**Main Figure Legends:**

**Figure 1:** Flow diagram of literature search and selection criteria.

**Figure 2:** Prevalence of RAS mutation in head and neck cancer.

**(A)** Prevalence of HRAS mutation is 7% (95 % CI = 5.38-9.06, p<0.01, I2 = 87%). **(B)** Prevalence of KRAS mutation is 2.89% (95 % CI = 2.19-3.80, p<0.0.1, I2 = 67%). **(C)** Prevalence of NRAS mutation is 2.20% (95 % CI = 1.86-2.59, p<0.01, I2 = 29%). Abbreviations: CI: Confidence interval. I2: Inconsistency index.

**Figure 3:** Worldwide prevalence of RAS mutations in head and neck cancer.

Cohort studies were grouped according to geographical origin of patients. The World map indicates HRAS, KRAS, and NRAS mutations frequency [%] in East Asia, South Asia, Europe, and North America. Dotted line and gray shading indicated overall prevalence and 95% CI. Abbreviations: CI: Confidence interval. I2: Inconsistency index.

**Figure 4:** Mutation and Codon Prevalence according to anatomic site.

**(A)** Prevalence of RAS mutation according to anatomical site. Dotted line and gray shading indicated overall prevalence and 95% CI. **(B)** Mutated codon location [%] according to tumors’ anatomical site. Abbreviations: CI: Confidence interval. I2: Inconsistency index.

**Figure 5:** Association between RAS mutations and tumor grade.

44 cohort reported details of patient stage or grade with mutation status. 1 and 2 stage or grade tumors were categorized as low-grade tumors while stage or grade of 3 and 4 were categorized as high-grade. Odds ratio analysis showed a significant association between HRAS and advanced stage. (OR = 3.63; 95% CI = 1.53-8.64) Abbreviations: CI: Confidence interval. I2: Inconsistency index. OR: Odds ratio.

**Figure 6:** Association between RAS mutations and with Human Papillomavirus (HPV) status.

17 cohort reported on mutations in both HPV positive and negative patients. Odds ratio analysis showed a significant association between KRAS and HPV infection (OR=2.09; 95% CI = 1.01-4.31). Abbreviations: CI: Confidence interval. I2: Inconsistency index. OR: Odds ratio.

**Supplementary Figure Legends:**

**Supplementary Figure 1:**

Begg’s funnel plots for publication bias analysis display the prevalence of mutation (x-axis) due to the standard error in each study (y-axis). Each dot represents one study. The white rectangle indicates a 95 % pseudo-confidence interval, and the solid middle line indicates the overall effect from the meta-analysis.

**Supplementary Figure 2:**

Forest plot of RAS mutation frequency [%] in head and neck cancer according to geographical region. Abbreviations: CI: Confidence interval. I2: Inconsistency index. OR: Odds ratio.

**Supplementary Figure 3:**

Forest plot of RAS mutation frequency [%] in head and neck cancer according to tumors anatomical site of origin. Abbreviations: CI: Confidence interval. I2: Inconsistency index. OR: Odds ratio.

**Supplementary Figure 4:**

**(A)** mutated codon [%] in HRAS, KRAS and NRAS mutated cases. **(B)** Amino Acid substitution [%] in KRAS G12 and G13 mutated cases **(C)** Amino Acid substitution [%] in HRAS G12, G13 and Q61 mutated cases. Abbreviations: D-Aspartic acid, C-Cysteine, V-Valine, S-Serine, R-Arginine, A-Alanine, K-Lysine, L-Leucine.

**Supplementary Figure 5:**

Odds ratio analysis of KRAS and NRAS mutations association with grade status. No significant correlation was found.

**Supplementary Figure 6:**

Odds ratio analysis of KRAS and NRAS mutations association with Human Papillomavirus (HPV). No significant correlation was found.