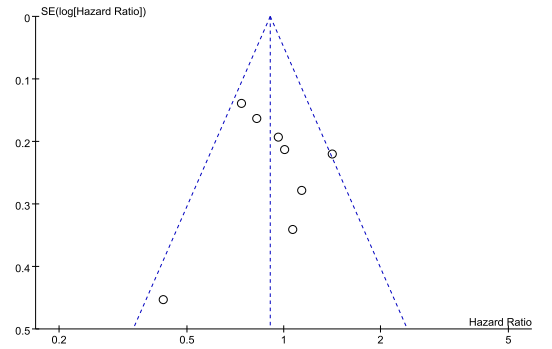
PS 1



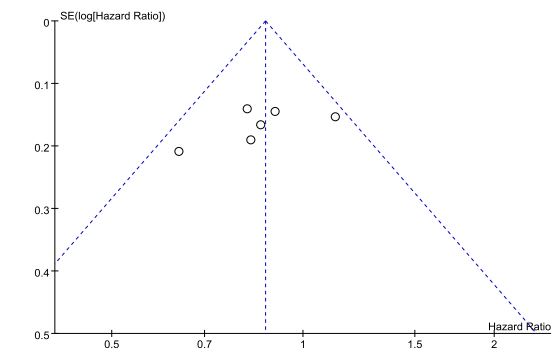
D Active or previous smokers



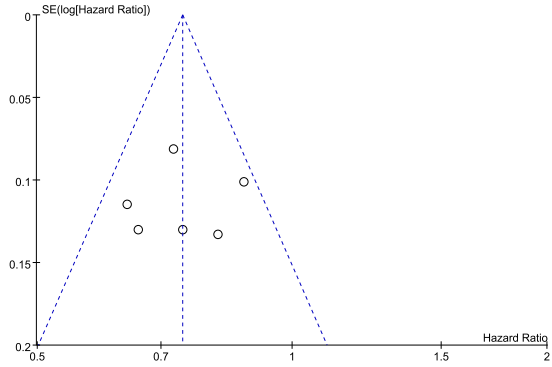
Never smoker



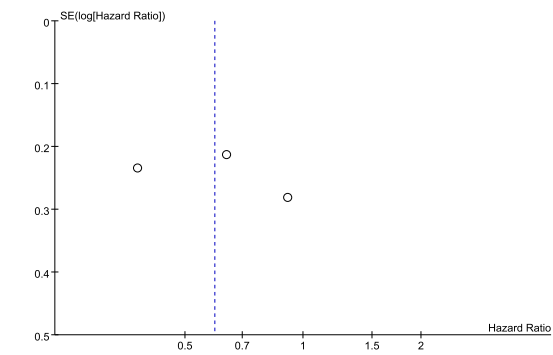
E With liver metastases



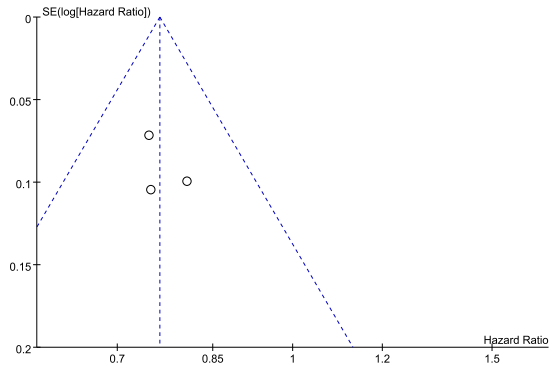
Without liver metastases



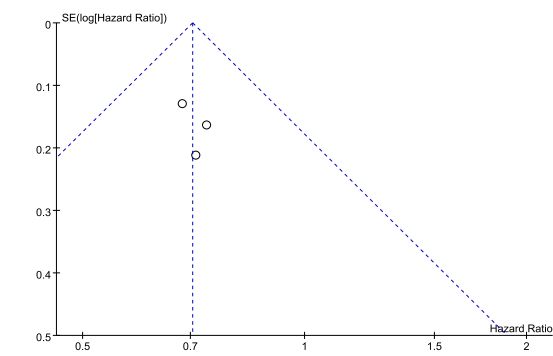
With brain metastases



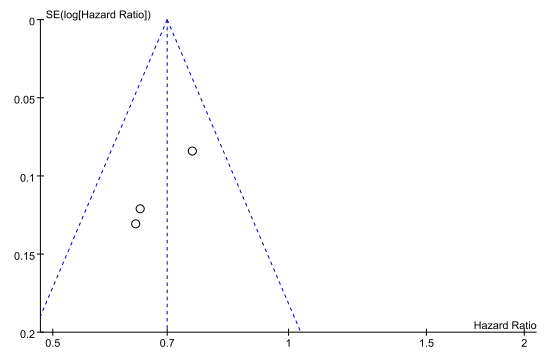
Without brain metastases



With bone metastases



Without bone metastases



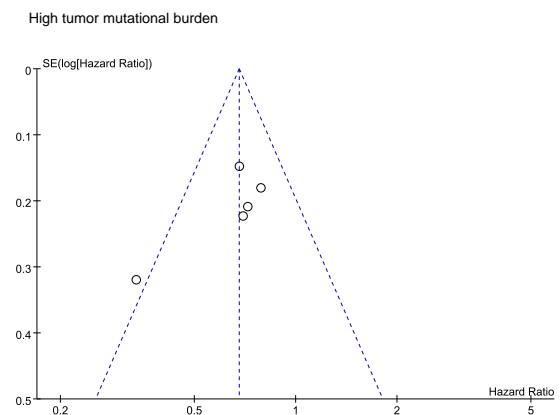
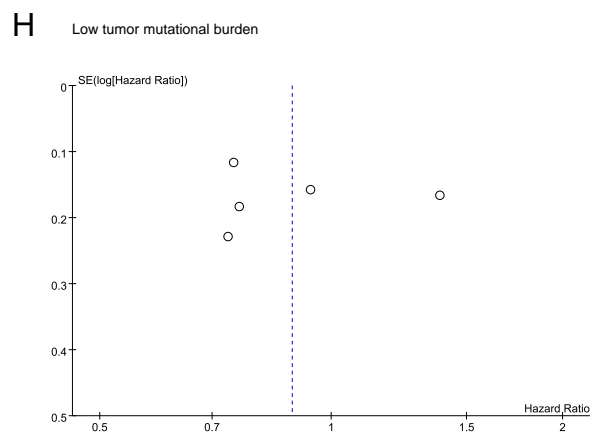
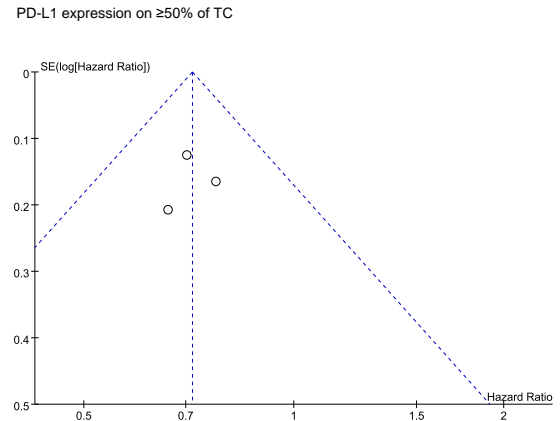
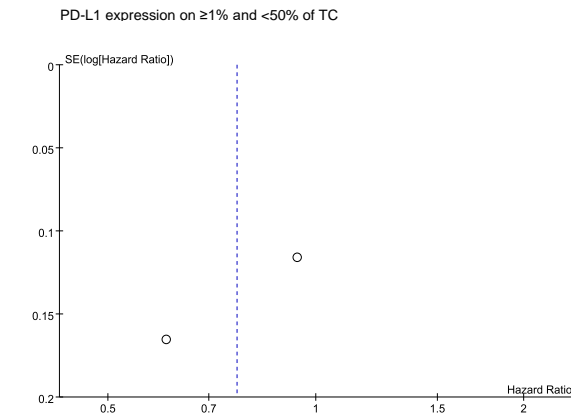
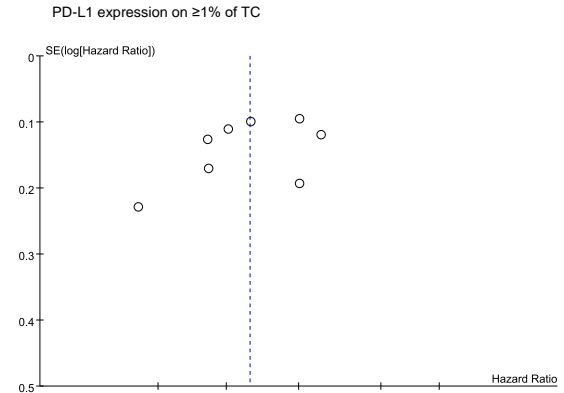
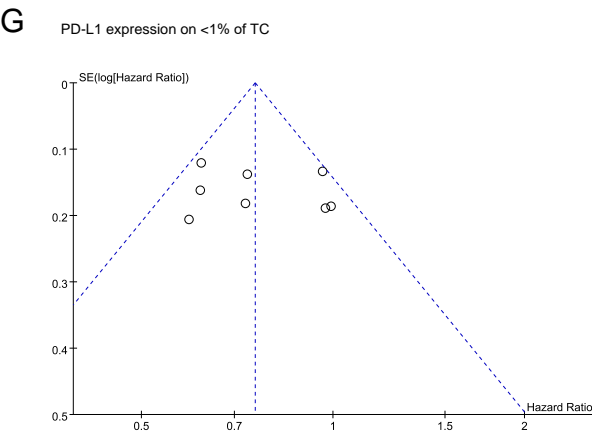
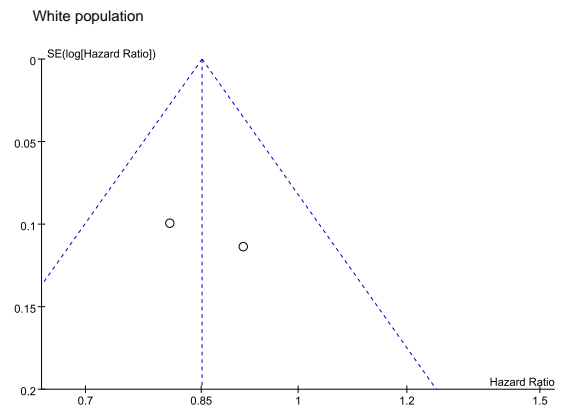
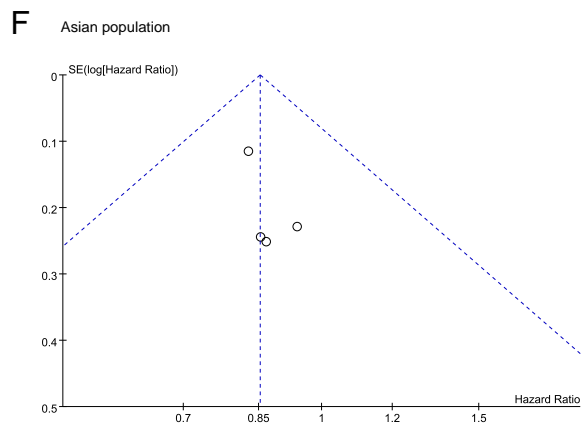


Figure S4: Funnel plots for OS in the subgroup with respect to (A) age group, (B) gender, (C) PS score, (D) smoking status, (E) metastases status/sites, (F) race, (G) PD-L1 expression status, (H) TMB. Statistical analyses were performed by using Review Manager 5.3 software; funnel plots were used to assess publication bias in each subgroup.