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Prognostic impact of fusobacterium nucleatum in head and neck cancers: a meta-analysis of critical oncological outcomes

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ADMINISTRATIVE INFORMATION

Support - N/A.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 November 2025 and was last updated on 18 November 2025.

INTRODUCTION

Review question / Objective The objective of this meta-analysis was to consolidate existing research on the prognostic relevance of Fusobacterium abundance in head and neck squamous cell carcinoma (HNSCC).

Condition being studied Fusobacterium nucleatum has been associated with both tumor development and clinical outcomes in various cancer types; however, its prognostic relevance in head and neck cancers is not yet well established.

METHODS

Search strategy The literature search was conducted using a combination of controlled vocabulary (MeSH and Emtree terms) and free-text keywords, linked through Boolean operators (AND, OR, NOT) to capture studies related to Fusobacterium (e.g., "Fusobacterium nucleatum," "Fusobacteriales"), head and neck malignancies (e.g., "HNSCC," "oral cancer," "oropharyngeal cancer," "laryngeal cancer"), and prognostic indicators (e.g., "survival," "mortality," "disease-free survival," "cancer-specific survival"). Core MeSH terms for pathogen-related exposure included "Fusobacterium"[MeSH], "Fusobacterium nucleatum"[MeSH], "Fusobacteriales," "oral microbiome," and "oral bacteria." Cancer site–related MeSH terms encompassed "Head and Neck Neoplasms"[MeSH], "Oropharyngeal Neoplasms"[MeSH], "Oral Neoplasms"[MeSH], "Laryngeal Neoplasms"[MeSH], "Hypopharyngeal Neoplasms"[MeSH], "Nasopharyngeal Neoplasms"[MeSH], and "Tongue Neoplasms"[MeSH]. Prognosis- and outcome-related MeSH terms included "Prognosis"[MeSH], "Survival Analysis"[MeSH], "Disease-Free Survival"[MeSH], "Neoplasm Recurrence, Local"[MeSH], "Mortality"[MeSH], "Survival Rate"[MeSH], and "Treatment Outcome"[MeSH].

Participant or population This review focused on adult patients aged 18 years or older with

histologically confirmed head and neck squamous cell carcinomas, including tumors of the oral cavity, oropharynx, hypopharynx, larynx, and nasopharynx.

Intervention The primary exposure of interest was the presence or elevated abundance of Fusobacterium—particularly Fusobacterium nucleatum—identified in tumor tissue or saliva through molecular techniques such as qPCR, next-generation sequencing, droplet digital PCR, or RNA sequencing.

Comparator These individuals were compared with patients exhibiting absent or low levels of Fusobacterium. The primary outcome evaluated was overall survival, while disease-specific survival or cancer-specific survival were considered secondary endpoints.

Study designs to be included Eligible studies consisted of original human research, including prospective or retrospective cohort designs and case–control studies, that reported time-to-event outcomes accompanied by hazard ratios and corresponding 95% confidence intervals, or provided adequate data to derive these estimates.

Eligibility criteria Studies that failed to satisfy the predefined eligibility criteria were excluded, and the reasons for exclusion were systematically recorded (e.g., irrelevant population, absence of prognostic outcomes, review articles, or non-original research). Ultimately, only investigations that evaluated the prognostic relationship between Fusobacterium—particularly F. nucleatum—and clinical outcomes in head and neck cancer were retained for inclusion in the final meta-analysis.

Information sources We conducted a comprehensive search of PubMed/MEDLINE, Web of Science, Scopus, and Embase covering the period from January 1, 2000, to October 15, 2025, applying no restrictions on language.

Main outcome(s) The primary outcome of this meta-analysis was overall survival (OS) stratified by Fusobacterium status in patients with head and neck cancers. OS was defined as the interval between diagnosis or the start of treatment and death from any cause.

Additional outcome(s) Secondary outcomes encompassed disease-specific survival (DSS) and cancer-specific survival (CSS), as reported in the included studies. For each outcome, multivariable-adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were preferentially extracted; when such adjusted estimates were unavailable, univariate HRs were used instead.

Quality assessment / Risk of bias analysis The methodological rigor of the included studies was evaluated using the Newcastle–Ottawa Scale (NOS) for cohort designs, which examines the domains of selection, comparability, and outcome assessment. Studies achieving a score of 7 or higher were classified as high quality. Two reviewers independently conducted the quality appraisal, and any disagreements were resolved through discussion or, when necessary, by consultation with a third evaluator.

Strategy of data synthesis All statistical analyses followed standard approaches for time-to-event meta-analysis, using hazard ratios (HRs) with 95% confidence intervals (CIs) as the effect measure. When available, multivariable-adjusted HRs were extracted; otherwise, univariate estimates were used. Log-transformed HRs and their standard errors were derived as needed. Meta-analyses were conducted in Stata 18 (metan command) and RevMan 5.4 using the inverse-variance method. A random-effects model was applied, and results were reported as pooled HRs with 95% CIs and 95% prediction intervals. A two-sided p-value < 0.05 was considered statistically significant.

Subgroup analysis N/A.

Sensitivity analysis Although a fixed-effect approach was initially planned, we rigorously assessed heterogeneity to confirm model suitability; if I^2 exceeded 50% or the Q test was significant ($p < 0.10$), sensitivity analyses and further investigation of heterogeneity sources were undertaken.

Language restriction There were no restrictions on language during the search process.No language restrictions.

Country(ies) involved Turkey.

Keywords Fusobacterium nucleatum; head and neck cancer; prognostic biomarker; overall survival; disease-specific survival; meta-analysis.

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