BMJ Open

Cohort profile: the Dutch oral cavity cancer cohort

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-092467
Article Type:	Cohort profile
Date Submitted by the Author:	15-Aug-2024
Complete List of Authors:	van Oorschot, Hanneke; Erasmus MC Cancer Center, Department of Otorhinolaryngology and Head and Neck Surgery; Dutch Institute for Clinical Auditing, Scientific Bureau Hardillo, Jose; Erasmus MC Cancer Center, Otorhinolaryngology and Head and Neck surgery Baatenburg de Jong, Rob; Erasmus MC Cancer Center, Department of Otorhinolaryngology Dutch head and neck audit , oral cavity collaborator group; Dutch Institute for Clinical Auditing, Scientific Bureau
Keywords:	ORAL & MAXILLOFACIAL SURGERY, Head & neck tumours < ONCOLOGY, Head & neck surgery < SURGERY, ONCOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Title:

Cohort profile: the Dutch oral cavity cancer cohort

Authors:

Hanneke Doremiek van Oorschot[1,2], MD (ORCID 0000-0001-6858-3984)

Jose Angelito Hardillo[1], MD, PhD (ORCID 0000-0001-5580-5613)

Robert Jan Baatenburg de Jong[1], MD, PhD (ORCID 0000-0001-7236-264X)

Dutch head and neck audit - oral cavity collaborator group:

Robert (R.J.J.) van Es[3], MD, PhD, Guido van den Broek[4], MD, PhD, Robert (R.P.) Takes[4], MD, PhD (ORCID 0000-0003-4784-0499), Gyorgy (G.B.) Halmos[5], MD, PhD (ORCID 0000-0003-2460-2260), Dominique (D.V.C.) de Jel[5], MD (ORCID 0000-0001-8159-0089), MD, Richard (R.) Dirven[6], MD, PhD, Martin (M.) Lacko[7], MD, PhD (ORCID 0000-0003-2868-4822), Lauretta (L.A.A.) Vaassen[8], MD, PhD, (ORCID 000-0002-1408-6146), Jan-Jaap (J.J.) Hendrickx[9], MD, PhD, Marjolijn (M.A.E.) Oomens[10], MD (ORCID 0000-0003-1526-559X), Hossein Ghaeminia[10], MD, PhD, Jeroen (J.C.) Jansen[11], MD, PhD, Annemarie Vesseur[12], MD (ORCID 0000-0002-6702-4360), Rolf Bun[13], MD, PhD, Noortje (L.Q.) Schwandt[14], MD, PhD, Christiaan (C.A.) Krabbe[14], MD, PhD, Thomas (T.J.W.) Klein Nulent[14], MD, Alexander (A.J.M) van Bemmel[16], MD (ORCID 0000-0003-0953-8408), Reinoud (R.) Klijn[17]

Author affiliations:

1. Department of Otorhinolaryngology and Head and Neck Surgery, Erasmus Medical Centre Cancer Institute, Rotterdam, The Netherlands
2. Scientific Bureau, Dutch Institute for Clinical Auditing, Leiden, the Netherlands
3. Department of Head and Neck Surgical Oncology, UMC Utrecht Cancer Centre, Utrecht
4. Department of Otorhinolaryngology, Head and Neck Surgery, Radboud University Medical Center, Nijmegen:
5. Department of Otorhinolaryngology/Head and Neck Surgery, University Medical Centre Groningen, University of Groningen, Groningen
6. Department of Head and Neck Oncology and Surgery, Netherlands Cancer Institute/Antoni van Leeuwenhoek, Amsterdam

7. Department of Otorhinolaryngology and Head and Neck Surgery, GROW School for Oncology and Reproduction, Maastricht University Medical Center, Maastricht
8. Department of Cranio-maxillofacial surgery, GROW School for Oncology and Reproduction, Maastricht University Medical Center, Maastricht
9. Department of Otorhinolaryngology, Head and Neck Surgery, Academic Medical Center, University of Amsterdam
10. Department of Oral and Maxillofacial Surgery, Rijnstate Hospital, Arnhem
11. Department of Otorhinolaryngology, Head and Neck Surgery, Leiden University Medical Centre, Leiden
12. Department of Otolaryngology, Head and Neck Surgery, Elisabeth Tweesteden Ziekenhuis Tilburg, Tilburg
13. Department of Oral and Maxillofacial Surgery/Head and Neck Oncology Noordwest Hospital group, Alkmaar en Dijklander Hospital, Hoorn
14. Department of Oral and Maxillofacial Surgery, Medical Centre Leeuwarden, Leeuwarden
15. Department of Oral and Maxillofacial Surgery, Haaglanden Medical Center, The Hague
16. Department of Otorhinolaryngology and Head and Neck Surgery, Medisch Spectrum Twente, Enschede
17. Department of Oral and Maxillofacial and Head and Neck Surgery, Medisch Spectrum Twente, Enschede

Corresponding author:

H.D. van Oorschot, MD

Department of Otorhinolaryngology and Head and Neck Surgery, P.O. Box 2040, 3000 CA Rotterdam, Erasmus Medical Centre Cancer Institute, Rotterdam, The Netherlands.

E: h.vanoorschot@erasmusmc.nl / T: 00107033106

Journal: BMJ open

Word count: 1558 words

Abstract word count: 243 words

Keywords: Head and neck cancer, oral cavity cancer, national cohort

Abstract

Purpose:

The Dutch Head and Neck Audit – Oral Cavity (DHNA-OC) cohort was collected to study quality of care, current treatment, and survival for oral cavity cancer (OCC) across all hospitals treating head and neck cancer (HNC) in the Netherlands.

Patients:

The DHNA-OC is a registry-based national cohort of 2,545 first primary OCC patients treated with curative intent between 2018 and 2021. All fourteen HNC hospitals in the Netherlands contributed, guaranteeing national coverage. The DHNA-OC cohort is an elaborate dataset including variables on patient and tumour characteristics, treatment, complications, recurrence rates, and survival.

Findings to date:

The median age at diagnosis was 67 years and most tumours were early stage (cT1 in 32% and cT2 in 31%). Tongue tumours were most common and surgery was performed in 91.3% of the patients. The number of included patients per hospital varied from 82 to 367. The proportion of advanced tumour stage varied significantly between hospitals. Substantial data completeness was acquired with only two variables exceeding 10% missing (comorbidities and performance score).

Future plans:

The DHNA-OC cohort will be used to study benchmarking of and current knowledge gaps in OCC care. Collaboration with other institutions or national/regional databases is highly encouraged. Some examples of planned studies are the assessment of hospital variation in outcome indicators for surgery and population-based treatment effects. The results of these studies will be used to identify best practices and continue improving quality of care. Longitudinal cohort follow-up and enrolment will continue prospectively.

Strengths and limitations of this study

- The main strength of the Dutch Head and Neck Audit—Oral Cavity (DHNA-OC) cohort is its nationwide inclusion, facilitated by population-based registries that are centrally managed.
- The DHNA-OC cohort is an elaborate dataset including variables on patient and tumour characteristics, given treatment, treatment complications, recurrence rates, and survival.
- The main limitations are the lack of data on socioeconomic status, education level, and medication use.
- Though all registrars adhere to the same manual and openly discuss questions when registering, variation in the interpretation of variables could exist.

Introduction

The Dutch Head and Neck Audit – Oral Cavity (DHNA-OC) cohort was designed to study current treatment, survival, and quality of care for oral cavity cancer (OCC). With an incidence of ~1000 in 2023, OCC is a relatively rare cancer in the Netherlands.[1] Despite the low incidence, OCC patients often require highly complex multidisciplinary integrated care.[2] As in other cancers with low incidence rates, clinical trials in HNC struggle to enroll enough participants. Therefore, real-world data is increasingly used to answer current knowledge gaps in clinical practice guidelines.

The Dutch Head and Neck Audit (DHNA) was established in 2014 to monitor and benchmark the quality of HNC nationally.[2] Auditing has been identified as an effective tool in improving quality of care for surgical oncological fields, such as in the Dutch Surgical Colorectal Audit.[3,4] By effective auditing and collaboration, the patient pathways were standardized, complication rates declined, and even mortality rates decreased.[4] Over the past years, DHNA data availability has improved, yet data is missing on crucial variables. To follow the lead of the colorectal audit, the DHNA-OC cohort was instigated.

Research questions that motivated the DHNA-OC cohort revolve around enhancing the quality of care and addressing current knowledge gaps. To study hospital variation, we first aim to develop a case-mix model for OCC.[5] This will enable us to investigate variation in surgical complications, resection margins, and textbook outcome.[6] Furthermore, the indication and value of adjuvant therapy in case of a resection margin of one to five millimeters remain unclear.[7] Also, debate is ongoing regarding the use of elective neck dissection versus sentinel lymph node biopsy in early-stage OCC.[8] Through the DHNA-OC, we aim to offer insights derived from real-world data, contributing to enhancing new clinical practice guidelines, which currently may lack a scientific foundation.

Cohort description

This research proposal was reviewed by the Institutional research review board Erasmus Medical Center (Rotterdam, The Netherlands), and the board confirmed that the rules laid down in the Medical Research Involving Human Subjects Act do not apply to this research proposal (MEC-2022-0816).

Cohort design

The DHNA-OC is based on data from the Dutch Head and Neck Audit (DHNA). HNC care in the Netherlands is centralized in 14 devoted hospitals: eight head and neck oncologic centres (HNOCs) and seven preferred partner hospitals.[9] HNC care is covered by the Dutch health insurance system, which is obligatory and socialized. The DHNA gained national coverage in 2019 and participation is mandatory. All patients with a first primary head and neck tumour are prospectively included. Patients with in situ carcinoma, a second primary tumour, recurrent HNC, melanomas, cutaneous malignancies, thyroid carcinomas, sarcomas, neuroendocrine cancers, and hematologic malignancies are currently not included in the DHNA. Data is collected by trained registrars, physician assistants, and administrative nurses employed by the HNC hospital or the Netherlands Comprehensive Cancer Organisation (IKNL). The complete DHNA data dictionary can be accessed online.[10] The DHNA is one of 26 quality registries maintained at the Dutch Institute for Clinical Auditing (DICA).[11] This institution guarantees data quality through annual data verification processes.[12]

Patient and public involvement

Patients were involved in the design of the DHNA.[2] Patients or the public were not involved in the planning or design, recruitment, or conduction of this cohort.

Participants

Data completeness is essential for reliable population-based research and evaluation of quality of care. Patients were selected from the DHNA based on the pathological conformation (biopsy) date between January 1 2018 and December 31 2021. Included ICD-O-3 codes for OCC were C00, C02-C04, C05.0, C5.8-9, and C06.0-8.[13] Patients of ≥18 years were selected if treated with curative intent in one of the 14 HNC hospitals during the study period. Missing variables in the DHNA cohort were complemented with data from the Netherlands Cancer Registry (NCR). This is the national registry on malignancies in the Netherlands.[14] Since 1989, IKNL has objectively registered all newly diagnosed patients in the NCR. Patients are assigned a unique uniform resource identifier (URI) in the treating hospital. DHNA and NCR data were matched on date of birth, hospital-URI, and treating hospital. The complemented dataset was returned to the individual hospitals to retrieve the remaining missing values from electronic patient files. A head and neck surgeon or clinical HNC researcher then executed data curation. The final dataset was delivered to update the DHNA dataset with missing values.

Variables and data management

Supplemental file 1 gives a complete overview of the DHNA-OC dataset. Comorbidity was scored using the ACE-27 and the TNM-classification followed the 8th edition of the Union for International Cancer Control TNM Classification.[15,16] Clinical TNM stage 0 was included in OCC cases with cTx/T0/TisN0M0 classification that were upstaged on pathological examination to pT1/T2/T3/T4. Surgical 30-day complications were classified utilizing the Clavien-Dindo classification.[17] Follow-up started on the date of last treatment (surgery, systemic therapy or radiotherapy). Follow-up was censored two years after the date of last treatment. As the DHNA is a prospective database, five-year follow-up will be registered yearly (data for 2018 in 2025, 2019 in 2026, and so on). As this study included national data a sample size calculation was deemed unnecessary.

To guarantee patient privacy and Dutch privacy regulations, DICA works with a third-trusted party: Medical Research Data Management (MRDM), Deventer, the Netherlands (NEN 7510:2011 and ISO 27001:2013 certified).[18] MRDM designs, develops, and manages registration systems for DICA's quality registrations, among others. MRDM processes the data from the hospital so that DICA receives only coded (pseudonymous) data. Hospitals sign an agreement with DICA and MRDM to process their data and deliver data manually (survey) or via batch. DICA's privacy committee guarantees that data handling complies with the Dutch Personal Data Protection Act. Statistical analyses are performed in protected digital areas and cannot be traced back to specific subjects.

Findings to date

A total of 2,545 patients were included (Figure 1). The final DHNA-OC cohort baseline characteristics are presented in Table 1.

Table 1: Demographic characteristics of patients included in the DHNA-OC cohort.
IQR = interquartile range, WHO = World Health Organization.

Characteristic	N = 2,545
Gender - female	1,171 (46%)
Age	67 (59, 75)
Body mass index (kg/m2)	
<18.5	102 (4.0%)
≥18.5 to <30	1,953 (77%)
≥30	419 (16%)
Unknown	71 (2.8%)

Smoking history	
No history of smoking	639 (25%)
Former smoker	852 (33%)
Current smoker	945 (37%)
Unknown	109 (4.3%)
Alcohol history	
No history of drinking	419 (16%)
Former drinker	196 (7.7%)
Current drinker	1,712 (67%)
Unknown	218 (8.6%)
ACE27 score	
Grade 0 - None	720 (28%)
Grade 1 - Mild	375 (15%)
Grade 2 - Moderate	248 (9.7%)
Grade 3 - Severe	90 (3.5%)
Unknown	1,112 (44%)
WHO performance status	
Normal activity (0)	1,268 (50%)
Symptomatic, fully ambulatory: cares for self (1)	501 (20%)
Ambulatory >50% of the time: occasional assistance (2)	178 (7.0%)
Ambulatory <50% of the time: nursing care needed (3)	41 (1.6%)
Bedridden (4)	1 (<0.1%)
Unknown	556 (22%)
Histology	
Squamous cell carcinoma	2,328 (91%)
Other	216 (9.0%)
Unknown	1 (<0.1%)
Oral cavity subsite (ICD-O-3)	
Lip	54 (2.1%)
Tongue	1,105 (43%)
Gum	449 (18%)
Floor of mouth	426 (17%)
Palate	86 (3.4%)
Other parts of oral cavity	423 (17%)
Not otherwise specified	2 (<0.1%)
cT-classification	
cTx	25 (1.0%)
cT0	7 (0.3%)
cTis	23 (0.9%)
cT1	825 (32%)
cT2	783 (31%)
cT3	343 (13%)
cT4	539 (21%)
cN-classification	
cNx	14 (0.6%)

cN0	2,001 (79%)
cN1	194 (7.6%)
cN2	292 (11%)
cN3	44 (1.7%)
cM-classification	
cMx	2 (<0.1%)
cM0	2,541 (100%)
cM1	2 (<0.1%)
cTNM stage	
Stage 0	53 (2.1%)
Stage I	791 (31%)
Stage II	643 (25%)
Stage III	342 (13%)
Stage IV	716 (28%)
Treatment	
Surgery	1,441 (57%)
Surgery & radiotherapy	724 (28%)
Surgery & chemoradiation	185 (7.3%)
Radiotherapy	111 (4.4%)
Chemoradiation	71 (2.8%)
Other	13 (0.5%)
Treating hospital	
HHOCs	1,926 (76%)
PPs	619 (24%)
Year of diagnosis	
2018	626 (25%)
2019	626 (25%)
2020	631 (25%)
2021	662 (26%)

The median age was 67 years (inter-quartile range [IQR] 59-75) and 46% was female. Body mass index (BMI in kg/m2) was unknown in 2.8%, with 77% of the patients at a BMI between 18.5 and 30 kg/m2. Most patients were current smoker or drinker (37% and 67% respectively) with missing data on smoking and drinking history in 4.3% and 8.6% respectively. Data on comorbidities was missing in 44%, leaving the grade 0 as the most observed ACE27 score (28%). A WHO-performance score of 0 was most seen in the cohort (50%), though data was missing in 22%.

Ninety-one percent of the tumours were squamous cell carcinoma and most were located in the tongue (43.%). Clinical TNM-stage 0 tumours were present in 2.1%, stage I in 31%, stage II in 25%, stage III in 13%, and stage IV in 28%. Surgery alone was performed in 57% of the patients. Surgery

was complemented by radiotherapy in 28% and by chemoradiation in 7.3%. Only 4.4% received radiotherapy as definitive treatment.

Seventy-six percent was treated in one of the HHOCs and annual inclusion rate was constant over the years. The number of patients that was included per hospital varied from 367 to 82 (Figure 2). The proportion of stage III-IV tumours varied significantly between treating hospitals (p-value <0.001) but was not directly proportional to hospital volume (Figure 3). Overall, a high data completeness was achieved, expecially regarding treatment and outcome variables.

The capture rate of the DHNA-OC cohort is compared to the annual incidence rate for OCC registered in the NCR in Figure 4. The difference in annual inclusion between the NCR and DHNA-OC cohort can be attributed to DHNA exclusion criteria. The DHNA excludes patients receiving no treatement, primary palliative treatment, and patients diagnosed with secondprimary OCC, melanoma's, and lip tumours.

As the DHNA is a prospective database, future OCC patients will be added to the DHNA-OC cohort. The authors welcome and encourage research collaborations using the DHNA-OC, and researchers interested in collaborating on the cohort are welcome to contact the research group. Data requests will be handled by PRISMA, the scientific advisory committee for research in head and neck cancer in the Netherlands (https://iknl.nl/kankersoorten/hoofd-halskanker/onderzoek/prisma).

Strengths and limitations

The DHNA-OC cohort is an elaborate dataset including variables on patient and tumour characteristics, given treatment, treatment complications, recurrence rates, and survival. As DHNA-OC data are population-based, the generalisability of future study results is facilitated. Considerable data completeness has been acquired compared to previous research. The only variables with >10% missing or unknown values were ACE27 score (44%) and the WHO performance score (22%). Described OCC cohorts in literature are mostly based on declaration data, lack national coverage, are completely retrospectively collected, or pool data for different HNC subsites[19–24].

The main limitations are the lack of data on socioeconomic status, education level, and medication use. These variables are currently not included in the DHNA, but DICA is working on implementing links with other databases to expand the DHNA. However, strict Dutch privacy laws

complicate linking processes. Though all registrars adhere to the same manual and openly discuss questions when registering, local variation in the interpretation of variables could exist. Annual numbers for the DHNA-OC cohort are lower compared to the OCC incidence rate in the Netherlands during the study period in the NCR (supplemental file 2). This can mostly be explained by exclusion of second primary tumours, cutaneous malignancies and palliative patients in the DHNA-OC. Taking these exclusions into account, we believe a reliable sample size has been aquired.

Acknowledgment

The authors thank all Dutch head and neck audit oral cavity collaborator group members for contributing. The authors thank all registrars, physician assistants, and administrative nurses who registered patients in the Dutch Head and Neck Audit. The authors thank the Netherlands Comprehensive Cancer Organisation (IKNL) registration team for collecting data for the Netherlands Cancer Registry. This work was supported by the Department of Otorhinolaryngology and Head and Neck Surgery of the Erasmus Medical Centre Cancer Institute (Rotterdam, the Netherlands).

Collaboration

The authors welcome and encourage research collaborations using the DHNA-OC cohort, and researchers interested in collaborating on the cohort are welcome to contact the research group. Data requests will be handled by PRISMA, the scientific advisory committee for research in head and neck cancer in the Netherlands (https://iknl.nl/kankersoorten/hoofd-halskanker/onderzoek/prisma).

Author contributions

HDvO: ethical permission, statistical analysis. HDvO, JAH, and RJBdJ: drafting of the manuscript. RJBdJ: initiator. All authors: conceptualisation, data extraction, data review, interpretation of the results, manuscript review, approval, and reading of the final manuscript.

Funding

This manuscript did not receive a grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of interest

Authors declare there was no conflict of interest.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication

Not applicable.

Research ethics and patient consent

This research proposal was reviewed by the Institutional research review board Erasmus Medical Center (Rotterdam, The Netherlands) and the board conforms that the rules laid down in the Medical Research Involving Human Subjects Act do not apply to this research proposal (MEC-2022-0816).

Data availability statement

Data may be obtained upon request after approval by PRISMA, the scientific advisory committee for research in head and neck cancer in the Netherlands. Any researcher requesting DHNA data has to collaborate with one of the participating Dutch head and neck cancer hospitals to ensure correct data and guideline interpretation.

References

1. Netherlands comprehensive cancer organisation. Netherlands Cancer Registry data & figures. Accessed June 24, 2024. https://iknl.nl/en/ncr/ncr-data-figures
2. van Overveld LF, Takes R, Smeele L, et al. Dutch Head and Neck Audit Group. The Dutch Head and Neck Audit: The First Steps. *Journal of Head and Neck Surgery*. 2018;1(1). doi:10.36959/605/528
3. Donabedian A. The Quality of Care How Can It Be Assessed? *JAMA*. 1988;260(12):1743-1748. https://jamanetwork.com/
4. Van Leersum NJ, Snijders HS, Henneman D, et al. The dutch surgical colorectal audit. *European Journal of Surgical Oncology*. 2013;39(10):1063-1070. doi:10.1016/j.ejso.2013.05.008
5. de Ridder M, Balm AJM, Baatenburg de Jong RJ, et al. Variation in head and neck cancer care in the Netherlands: A retrospective cohort evaluation of incidence, treatment and outcome. *European Journal of Surgical Oncology*. 2017;43(8):1494-1502. doi:10.1016/j.ejso.2017.02.017

6. van der Heide MFJ, de Jel DVC, Hoeijmakers F, et al. Defining High-Quality Integrated Head and Neck Cancer Care Through a Composite Outcome Measure: Textbook Outcome. *Laryngoscope*. 2022;132(1):78-87. doi:10.1002/lary.29720

7. Margalit DN, Sacco AG, Cooper JS, et al. Systematic review of postoperative therapy for resected squamous cell carcinoma of the head and neck: Executive summary of the American Radium Society appropriate use criteria. *Head Neck*. 2021;43(1):367-391. doi:10.1002/hed.26490

8. Al-Moraissi EA, Alkhutari AS, de Bree R, et al. Management of clinically node-negative early-stage oral cancer: network meta-analysis of randomized clinical trials. *Int J Oral Maxillofac Surg*. Published online 2023. doi:10.1016/j.ijom.2023.08.004

9. Platform Oncologie-SONCOS. *Multidisciplinaire Normering Oncologische Zorg in Nederland*.; 2023. Accessed January 22, 2024. https://demedischspecialist.nl/sites/default/files/2023-02/soncos_normeringsrapport_versie_11_2023.pdf

10. DICA support - DHNA (hoofd-halsoncologie). Accessed January 22, 2024. https://support.mrdm.com/nl/downloads/documenten/?org=dica&set=dhna

11. Beck N, Van Bommel AC, Eddes EH, et al. The Dutch Institute for Clinical Auditing: Achieving Codman's Dream on a Nationwide Basis. *Ann Surg*. 2020;271:627-631. doi:10.1097/SLA.0000000000003665

12. van der Werf LR, Voeten SC, van Loe CMM, et al. Data verification of nationwide clinical quality registries. *BJS Open*. 2019;3(6):857-864. doi:10.1002/bjs5.50209

13. Fritz AG, Percy C, Jack A, et al. *International Classification of Diseases for Oncology (ICD-O) - 3rd Edition*.

14. Netherlands Cancer Registry (NCR). Accessed January 22, 2024. https://iknl.nl/en/ncr

15. Brierley J, Gospodarowicz M, Wittekind C. *TNM Classification of Malignant Tumours, 8th Edition.* Wiley-Blackwell; 2016.

16. Agarwal JP, Adulkar D, Swain M, et al. Influence of comorbidity on therapeutic decision making and impact on outcomes in patients with head and neck squamous cell cancers: Results from a prospective cohort study. *Head Neck*. 2019;41(3):765-773. doi:10.1002/HED.25408

17. Clavien PA, Barkun J, De Oliveira ML, et al. The clavien-dindo classification of surgical complications: Five-year experience. *Ann Surg*. 2009;250(2):187-196. doi:10.1097/SLA.0b013e3181b13ca2

18. MRDM - about us. Accessed January 22, 2024. https://mrdm.com/company/

19. Nouraei SAR, Mace AD, Middleton SE, et al. A stratified analysis of the perioperative outcome of 17623 patients undergoing major head and neck cancer surgery in England over 10 years: Towards an Informatics-based Outcomes Surveillance Framework. *Clinical Otolaryngology*. 2017;42(1):11-28. doi:10.1111/coa.12649

20. Zhao Z, Hao J, He Q, et al. Unplanned Reoperations in Oral and Maxillofacial Surgery. *Journal of Oral and Maxillofacial Surgery*. 2019;77(1):135.e1-135.e5. doi:10.1016/j.joms.2018.08.017

21. Schwam ZG, Sosa JA, Roman S, et al. Complications and mortality following surgery for oral cavity cancer: Analysis of 408 cases. *Laryngoscope*. 2015;125(8):1869-1873. doi:10.1002/lary.25328

22. Tighe D, Sassoon I, Hills A, et al. Case-mix adjustment in audit of length of hospital stay in patients operated on for cancer of the head and neck. *British Journal of Oral and Maxillofacial Surgery*. 2019;57(9):866-872. doi:10.1016/j.bjoms.2019.07.007

23. Schoppy DW, Rhoads KF, Ma Y, et al. Measuring institutional quality in head and neck surgery using hospital-level data: Negative margin rates and neck dissection yield. *JAMA Otolaryngol Head Neck Surg*. 2017;143(11):1111-1116. doi:10.1001/jamaoto.2017.1694

24. Chiou LJ, Lee CC. Textbook outcome was associated with better survival in oral cancer surgery in southern Taiwan. *Oral Dis*. 2023;(March):1-11. doi:10.1111/odi.14587

Figure legends:

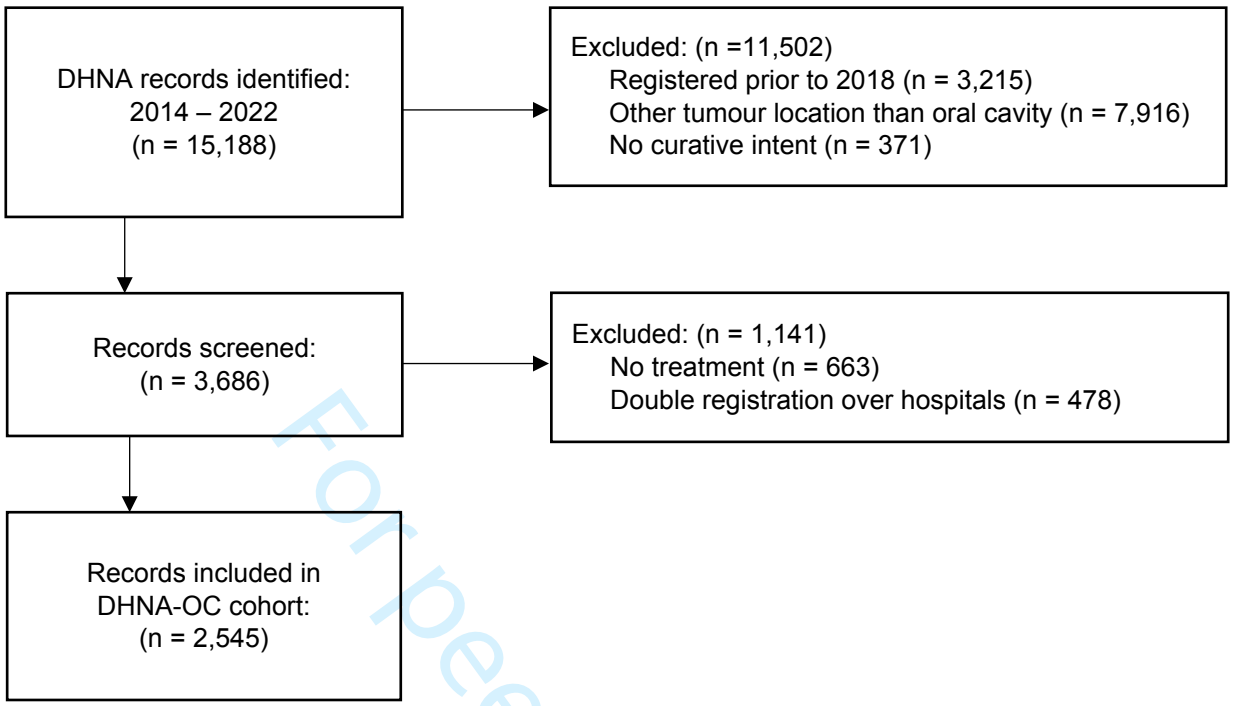
Figure 1 – Flow chart for inclusion in the Dutch Head and Neck Audit – Oral Cavity (DHNA-OC) cohort.

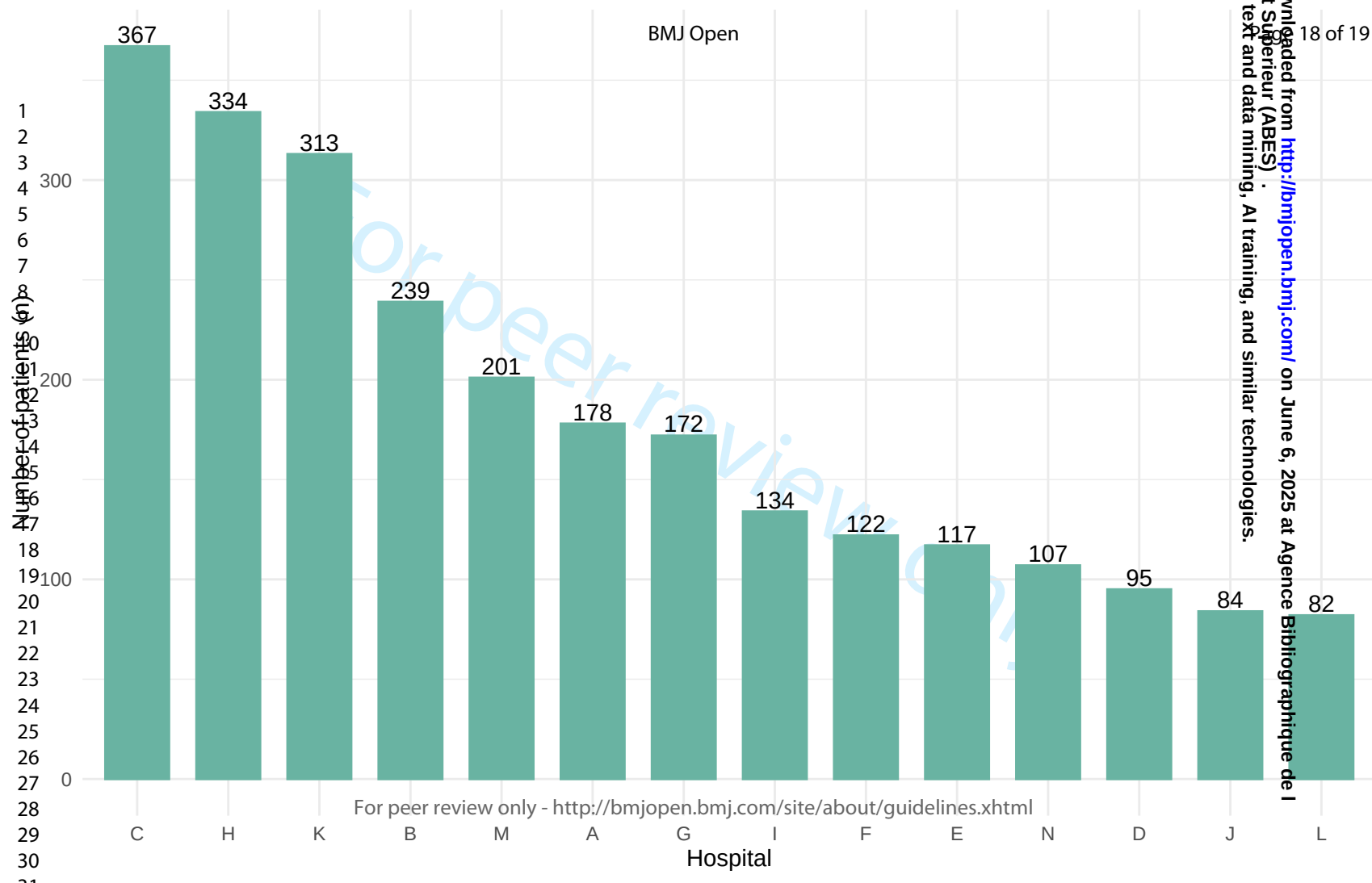
Figure 2 – Number of patients curatively treated for first primary oral cavity cancer in the 14 head and neck oncology hospitals in the Netherlands between 2018 and 2021 (N = 2,545).

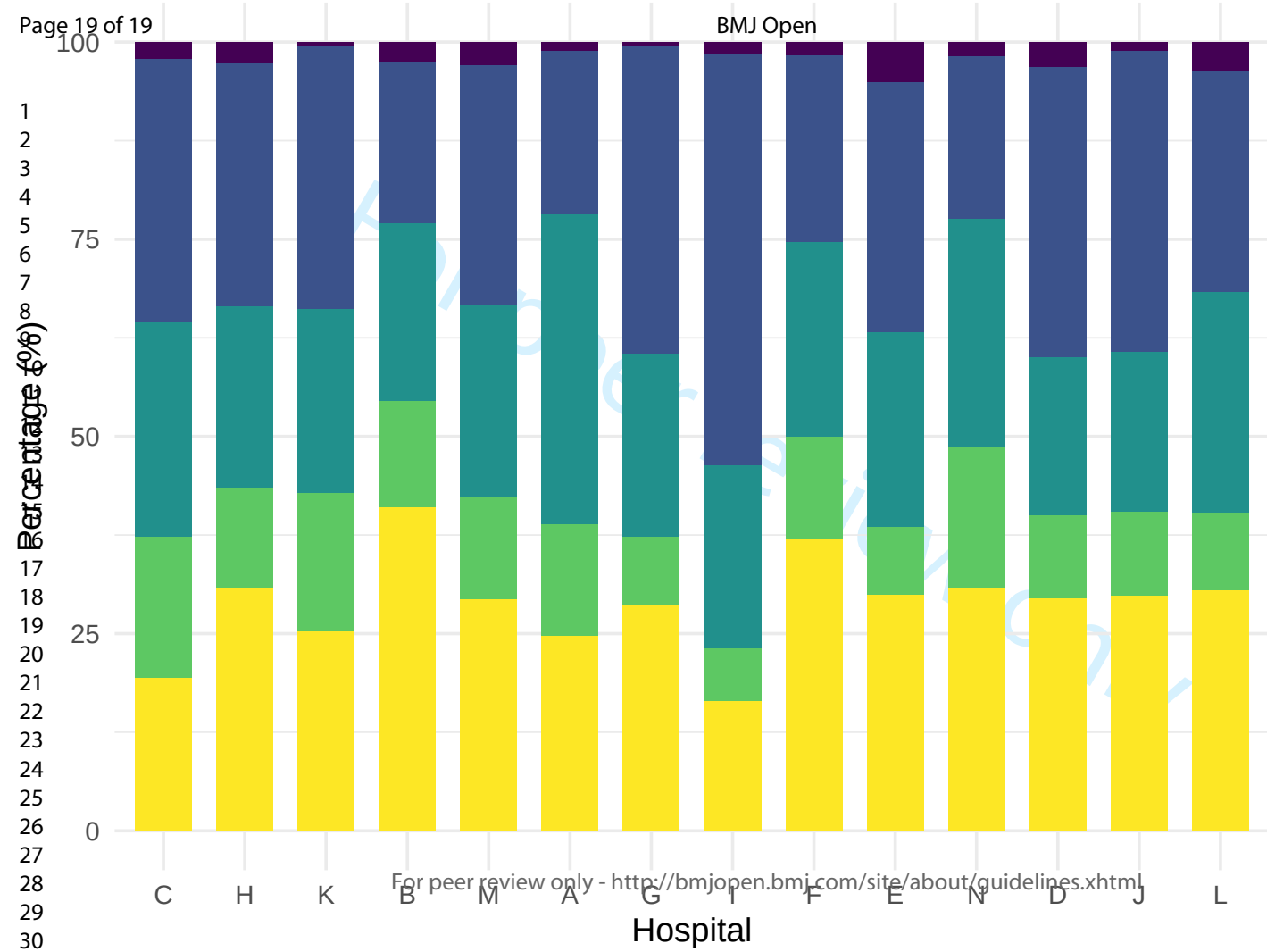
Figure 3 – Tumour stage for first primary oral cavity cancer patients curatively treated in the 14 head and neck oncology hospitals in the Netherlands between 2018 and 2021 (N = 2,545).

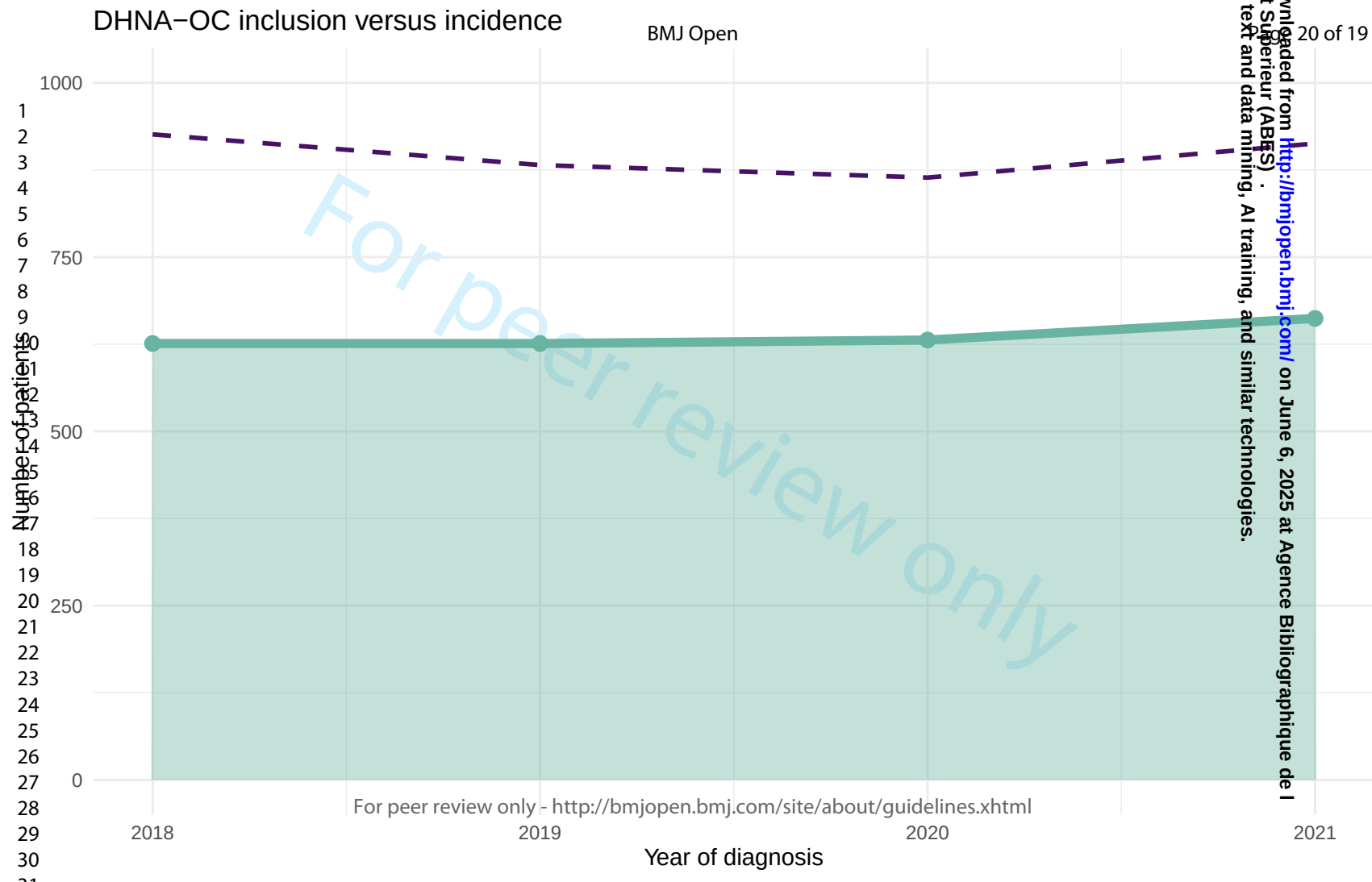
Figure 4 – Inclusion of Dutch Head and Neck Audit – Oral Cavity cohort (blue) compared to the oral cavity cancer incidence (purple line) in the Netherlands between 2018 and 2021.

Figure 1 – Flow chart for inclusion in the Dutch Head and Neck Audit – Oral Cavity (DHNA-OC) cohort.









BMJ Open

Cohort profile: the Dutch oral cavity cancer cohort

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-092467.R1
Article Type:	Cohort profile
Date Submitted by the Author:	22-Apr-2025
Complete List of Authors:	van Oorschot, Hanneke; Erasmus MC Cancer Center, Department of Otorhinolaryngology and Head and Neck Surgery; Dutch Institute for Clinical Auditing, Scientific Bureau Hardillo, Jose; Erasmus MC Cancer Center, Otorhinolaryngology and Head and Neck surgery Baatenburg de Jong, Rob; Erasmus MC Cancer Center, Department of Otorhinolaryngology Dutch head and neck audit , oral cavity collaborator group; Dutch Institute for Clinical Auditing, Scientific Bureau
Primary Subject Heading:	Dentistry and oral medicine
Secondary Subject Heading:	Ear, nose and throat/otolaryngology, Oncology
Keywords:	ORAL & MAXILLOFACIAL SURGERY, Head & neck tumours < ONCOLOGY, Head & neck surgery < SURGERY, ONCOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Title:

Cohort profile: the Dutch oral cavity cancer cohort

Authors:

Hanneke Doremiek van Oorschot[1,2], MD (ORCID 0000-0001-6858-3984)

Jose Angelito Hardillo[1], MD, PhD (ORCID 0000-0001-5580-5613)

Robert Jan Baatenburg de Jong[1], MD, PhD (ORCID 0000-0001-7236-264X)

Dutch head and neck audit - oral cavity collaborator group:

Robert (R.J.J.) van Es[3], MD, PhD, Guido van den Broek[4], MD, PhD, Robert (R.P.) Takes[4], MD, PhD (ORCID 0000-0003-4784-0499), Gyorgy (G.B.) Halmos[5], MD, PhD (ORCID 0000-0003-2460-2260), Dominique (D.V.C.) de Jel[5], MD (ORCID 0000-0001-8159-0089), MD, Richard (R.) Dirven[6], MD, PhD, Martin (M.) Lacko[7], MD, PhD (ORCID 0000-0003-2868-4822), Lauretta (L.A.A.) Vaassen[8], MD, PhD, (ORCID 000-0002-1408-6146), Jan-Jaap (J.J.) Hendrickx[9], MD, PhD, Marjolijn (M.A.E.) Oomens[10], MD (ORCID 0000-0003-1526-559X), Hossein Ghaeminia[10], MD, PhD, Jeroen (J.C.) Jansen[11], MD, PhD, Annemarie Vesseur[12], MD (ORCID 0000-0002-6702-4360), Rolf Bun[13], MD, PhD, Noortje (L.Q.) Schwandt[14], MD, PhD, Christiaan (C.A.) Krabbe[14], MD, PhD, Thomas (T.J.W.) Klein Nulent[14], MD, Alexander (A.J.M) van Bemmel[16], MD (ORCID 0000-0003-0953-8408), Reinoud (R.) Klijn[17]

Author affiliations:

1. Department of Otorhinolaryngology and Head and Neck Surgery, Erasmus Medical Centre Cancer Institute, Rotterdam, The Netherlands
2. Scientific Bureau, Dutch Institute for Clinical Auditing, Leiden, the Netherlands
3. Department of Head and Neck Surgical Oncology, UMC Utrecht Cancer Centre, Utrecht
4. Department of Otorhinolaryngology, Head and Neck Surgery, Radboud University Medical Center, Nijmegen:
5. Department of Otorhinolaryngology/Head and Neck Surgery, University Medical Centre Groningen, University of Groningen, Groningen
6. Department of Head and Neck Oncology and Surgery, Netherlands Cancer Institute/Antoni van Leeuwenhoek, Amsterdam

7. Department of Otorhinolaryngology and Head and Neck Surgery, GROW School for Oncology and Reproduction, Maastricht University Medical Center, Maastricht
8. Department of Cranio-maxillofacial surgery, GROW School for Oncology and Reproduction, Maastricht University Medical Center, Maastricht
9. Department of Otorhinolaryngology, Head and Neck Surgery, Academic Medical Center, University of Amsterdam
10. Department of Oral and Maxillofacial Surgery, Rijnstate Hospital, Arnhem
11. Department of Otorhinolaryngology, Head and Neck Surgery, Leiden University Medical Centre, Leiden
12. Department of Otolaryngology, Head and Neck Surgery, Elisabeth Tweesteden Ziekenhuis Tilburg, Tilburg
13. Department of Oral and Maxillofacial Surgery/Head and Neck Oncology Noordwest Hospital group, Alkmaar en Dijklander Hospital, Hoorn
14. Department of Oral and Maxillofacial Surgery, Medical Centre Leeuwarden, Leeuwarden
15. Department of Oral and Maxillofacial Surgery, Haaglanden Medical Center, The Hague
16. Department of Otorhinolaryngology and Head and Neck Surgery, Medisch Spectrum Twente, Enschede
17. Department of Oral and Maxillofacial and Head and Neck Surgery, Medisch Spectrum Twente, Enschede

Corresponding author:

H.D. van Oorschot, MD

Department of Otorhinolaryngology and Head and Neck Surgery, P.O. Box 2040, 3000 CA Rotterdam, Erasmus Medical Centre Cancer Institute, Rotterdam, The Netherlands.

E: h.vanoorschot@erasmusmc.nl / T: 00107033106

Journal: BMJ open

Word count: 1616 words

Abstract word count: 242 words

Keywords: Head and neck cancer, oral cavity cancer, national cohort

Abstract

Purpose:

The Dutch Head and Neck Audit – Oral Cavity (DHNA-OC) cohort was collected to study the quality of care, current treatment, and survival for oral cavity cancer (OCC) across all hospitals treating head and neck cancer (HNC) in the Netherlands.

Patients:

The DHNA-OC is a registry-based national cohort of 2,545 first primary OCC patients treated with curative intent between 2018 and 2021. All fourteen HNC hospitals in the Netherlands contributed, guaranteeing national coverage. The DHNA-OC cohort is an elaborate dataset including variables on patient and tumour characteristics, treatment, complications, recurrence rates, and survival.

Findings to date:

The median age at diagnosis was 67 years and most tumours were early stage (cT1 in 32% and cT2 in 31%). Tongue tumours were most common and surgery was performed in 91.3% of the patients. The number of included patients per hospital varied from 82 to 367. The proportion of advanced tumour stage varied significantly between hospitals. Substantial data completeness was acquired with only two variables exceeding 10% missing (comorbidities and performance score).

Future plans:

The DHNA-OC cohort will be used to study benchmarking of and current knowledge gaps in OCC care. Collaboration with other institutions or national/regional databases is highly encouraged. Some examples of planned studies are the assessment of hospital variation in outcome indicators for surgery and population-based treatment effects. The results of these studies will be used to identify best practices and continue improving quality-of-care. Longitudinal cohort follow-up and enrolment will continue prospectively.

Strengths and limitations of this study

- The main strength of the Dutch Head and Neck Audit—Oral Cavity (DHNA-OC) cohort is its nationwide inclusion, facilitated by population-based registries that are centrally managed.
- The DHNA-OC cohort is an elaborate dataset including variables on patient and tumour characteristics, given treatment, treatment complications, recurrence rates, and survival.
- The main limitations are the lack of data on socioeconomic status, education level, and medication use.
- Though all registrars adhere to the same manual and openly discuss questions when registering, variation in the interpretation of variables could exist.

Introduction

The Dutch Head and Neck Audit – Oral Cavity (DHNA-OC) cohort was designed to study current treatment, survival, and quality of care for oral cavity cancer (OCC). With an incidence of ~1000 in 2023, OCC is a relatively rare cancer in the Netherlands.[1] Despite the low incidence, OCC patients often require highly complex multidisciplinary integrated care.[2] As in other cancers with low incidence rates, clinical trials in HNC struggle to enrol enough participants. Therefore, real-world data is increasingly used to answer current knowledge gaps in clinical practice guidelines.

The Dutch Head and Neck Audit (DHNA) was established in 2014 to monitor and benchmark the quality of HNC nationally.[2] Auditing has been identified as an effective tool in improving quality-of-care for surgical oncological fields, such as in the Dutch Surgical Colorectal Audit.[3,4] By effective auditing and collaboration, the patient pathways were standardized, complication rates declined, and even mortality rates decreased.[4] Over the past years, DHNA data availability has improved, yet data is missing on crucial variables. To follow the lead of the colorectal audit, the DHNA-OC cohort was instigated.

Research questions that motivated the DHNA-OC cohort revolve around enhancing the quality of care and addressing current knowledge gaps. To study hospital variation, we first aim to develop a case-mix model for OCC.[5] This will enable us to investigate variation in surgical complications, resection margins, and textbook outcome.[6] Furthermore, the indication and value of adjuvant therapy in case of a resection margin of one to five millimetres remain unclear.[7] Also, debate is ongoing regarding the use of elective neck dissection versus sentinel lymph node biopsy in early-stage OCC.[8] Through the DHNA-OC, we aim to offer insights derived from real-world data, contributing to enhancing new clinical practice guidelines, which currently may lack a scientific foundation.

Cohort description

This research proposal was reviewed by the Institutional research review board Erasmus Medical Center (Rotterdam, The Netherlands), and the board confirmed that the rules laid down in the Medical Research Involving Human Subjects Act do not apply to this research proposal (MEC-2022-0816).

Cohort design

The DHNA-OC is based on data from the Dutch Head and Neck Audit (DHNA). HNC care in the Netherlands is centralized in 14 devoted hospitals: eight head and neck oncologic centres (HNOCs) and seven preferred partner hospitals.[9] HNC care is covered by the Dutch health insurance system, which is obligatory and socialized. The DHNA gained national coverage in 2019 and participation is mandatory. All patients with a first primary head and neck tumour are prospectively included. Patients with in situ carcinoma, a second primary tumour, recurrent HNC, melanomas, cutaneous malignancies, thyroid carcinomas, sarcomas, neuroendocrine cancers, and hematologic malignancies are currently not included in the DHNA. Data is collected by trained registrars, physician assistants, and administrative nurses employed by the HNC hospital or the Netherlands Comprehensive Cancer Organisation (IKNL). The complete DHNA data dictionary can be accessed online.[10] The DHNA is one of 26 quality registries maintained at the Dutch Institute for Clinical Auditing (DICA).[11] This institution guarantees data quality through annual data verification processes.[12]

Patient and public involvement

Patients were involved in the design of the DHNA.[2] Patients or the public were not involved in the planning or design, recruitment, or conduction of this cohort.

Participants

Data completeness is essential for reliable population-based research and evaluation of quality of care. Patients were selected from the DHNA based on the pathological conformation (biopsy) date between January 1 2018 and December 31 2021. Included ICD-O-3 codes for OCC were C00, C02-C04, C05.0, C5.8-9, and C06.0-8.[13] Patients of ≥18 years were selected if treated with curative intent in one of the 14 HNC hospitals during the study period. Missing variables in the DHNA cohort were complemented with data from the Netherlands Cancer Registry (NCR). This is the national registry on malignancies in the Netherlands.[14] Since 1989, IKNL has objectively registered all newly diagnosed patients in the NCR. Patients are assigned a unique uniform resource identifier (URI) in the treating hospital. DHNA and NCR data were matched on date of birth, hospital-URI, and treating hospital. The complemented dataset was returned to the individual hospitals to retrieve the remaining missing values from electronic patient files. A head and neck surgeon or clinical HNC researcher then executed data curation. The final dataset was delivered to update the DHNA dataset with missing values.

Variables and data management

Supplemental file 1 gives a complete overview of the DHNA-OC dataset. Comorbidity was scored using the ACE-27 and the TNM-classification followed the 8th edition of the Union for International Cancer Control TNM Classification.[15,16] Clinical TNM stage 0 was included in OCC cases with cTx/T0/TisN0M0 classification that were upstaged on pathological examination to pT1/T2/T3/T4. Surgical 30-day complications were classified utilizing the Clavien-Dindo classification.[17] Follow-up started on the date of last treatment (surgery, systemic therapy or radiotherapy). Follow-up was censored two years after the date of the last treatment. As the DHNA is a prospective database, a five-year follow-up will be registered yearly (data for 2018 in 2025, 2019 in 2026, and so on). As this study included national data a sample size calculation was deemed unnecessary.

To guarantee patient privacy and Dutch privacy regulations, DICA works with a third-trusted party: Medical Research Data Management (MRDM), Deventer, the Netherlands (NEN 7510:2011 and ISO 27001:2013 certified).[18] MRDM designs, develops, and manages registration systems for DICA's quality registrations, among others. MRDM processes the data from the hospital so that DICA receives only coded (pseudonymous) data. Hospitals sign an agreement with DICA and MRDM to process their data and deliver data manually (survey) or via batch. DICA's privacy committee guarantees that data handling complies with the Dutch Personal Data Protection Act. Statistical analyses are performed in protected digital areas and cannot be traced back to specific subjects.

Findings to date

A total of 2,545 patients were included (Figure 1). The final DHNA-OC cohort baseline characteristics are presented in Table 1.

Table 1: Demographic characteristics of patients included in the DHNA-OC cohort.
IQR = interquartile range, WHO = World Health Organization.
**Histology types included in other are basaloid squamous cell, spindle cell, adenosquamous, verrucous, papillary squamous cell, and minor salivary gland carcinomas.*

Characteristic	N = 2,545
Gender - female	1,171 (46%)
Age	67 (59, 75)
Body mass index (kg/m2)	
<18.5	102 (4.0%)

≥18.5 to <30	1,953 (77%)
≥30	419 (16%)
Unknown	71 (2.8%)
Smoking history	
No history of smoking	639 (25%)
Former smoker	852 (33%)
Current smoker	945 (37%)
Unknown	109 (4.3%)
Alcohol history	
No history of drinking	419 (16%)
Former drinker	196 (7.7%)
Current drinker	1,712 (67%)
Unknown	218 (8.6%)
ACE27 score	
Grade 0 - None	720 (28%)
Grade 1 - Mild	375 (15%)
Grade 2 - Moderate	248 (9.7%)
Grade 3 - Severe	90 (3.5%)
Unknown	1,112 (44%)
WHO performance status	
Normal activity (0)	1,268 (50%)
Symptomatic, fully ambulatory: cares for self (1)	501 (20%)
Ambulatory >50% of the time: occasional assistance (2)	178 (7.0%)
Ambulatory <50% of the time: nursing care needed (3)	41 (1.6%)
Bedridden (4)	1 (<0.1%)
Unknown	556 (22%)
Histology	
Squamous cell carcinoma	2,328 (91%)
Other	216 (9.0%)
Unknown	1 (<0.1%)
Oral cavity subsite (ICD-O-3)	
Lip	54 (2.1%)
Tongue	1,105 (43%)
Gum	449 (18%)
Floor of mouth	426 (17%)
Palate	86 (3.4%)
Other parts of oral cavity	423 (17%)
Not otherwise specified	2 (<0.1%)
cT-classification	
cTx	25 (1.0%)
cT0	7 (0.3%)
cTis	23 (0.9%)
cT1	825 (32%)
cT2	783 (31%)
cT3	343 (13%)

cT4	539 (21%)
cN-classification	
cNx	14 (0.6%)
cN0	2,001 (79%)
cN1	194 (7.6%)
cN2	292 (11%)
cN3	44 (1.7%)
cM-classification	
cMx	2 (<0.1%)
cM0	2,541 (100%)
cM1	2 (<0.1%)
cTNM stage	
Stage 0	53 (2.1%)
Stage I	791 (31%)
Stage II	643 (25%)
Stage III	342 (13%)
Stage IV	716 (28%)
Treatment	
Surgery	1,441 (57%)
Surgery & radiotherapy	724 (28%)
Surgery & chemoradiation	185 (7.3%)
Radiotherapy	111 (4.4%)
Chemoradiation	71 (2.8%)
Other*	13 (0.5%)
Treating hospital	
HHOCs	1,926 (76%)
PPs	619 (24%)
Year of diagnosis	
2018	626 (25%)
2019	626 (25%)
2020	631 (25%)
2021	662 (26%)
Follow-up survival status	
No evidence of disease	1942 (76%)
Alive with disease	63 (2.5%)
Dead of disease	188 (7.4%)
Dead of other causes	97 (3.9%)
Dead of treatment complications	10 (0.4%)
Dead of unknown causes	167 (6.6%)
Unknown	78 (3.1%)

The median age was 67 years (interquartile range [IQR] 59-75) and 46% was female. Body mass index (BMI in kg/m2) was unknown in 2.8%, with 77% of the patients at a BMI between 18.5 and 30 kg/m2.

Most patients were current smokers or drinkers (37% and 67% respectively) with missing data on smoking and drinking history in 4.3% and 8.6% respectively. Data on comorbidities was missing in 44%, leaving the grade 0 as the most observed ACE27 score (28%). A WHO-performance score of 0 was most seen in the cohort (50%), though data was missing in 22%.

Ninety-one per cent of the tumours were squamous cell carcinoma and most were located in the tongue (43.%). Clinical TNM-stage 0 tumours were present in 2.1%, stage I in 31%, stage II in 25%, stage III in 13%, and stage IV in 28%. Surgery alone was performed in 57% of the patients. Surgery was complemented by radiotherapy in 28% and by chemoradiation in 7.3%. Only 4.4% received radiotherapy as definitive treatment. Seventy-six percent was treated in one of the HHOCs and the annual inclusion rate was constant over the years. The number of patients that were included per hospital varied from 367 to 82 (Figure 2). The proportion of stage III-IV tumours varied significantly between treating hospitals (p-value <0.001) but was not directly proportional to hospital volume (Figure 3). Overall, high data completeness was achieved, especially regarding treatment and outcome variables.

Two-year follow-up indicated 76% of the patients alive without and 2.5% of the patients alive with disease (Figure 4). Follow-up data was missing in 78 patients (3.1%). Of the deceased patients (n=462), the cause of death was unknown in 36% (n=167). The remaining patients died of disease (7.4%), other causes (3.8%), or treatment complications (0.4%).The capture rate of the DHNA-OC cohort is compared to the annual incidence rate for OCC registered in the NCR in Figure 5. The difference in annual inclusion between the NCR and DHNA-OC cohort can be attributed to DHNA exclusion criteria. The DHNA excludes patients receiving no treatment, primary palliative treatment, and patients diagnosed with second primary OCC, melanoma, and lip tumours.

As the DHNA is a prospective database, future OCC patients will be added to the DHNA-OC cohort. The authors welcome and encourage research collaborations using the DHNA-OC, and researchers interested in collaborating on the cohort are welcome to contact the research group. Data requests will be handled by PRISMA, the scientific advisory committee for research in head and neck cancer in the Netherlands (https://iknl.nl/kankersoorten/hoofd-halskanker/onderzoek/prisma).

Strengths and limitations

The DHNA-OC cohort is an elaborate dataset including variables on patient and tumour characteristics, given treatment, treatment complications, recurrence rates, and survival. As DHNA-OC data are population-based, the generalisability of future study results is facilitated. Considerable data completeness has been acquired compared to previous research. The only variables with >10% missing or unknown values were the ACE27 score (44%) and the WHO performance score (22%). Described OCC cohorts in literature are mostly based on declaration data, lack national coverage, are completely retrospectively collected, or pool data for different HNC subsites[19–24].

The main limitations are the lack of data on socioeconomic status, education level, and medication use. These variables are currently not included in the DHNA, but DICA is working on implementing links with other databases to expand the DHNA. However, strict Dutch privacy laws complicate linking processes. Though all registrars adhere to the same manual and openly discuss questions when registering, local variation in the interpretation of variables could exist. Annual numbers for the DHNA-OC cohort are lower compared to the OCC incidence rate in the Netherlands during the study period in the NCR (Figure 5). This can mostly be explained by the exclusion of second primary tumours, cutaneous malignancies and palliative patients in the DHNA-OC. Taking these exclusions into account, we believe a reliable sample size has been acquired.

Acknowledgement

The authors thank all Dutch head and neck audit oral cavity collaborator group members for contributing. The authors thank all registrars, physician assistants, and administrative nurses who registered patients in the Dutch Head and Neck Audit. The authors thank the Netherlands Comprehensive Cancer Organisation (IKNL) registration team for collecting data for the Netherlands Cancer Registry. This work was supported by the Department of Otorhinolaryngology and Head and Neck Surgery of the Erasmus Medical Centre Cancer Institute (Rotterdam, the Netherlands).

Collaboration

The authors welcome and encourage research collaborations using the DHNA-OC cohort, and researchers interested in collaborating on the cohort are welcome to contact the research group. Data

requests will be handled by PRISMA, the scientific advisory committee for research in head and neck cancer in the Netherlands (https://iknl.nl/kankersoorten/hoofd-halskanker/onderzoek/prisma).

Author contributions

HDvO: ethical permission, statistical analysis. HDvO, JAH, and RJBdJ: drafting of the manuscript. RJBdJ: initiator and guarantor. All authors: conceptualisation, data extraction, data review, interpretation of the results, manuscript review, approval, and reading of the final manuscript.

Funding

This manuscript did not receive a grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of interest

Authors declare there was no conflict of interest.

Patient and public involvement

Patients or the public were not involved in the planning or design, recruitment, or conduction of this cohort.

Patient consent for publication

Not applicable.

Research ethics and patient consent

This research proposal was reviewed by the Institutional research review board Erasmus Medical Center (Rotterdam, The Netherlands) and the board conforms that the rules laid down in the Medical Research Involving Human Subjects Act do not apply to this research proposal (MEC-2022-0816).

Data availability statement

Data may be obtained upon request after approval by PRISMA, the scientific advisory committee for research in head and neck cancer in the Netherlands. Any researcher requesting DHNA data has to collaborate with one of the participating Dutch head and neck cancer hospitals to ensure correct data and guideline interpretation.

References

1. Netherlands comprehensive cancer organisation. Netherlands Cancer Registry data & figures. Accessed June 24, 2024. https://iknl.nl/en/ncr/ncr-data-figures
2. van Overveld LF, Takes R, Smeele L, et al. Dutch Head and Neck Audit Group. The Dutch Head and Neck Audit: The First Steps. *Journal of Head and Neck Surgery*. 2018;1(1). doi:10.36959/605/528
3. Donabedian A. The Quality of Care How Can It Be Assessed? *JAMA*. 1988;260(12):1743-1748. https://jamanetwork.com/
4. Van Leersum NJ, Snijders HS, Henneman D, et al. The dutch surgical colorectal audit. *European Journal of Surgical Oncology*. 2013;39(10):1063-1070. doi:10.1016/j.ejso.2013.05.008
5. de Ridder M, Balm AJM, Baatenburg de Jong RJ, et al. Variation in head and neck cancer care in the Netherlands: A retrospective cohort evaluation of incidence, treatment and outcome. *European Journal of Surgical Oncology*. 2017;43(8):1494-1502. doi:10.1016/j.ejso.2017.02.017
6. van der Heide MFJ, de Jel DVC, Hoeijmakers F, et al. Defining High-Quality Integrated Head and Neck Cancer Care Through a Composite Outcome Measure: Textbook Outcome. *Laryngoscope*. 2022;132(1):78-87. doi:10.1002/lary.29720
7. Margalit DN, Sacco AG, Cooper JS, et al. Systematic review of postoperative therapy for resected squamous cell carcinoma of the head and neck: Executive summary of the American Radium Society appropriate use criteria. *Head Neck*. 2021;43(1):367-391. doi:10.1002/hed.26490
8. Al-Moraissi EA, Alkhutari AS, de Bree R, et al. Management of clinically node-negative early-stage oral cancer: network meta-analysis of randomized clinical trials. *Int J Oral Maxillofac Surg*. Published online 2023. doi:10.1016/j.ijom.2023.08.004
9. Platform Oncologie-SONCOS. *Multidisciplinaire Normering Oncologische Zorg in Nederland*.; 2023. Accessed January 22, 2024. https://demedischspecialist.nl/sites/default/files/2023-02/soncos_normeringsrapport_versie_11_2023.pdf
10. DICA support - DHNA (hoofd-halsoncologie). Accessed January 22, 2024. https://support.mrdm.com/nl/downloads/documenten/?org=dica&set=dhna
11. Beck N, Van Bommel AC, Eddes EH, et al. The Dutch Institute for Clinical Auditing: Achieving Codman's Dream on a Nationwide Basis. *Ann Surg*. 2020;271:627-631. doi:10.1097/SLA.0000000000003665
12. van der Werf LR, Voeten SC, van Loe CMM, et al. Data verification of nationwide clinical quality registries. *BJS Open*. 2019;3(6):857-864. doi:10.1002/bjs5.50209
13. Fritz AG, Percy C, Jack A, et al. *International Classification of Diseases for Oncology (ICD-O) - 3rd Edition*.
14. Netherlands Cancer Registry (NCR). Accessed January 22, 2024. https://iknl.nl/en/ncr
15. Brierley J, Gospodarowicz M, Wittekind C. *TNM Classification of Malignant Tumours, 8th Edition.* Wiley-Blackwell; 2016.
16. Agarwal JP, Adulkar D, Swain M, et al. Influence of comorbidity on therapeutic decision making and impact on outcomes in patients with head and neck squamous cell cancers: Results from a prospective cohort study. *Head Neck*. 2019;41(3):765-773. doi:10.1002/HED.25408

17. Clavien PA, Barkun J, De Oliveira ML, et al. The clavien-dindo classification of surgical complications: Five-year experience. *Ann Surg*. 2009;250(2):187-196. doi:10.1097/SLA.0b013e3181b13ca2

18. MRDM - about us. Accessed January 22, 2024. https://mrdm.com/company/

19. Nouraei SAR, Mace AD, Middleton SE, et al. A stratified analysis of the perioperative outcome of 17623 patients undergoing major head and neck cancer surgery in England over 10 years: Towards an Informatics-based Outcomes Surveillance Framework. *Clinical Otolaryngology*. 2017;42(1):11-28. doi:10.1111/coa.12649

20. Zhao Z, Hao J, He Q, et al. Unplanned Reoperations in Oral and Maxillofacial Surgery. *Journal of Oral and Maxillofacial Surgery*. 2019;77(1):135.e1-135.e5. doi:10.1016/j.joms.2018.08.017

21. Schwam ZG, Sosa JA, Roman S, et al. Complications and mortality following surgery for oral cavity cancer: Analysis of 408 cases. *Laryngoscope*. 2015;125(8):1869-1873. doi:10.1002/lary.25328

22. Tighe D, Sassoon I, Hills A, et al. Case-mix adjustment in audit of length of hospital stay in patients operated on for cancer of the head and neck. *British Journal of Oral and Maxillofacial Surgery*. 2019;57(9):866-872. doi:10.1016/j.bjoms.2019.07.007

23. Schoppy DW, Rhoads KF, Ma Y, et al. Measuring institutional quality in head and neck surgery using hospital-level data: Negative margin rates and neck dissection yield. *JAMA Otolaryngol Head Neck Surg*. 2017;143(11):1111-1116. doi:10.1001/jamaoto.2017.1694

24. Chiou LJ, Lee CC. Textbook outcome was associated with better survival in oral cancer surgery in southern Taiwan. *Oral Dis*. 2023;(March):1-11. doi:10.1111/odi.14587

Figure legends:

Figure 1 – Flow chart for inclusion in the Dutch Head and Neck Audit – Oral Cavity (DHNA-OC) cohort.

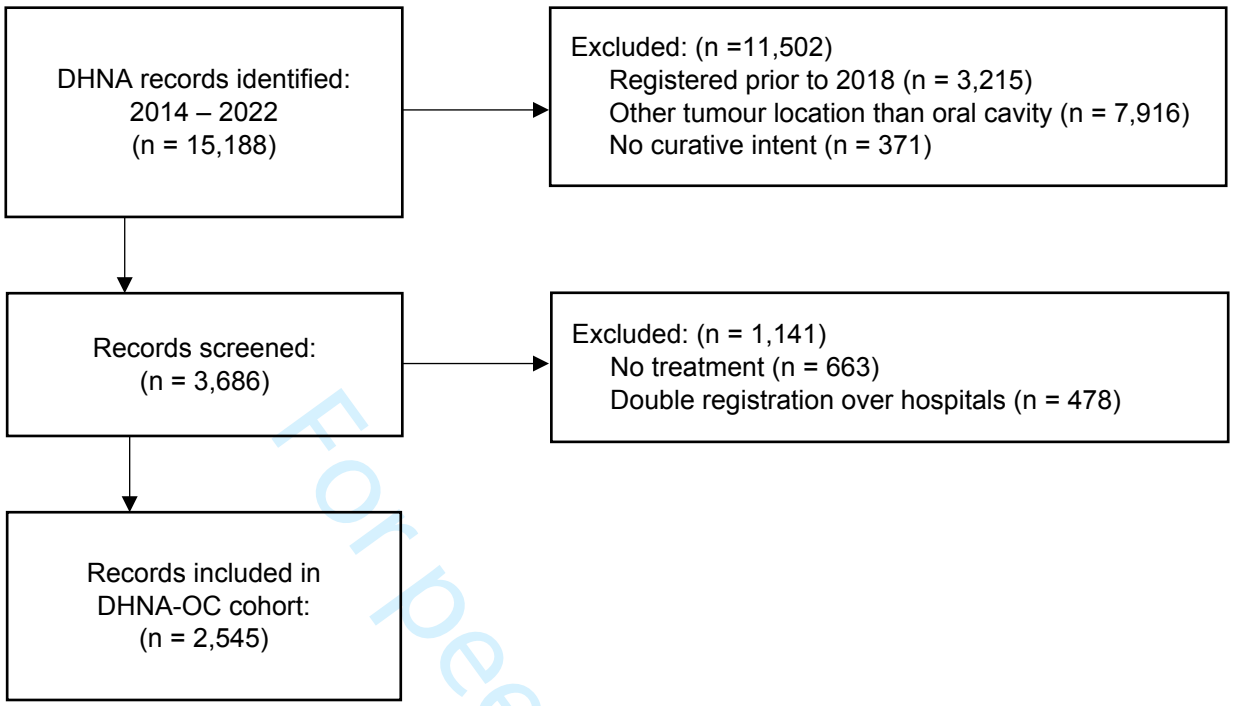
Figure 2 – Number of patients curatively treated for first primary oral cavity cancer in the 14 head and neck oncology hospitals in the Netherlands between 2018 and 2021 (N = 2,545).

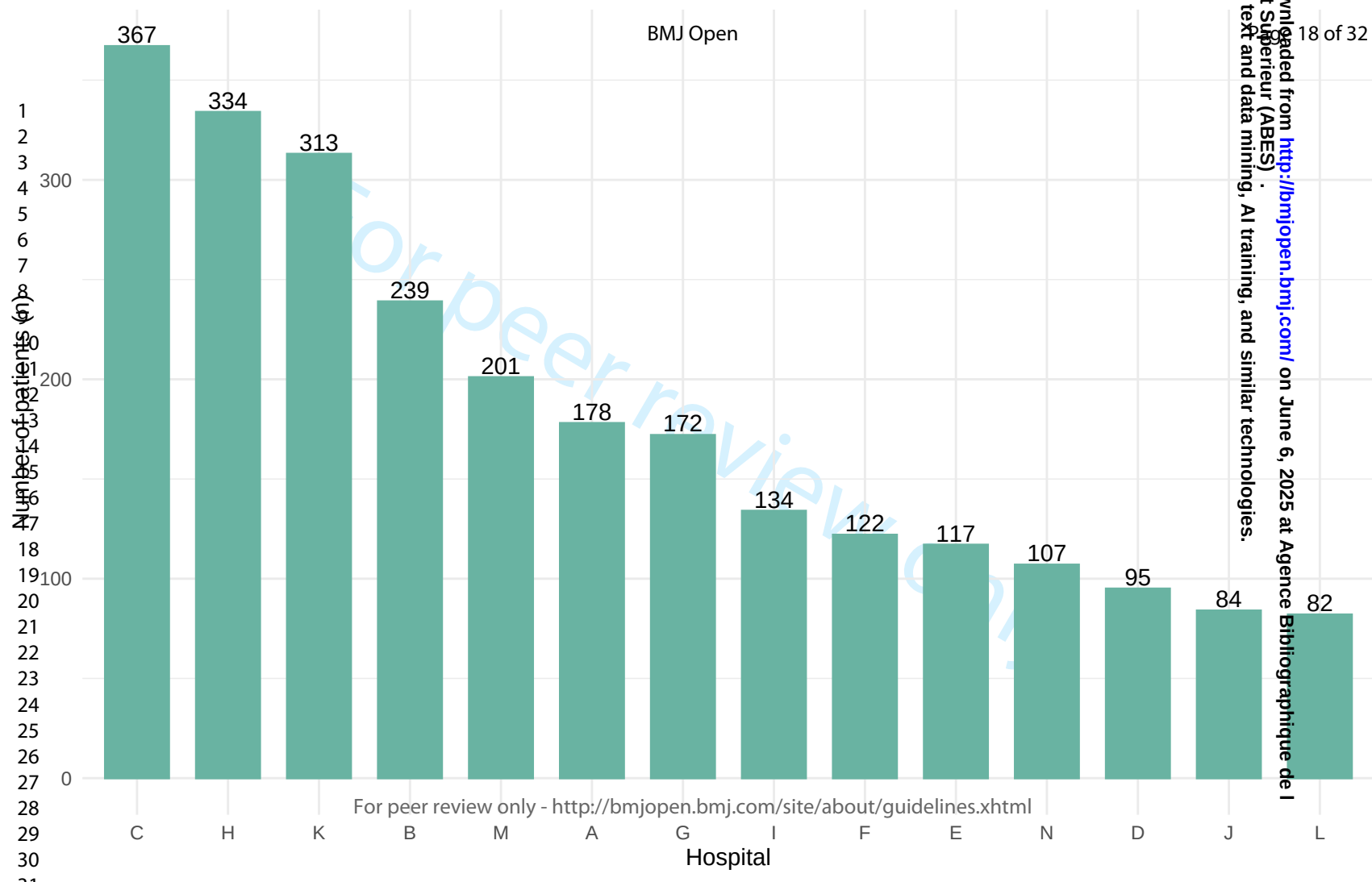
Figure 3 – Tumour stage for first primary oral cavity cancer patients curatively treated in the 14 head and neck oncology hospitals in the Netherlands between 2018 and 2021 (N = 2,545).

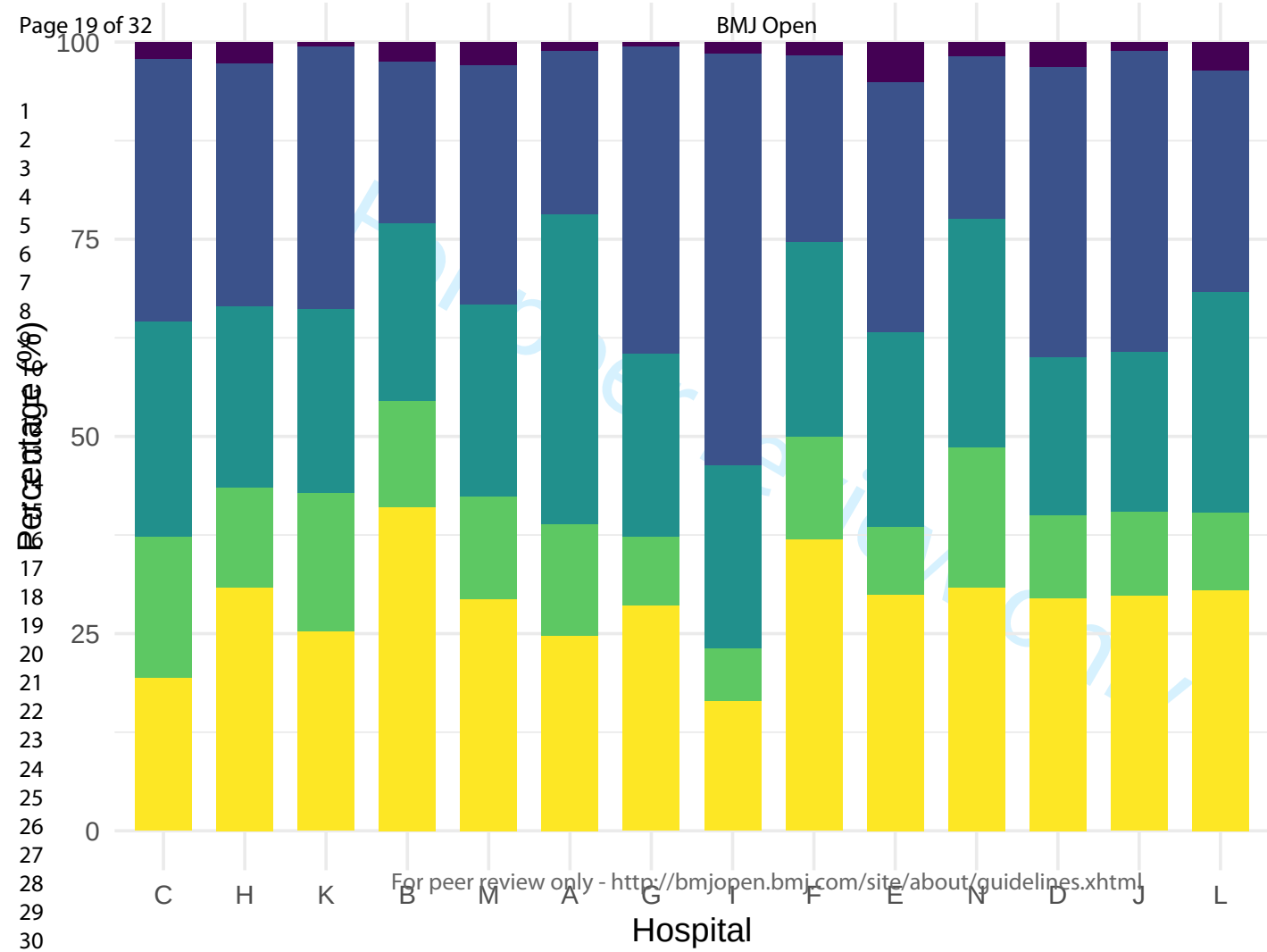
Figure 4 – Kaplan Meier curve for two-year overall survival.

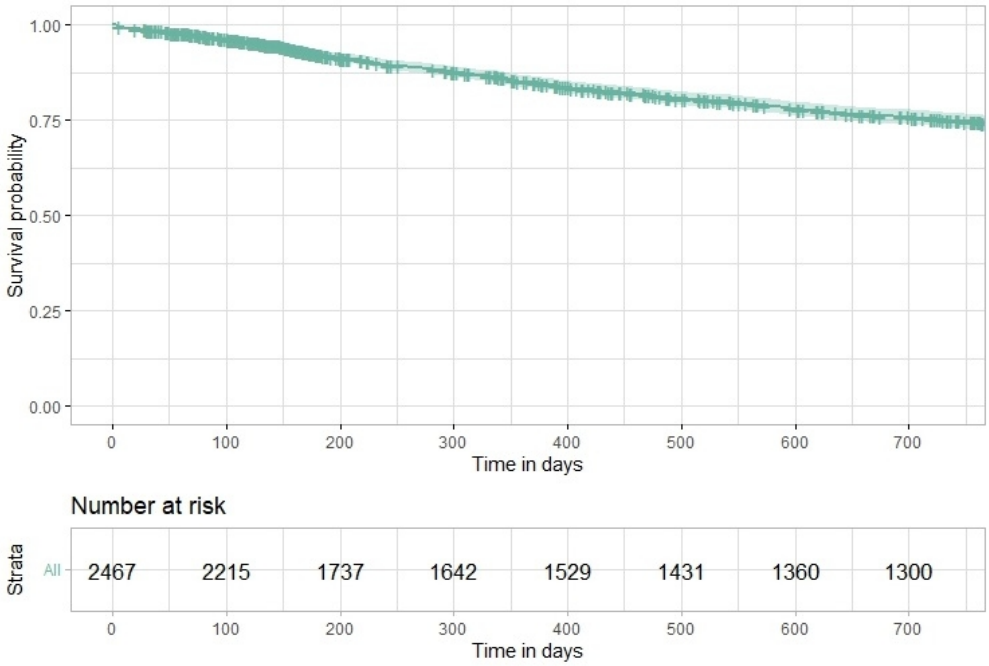
Figure 5 – Inclusion of Dutch Head and Neck Audit – Oral Cavity cohort (blue) compared to the oral cavity cancer incidence (purple line) in the Netherlands between 2018 and 2021.

Figure 1 – Flow chart for inclusion in the Dutch Head and Neck Audit – Oral Cavity (DHNA-OC) cohort.





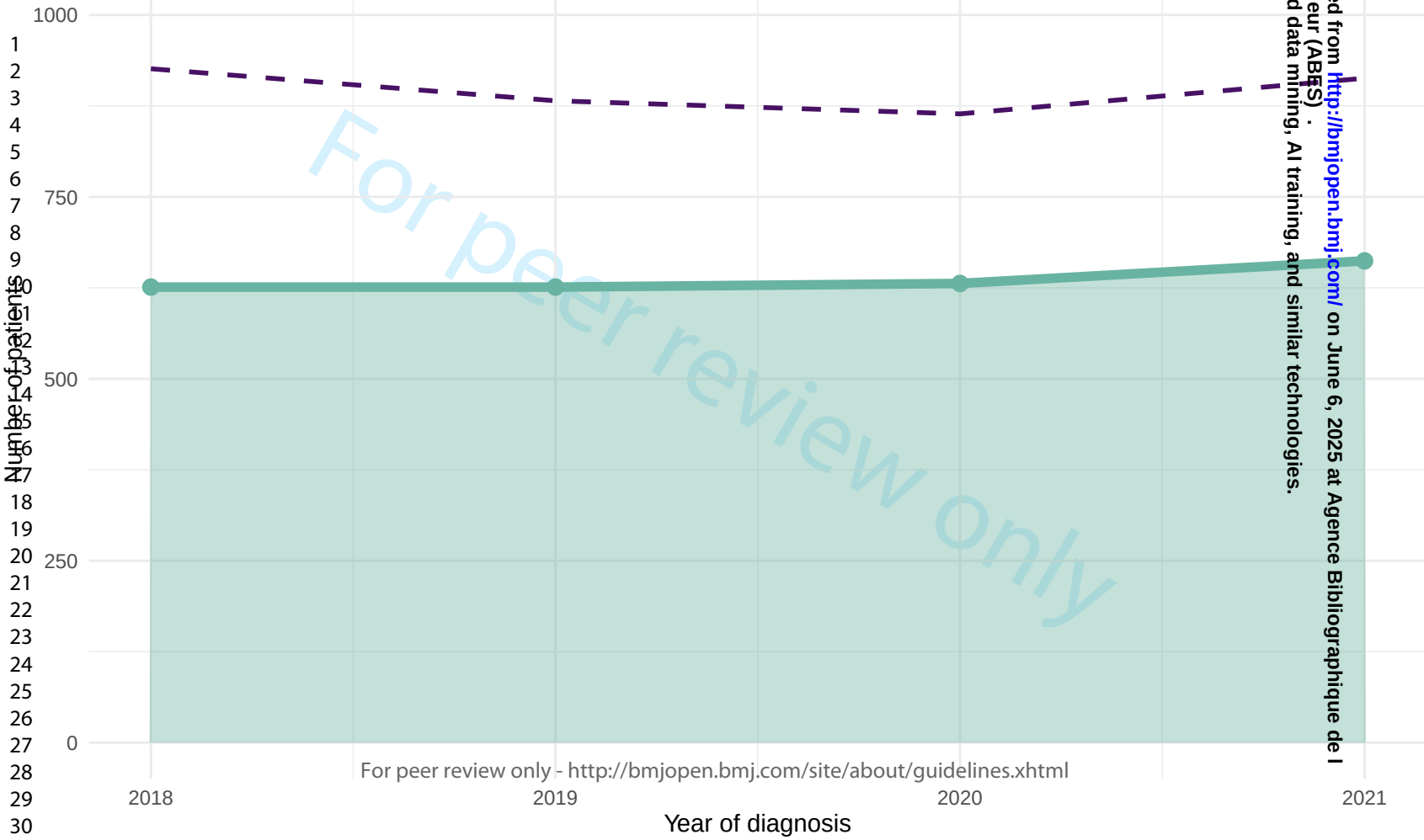




Kaplan Meier curve for two-year overall survival.

197x146mm (96 x 96 DPI)

DHNA−OC inclusion versus incidence



Variable
Hospital
Unique patient identifier
Gender
Date of birth
Length in cm
Weigth in kg
Smoking habit
Packyears
Alcohol habit
Units of alcohol per week
Are there known comorbidities?
ACE-27 comorbidity score
Sublocalisation ICD-O-3 code
Date of biopsy
WHO performance status
Hb-level at diagnosis
Histologic type of oral cavity tumour
Performance of a sentinel lymph node biopsy

cT-classification following the TNM8
cN-classification following the TNM8
cM-classification following the TNM8
Surgical treatment
Radiotherapy treatment
Systemic therapy treatment
Resection of primary tumour
Date of resection primary tumour
ASA score
Neck dissection, unilateral
Neck dissection, bilateral
Date of neck dissection

Type of resection (1)
Type of resection (2)
Performance of tracheostomy with primary resection
Reconstructive surgery after ablative surgeyr
Type of reconstructive surgery performed (not donorsite)
Type of free flap reconstruction performed
pT-classification following TNM8

pN-classification following TNM8
pM-classification following TNM8
Resection margin classification
Pattern of invasion
Perineural or vasoinvasive growth
Numer of lymph nodes pathologically assessed
Number of positive lymphnodes on pathology
Date of discharge after primary surgery
Did an unplanned reoperation occur within 30 days after primary surgery?
Date of reoperation
Did an unplanned readmission occur after discharge for primary surgery?
Date of readmission
Date of discharge after readmission
Did surgical complications occur within 30 days after primary surgery?

Did postoperative bleeding occur within 30 days after primary surgery?
Date of postoperative bleeding
Did chyle leakage occur within 30 days after primary surgery?
Data of chyle leakage
Did a wound infection occur within 30 days after primary surgery?
Data of wound infection
Did wound dehiscence occur within 30 days after primary surgery?
Date of wound dehiscence
Did free flap failure occur within 30 days after primary surgery?
Date of free flap failure
Did fistula formation occur within 30 days after primary surgery?

Date of fistula formation
Start date of chemotherapy
Was the chemotherapy treatment executed as plannen?
Stop date of chemotherapy
Start date of radiotherapy
Was the radiotherapy treatment executed as plannen?
Stop date of raditoherapy
Date of death
Survival status
Data of determination of survival status
Has tumour tissue been detected after treatment, in the form of local tumour, regional tumour, distant metastasis or a second primary tumour?
Local tumour
Incidence date local tumour
Regional tumour
Incidence date regional tumour
Distant metastasis
Incidence date of distant metastasis
Second primary tumour in the head and neck region
Incidence date of second primary tumour in head and neck region

Optionset
number
number
1: Male 2: Female 7: Undifferentiated 9: Unknown
YYMMDD
number
number
1: Never smoked 2: Stopped smoking 3: Current smoker 9: Unknown
number
1: Never drinker 2: Stopped drinking 3: Current drinker 9: Unknown
number
0: No 1: Yes
number
C999
YYMMDD
0: 0 = Normal activity 1: 1 = Symptomatic 2: 2 = More than 50% of the time ambulatory state, can take care of oneself. Not capable of working. 3: 3 = More than 50% of the daytime in bed or chair. Cannot fully take care of oneself 4: 4 = Completely ill. Cannot take care of oneself. All day in bed or chair.
number
1: Squamous cell carcinoma 2: Basaloid squamous cell carcinoma 3: Spindle cell carcinoma 4: Adenosquamous carcinoma 5: Verrucous carcinoma 6: Lymphoepithelial carcinoma 7: Papillary squamous cell carcinoma 8: Acantholytic squamous cell carcinoma 77: Other 99: Unknown
0: No 1: Yes

1: x 2: 0 3: is 5: 1 7: 1a 8: 1b 10: 2 11: 2a 12: 2b 13: 3 14: 4 15: 4a 16: 4b 99: Unknown
0: x 1: 0 2: 1 3: 2 4: 2a 5: 2b 7: 2c 8: 3 10: 3a 11: 3b 99: Unknown
1: x 2: 0 3: 1 9: Unknown
0: No 1: Yes
0: No 1: Yes
0: No 1: Yes
0: No 1: Yes
YYMMDD
1: I 2: II 3: III 4: IV 5: V
0: No 1: Yes
0: No 1: Yes
YYMMDD

1: Oral cavity - Local resection (other than tongue) 2: Oral cavity - Partial tongue resection (to hemi oral tongue) 3: Oral cavity - (Sub)total tongue resection (more than hemi oral tongue, incl. extension to tonguebase) 4: Oral cavity - Marginal/partial resection with marginal mandible (preservation of continuity) 5: Oral cavity - Segmental mandible resection ((sub)total, loss of continuity) 6: Oral cavity - Partial maxilla resection 7: Oral cavity - (Sub)total maxilla resection
1: Oral cavity - Local resection (other than tongue) 2: Oral cavity - Partial tongue resection (to hemi oral tongue) 3: Oral cavity - (Sub)total tongue resection (more than hemi oral tongue, incl. extension to tonguebase) 4: Oral cavity - Marginal/partial resection with marginal mandible (preservation of continuity) 5: Oral cavity - Segmental mandible resection ((sub)total, loss of continuity) 6: Oral cavity - Partial maxilla resection 7: Oral cavity - (Sub)total maxilla resection
0: No 1: Yes 9: Unknown
0: No 1: Yes
1: Free flap 2: Pedicled flap 3: Local transposition 4: Skintransplant, unvascularised 7: Other, namely 9: Unknown
1: Radial forearm flap 2: Anterolateral thigh flap 3: Fibula (+/- skinisland) 7: Other, namely 9: Unknown
1: x 2: 0 3: is 5: 1 7: 1a 8: 1b 10: 2 11: 2a 12: 2b 13: 3 14: 4 15: 4a 16: 4b 99: Unknown

0: x 1: 0 2: 1 3: 2 4: 2a 5: 2b 7: 2c 8: 3 10: 3a 11: 3b 99: Unknown
1: x 2: 0 3: 1 9: Unknown
2: Resection margin involved 3: <1mm 4: 1-5 mm 5: >5 mm 9: Unknown
1: Spidery growth 9: Unknown
1: Perineural 2: Vaso-invasive 3: Both 4: None 9: Unknown
1: Number of lympnodes 98: No lymphnodes assessed 99: Unknown
1: Numbe rof lymphnodes 98: No positive lymphnodes 99: Unknown
YYMMDD
0: No 1: Yes, due to complications 2: Yes, due to an irradical resection 9: Unknown
YYMMDD
0: No 1: Yes 9: Unknown
YYMMDD
YYMMDD
0: No 1: Yes

0: No 1: Yes, grade Clavien Dindo1: hematoma/compression 2: Yes, grade Clavien Dindo2: Conservative, transfusion 3: Yes, grade Clavien Dindo3: Reexploration under anesthesia 4: Yes, grade Clavien Dindo4: Lifethreatening bleeding with intensive care admission 5: Yes, grade Clavien Dindo5: Death 9: Unknown
YYMMDD
0: No 1: Yes, grade Clavien Dindo1: Conservative, puntion 2: Yes, grade Clavien Dindo2: Parenteral feeding 3: Yes, grade Clavien Dindo3: Reexploration under anesthesia 4: Yes, grade Clavien Dindo4: Lifethreatening with intensive care admission 5: Yes, grade Clavien Dindo5: Death 9: Unknown
YYMMDD
0: No 1: Yes, grade Clavien Dindo1: Conservative; local decomnpression of infected hematoma including incision and drainage 2: Yes, grade Clavien Dindo2: Longer (than profylaxtic) use of antibiotica prescribed 3: Yes, grade Clavien Dindo3: Reexploration under anesthesia 4: Yes, grade Clavien Dindo4: Septicaemia with with intensive care admission 5: Yes, grade Clavien Dindo5: Death 9: Unknown
YYMMDD
0: No 1: Yes, grade Clavien Dindo1: Some loose stitches 2: Yes, grade Clavien Dindo2: Local tamponnade / secundary granulation 3: Yes, grade Clavien Dindo3: Reexploration under anesthesia 4: Yes, grade Clavien Dindo4: Lifethreatening with intensive care admission 5: Yes, grade Clavien Dindo5: Death 9: Unknown
YYMMDD
0: No 1: Yes, grade G1: Revision of anestamosis with full recovery 2: Yes, grade G2: Partial flapp loss (such as necrosis of border, secondary granulation); Small revision sugery with re-fixation of plate? 3: Yes, grade G3: total loss of reconstruction 9: Unknown
YYMMDD
0: No 1: Yes 9: Unknown

YYMMDD
YYMMDD
1: Yes 2: Yes, with dosis reduction 0: No, decision of treating specialist 3: No, decision of patient 4: No, death of patient 9: Unknown
YYMMDD
YYMMDD
1: Yes 2: Yes, with dosis reduction 0: No, decision of treating specialist 3: No, decision of patient 4: No, death of patient 9: Unknown
YYMMDD
YYMMDD
1: NED: No evidence of disease 2: AWD: Alive with disease 3: DOD: Dead of disease 4: DOC: Dead of other causes 5: DTC: Dead of treatment complications 99: Unknown
YYMMDD
0: No 1: Yes 9: Unknown
0: No 1: Yes
YYMMDD
0: No 1: Yes
YYMMDD
0: No 1: Yes
YYMMDD
0: No 1: Yes
YYMMDD