

Prof. Christian Simon

Chef-de-service

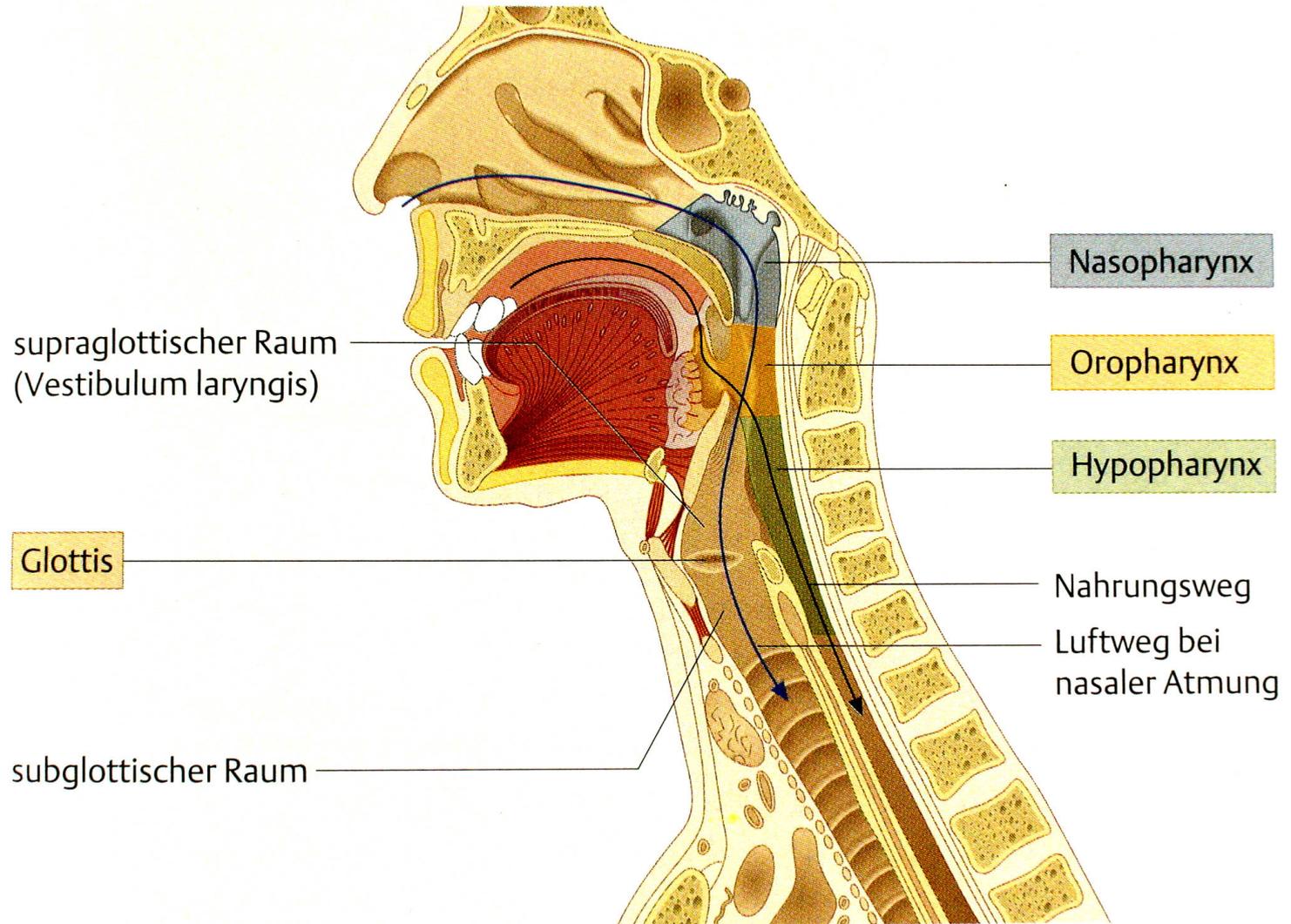
**Service de l'oto- rhino-laryngology et chirurgie
cervico-faciale**

CHUV, University of Lausanne

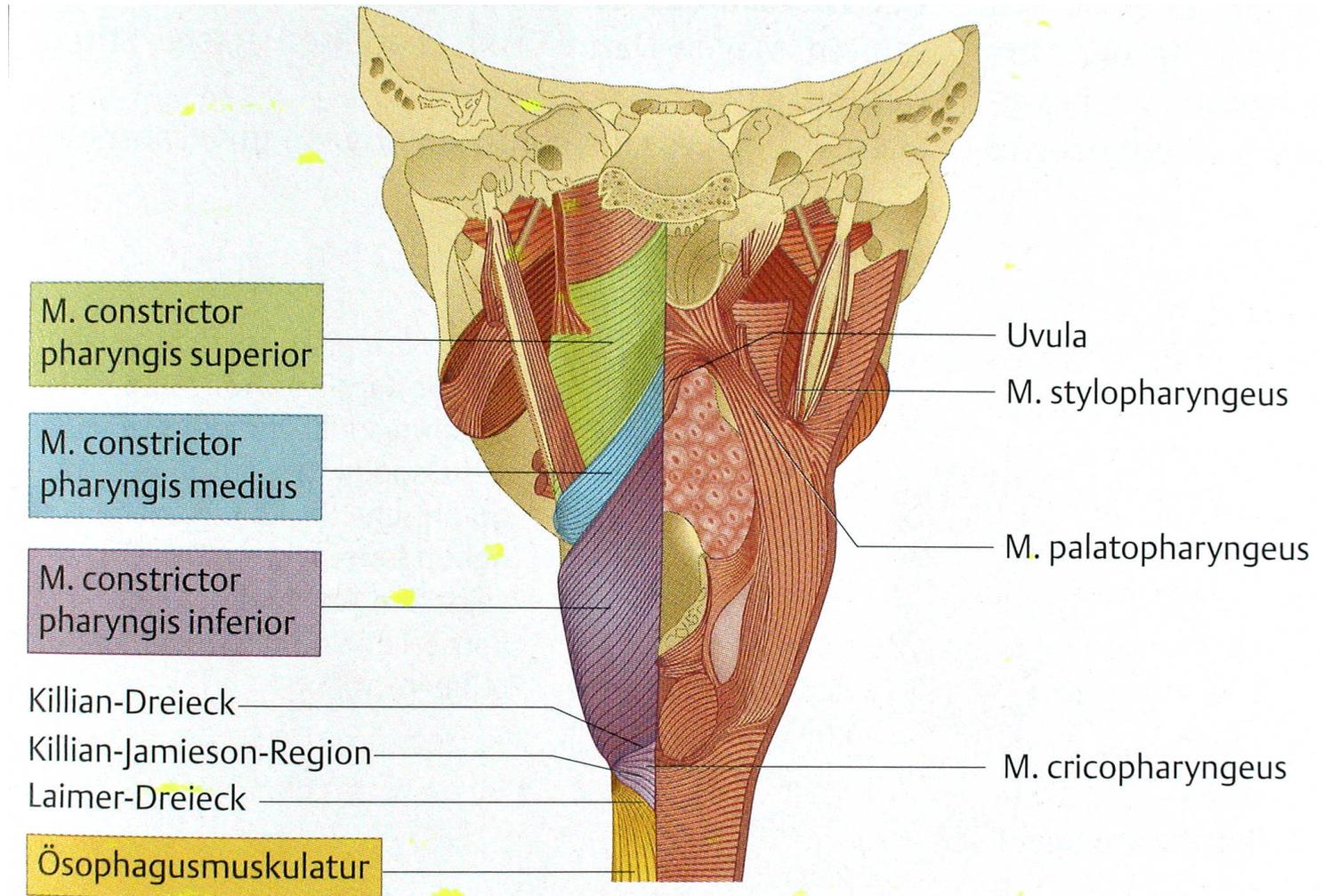
Pharyngeal tumors



Anatomy: Pharynx



Anatomy: Pharynx



Anatomy of the lymphatic system

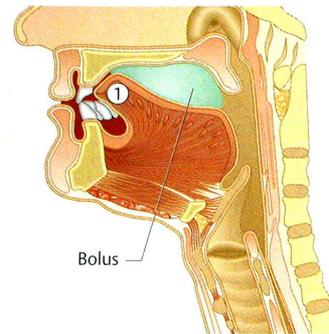
Waldeyer ring:

- 1) Adenoids
- 2) Tonsils
- 3) Base-of-tongue
- 4) Follicles at the posterior pharyngeal wall

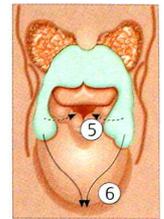
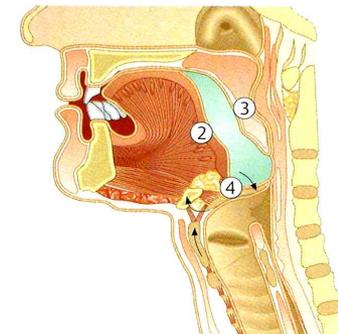
Physiology

- Swallowing
- Speech
- Respiration
- Immune system

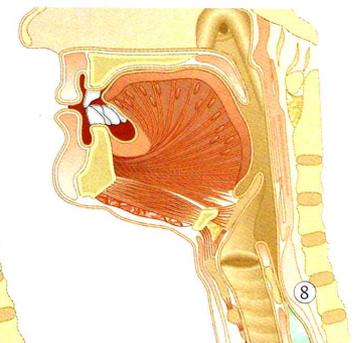
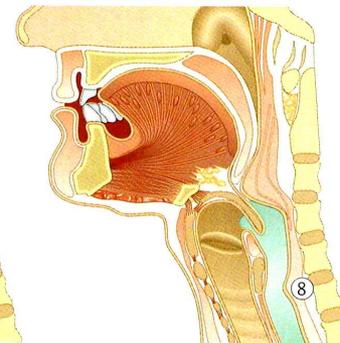
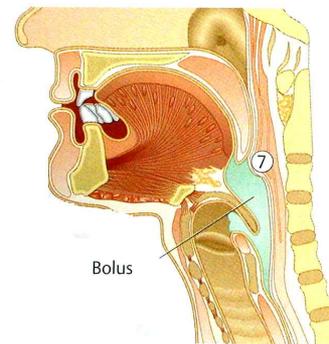
a orale Phase



b pharyngeale Phase



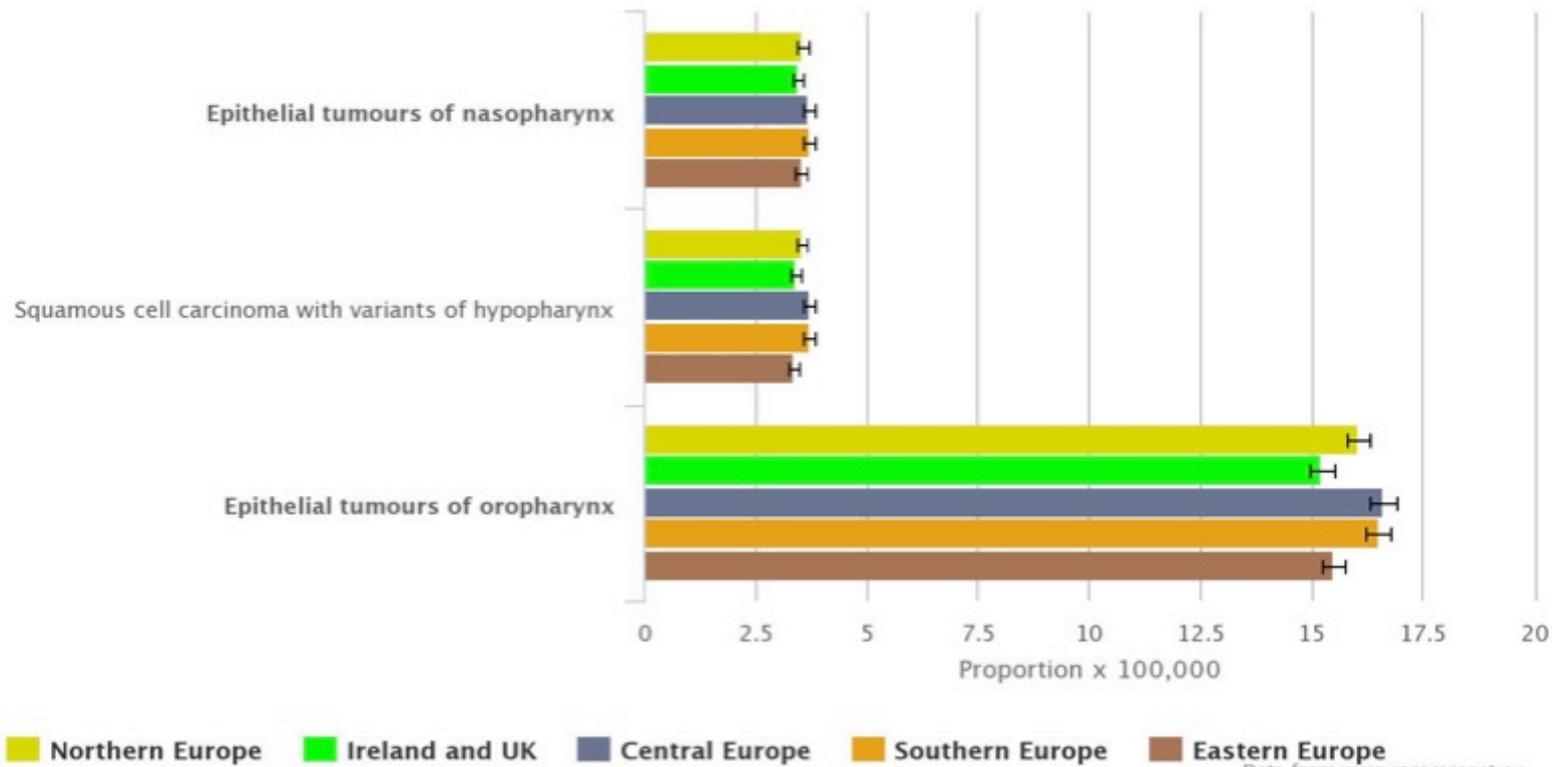
c ösophageale Phase



Epidemiology

Complete prevalence by European area

Proportion x 100,000 at 2008. 26 CRs.
Error bars are 95% confidence intervals.

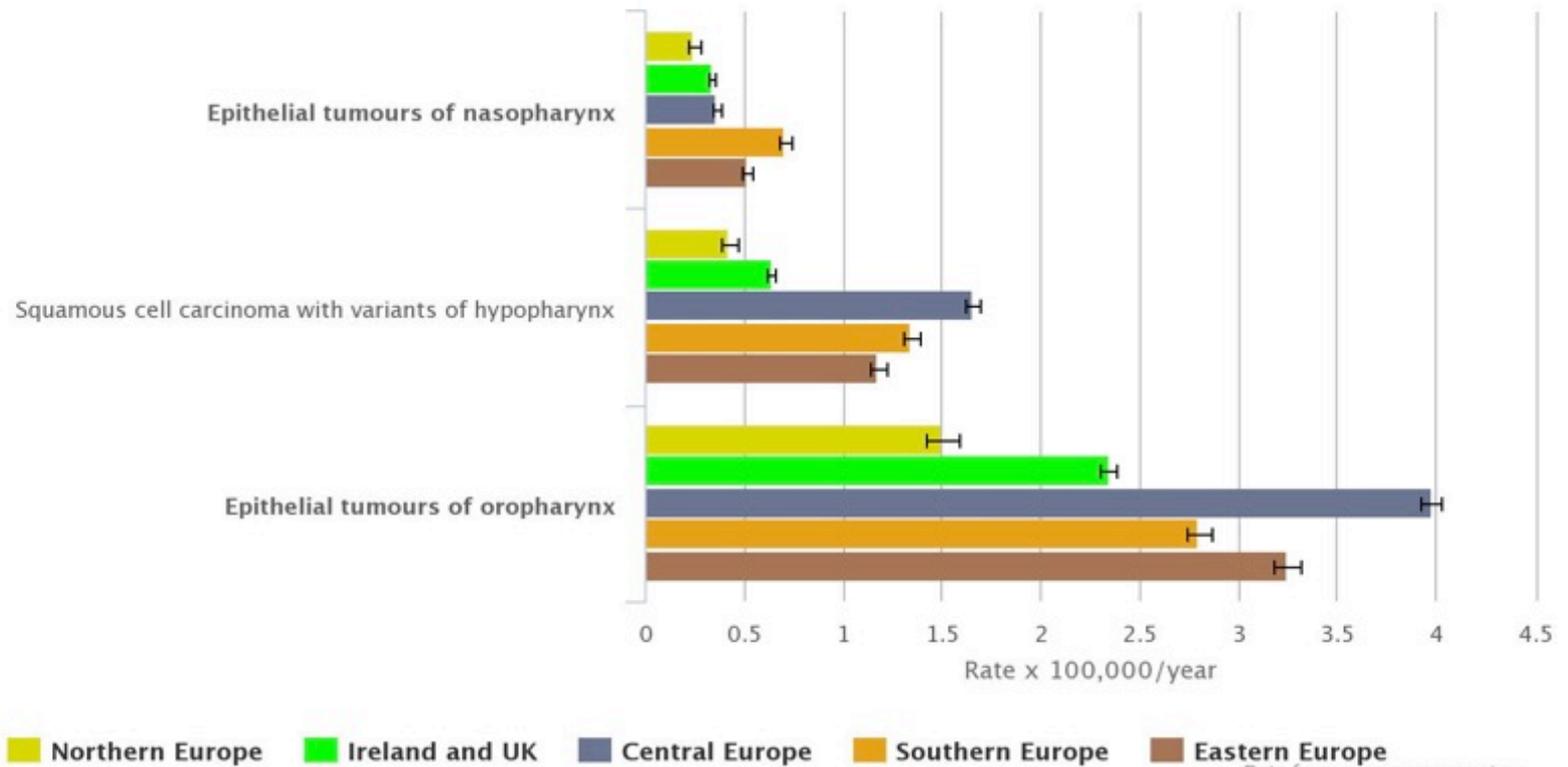


Data from www.rarecarenet.eu

Epidemiology

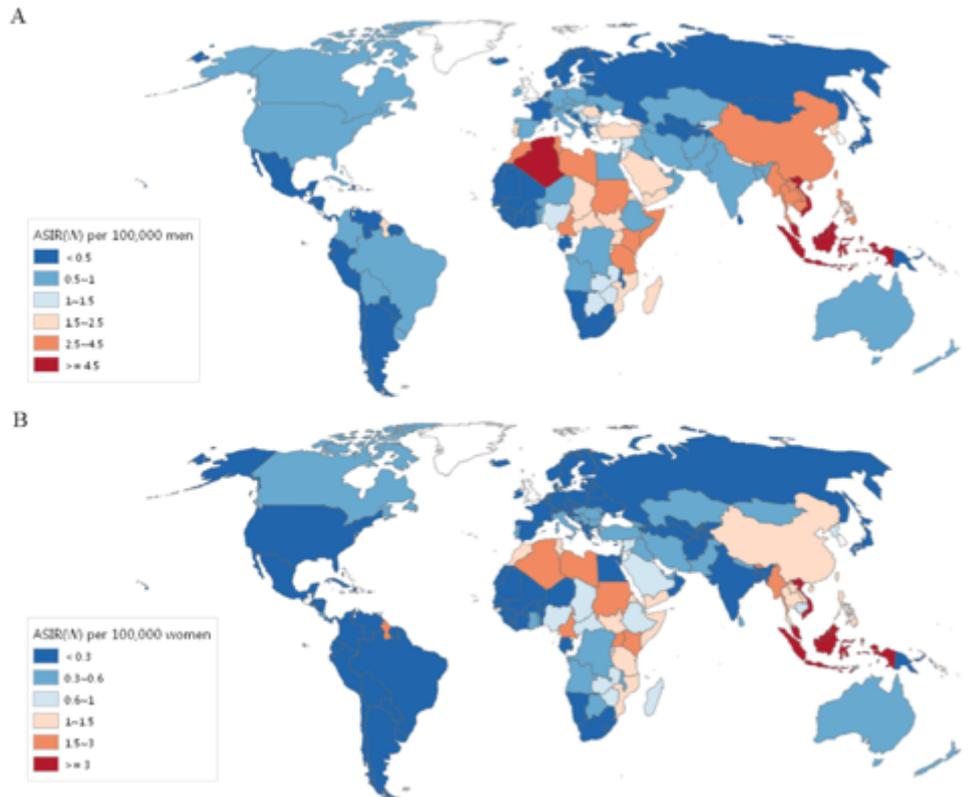
Age-adjusted incidence rate by European area

Rate x 100,000/year (European standard population). Period of diagnosis 2000–2007. 83 CRs.
Error bars are 95% confidence intervals.



Data from www.rarecarenet.eu

Epidemiology: Countries with high incidence of nasopharyngeal cancer



Age standardized incidence rates (ASIR):

A) For men

B) For women

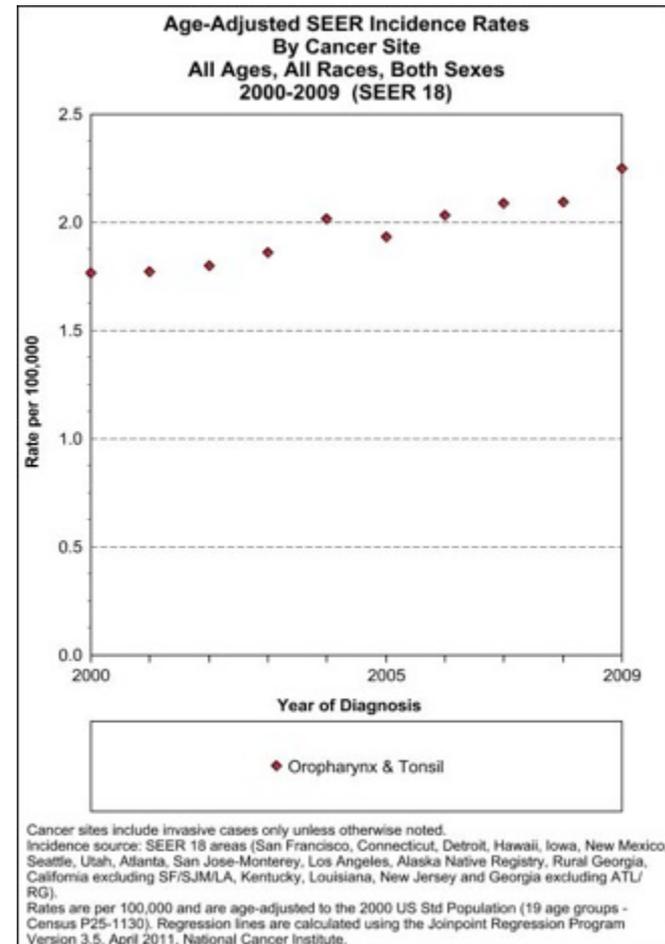
Countries with highest ASIR:

- China
- Hong Kong
- Singapore
- Malaysia
- Algeria

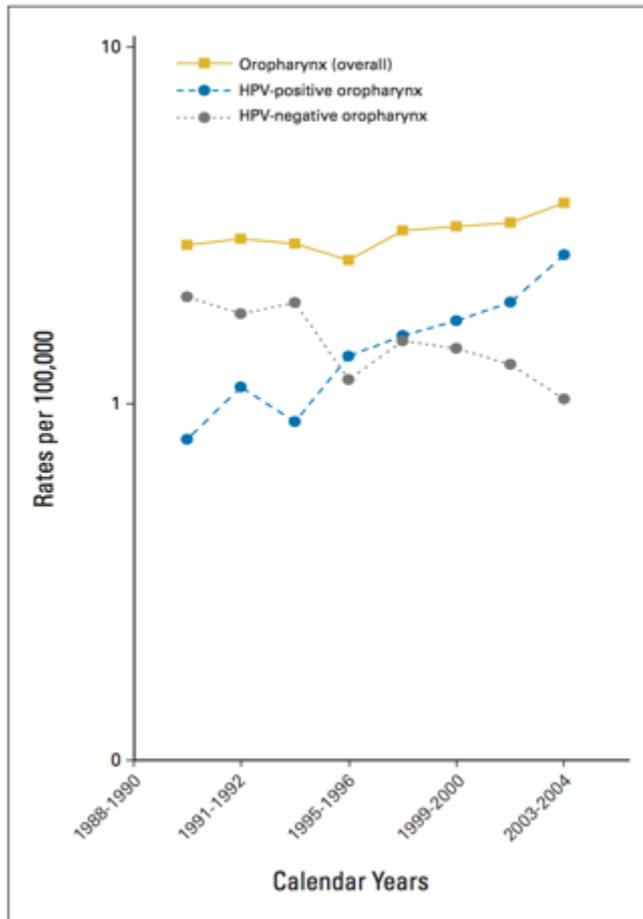
Fig. 1. Global estimates of national age-standardized incidence rates of nasopharyngeal carcinoma in (A) men and (B) women for all ages.

Epidemiology of oropharyngeal cancer

- Incidence of oropharyngeal cancer (OPC) in the US is 2.2/100.000 in 2009 (SEER 2013)
- Early stage OPC between 16.5% and 26% of all OPCs (Carvalho 2005)



Epidemiology: HPV and oropharyngeal cancer (US)



- Population level incidence /100.000 of HPV positive OPC increased from 0,8 (1988) to 2,6 (2004) corresponding to an increase of 225%
- Incidence of HPV negative OPC declined by 50%

Chaturvedi et al. JCO 2011

Histology types and etiology of nasopharyngeal cancers

- Histological subtypes:
 - Keratinising (associated with HPV)
 - Non-keratinising (differentiated or undifferentiated; associated with EBV)
 - Basaloid (no association known)

	Epidemiology	Overall survival	Local control	Distant metastasis-free survival
HPV-negative/EBV-positive	Endemic regions	Most superior	Most superior	Lowest
HPV-positive/EBV-negative	Non-endemic regions	Moderate	Moderate	Moderate
HPV-negative/EBV-negative	Non-endemic regions	Lowest	Lowest	Moderate

HPV=human papillomavirus. EBV=Epstein-Barr virus.

Table 1: Characteristics of the different types of viral-associated nasopharyngeal carcinoma

Histological types of oropharyngeal malignancies

- Malignant epithelial tumors
 - Squamous cell carcinoma
 - Lympho-epithelial carcinoma
- Salivary gland tumors
 - Salivary gland carcinomas
 - Adenoid cystic carcinoma etc.
- Myoepithelial carcinoma
- Carcinoma ex pleomorphic carcinoma
- Soft tissue tumors
- Hemato-lymphoid tumors
- Mucosal malignant melanoma
- Secondary tumors

Etiology and risk factors of oropharyngeal carcinomas

- Tobacco: <20 cig./day 1.6 fold increased risk for OPC, >20 cig./day 3.1 fold increased risk for OPC, reduction of risk down to 1.2 10 years after quitting smoking (Ansary et al., 2009)
- Alcohol: 36 fold increased risk for OPC in heavy drinkers and heavy smokers (Ansary et al., 2009)
- Ethnicity: Increased risk in African-Americans in the US (Lambert et al., 2011)

Etiology and risk factors of oropharyngeal carcinomas

- HPV:
 - 20-25% HPV-positivity in HNSCC-patients (D'Souza et al, 2007)
 - 40%-80% of OPCs positive for HPV (Miller et al., 2012)
 - Associated mostly with HPV16 (Gillison, 2006)
 - Sexually transmitted disease (Gillison, 2006)
 - Increase of HPV+OPC by 225% in population-level incidence 1984-2004 (Chaturvdei et al., 2011)

Smoking and HPV positive oropharyngeal cancer

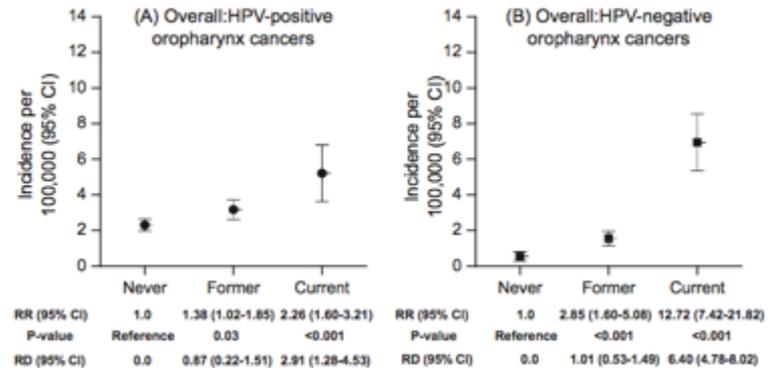
Odds ratio (OR) to have an HPV-positive tumor higher in never-smokers

Relative risk (RR) to develop an HPV-positive tumor higher in former and current smokers

TABLE 3. Multivariate analyses of association of human papillomavirus positivity for all subjects using a model without selection.

Risk factor	Coefficient, β (SE)	p value	OR for combined HPV/p16 positivity (95% CI)
Intercept	-0.827 (1.583)	.80	-
Smoking status			
Never smoked, reference	-	-	1
Current	-2.02 (0.43)	<.0001	0.133 (0.06-0.31)
Former	-1.39 (0.38)	.0003	0.250 (0.12-0.53)
Sex			
Male, reference group	-	-	1
Female	-0.07 (0.34)	.83	0.93 (0.475-1.818)
Region			
Eastern Europe, reference	-	-	1
Asia	-0.71 (0.77)	.36	0.49 (0.11-2.23)
Western Europe	1.91 (0.46)	<.0001	6.74 (2.72-16.72)
Tumor site			
Oropharyngeal, reference	-	-	1
Nonoropharyngeal	-4.38 (0.48)	<.0001	0.013 (0.005-0.03)
Disease stage			
II, reference group	-	-	1
III/IV	1.55 (1.33)	.25	4.70 (0.35-63.9)
Age, y	-0.01 (0.02)	.45	0.99 (0.96-1.02)

Abbreviations: OR, odds ratio; HPV, human papillomavirus; 95% CI, 95% confidence interval. The model using a stepwise logistic regression model is included as Supplementary Table S2, online only. Age, sex, primary site, stage, smoking status, and region were introduced into the model. All subjects, considering sex, disease stage, age, region (Eastern/Western Europe and Asia), tumor site, and smoking status without selection. Similar findings were observed when analyses were repeated for oropharyngeal cancer subjects only (Supplementary Table S3, online only).



Histological types of hypopharyngeal malignancies

- Squamous cell carcinomas
- Lympho-epithelial carcinomas
- Lymphomas
 - T-cell lymphomas
 - Non-Hodgkin Lymphomas
- Adenocarcinomas
- Soft tissue tumors
- Secondary tumors (i.e. thyroid cancer by direct infiltration)

Etiology of hypopharyngeal cancer

- Alcohol consumption (more important)
- Tobacco
- Plummer-Vinson syndrome (postcricoid cancer)
- Paterson-brown-Kelly syndrome (postcricoid cancer)

Cummings 2005

Prevention: EBV-screening to predict NPC-occurrence

TABLE 4. MULTIVARIATE-ADJUSTED RELATIVE RISK OF NASOPHARYNGEAL CARCINOMA ACCORDING TO STUDY PERIOD.*

VARIABLE	RELATIVE RISK OF NASOPHARYNGEAL CARCINOMA					
	ENTIRE STUDY PERIOD	P VALUE	1-5 YR AFTER ENROLLMENT	P VALUE	>5 YR AFTER ENROLLMENT	P VALUE
	RR (95% CI)		RR (95% CI)		RR (95% CI)	
IgA antibodies against EBV capsid antigen						
Negative	1.0		1.0		1.0	
Positive	22.0 (7.3-66.9)	<0.001	55.5 (8.9-345.4)	<0.001	13.9 (3.1-61.7)	<0.001
Anti-EBV DNase antibodies						
Negative	1.0		1.0		1.0	
Positive	3.5 (1.4-8.7)	0.006	4.7 (0.8-28.5)		3.2 (1.1-9.2)	0.03
Both serologic markers						
Neither positive	1.0		1.0		1.0	
Either positive	4.0 (1.6-10.2)	0.003	7.1 (1.0-50.6)	0.05	3.5 (1.2-10.0)	0.02
Both positive	32.8 (7.3-147.2)	<0.001	85.3 (7.4-978.4)	<0.001	20.7 (2.6-162.0)	0.004

*The relative risks (RRs) have been adjusted for age and the presence or absence of a family history of nasopharyngeal carcinoma. P values for "either positive" and "both positive" are for the comparisons with "neither positive." CI denotes confidence interval, and EBV Epstein-Barr virus.

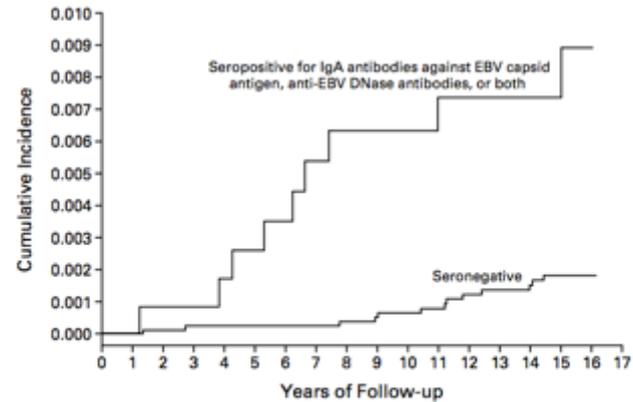


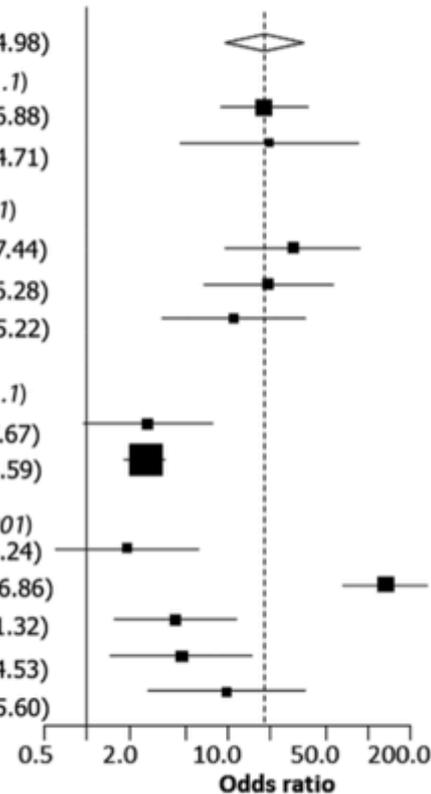
Figure 1. Cumulative Incidence of Nasopharyngeal Carcinoma during Follow-up among 9688 Study Subjects, According to Whether They Tested Positive or Negative for Either Serologic Marker of Epstein-Barr Virus (EBV) Infection (or Both) at the Time of Enrollment between 1984 and 1986.

Chien et al. N Engl J Med 2001

Prevention: HPV-screening to predict OPCs

B

HPV16 E6	Controls Seropositivity (%) [†]	Cases Seropositivity (%) [†]	OR (95% CI)
Overall	11 (0.8)	118 (8.0)	18.44 (9.72 to 34.98)
By sex			(<i>P</i> > .1)
Men	9 (0.9)	90 (7.7)	18.04 (8.83 to 36.88)
Women	2 (0.6)	28 (9.5)	19.71 (4.59 to 84.71)
By smoking status			(<i>P</i> > .1)
Never	4 (0.8)	24 (14.3)	29.02 (9.63 to 87.44)
Former	4 (0.9)	38 (10.7)	19.53 (6.78 to 56.28)
Current	3 (0.7)	56 (5.9)	10.88 (3.36 to 35.22)
By alcohol consumption			(<i>P</i> > .1)
Never	1 (0.6)	7 (7.9)	2.68 (0.94 to 7.67)
Ever	10 (0.8)	111 (8.0)	2.58 (1.85 to 3.59)
By cancer site			(<i>P</i> < .0001)
Oral cavity		4 (1.1)	1.91 (0.59 to 6.24)
Oropharynx		97 (30.2)	132.0 (65.29 to 266.86)
Larynx		8 (1.5)	4.18 (1.54 to 11.32)
Esophagus		5 (2.6)	4.63 (1.48 to 14.53)
Overlapping sites		4 (5.3)	9.76 (2.68 to 35.60)



D

Prevention: Vaccination strategies against HPV-driven tumors

- Costa-Rica HPV-vaccine trial (CVT): Prevalence of HPV overall 0,7% vs. 1,3% and HPV 16 and/or 18 (0,03% vs. 0,5%), vaccine efficacy of 93,3%
- Vaccination trials for the prevention of HPV positive OPCs difficult, because endpoints are difficult to determine

Symptoms: Nasopharynx cancer

- Neck mass
- Blood in saliva
- Deafness
- Epistaxis
- Nasal obstruction
- Tinnitus
- Cranial nerve palsy



High likelihood

Low likelihood

Cummings 2005

Symptoms: Oropharynx cancer

- Neck mass
- Dysphagia
- Odynophagia
- Otalgia
- Oral bleeding



Cummings 2005

Symptoms: Hypopharynx cancer

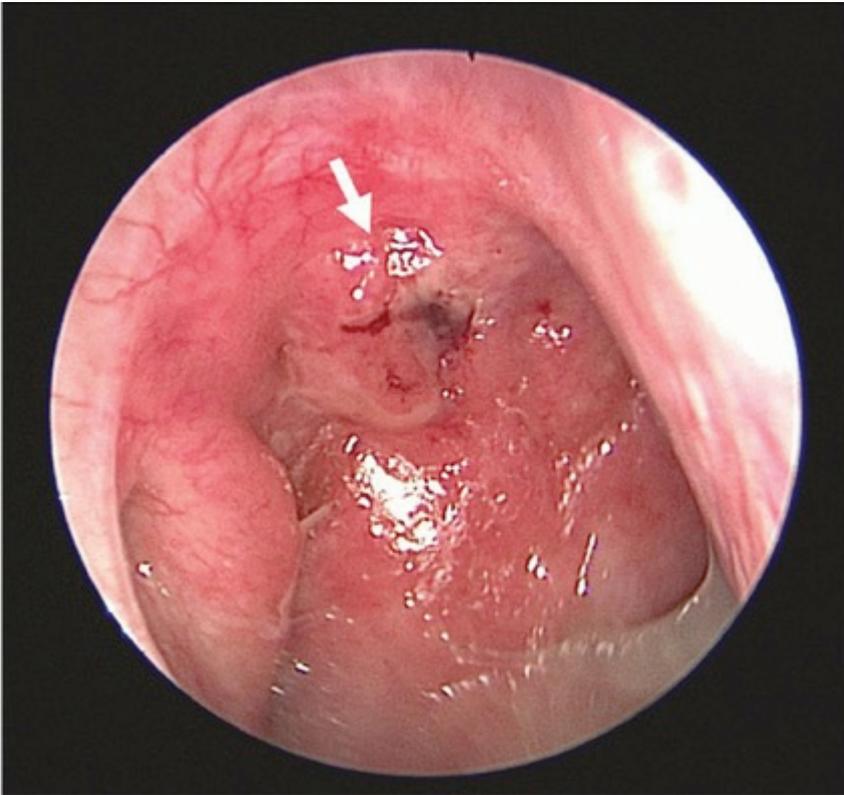
- Dysphagia
- Neck mass
- Sore throat
- Hoarseness
- Otalgia
- Shortness of breath
- Hemoptysis
- Gastro-esophageal reflux



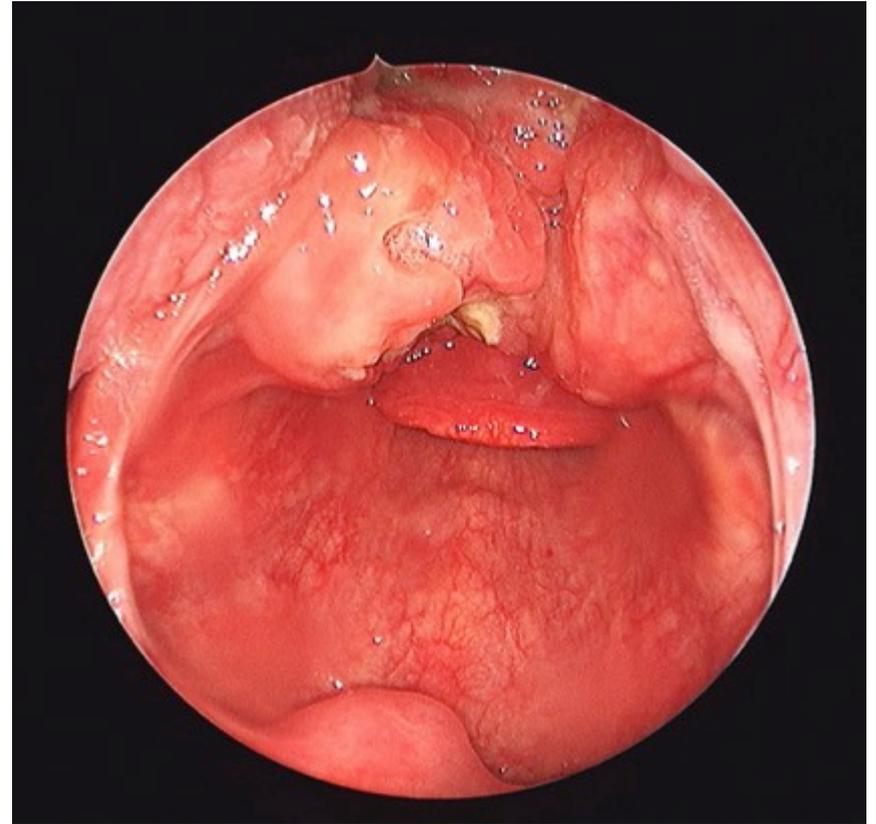
Hoffmann et al. Laryngoscope 1997

Presentation

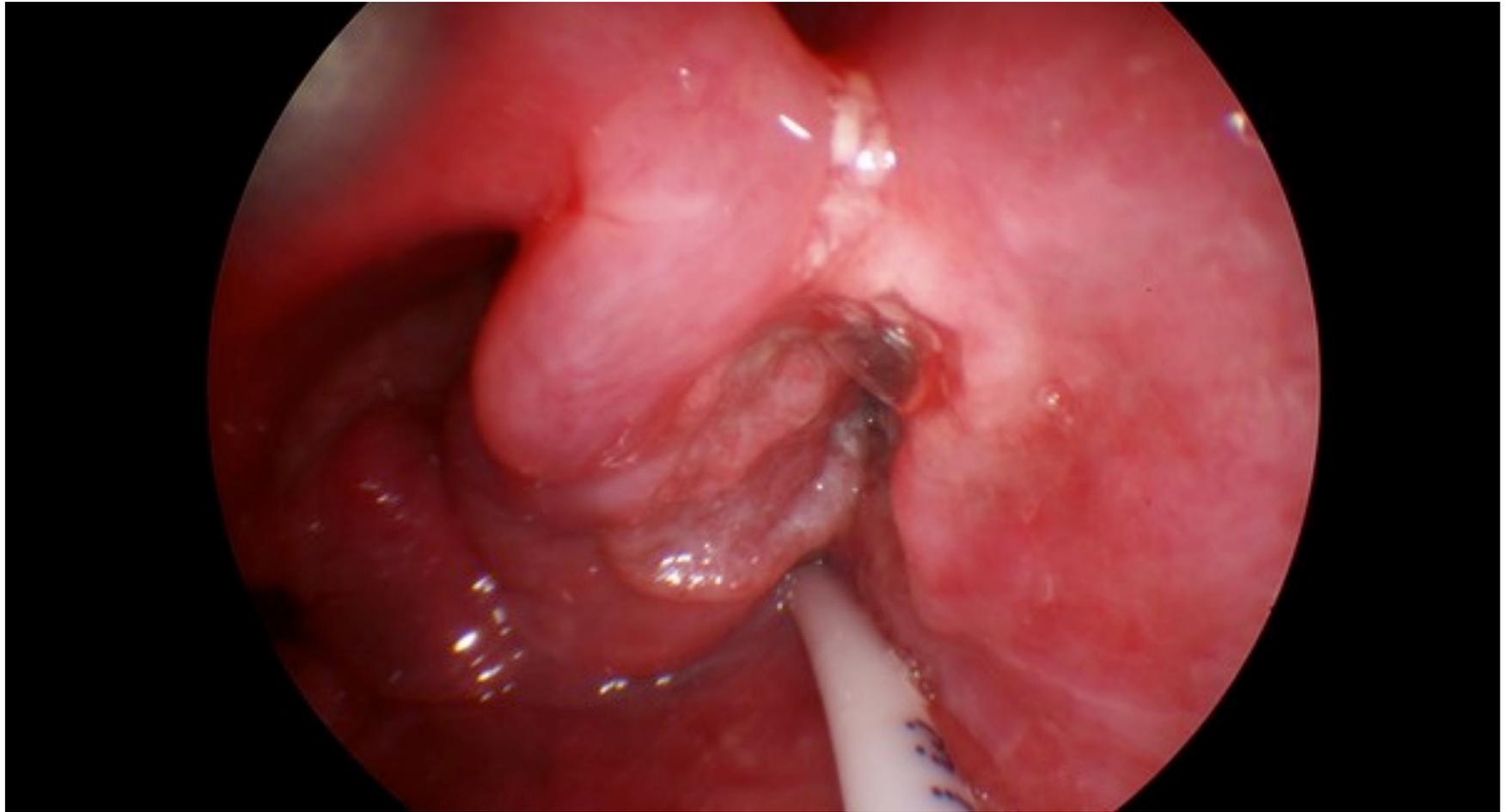
Nasopharynx



Oropharynx



Presentation: Hypopharynx



Work-up for nasopharyngeal carcinomas

- **H&P^{a,b} including a complete head and neck exam; mirror examination as clinically indicated**
- **Nasopharyngeal fiberoptic examination**
- **Biopsy of primary site or FNA of the neck**
- **MRI with contrast of skull base to clavicle ± CT of skull base/neck with contrast as clinically indicated to evaluate skull base erosion**
- **Dental,^c nutritional, speech and swallowing, and audiology evaluations as clinically indicated^d**
- **Imaging for distant metastases with FDG-PET/CT and/or chest CT with contrast, especially for nonkeratinizing histology, endemic phenotype, or N2-3 disease; may be considered for stage III-IV disease**
- **Consider EBV/DNA testing^e**
- **Consider ophthalmologic and endocrine evaluation as clinically indicated.**

Multidisciplinary consultation as clinically indicated

Work-up for oropharyngeal carcinomas

- **H&P^{a,b} including a complete head and neck exam; mirror and fiberoptic examination as clinically indicated**
- **Biopsy of primary site or fine-needle aspiration (FNA) of the neck**
- **Tumor human papillomavirus (HPV) testing recommended^c**
- **Chest CT^d (with or without contrast) as clinically indicated**
- **CT with contrast and/or MRI with contrast of primary and neck**
- **Consider FDG-PET/CT for stage III-IV disease**
- **Dental evaluation,^e including panorex as clinically indicated**
- **Nutrition, speech and swallowing evaluation/therapy, and audiogram as clinically indicated^f**
- **EUA with endoscopy as clinically indicated**
- **Pre-anesthesia studies**

Multidisciplinary consultation as clinically indicated

Work-up for hypopharyngeal carcinomas

- **H&P^{a,b} including a complete head and neck exam; mirror and/or fiberoptic examination as clinically indicated**
 - **Biopsy of primary site or FNA of neck**
 - **Chest CT (with or without contrast) as clinically indicated^c**
 - **CT with contrast and/or MRI with contrast of primary and neck**
 - **Consider FDG-PET/CT^d for stage III-IV disease**
 - **EUA with endoscopy**
 - **Preanesthesia studies as clinically indicated**
 - **Nutrition, speech and swallowing evaluation/therapy, and audiogram as clinically indicated^e**
 - **Dental evaluation^f**
 - **Consider pulmonary function tests for conservation surgery candidates**
- Multidisciplinary consultation as clinically indicated**

Staging: Important changes between 7th and 8th AJCC classification

TABLE 1. Clinical and Pathologic T Category for Human Papillomavirus-Associated (p16-Positive) Oropharyngeal Cancer, 8th Edition Staging Manual^a

T CATEGORY	T CRITERIA
T0	No primary identified
T1	Tumor 2 cm or smaller in greatest dimension
T2	Tumor larger than 2 cm but not larger than 4 cm in greatest dimension
T3	Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis
T4	Moderately advanced local disease; tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible or beyond ^b

^aTable 1 is used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer Science and Business Media LLC (springer.com) (Amin MB, Edge SB, Greene FL, et al, eds. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017, with permission²). ^bMucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.

TABLE 2. Clinical and Pathologic T Category for Non-Human Papillomavirus-Associated (p16-Negative) Oropharyngeal Cancer, 8th Edition Staging Manual^a

T CATEGORY	T CRITERIA
Tx	Primary tumor cannot be assessed
Tis	Carcinoma in situ
T1	Tumor 2 cm or smaller in greatest dimension
T2	Tumor larger than 2 cm but not larger than 4 cm in greatest dimension
T3	Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis
T4	Moderately advanced or very advanced local disease
T4a	Moderately advanced local disease; tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible ^b
T4b	Very advanced local disease; tumor invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base or encases carotid artery

^aTable 2 is used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer Science and Business Media LLC (springer.com) (Amin MB, Edge SB, Greene FL, et al, eds. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017, with permission²). ^bMucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.

Staging: Important changes between 7th and 8th AJCC classification

TABLE 3. Clinical N Category Human Papillomavirus-Associated (p16-Positive) Oropharyngeal Cancer, 8th Edition Staging Manual^a

N CATEGORY	N CRITERIA
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	One or more ipsilateral lymph nodes, none larger than 6 cm
N2	Contralateral or bilateral lymph nodes, none larger than 6 cm
N3	Lymph node(s) larger than 6 cm

^aTable 3 is used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer Science and Business Media LLC (springer.com) (Amin MB, Edge SB, Greene FL, et al, eds. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017, with permission²).

TABLE 4. Clinical N Category for Non-Human Papillomavirus-Associated (p16-Negative) Oropharyngeal Cancer, 8th Edition Staging Manual^a

N CATEGORY	N CRITERIA
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE-negative
N2	Metastasis in a single ipsilateral lymph node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE-negative; or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE-negative; or metastasis in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE-negative
N2a	Metastasis in a single ipsilateral lymph node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE-negative
N2b	Metastasis in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE-negative
N2c	Metastasis in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE-negative
N3	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE-negative; or metastasis in any lymph node(s) and clinically overt ENE-positive
N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE-negative
N3b	Metastasis in any node(s) and clinically overt ENE-positive

Abbreviations: ENE, extranodal extension. ^aTable 4 is used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer Science and Business Media LLC (springer.com) (Amin MB, Edge SB, Greene FL, et al, eds. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017, with permission²).

Staging: Important changes between 7th and 8th AJCC classification

TABLE 5. Pathologic N Category Human Papillomavirus-Associated (p16-Positive) Oropharyngeal Cancer, 8th Edition Staging Manual^a

N CATEGORY	N CRITERIA
NX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in 4 or fewer lymph nodes
pN2	Metastasis in more than 4 lymph nodes

^aTable 5 is used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer Science and Business Media LLC (springer.com) (Amin MB, Edge SB, Greene FL, et al, eds. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017, with permission²).

Staging: Important changes between 7th and 8th AJCC classification

TABLE 6. Anatomic Stage and Prognostic Groups for *Clinical* TNM Grouping of Human Papillomavirus-Associated (p16-Positive) Oropharyngeal Cancer, 8th Edition Staging Manual^a

T CATEGORY	N CATEGORY			
	N0	N1	N2	N3
T0	NA	I	II	III
T1	I	I	II	III
T2	I	I	II	III
T3	II	II	II	III
T4	III	III	III	III

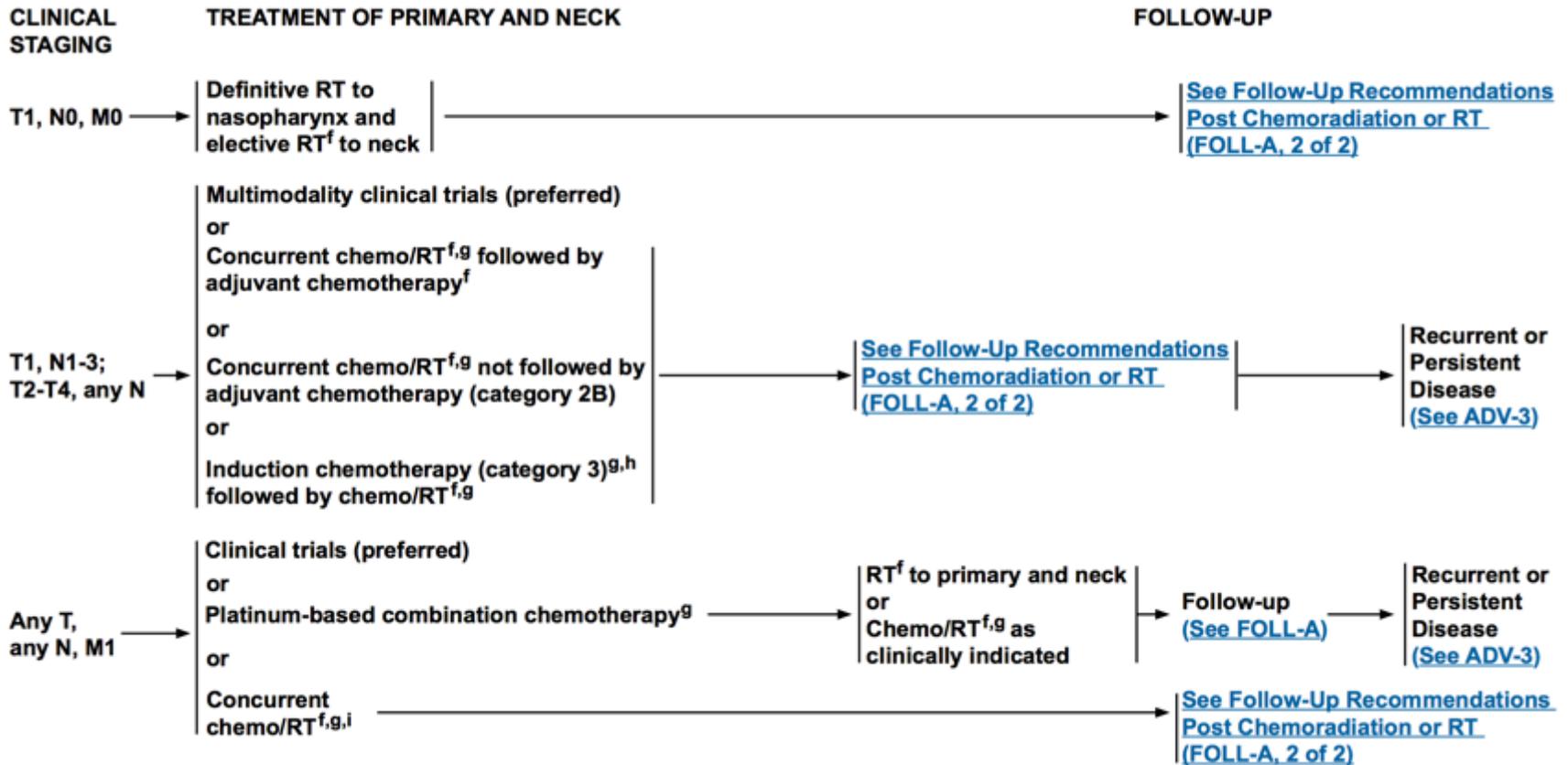
^aAny M1 is stage IV.

TABLE 8. Anatomic Stage and Prognostic Groups for *Clinical* and *Pathologic* TNM Grouping of Non-Human Papillomavirus-Associated (p16-Negative) Oropharyngeal Cancer, 8th Edition Staging Manual^a

T CATEGORY	N CATEGORY			
	N0	N1	N2a,b,c	N3a,b
T1	I	III	IVA	IVB
T2	II	III	IVA	IVB
T3	III	III	IVA	IVB
T4a	IVA	IVA	IVA	IVB
T4b	IVB	IVB	IVB	IVB

^aAny M1 is stage IVC.

Treatment: Nasopharynx



Treatment: Nasopharynx

Concomitant CRT with adjuvant CT provides best results

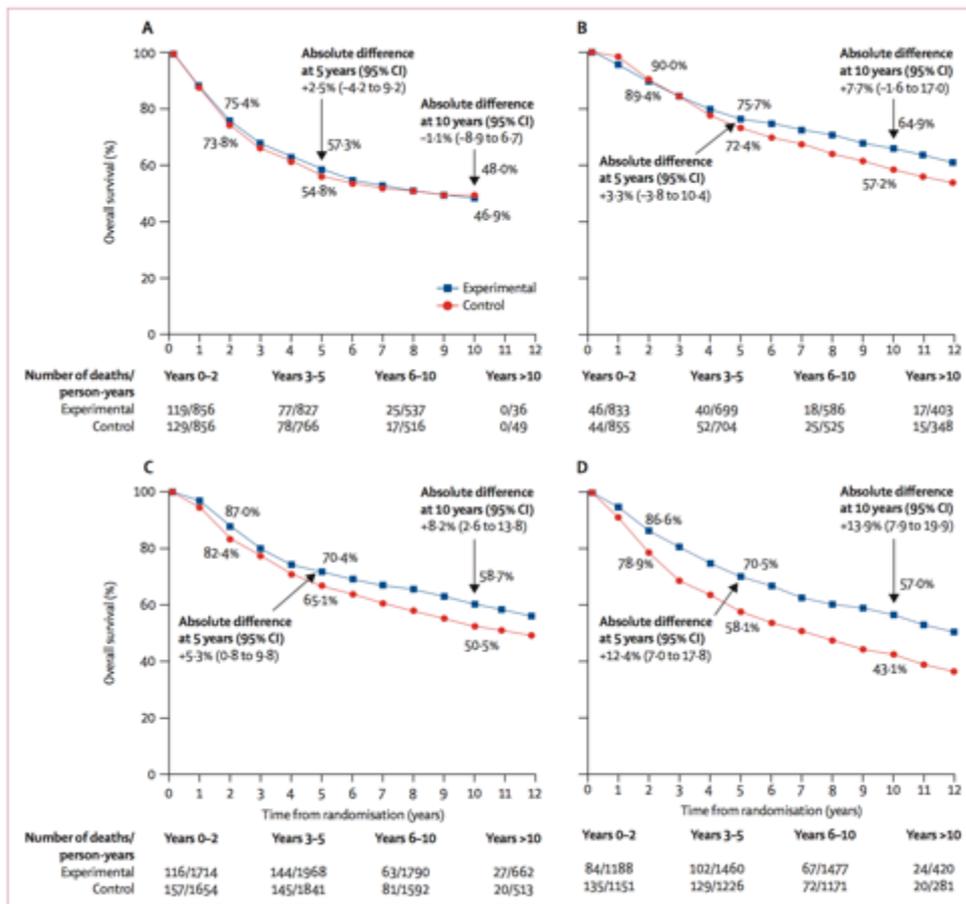


Figure 3: Survival curves for overall survival in trials investigating (A) induction, (B) adjuvant, (C) concomitant, and (D) concomitant plus adjuvant chemotherapy

Treatment: Nasopharynx

Induction TPF followed by CRT better than CRT alone (for stage III – IVb)

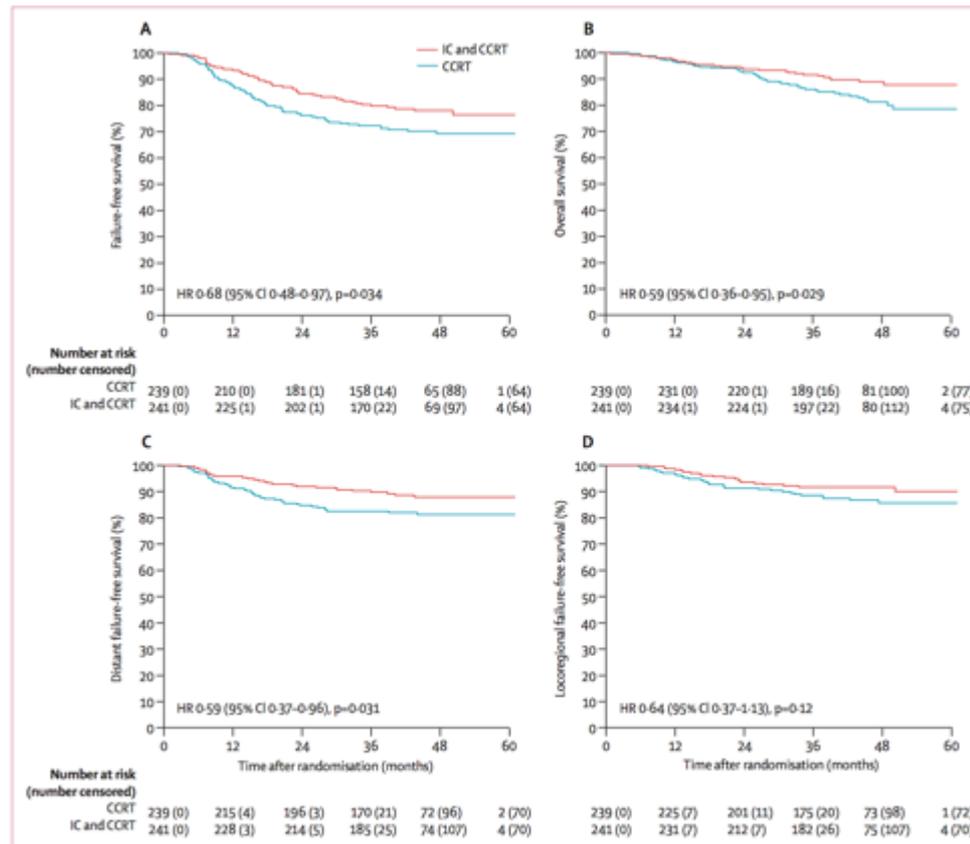


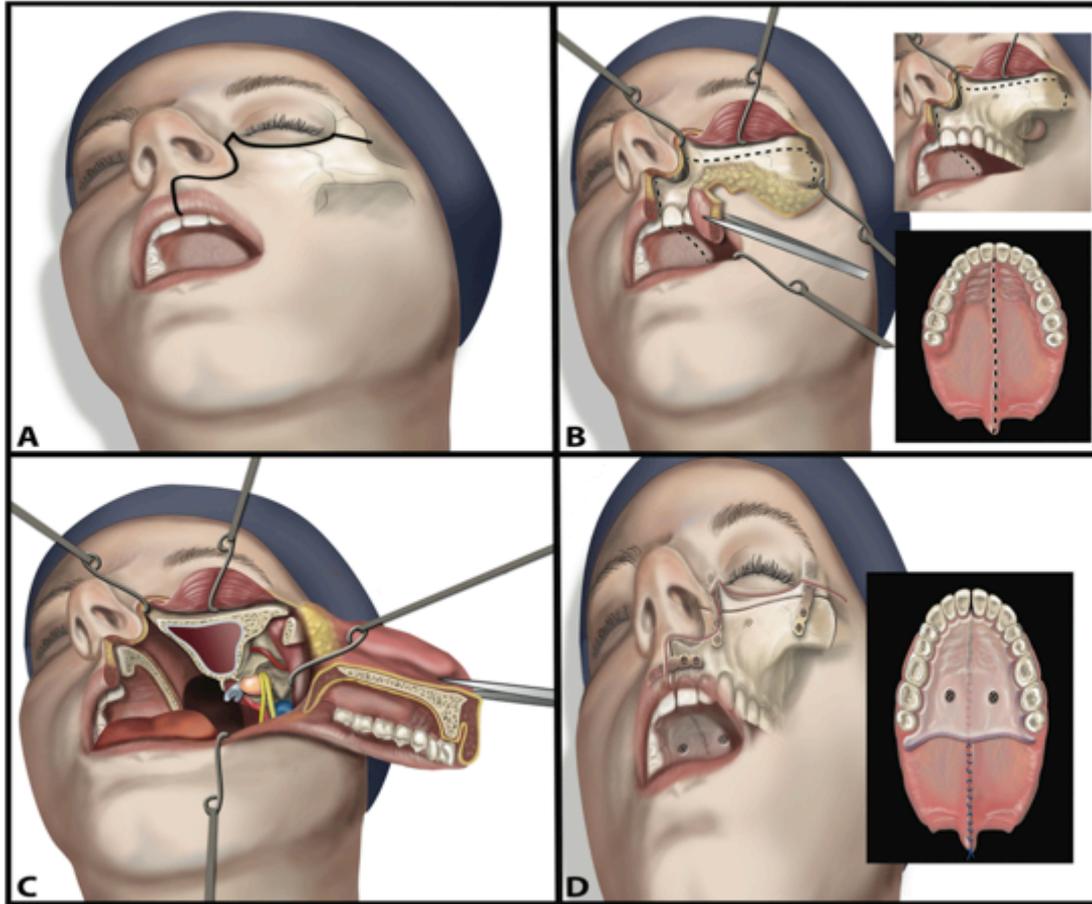
Figure 2: Kaplan-Meier survival curves for the two treatment groups (A) Failure-free survival, (B) overall survival, (C) distant failure-free survival, and (D) locoregional failure-free survival, all from the start of treatment. Hazard ratios (HRs) were calculated with the unadjusted Cox proportional-hazards model; p values were calculated with the unadjusted log-rank test. CCRT=concurrent chemoradiotherapy. IC=induction chemotherapy.

Treatment: Recurrent nasopharyngeal carcinoma

- rT1-T2:
 - Surgery
 - Endoscopic
 - Maxillary swing
 - Robotics (experimental)
 - RT
 - Brachytherapy
 - stereotactic RT
 - IMRT
- rT3-T4
 - IMRT

Chua et al. Lancet 2016

Maxillary swing



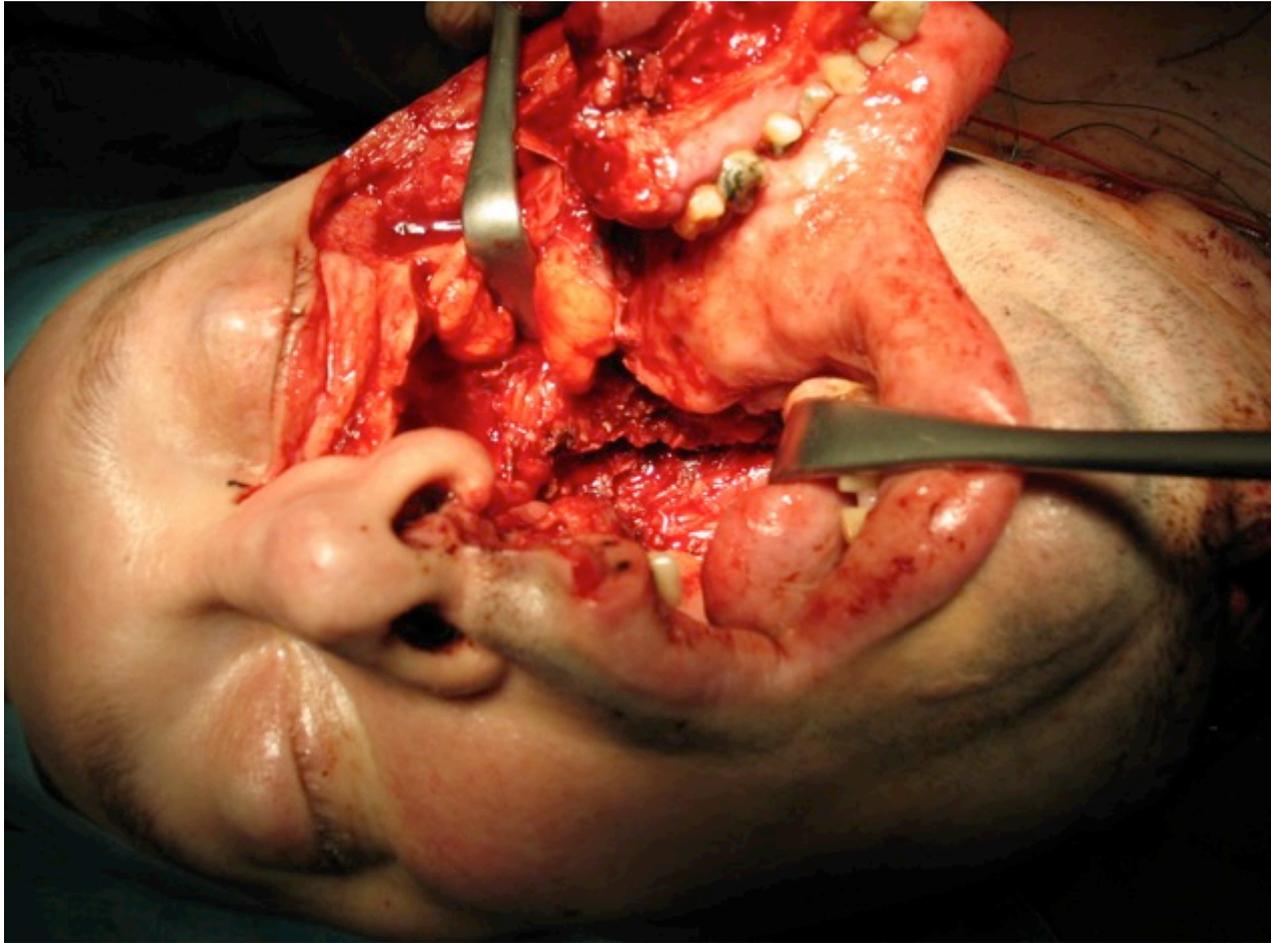
Maxillary swing incision = Weber-Fergusson incision



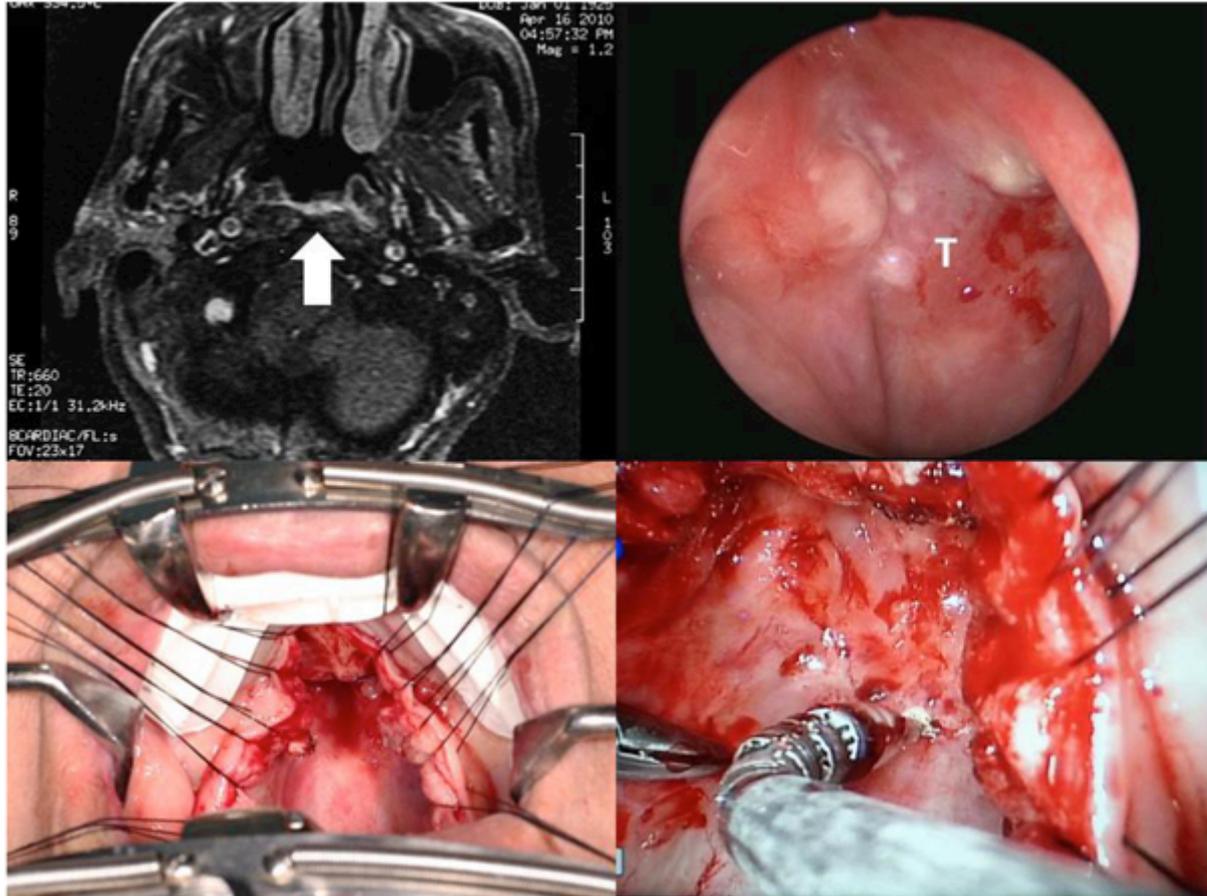
Execution of the incision



Hard palate is left attached to the cheek

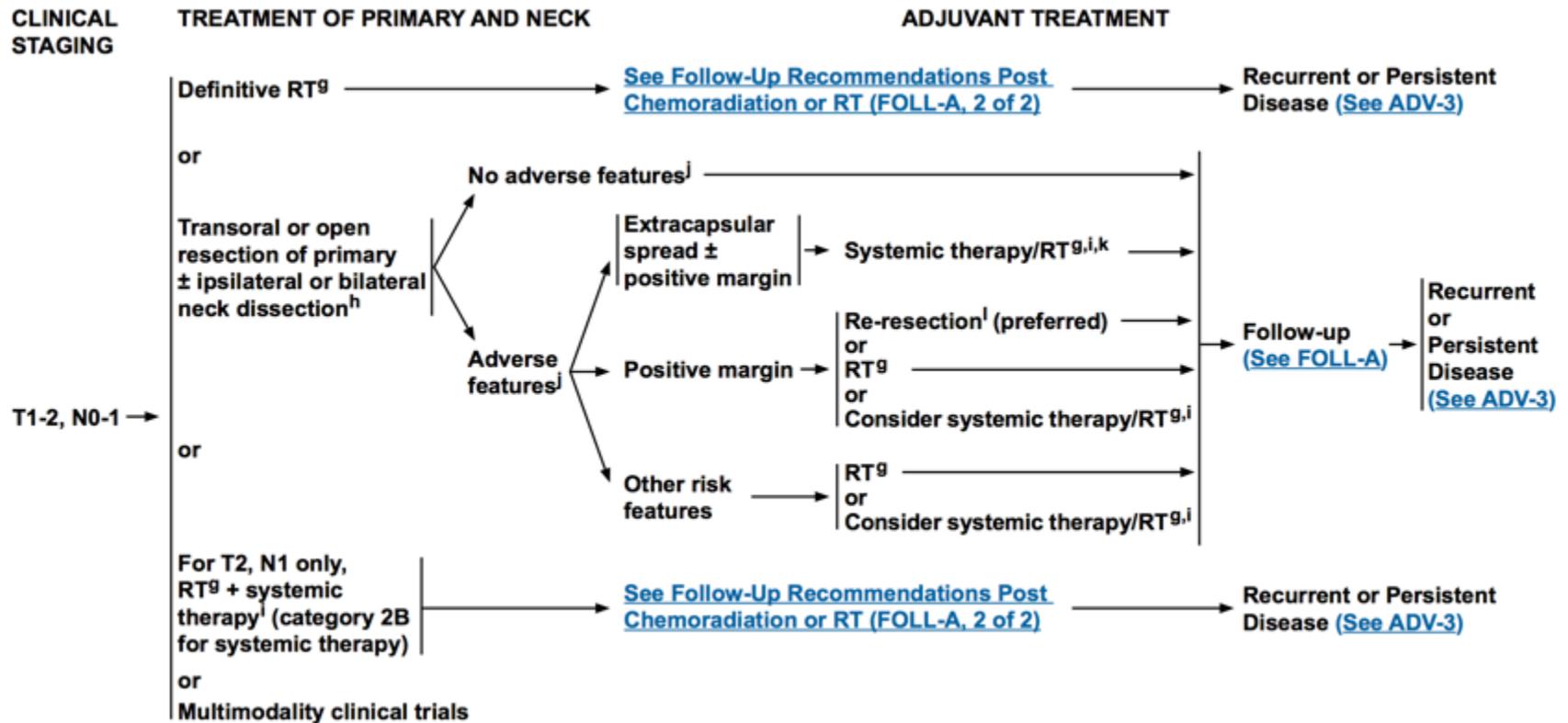


Robotic approach

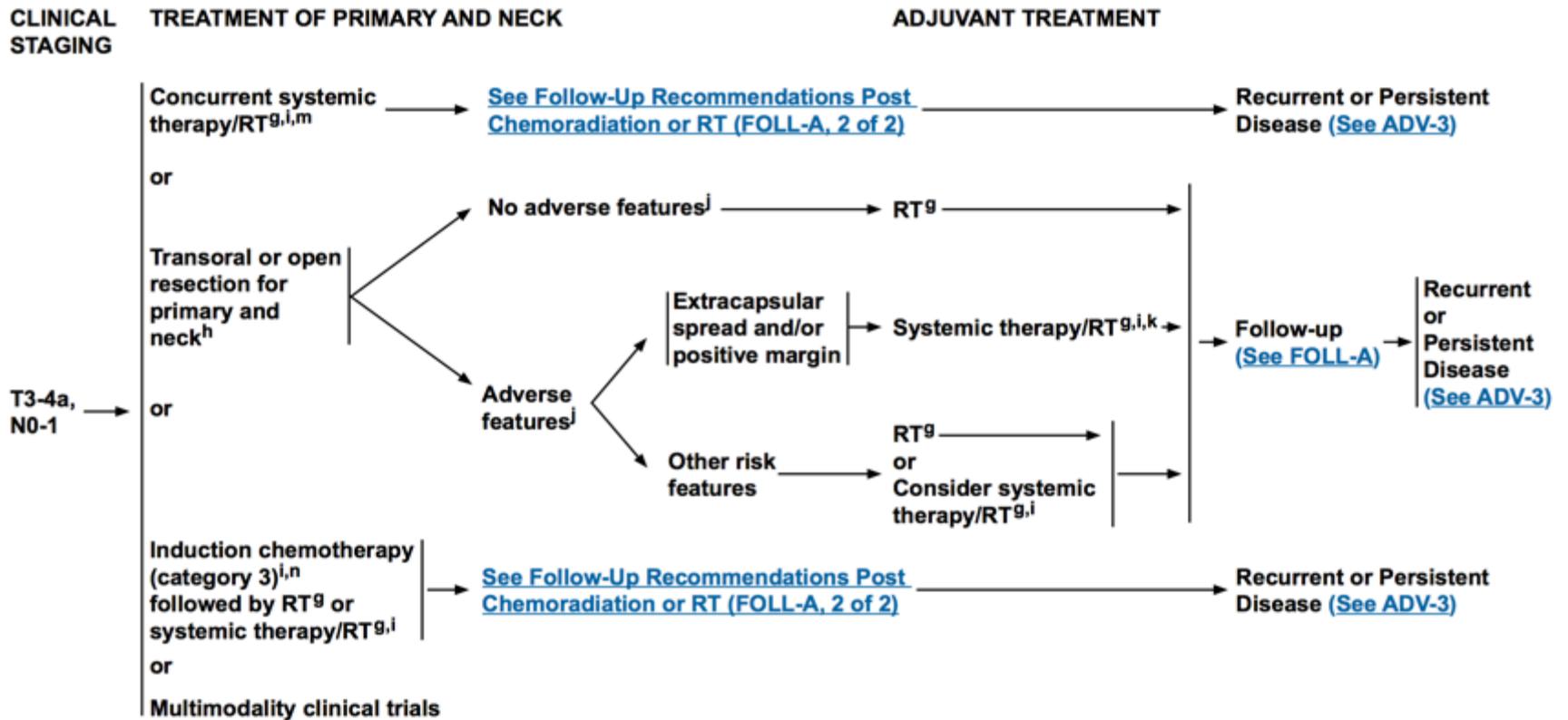


Chan et al. Oral Onc. 2014

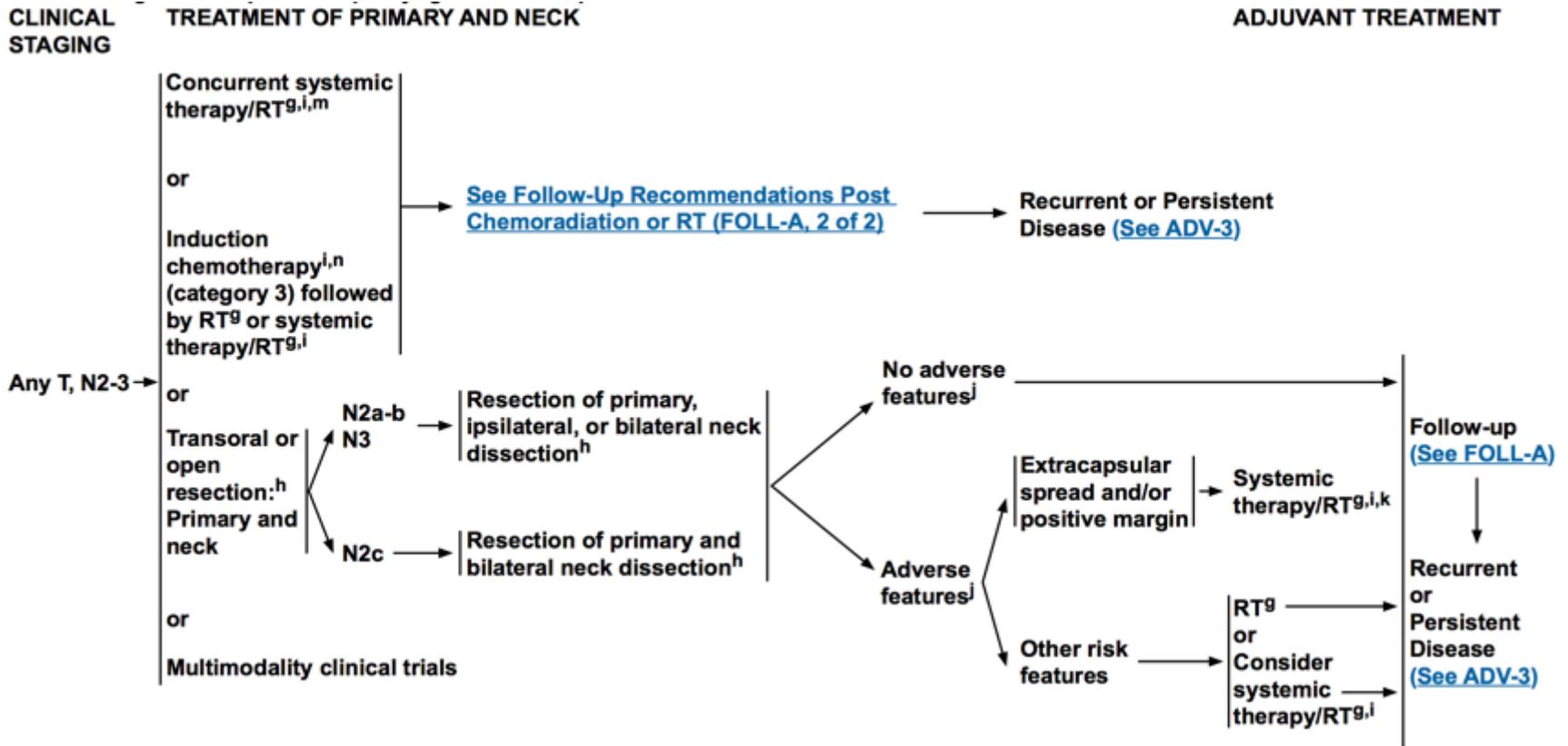
Treatment: Oropharyngeal cancers



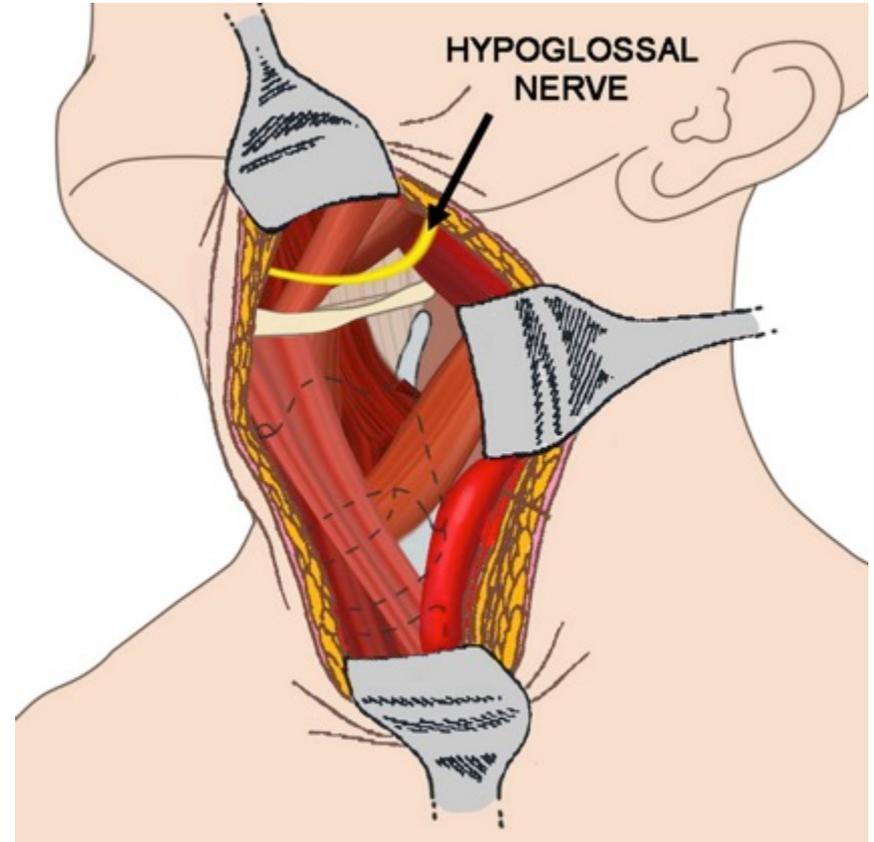
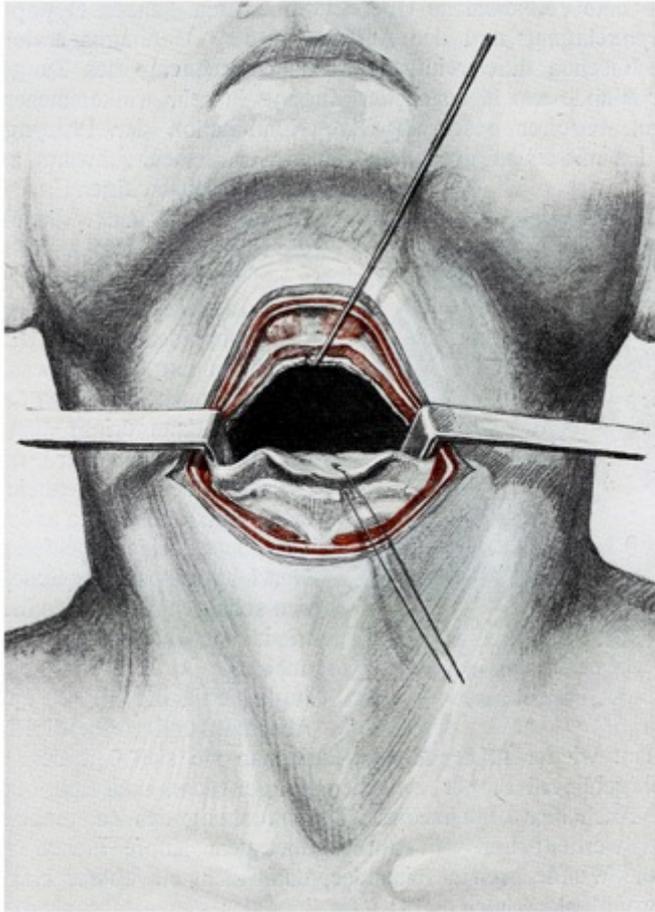
Treatment: Oropharyngeal cancers



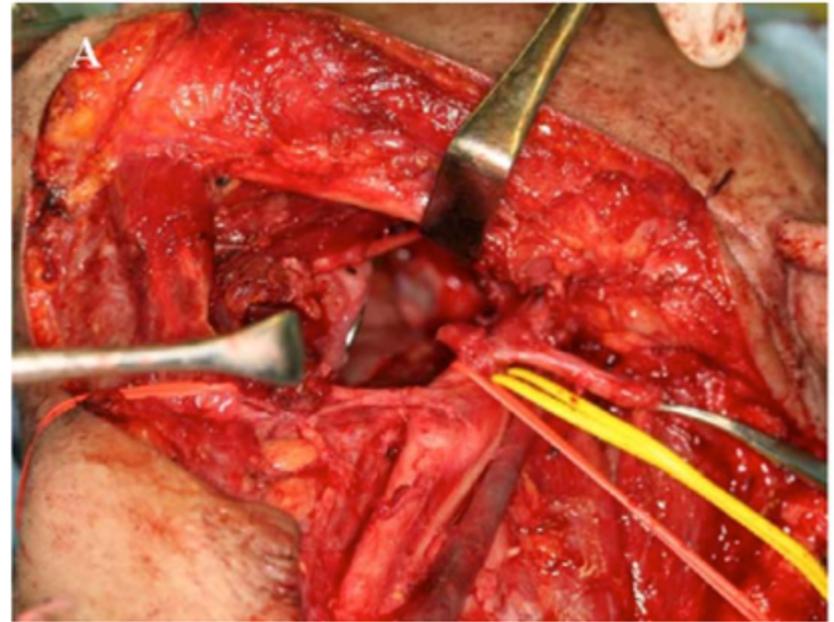
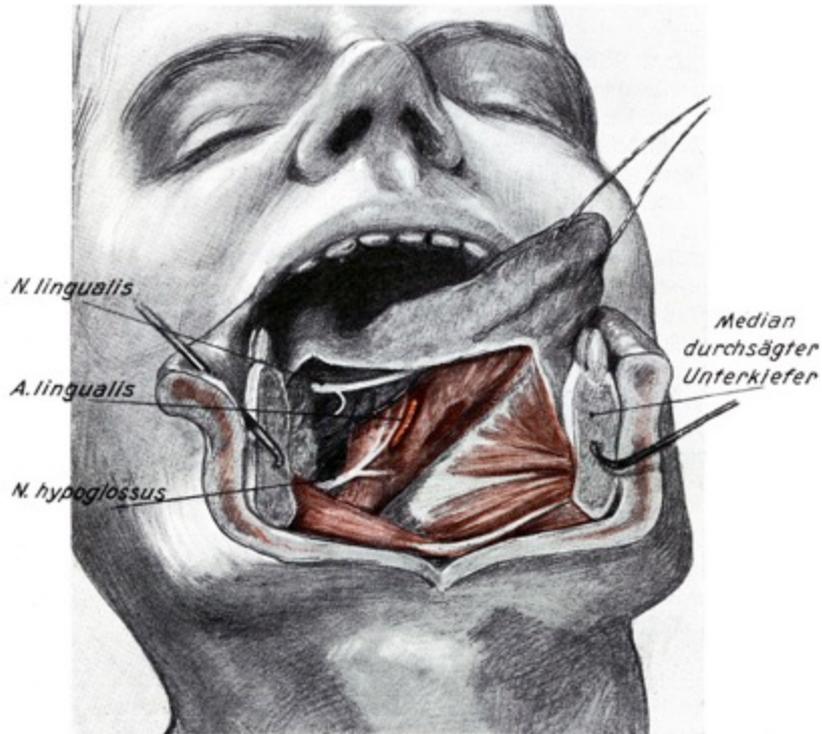
Treatment: Oropharyngeal cancers



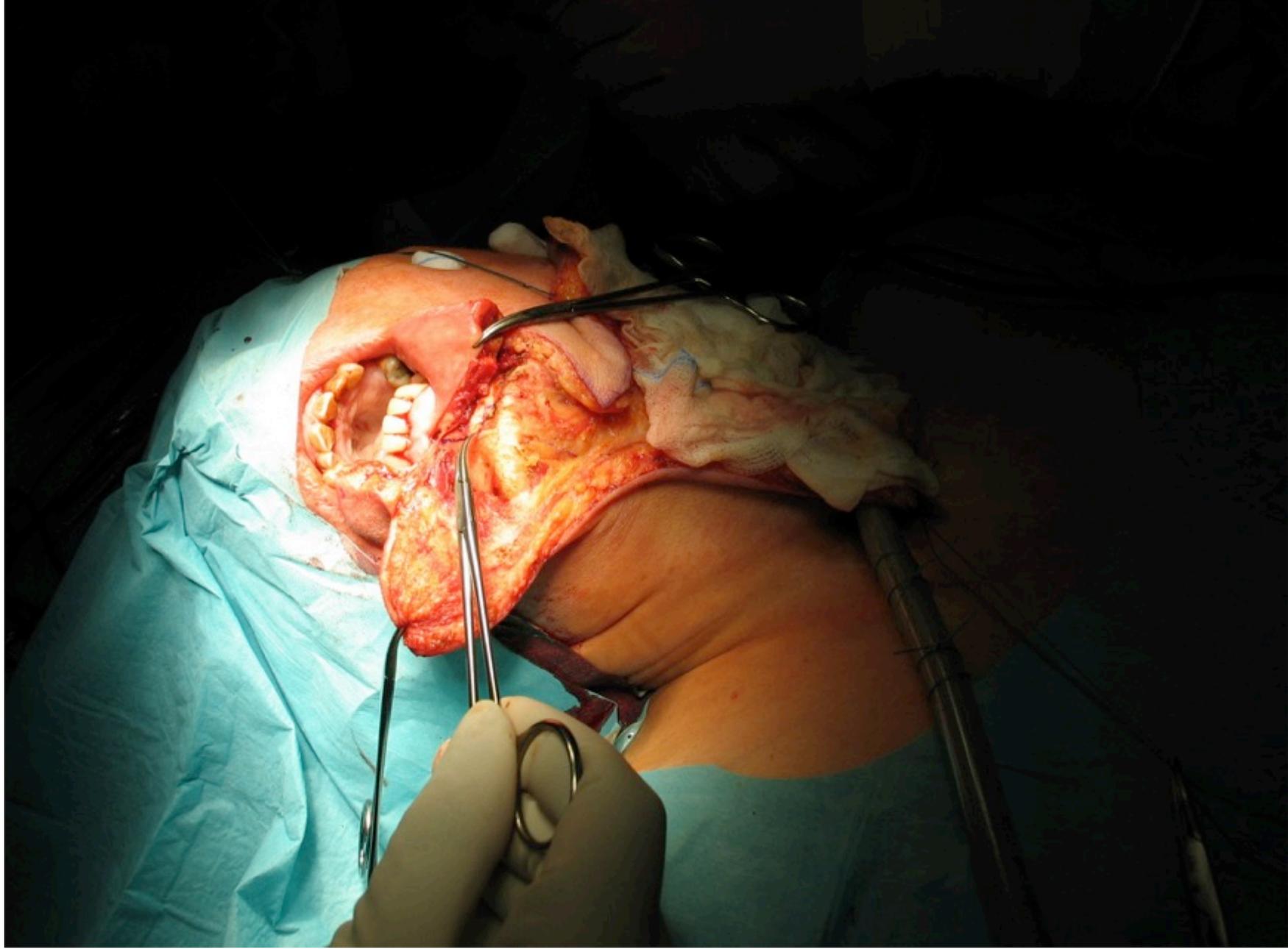
Open approach to the oropharynx: Lateral und median pharyngotomy

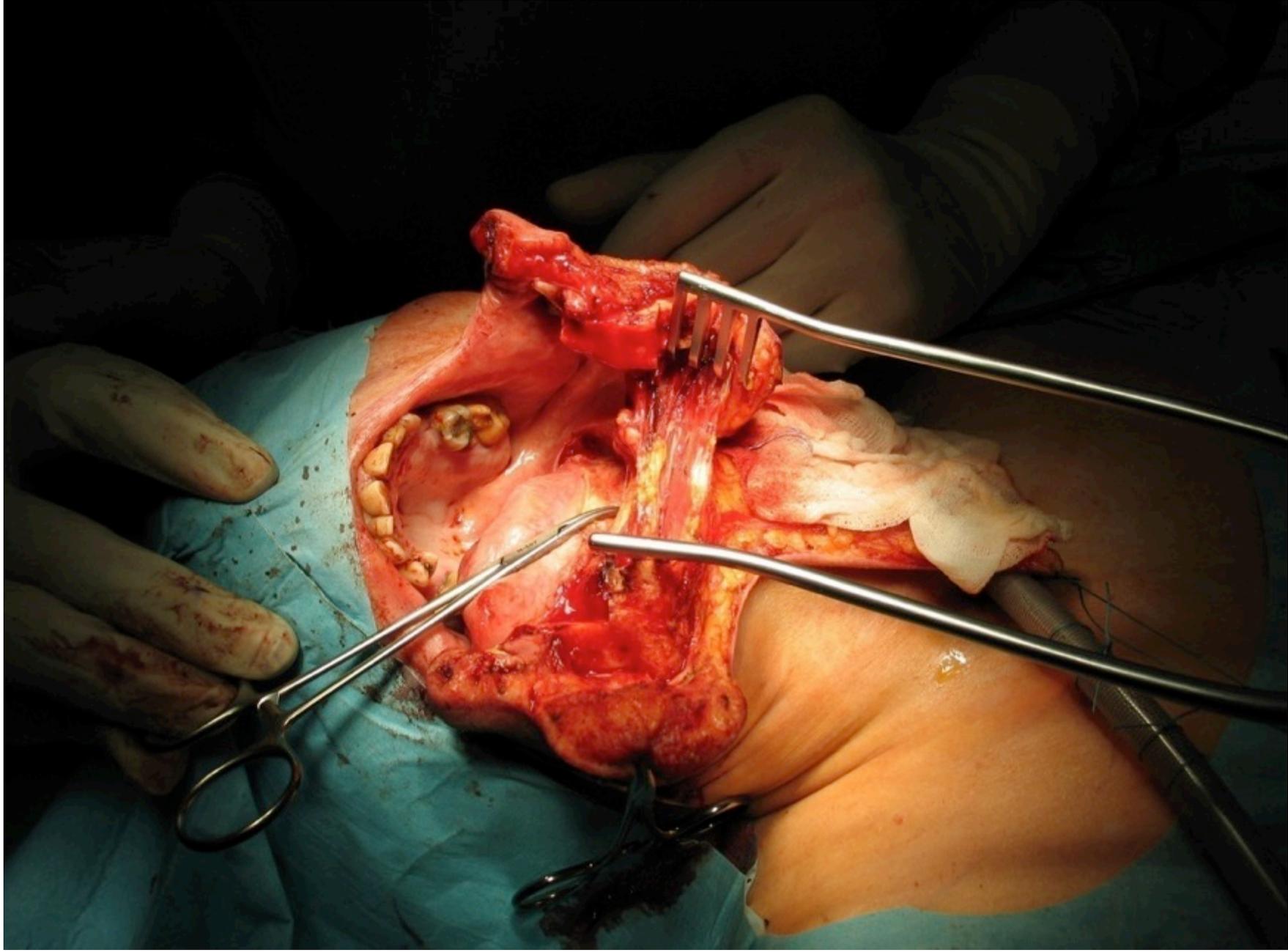


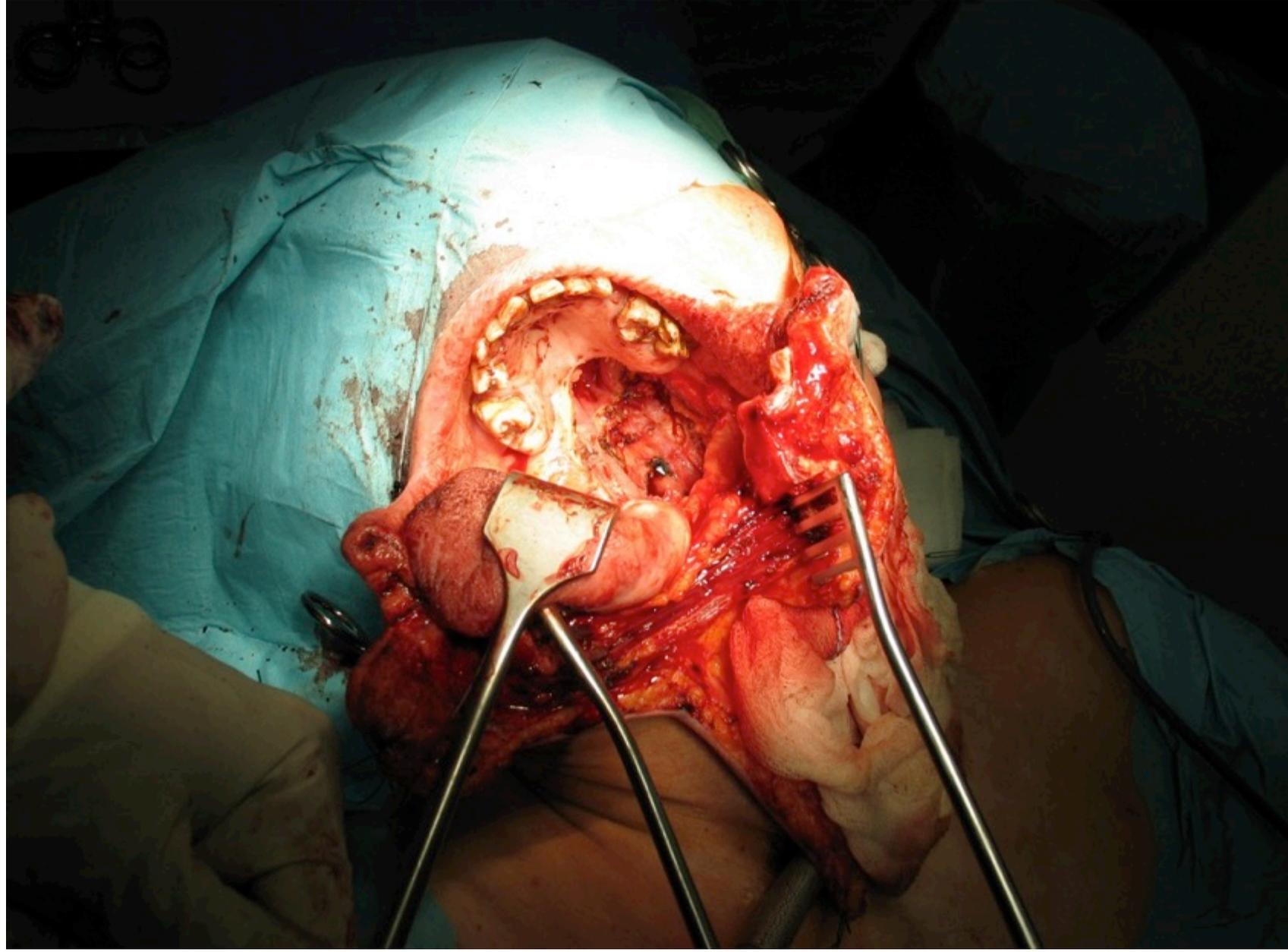
Open approach to the oropharynx: Median mandibulotomy vs. pull through



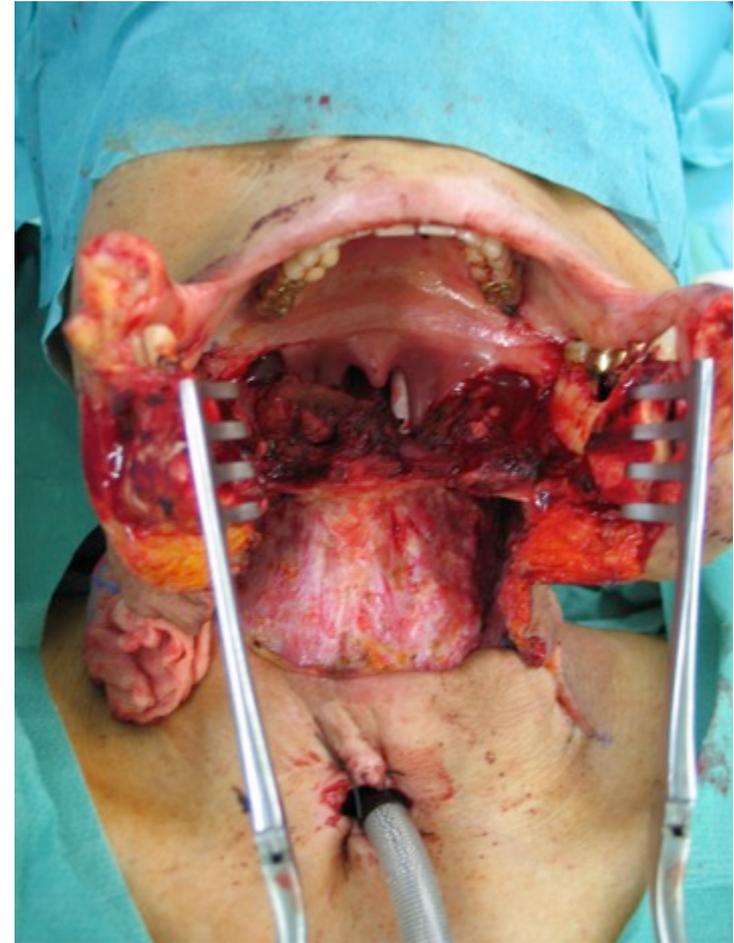
Masuda et al. *Auris Nasus Larynx* 2011







Reconstruction of the anterior $\frac{3}{4}$ of the tongue and FOM for a tongue cancer recurrence



Surgery provides similar oncological outcome for advanced OPSCCs as radiation therapy...

TABLE 3
Base of Tongue Carcinoma: Five-Year Survival^a

Institution	No. of patients	T4 (%)	Stage IV (%)	Survival (%)	
				Absolute	Cause specific
S with or without adjuvant RT					
Mayo Clinic, Rochester, MN (1960–1967) (1972) ³⁵	102	ND	7	44	ND
Washington University, St. Louis, MO (1983) ¹⁹	101	9	45	45	ND
Stanford University, Palo Alto, CA (1974–1982) (1985) ²⁰	14	0	21	51	ND
Memorial Sloan-Kettering Cancer Center, New York, NY (1979–1989) (1993) ²²	100	19	36	55	65
University of Pennsylvania, Philadelphia, PA (1997) ²³	17	41	59	46 (3 yr)	ND
Mayo Clinic, Rochester, MN (1971–1993) (1998) ²⁴	79	0	33	51	65
University of Pittsburgh, Pittsburgh, PA (1980–1987) (2000) ³⁶	87	ND	ND	49	56
Weighted average	500	11	31	49	62
RT with or without neck dissection					
Stanford University, Palo Alto, CA (1958–1980) (1983) ³⁷	64	ND	50	35	ND
Memorial Medical Center, Long Beach, CA (1988) ³⁴	70	17	57	35	60
M. D. Anderson Cancer Center, Houston, TX (1984–1992) (1995) ²⁷	54	2	63	59	65
Memorial Sloan-Kettering Cancer Center, New York, NY (1981–1995) (1998) ³⁰	68	3	51	87	ND
University of Florida, Gainesville, FL (2000) ³¹	217	19	71	50	64
Weighted average	473	14	62	52	63

ND: no data.

^a Modified from Table 3 in Mendenhall et al., 2000.³¹

...but the rate of severe complications is higher

Institution	No. of patients	T4 (%)	Boost technique	Complications (%)	
				Severe	Fatal
S with or without adjuvant RT					
M. D. Anderson Cancer Center, Houston, TX (1964–1973) (1978) ³²	34	41	NA	26	18
Indiana University, Indianapolis, IN (1983) ³⁸	8	38	NA	38	12
Washington University, St. Louis, MO (1983) ¹⁹	101	9	NA	28	4
Stanford University, Palo Alto, CA (1985) ²⁰	14	0	NA	64	0
M. D. Anderson Cancer Center, Houston, TX (1974–1984) (1990) ³	51	ND	NA	28	2
University of California, Los Angeles, CA (1990) ³⁹	13	0	NA	23	0
University of Pittsburgh, Pittsburgh, PA (1992) ⁵	14	0	NA	0	0
Memorial Sloan-Kettering Cancer Center, New York, NY (1979–1989) (1993) ²²	100	19	NA	ND	0
Mayo Clinic, Rochester, MN (1971–1986) (1993) ²	55	0	NA	49	4
University of Pennsylvania, Philadelphia, PA (1997) ²³	17	41	NA	29	0
Weighted average	407	15		32	3.5
RT with or without neck dissection					
Stanford University, Palo Alto, CA (1956–1973) (1976) ⁴⁰	104	ND	EBRT	7	1
M. D. Anderson Cancer Center, Houston, TX (1954–1971) (1976) ²⁵	174	17	EBRT	3	0
Stanford University, Palo Alto, CA (1974–1982) (1985) ²⁰	14	14	¹⁹² Ir	7	0
Memorial Medical Center, Long Beach, CA (1988) ³⁴	70	17	¹⁹² Ir	6	0
M. D. Anderson Cancer Center, Houston, TX (1974–1984) (1990) ³	121	ND	EBRT	2	0
M. D. Anderson Cancer Center, Houston, TX (1984–1992) (1995) ²⁷	54	2	EBRT	0	0
William Beaumont Hospital, Royal Oak, MI (1996) ²⁹	20	25	¹⁹² Ir	10	0
Memorial Sloan-Kettering Cancer Center, New York, NY (1981–95) (1998) ³⁰	68	3	¹⁹² Ir	3	0
University of Florida, Gainesville, FL (2000) ³¹	217	19	EBRT	4	1
Weighted average	842	14	—	3.8	0.4

NA: not applicable; ND: no data; EBRT: external beam radiation therapy; ¹⁹²Ir: iridium-192 interstitial brachytherapy; boost: S: surgery; RT: radiation therapy

Types of trans-oral surgery (TOS)

- Conventional trans-oral approach
- Trans-oral robotic surgery (TORS)
- Trans-oral laser microsurgery (TLM)

Differences between TLM and TORS

TLM



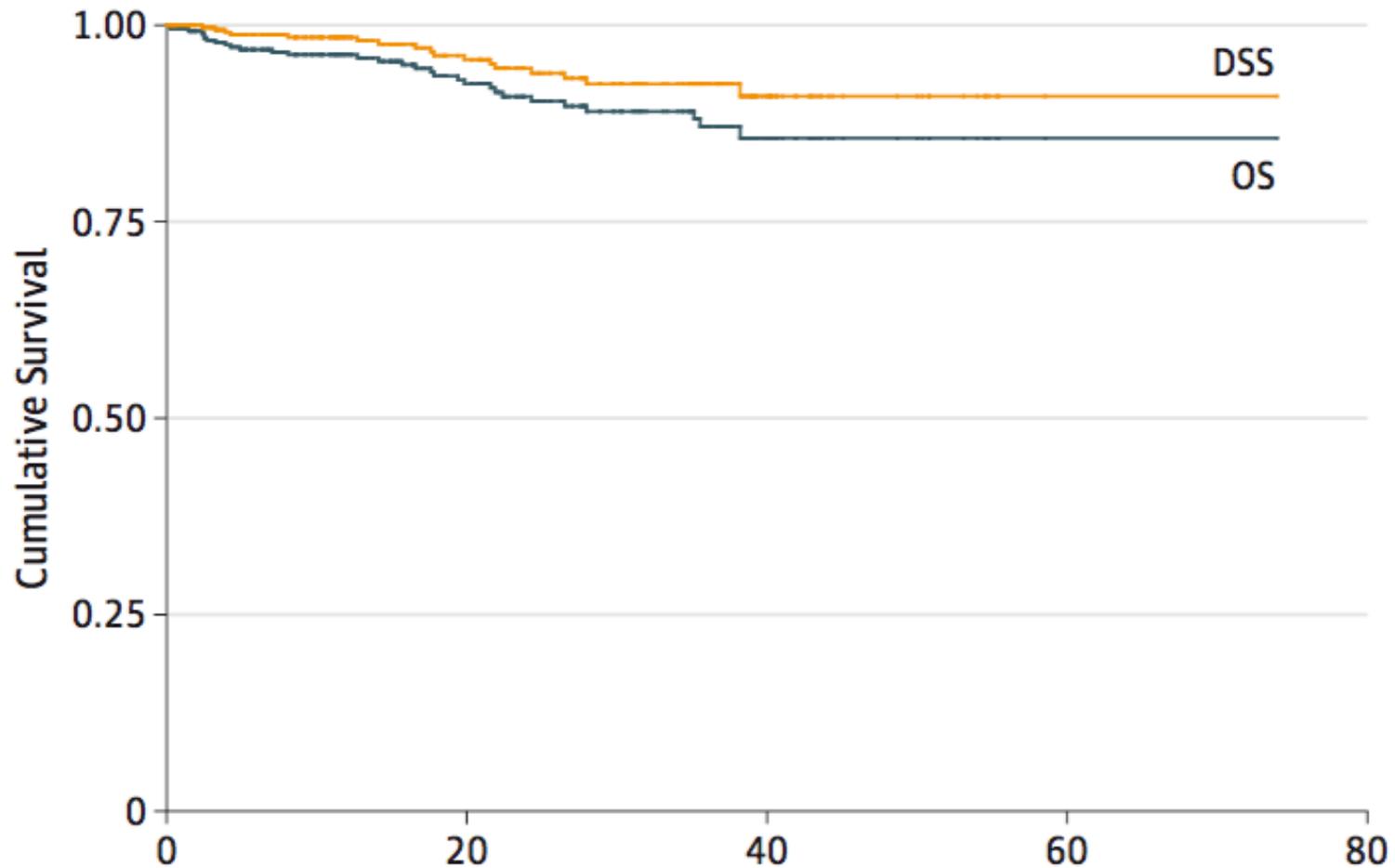
microscope

TORS



Robot with endoscope

Experience with TORS in patients with OPCs

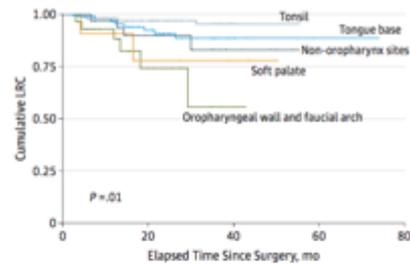


de Almeida, JAMA Otolaryngol Head Neck Surg; 2015

Parameters influencing LRC

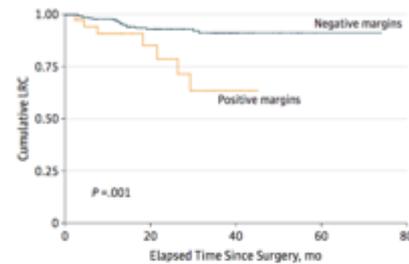
Figure 1. Locoregional Control (LRC) for Patients Treated With Transoral Robotic Surgery (TORS)

A LRC in patients with oropharyngeal cancer treated with TORS



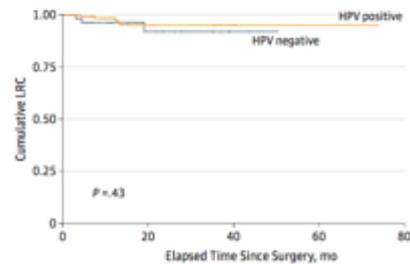
No. at risk	0	20	40	60
Non-OP sites	40	21	5	0
Tongue base	128	59	11	1
OP wall and faucial arch	33	8	1	0
Soft palate	14	5	3	0
Tonsil	181	86	17	0

B LRC by pathologic margin status



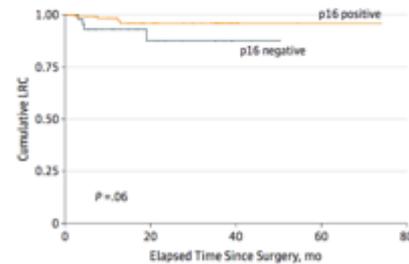
No. at risk	0	20	40	60
Negative margin	342	160	34	1
Positive margin	39	15	3	0

C LRC by HPV status in patients with oropharyngeal cancer treated with TORS



No. at risk	0	20	40	60
HPV negative	67	21	3	0
HPV positive	155	70	16	1

D LRC by p16 status in patients with oropharyngeal cancer treated with TORS



No. at risk	0	20	40	60
p16 negative	58	16	2	0
p16 positive	154	64	13	1

Locoregional control by oropharyngeal subsite in all patients and pathologic margin status, human papillomavirus (HPV) status, and p16 status in patients with oropharyngeal primary tumors.

Functional outcome with TORS/TLM and adjuvant (C)RT

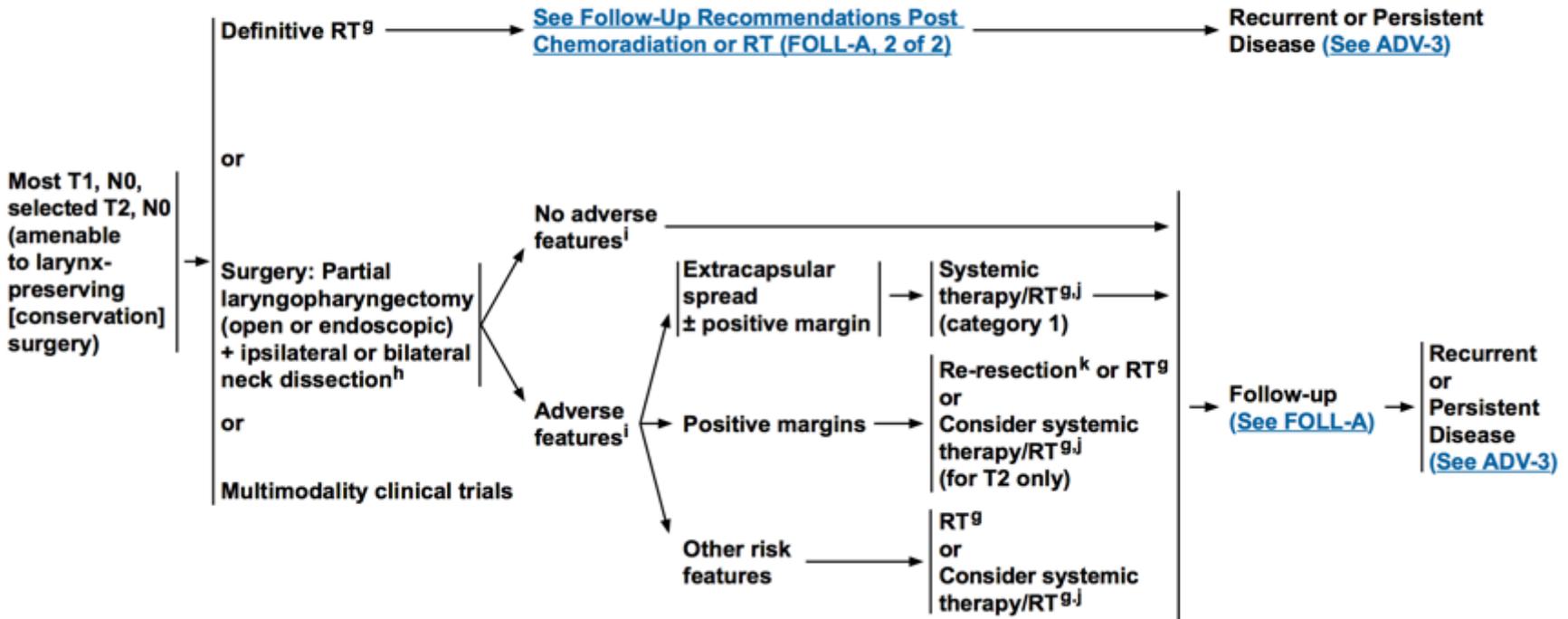
	TORS/ TLM	TNM	Adj. tx	Functional outcome 1Y
Morisod 2017	TORS	T1-2/N0-2c (No ECS, 45% secondary primaries)	CRT 3% / RT 28%	FOSS back to 0-2 in 70%
Choby 2015	TORS	T1-3/N0-2c	CRT 0%/ RT 0%	UW_QOL for swallowing at 100/100
Chen 2014	TORS/TLM	T1-3/N1-2c	RT 100%	UW_QOL for swallowing at 91.5/100
Sinclair 2011	TORS	T1-2/N0-2c	CRT 31% / RT 45%	MDADI from pre-tx 82 to post-tx 74
Genden 2011	TORS	T1-2/N0-2c	CRT 60% / RT 20%	PSS-HN and FOIS back to baseline
Leonhardt 2012	TORS	T1-4/N0-2b	CRT 19% / RT 60%	PSS-HN back to baseline for diet and eating, reduced for speech
More 2012	TORS	T1-3/N0-2c	CRT 60% / RT 20%	MDADI back to baseline
Haughey 2011	TLM	T1-4/N0-3	CRT 16% / RT 58%	FOSS back to 0-2 in 87%
Grant 2006	TLM	T1-4/N0-3	CRT 0% / RT 47%	FOSS back to baseline

Treatment: Hypopharyngeal cancers

CLINICAL STAGING

TREATMENT OF PRIMARY AND NECK

ADJUVANT TREATMENT



Treatment: Hypopharyngeal cancers

CLINICAL STAGING

T2-3, any N
(if requiring [amenable to] pharyngectomy with partial or total laryngectomy); T1, N+

TREATMENT OF PRIMARY AND NECK

Induction chemotherapy^{j,l} → CT or MRI (with contrast) of primary site/neck

or

Partial or total laryngopharyngectomy + neck dissection,^h including level VI

No adverse featuresⁱ

Adverse featuresⁱ

Extracapsular spread and/or positive margin

Other risk features

ADJUVANT TREATMENT

[See Response After Induction Chemotherapy \(HYPO-4\)](#)

Systemic therapy/RT^{g,j}
(category 1)

RT^g
or
Consider systemic therapy/RT^{g,j}

Follow-up
([See FOLL-A](#))

Recurrent or Persistent Disease
([See ADV-3](#))

Concurrent systemic therapy/RT^{g,j,m}

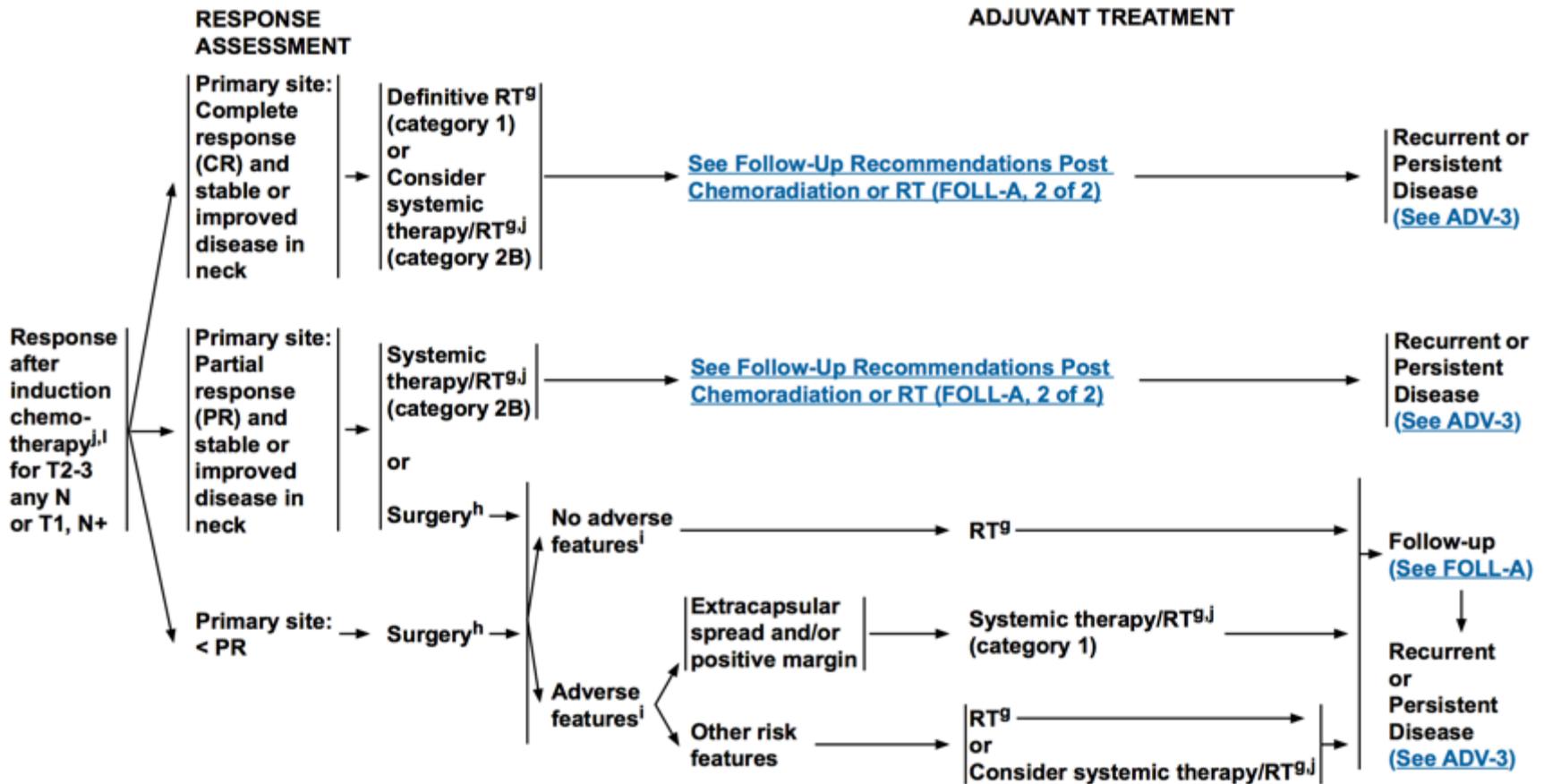
[See Follow-Up Recommendations Post Chemoradiation or RT \(FOLL-A, 2 of 2\)](#)

Recurrent or Persistent Disease
([See ADV-3](#))

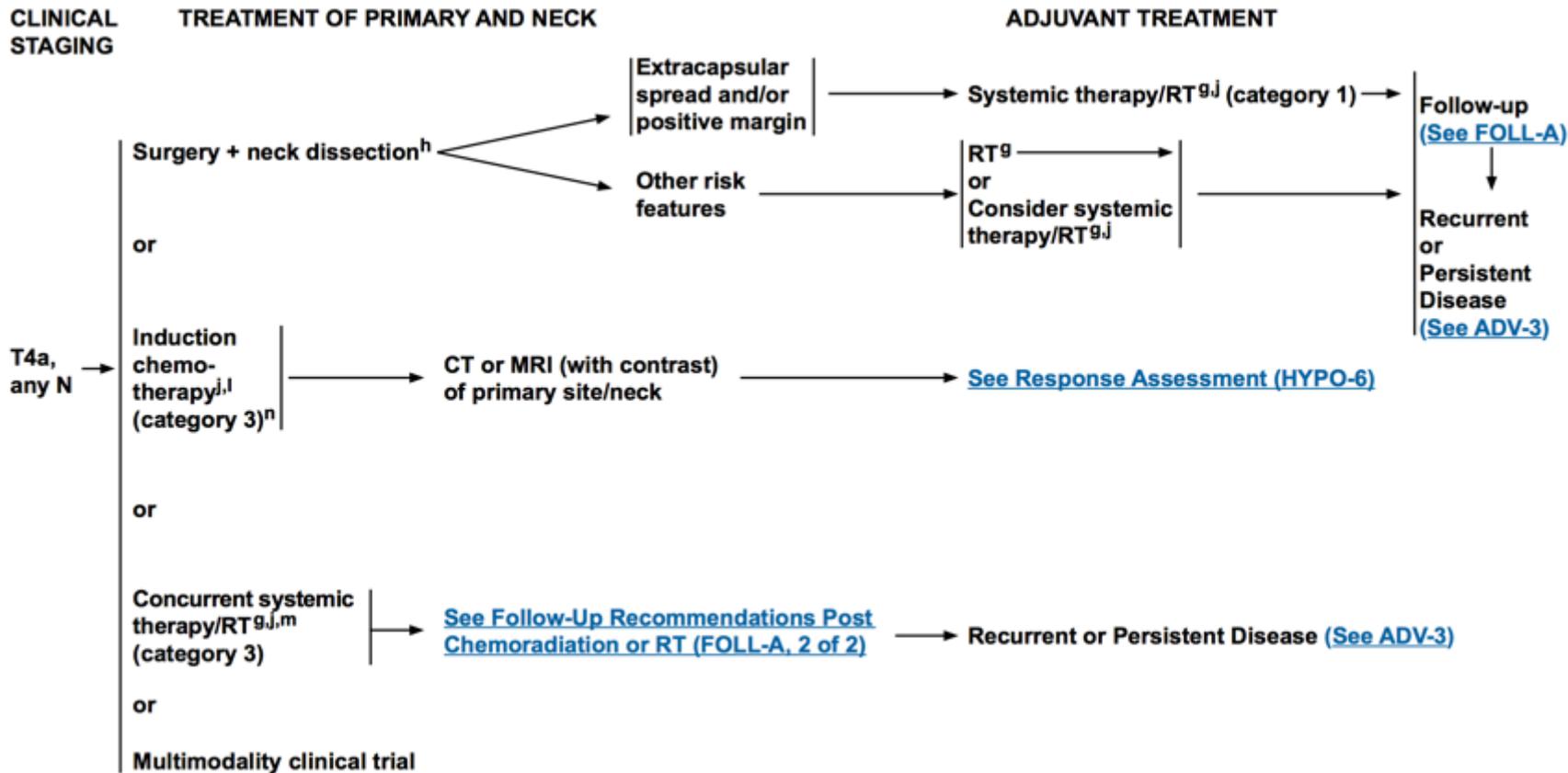
or

Multimodality clinical trials

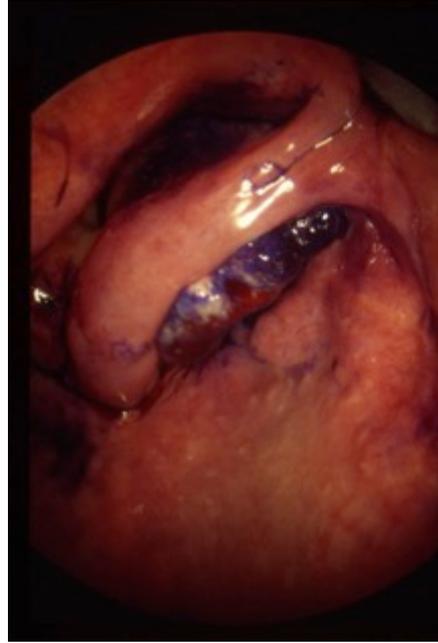
Treatment: Hypopharyngeal cancers



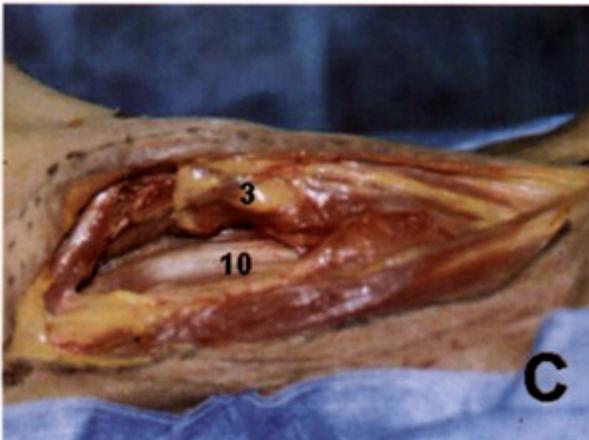
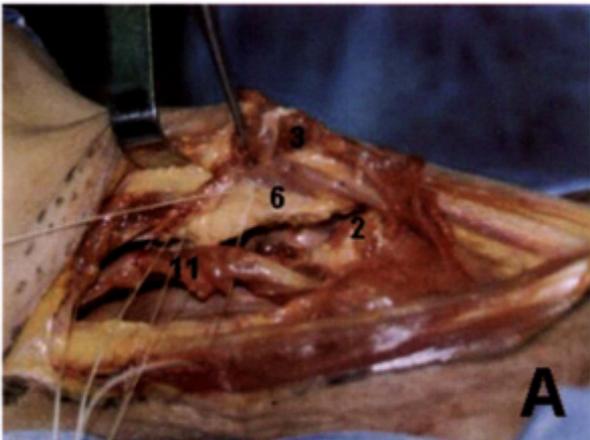
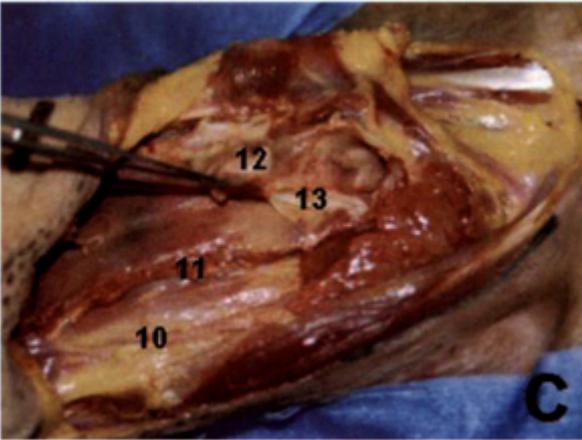
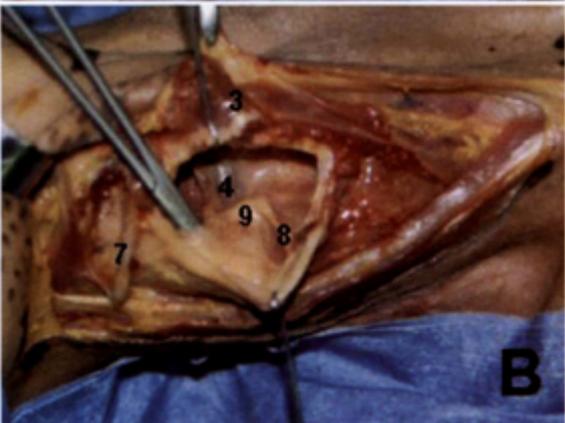
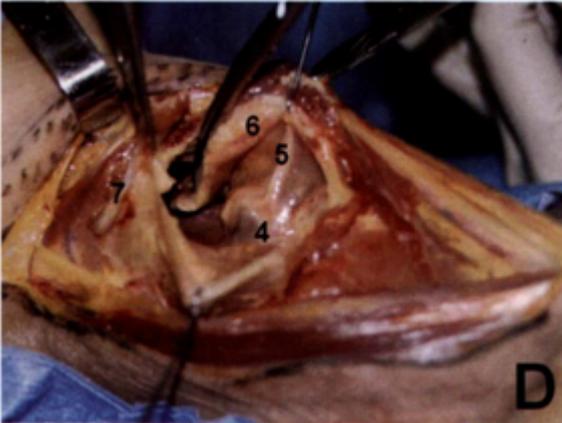
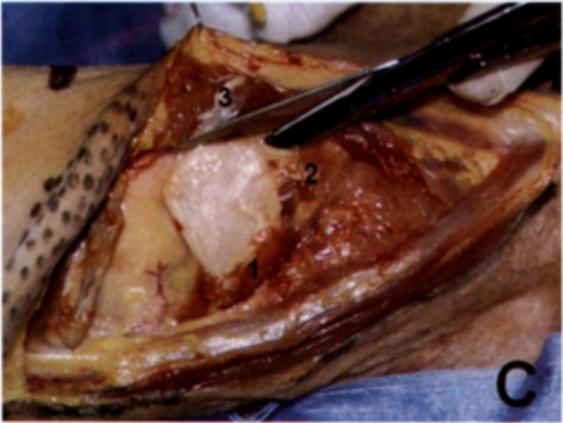
Treatment: Hypopharyngeal cancers



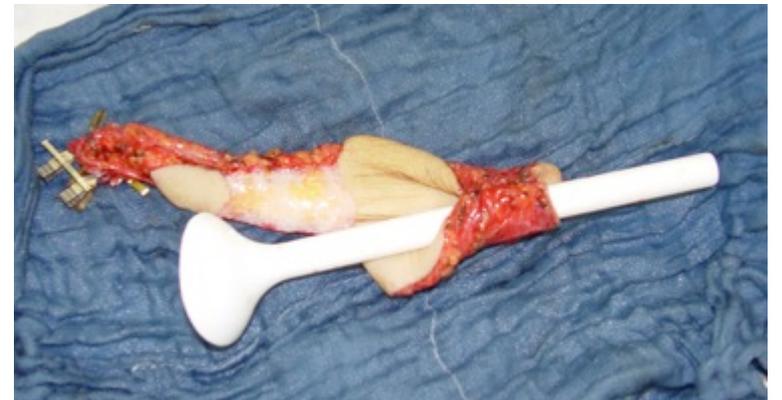
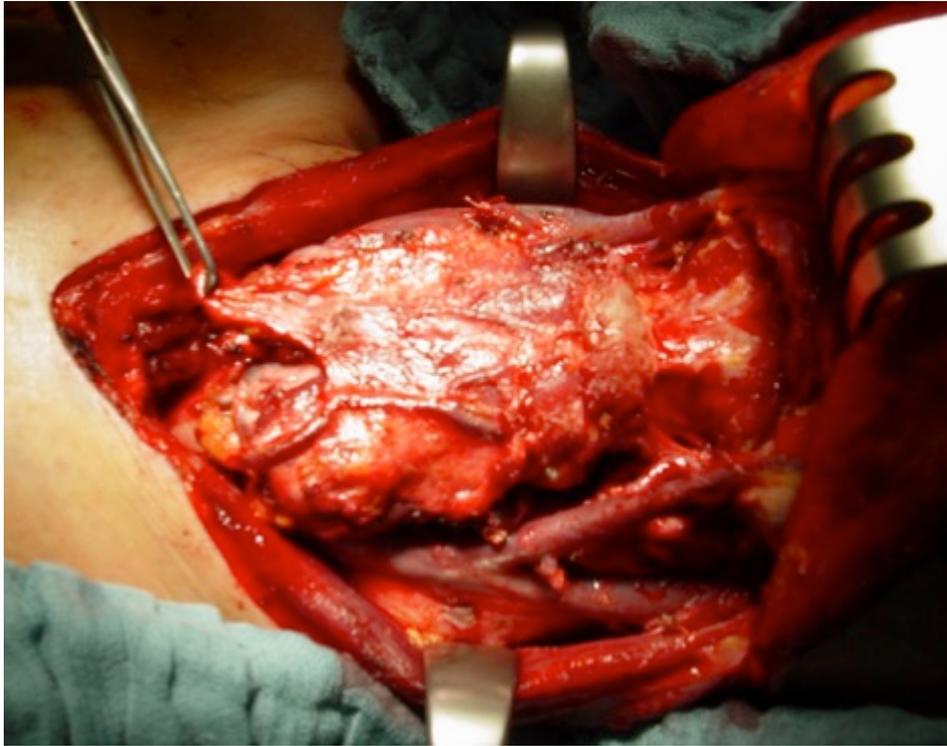
Laser surgery

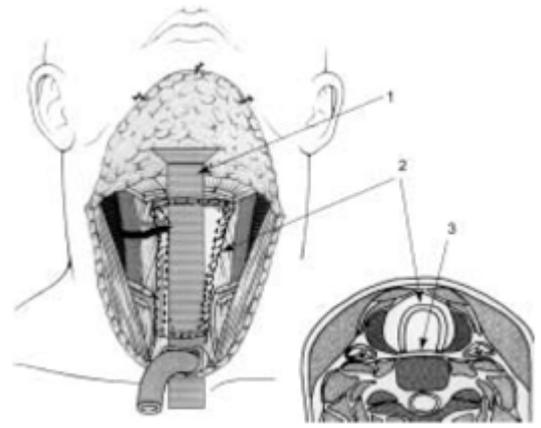
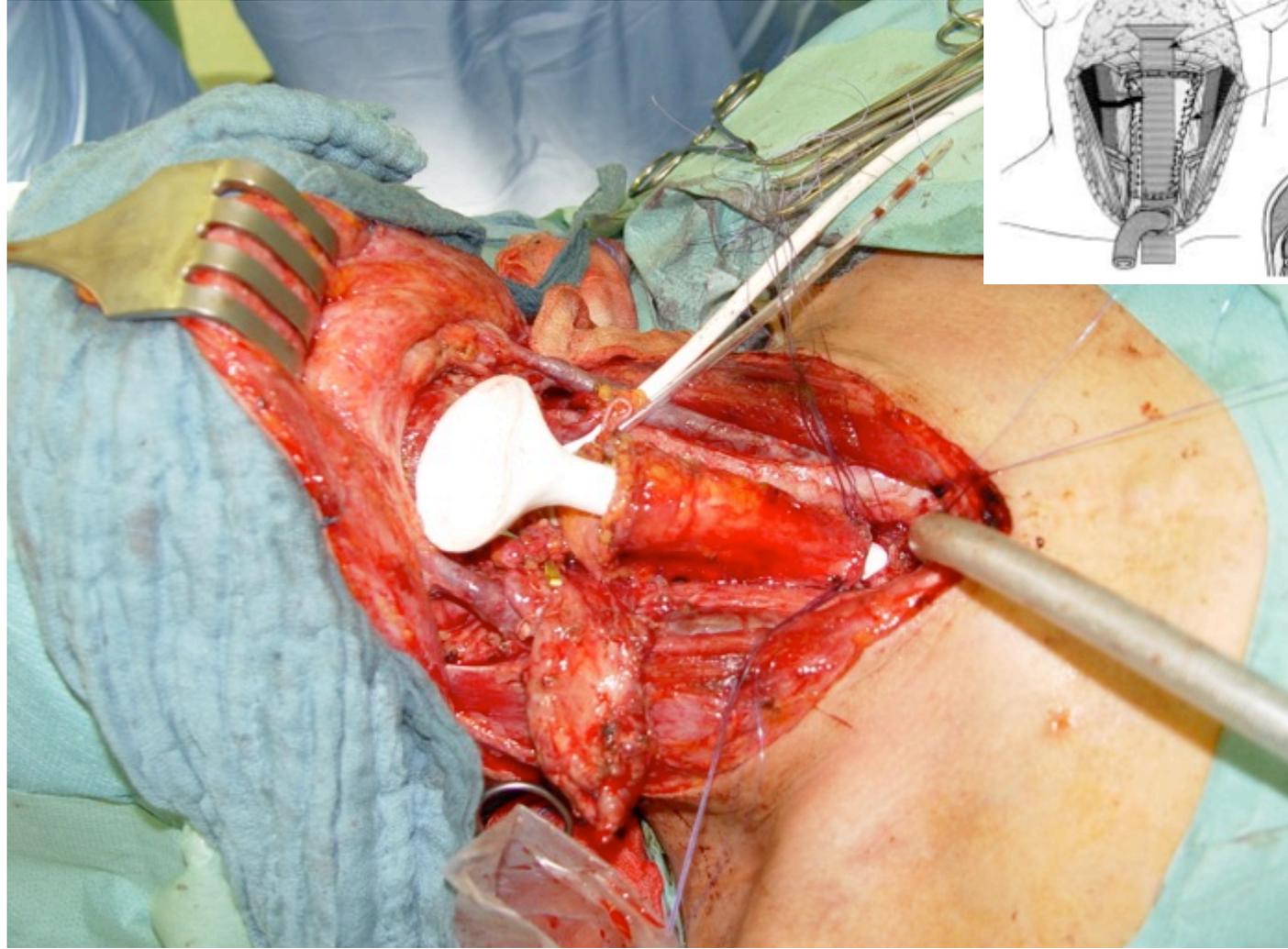


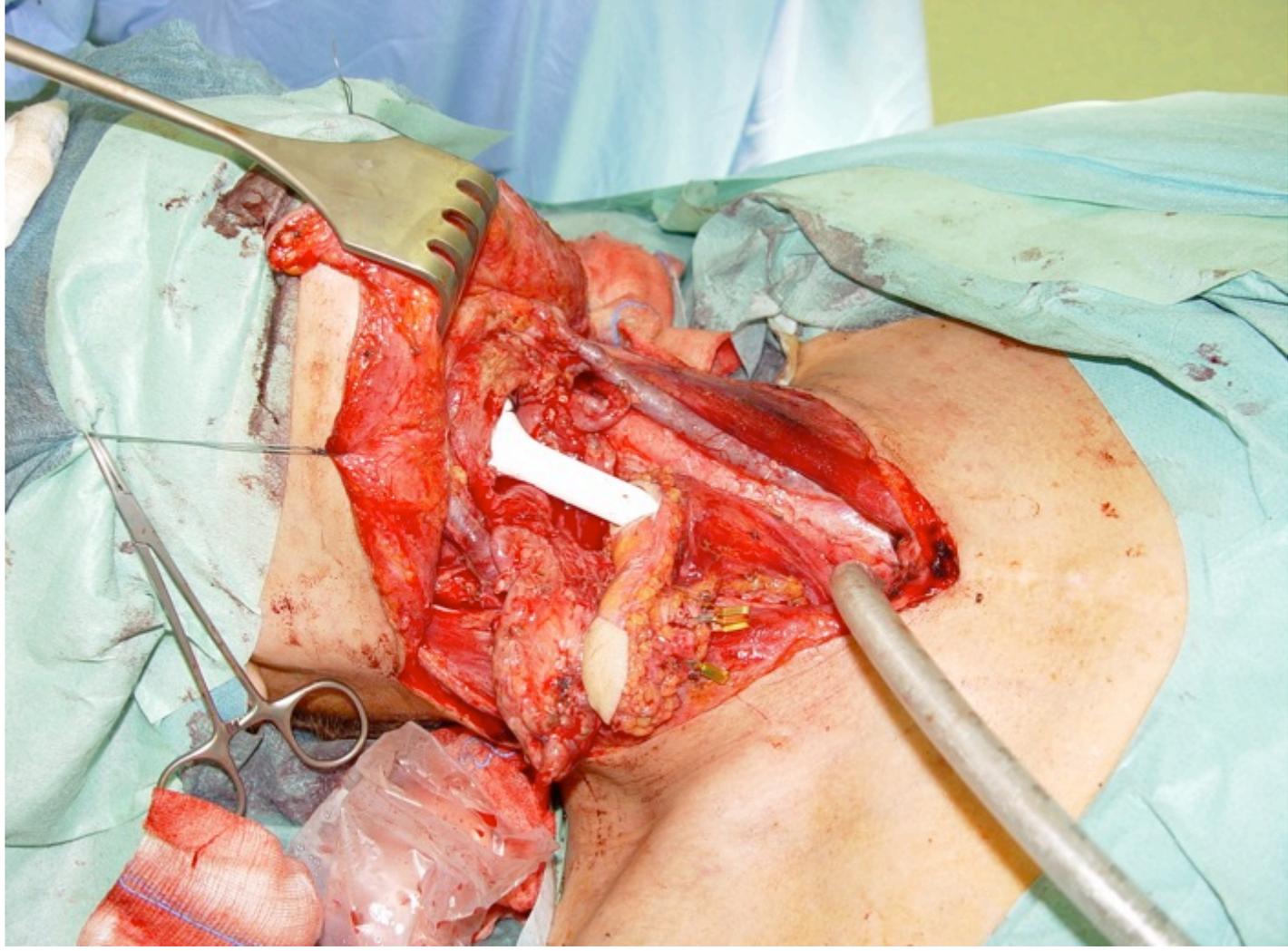
Partial laryngo-pharyngectomy



Total laryngo-pharyngectomy







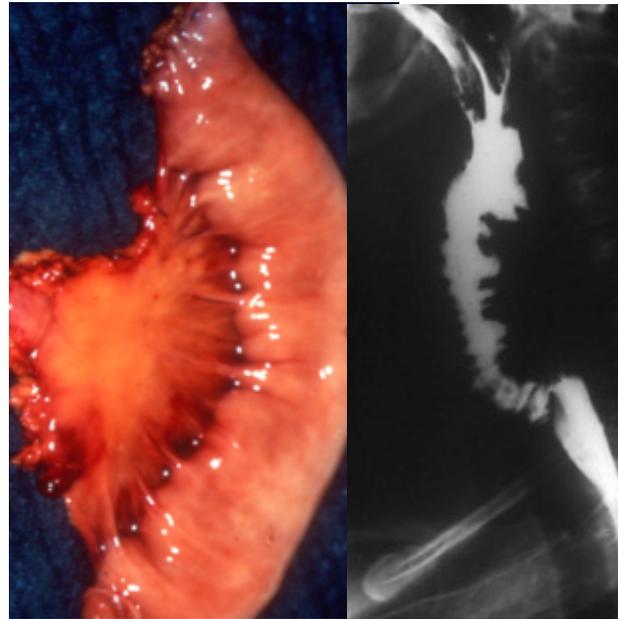
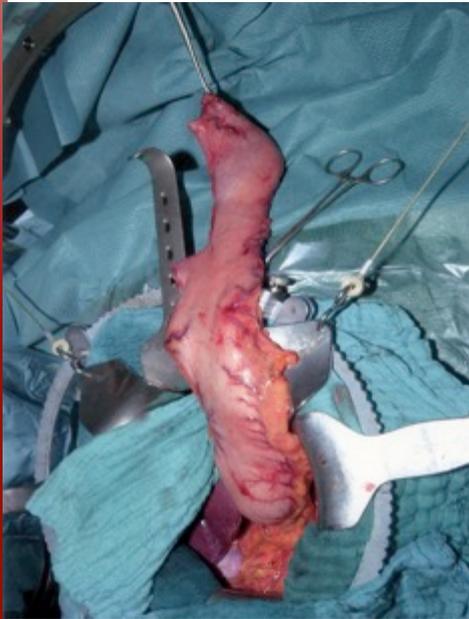


Options for the reconstruction of total laryngo-pharyngectomy defects

1. Gastric pull-up

2. Jejunum

3. RFF, ALT



Büchler et al. (1996) J
Am Coll Surg 182:
241-245

- Thank you for your attention

