

Supplementary Online Content

eMethods

Search strategy

The databases Medline (via Ovid), Embase (via Ovid), Cochrane Library, Scopus, and Web of Science (Core Collection) were searched by VP from inception to December 2022. For exact search terms used in each database, see below.

The search strategy was peer-reviewed by two librarian colleagues of VP using the PRESS checklist and evaluated against the PRISMA-S guidelines [1]. Databases were searched separately, rather than multiple databases being searched simultaneously on the same platform. The search syntax was adapted for each database, and to account for variation between thesaurus terms/controlled vocabulary across each database.

Results were deduplicated using Endnote 20 software. Endnote was set to identify articles as duplicates if they matched in the Author, Year, Title, Short Title, and Reference Type fields, and was also set to ignore differences in item record spacing and punctuation in these fields when identifying duplicates.

Medline via Ovid

"Head and Neck Neoplasms"/ OR Carcinoma, Squamous Cell/ OR Mouth Neoplasms/ OR Oropharyngeal Neoplasms/ OR Hypopharyngeal Neoplasms/ OR ("oral cavity neoplasm*" OR "Esophageal Neoplasm*" OR "Facial Neoplasm*" OR "oropharyngeal neoplasm*" OR "Mouth Neoplasm*" OR "Otorhinolaryngologic Neoplasm*" OR "Parathyroid Neoplasm*" OR "Thyroid Neoplasm*" OR "Tracheal Neoplasm*" OR "head and neck neoplasm*" OR "hypopharyngeal neoplasm*" OR ("head and neck" adj2 cancer*) OR (Esophageal adj2 cancer*) OR (fac* adj2 cancer*) OR (mouth adj2 cancer*) OR "Otorhinolaryngologic cancer*" OR "Parathyroid cancer*" OR (thyroid adj2 cancer*) OR (trachea* adj2 cancer*) OR "squamous cell carcinoma" OR "Oropharyngeal cancer*" OR "Hypopharyngeal cancer*").ti,ab,kw.

AND

telomerase.ti,ab,kw. OR TERT.ti,ab,kw. OR TERTp.ti,ab,kw. OR telomerase/

Embase via Ovid

"Head and Neck Neoplasms"/ OR Carcinoma, Squamous Cell/ OR Mouth Neoplasms/ OR Oropharyngeal Neoplasms/ OR exp Hypopharyngeal Neoplasms/ OR ("Esophageal Neoplasm*" OR "Facial Neoplasm*" OR "Mouth Neoplasm*" OR "Otorhinolaryngologic Neoplasm*" OR "Parathyroid Neoplasm*" OR "Thyroid Neoplasm*" OR "Tracheal Neoplasm*" OR "head and neck neoplasm*" OR "oral cavity neoplasm*" OR "oropharyngeal neoplasm*" OR "hypopharyngeal neoplasm*" OR ("head and neck" adj2 cancer*) OR (Esophageal adj2 cancer*) OR (fac* adj2 cancer*) OR (mouth adj2 cancer*) OR "Otorhinolaryngologic cancer*" OR "Parathyroid cancer*" OR (thyroid adj2 cancer*) OR (trachea* adj2 cancer*) OR "squamous cell carcinoma" OR "Oropharyngeal cancer*" OR "Hypopharyngeal cancer*").ti,ab,kw.

AND

telomerase.ti,ab,kw. OR TERT.ti,ab,kw. OR TERTp.ti,ab,kw. OR telomerase/

Web of Science core collection

TS=("Facial Neoplasm*" OR "Mouth Neoplasm*" OR "Otorhinolaryngologic Neoplasm*" OR "Parathyroid Neoplasm*" OR "Thyroid Neoplasm*" OR "Tracheal Neoplasm*" OR "head and neck neoplasm*" OR "oropharyngeal neoplasm*" OR "hypopharyngeal neoplasm*" OR ("head and neck" NEAR/2 cancer*) OR (Esophageal NEAR/2 cancer*) OR (fac* NEAR/2 cancer*) OR (mouth NEAR/2 cancer*) OR "Otorhinolaryngologic cancer*" OR "Parathyroid cancer*" OR (thyroid NEAR/2 cancer*) OR (trachea* NEAR2 cancer*) OR "squamous cell carcinoma" OR "Oropharyngeal cancer*" OR "Hypopharyngeal cancer*")

AND

TS=(telomerase OR TERT OR TERTp)

Scopus

TITLE-ABS-KEY ("Facial Neoplasm*" OR "Mouth Neoplasm*" OR "Otorhinolaryngologic Neoplasm*" OR "Parathyroid Neoplasm*" OR "Thyroid Neoplasm*" OR "Tracheal Neoplasm*" OR "head and neck neoplasm*" OR "oropharyngeal neoplasm*" OR "hypopharyngeal neoplasm*" OR ("head and neck" W/2 cancer*) OR (Esophageal W/2 cancer*) OR (fac* W/2 cancer*) OR (mouth W/2 cancer*) OR "Otorhinolaryngologic cancer*" OR "Parathyroid cancer*" OR (thyroid W/2 cancer*) OR (trachea* W/2 cancer*) OR "squamous cell carcinoma" OR "Oropharyngeal cancer*" OR "Hypopharyngeal cancer*")

AND

TITLE-ABS-KEY (telomerase OR TERT OR TERTp)

Cochrane Library

("Facial Neoplasm*" OR "Mouth Neoplasm*" OR "Otorhinolaryngologic Neoplasm*" OR "Parathyroid Neoplasm*" OR "Thyroid Neoplasm*" OR "Tracheal Neoplasm*" OR "head and neck neoplasm*" OR "oropharyngeal neoplasm*" OR "hypopharyngeal neoplasm*" OR ("head and neck" NEAR/2 cancer*) OR (Esophageal NEAR/2 cancer*) OR (fac* NEAR/2 cancer*) OR (mouth NEAR/2 cancer*) OR "Otorhinolaryngologic cancer*" OR "Parathyroid cancer*" OR (thyroid NEAR/2 cancer*) OR (trachea* NEAR/2 cancer*) OR "squamous cell carcinoma" OR "Oropharyngeal cancer*" OR "Hypopharyngeal cancer*"):ti,ab,kw OR MeSH descriptor: [Head and Neck Neoplasms] this term only OR MeSH descriptor: [Neoplasms, Squamous Cell] this term only OR MeSH descriptor: [Oropharyngeal Neoplasms] this term only OR MeSH descriptor: [Mouth Neoplasms] this term only OR MeSH descriptor: [Hypopharyngeal Neoplasms] this term only

AND

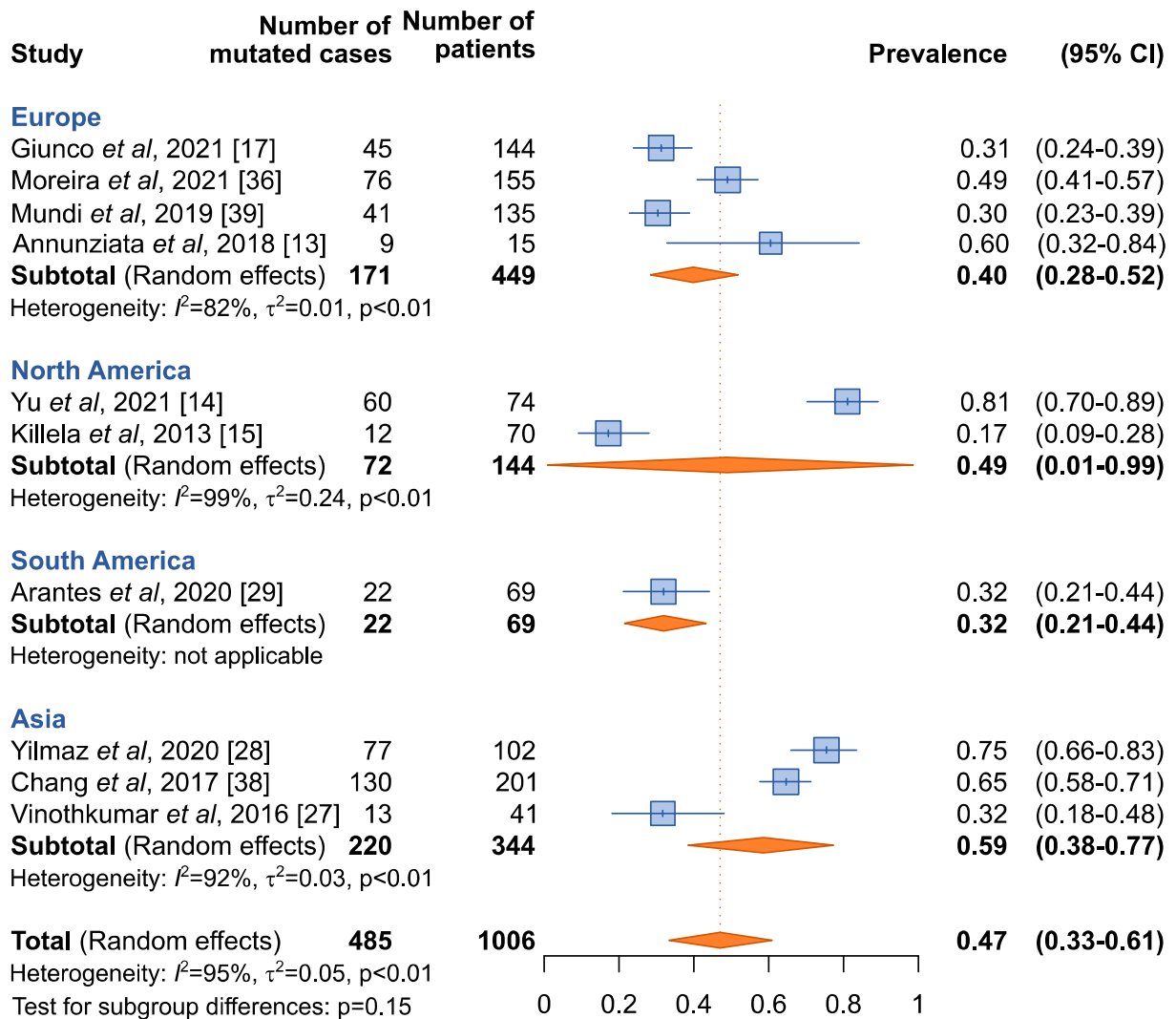
(telomerase OR TERT OR TERTp):ti,ab,kw OR MeSH descriptor: [telomerase] this term only

eTable. Quality assessment of included studies according to the Newcastle-Ottawa Scale [2]

Study	Selection				Comparability ^a	Outcome			Total Score (0-9)
	Representativeness of exposed cohort	Selection of non-exposed cohort	Exposure ascertainment	Outcome not present prior to exposure		Independent assessment	Adequacy of follow-up (median ≥ 24 months)	Completeness of follow-up ascertainment	
Studies for prevalence and prognosis									
Giunco <i>et al</i> , 2021 [3]	●	●	●	○	●●	●	●	●	8
Kim <i>et al</i> , 2021 [4]	●	●	●	●	●●	●	○	○	7
Arantes <i>et al</i> , 2020 [5]	●	●	●	●	●●	●	●	○	8
Yilmaz <i>et al</i> , 2020 [6]	●	●	●	○	●○	●	○	●	6
Boscolo-Rizzo <i>et al</i> , 2020 [7]	●	●	●	●	●●	●	●	○	8
Dogan <i>et al</i> , 2019 [8]	●	●	●	●	●●	●	●	●	9
Mundi <i>et al</i> , 2019 [9]	●	●	●	●	○○	●	●	●	7
Qu <i>et al</i> , 2014 [10]	●	●	●	○	○○	●	○	○	4
Studies for prevalence only									
Moreira <i>et al</i> , 2021 [11]	●	●	●	○	○○	●	●	○	5
Yu <i>et al</i> , 2021 [12]	●	●	●	●	○○	●	●	○	7
Annunziata <i>et al</i> , 2018 [13]	●	●	○	●	●●	●	○	○	6
Schwaederle <i>et al</i> , 2018 [14]	●	●	●	○	●●	●	○	○	6
Morris <i>et al</i> , 2017 [15]	●	●	●	○	○○	●	○	○	4
Chang <i>et al</i> , 2017 [16]	●	●	●	●	●●	●	●	●	9
Vinothkumar <i>et al</i> , 2016 [17]	●	●	●	○	○○	●	○	○	5
Cheng <i>et al</i> , 2015 [18]	○	●	●	○	○○	●	○	○	4
Killela <i>et al</i> , 2013 [19]	●	●	●	○	○○	●	○	○	4

○ Absent ● Present

eFigure. Forest-plot of prevalence of *TERT* promoter mutations in oral cavity SCC according the geographic area of the included patients



References

- [1] McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. *J Clin Epidemiol* 2016;75:40–6. <https://doi.org/10.1016/j.jclinepi.2016.01.021>.
- [2] Wells G, Wells G, Shea B, Shea B, O'Connell D, Peterson J, et al. *The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses*, 2014.
- [3] Giunco S, Boscolo-Rizzo P, Rampazzo E, Tirelli G, Alessandrini L, Di Carlo R, et al. TERT Promoter Mutations and rs2853669 Polymorphism: Useful Markers for Clinical Outcome Stratification of Patients With Oral Cavity Squamous Cell Carcinoma. *Front Oncol* 2021;11:782658. <https://doi.org/10.3389/fonc.2021.782658>.
- [4] Kim H, Kwon MJ, Park B, Choi HG, Nam ES, Cho SJ, et al. Negative Prognostic Implication of TERT Promoter Mutations in Human Papillomavirus-Negative Tonsillar Squamous Cell Carcinoma Under the New 8th AJCC Staging System. *Indian J Surg Oncol* 2021;12:134–43. <https://doi.org/10.1007/s13193-020-01200-9>.
- [5] Arantes LMRB, Cruvinel-Carlioni A, de Carvalho AC, Sorroche BP, Carvalho AL, Scapulatempo-Neto C, et al. TERT Promoter Mutation C228T Increases Risk for Tumor Recurrence and Death in Head and Neck Cancer Patients. *Front Oncol* 2020;10:1275. <https://doi.org/10.3389/fonc.2020.01275>.
- [6] Yilmaz I, Erkul BE, Ozturk Sari S, Issin G, Tural E, Terzi Kaya Terzi N, et al. Promoter region mutations of the telomerase reverse transcriptase (TERT) gene in head and neck squamous cell carcinoma. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2020;130:63–70. <https://doi.org/10.1016/j.oooo.2020.02.015>.
- [7] Boscolo-Rizzo P, Giunco S, Rampazzo E, Brutti M, Spinato G, Menegaldo A, et al. TERT promoter hotspot mutations and their relationship with TERT levels and telomere erosion in patients with head and neck squamous cell carcinoma. *J Cancer Res Clin Oncol* 2020;146:381–9. <https://doi.org/10.1007/s00432-020-03130-z>.
- [8] Dogan S, Xu B, Middha S, Vanderbilt CM, Bowman AS, Migliacci J, et al. Identification of prognostic molecular biomarkers in 157 HPV-positive and HPV-negative squamous cell carcinomas of the oropharynx. *Int J Cancer* 2019;145:3152–62. <https://doi.org/10.1002/ijc.32412>.

- [9] Mundi N, Prokopec SD, Ghasemi F, Warner A, Patel K, MacNeil D, et al. Genomic and human papillomavirus profiling of an oral cancer cohort identifies TP53 as a predictor of overall survival. *Cancers Head Neck* 2019;4:5. <https://doi.org/10.1186/s41199-019-0045-0>.
- [10] Qu Y, Dang S, Wu K, Shao Y, Yang Q, Ji M, et al. TERT promoter mutations predict worse survival in laryngeal cancer patients. *Int J Cancer* 2014;135:1008–10.
- [11] Moreira A, Poulet A, Masliah-Planchon J, Lecerf C, Vacher S, Larbi Chérif L, et al. Prognostic value of tumor mutational burden in patients with oral cavity squamous cell carcinoma treated with upfront surgery. *ESMO Open* 2021;6:100178. <https://doi.org/10.1016/j.esmoop.2021.100178>.
- [12] Yu Y, Fan D, Song X, Zakeri K, Chen L, Kang J, et al. TERT Promoter Mutations Are Enriched in Oral Cavity Cancers and Associated With Locoregional Recurrence. *JCO Precis Oncol* 2021;5:PO.20.00515. <https://doi.org/10.1200/PO.20.00515>.
- [13] Annunziata C, Pezzuto F, Greggi S, Ionna F, Losito S, Botti G, et al. Distinct profiles of TERT promoter mutations and telomerase expression in head and neck cancer and cervical carcinoma. *Int J Cancer* 2018;143:1153–61. <https://doi.org/10.1002/ijc.31412>.
- [14] Schwaederle M, Krishnamurthy N, Daniels GA, Piccioni DE, Kesari S, Fanta PT, et al. Telomerase reverse transcriptase promoter alterations across cancer types as detected by next-generation sequencing: A clinical and molecular analysis of 423 patients. *Cancer* 2018;124:1288–96. <https://doi.org/10.1002/cncr.31175>.
- [15] Morris LGT, Chandramohan R, West L, Zehir A, Chakravarty D, Pfister DG, et al. The Molecular Landscape of Recurrent and Metastatic Head and Neck Cancers: Insights From a Precision Oncology Sequencing Platform. *JAMA Oncol* 2017;3:244–55. <https://doi.org/10.1001/jamaoncol.2016.1790>.
- [16] Chang K-P, Wang C-I, Pickering CR, Huang Y, Tsai C-N, Tsang N-M, et al. Prevalence of promoter mutations in the TERT gene in oral cavity squamous cell carcinoma. *Head Neck* 2017;39:1131–7. <https://doi.org/10.1002/hed.24728>.
- [17] Vinothkumar V, Arunkumar G, Revathidevi S, Arun K, Manikandan M, Rao AKDM, et al. TERT promoter hot spot mutations are frequent in Indian cervical and oral squamous cell carcinomas. *Tumour Biol J Int Soc Oncodevelopmental Biol Med* 2016;37:7907–13. <https://doi.org/10.1007/s13277-015-4694-2>.

- [18] Cheng KA, Kurtis B, Babayeva S, Zhuge J, Tantchou I, Cai D, et al. Heterogeneity of TERT promoter mutations status in squamous cell carcinomas of different anatomical sites. *Ann Diagn Pathol* 2015;19:146–8. <https://doi.org/10.1016/j.anndiagpath.2015.03.005>.
- [19] Killela PJ, Reitman ZJ, Jiao Y, Bettegowda C, Agrawal N, Diaz LA, et al. TERT promoter mutations occur frequently in gliomas and a subset of tumors derived from cells with low rates of self-renewal. *Proc Natl Acad Sci U S A* 2013;110:6021–6. <https://doi.org/10.1073/pnas.1303607110>.