TAIPEI VETERANS GENERAL HOSPITAL PRACTICES GUIDELINES IN ONCOLOGY

Head and Neck Cancers

Cancer of the Oral Cavity

Cancer of the Oropharynx

Cancer of the Hypopharynx

Cancer of the Larynx

Salivary Gland Tumors

Occult Head & Neck Primaries

v.1. 2021.09.09

Table of Content

Multidisciplinary Team

- **Surgical Oncologist specialized in Oral Cancers**
  - Otorhinolaryngologist (ENT)
  - Oral and maxillofacial surgeon (OS)
  - Plastic and reconstructive surgeon (PS)
- **Radiation Oncology**
  - Radiation Oncologist; Radiation Physicist; Radiation Technologist
- **Medical Oncology**
- **Pathology**
- **Diagnostic Radiology**
- **Nuclear Medicine**
- **Dentistry/Prosthodontics**
- **Speech & Swallowing Therapy**
- **Specialized Nursing Care**
- **Social Workers**
- **Nutritional Support**

Head and Neck Cancer* Panel Members

(*Nasopharyngeal, sinonasal cancer are not included*)

- **Surgical Oncology**

  Otorhinolaryngologist :

  – 朱本元†；戴世光§ ；王怡芬；許彥彬；李宗倫；張嘉帆

  Oral and Maxillofacial Surgeon:

  – 高壽延 ；雷文天；羅文良 ；吳政憲§；楊政杰；成函潔

- **Radiation Oncology**

  – 王令瑋§ ；蕭正英§ ；黃品逸；藍耿立；陳一瑋；胡育文；吳元宏

- **Medical Oncology**

  – 陳盛鈺§ ；楊慕華¶§ ；張牧新

- **Diagnostic Radiology**

  – 凌憬峯

- **Nuclear Medicine**

  – 黃文盛；張智勇

- **Pathology**

  – 郭盈汝

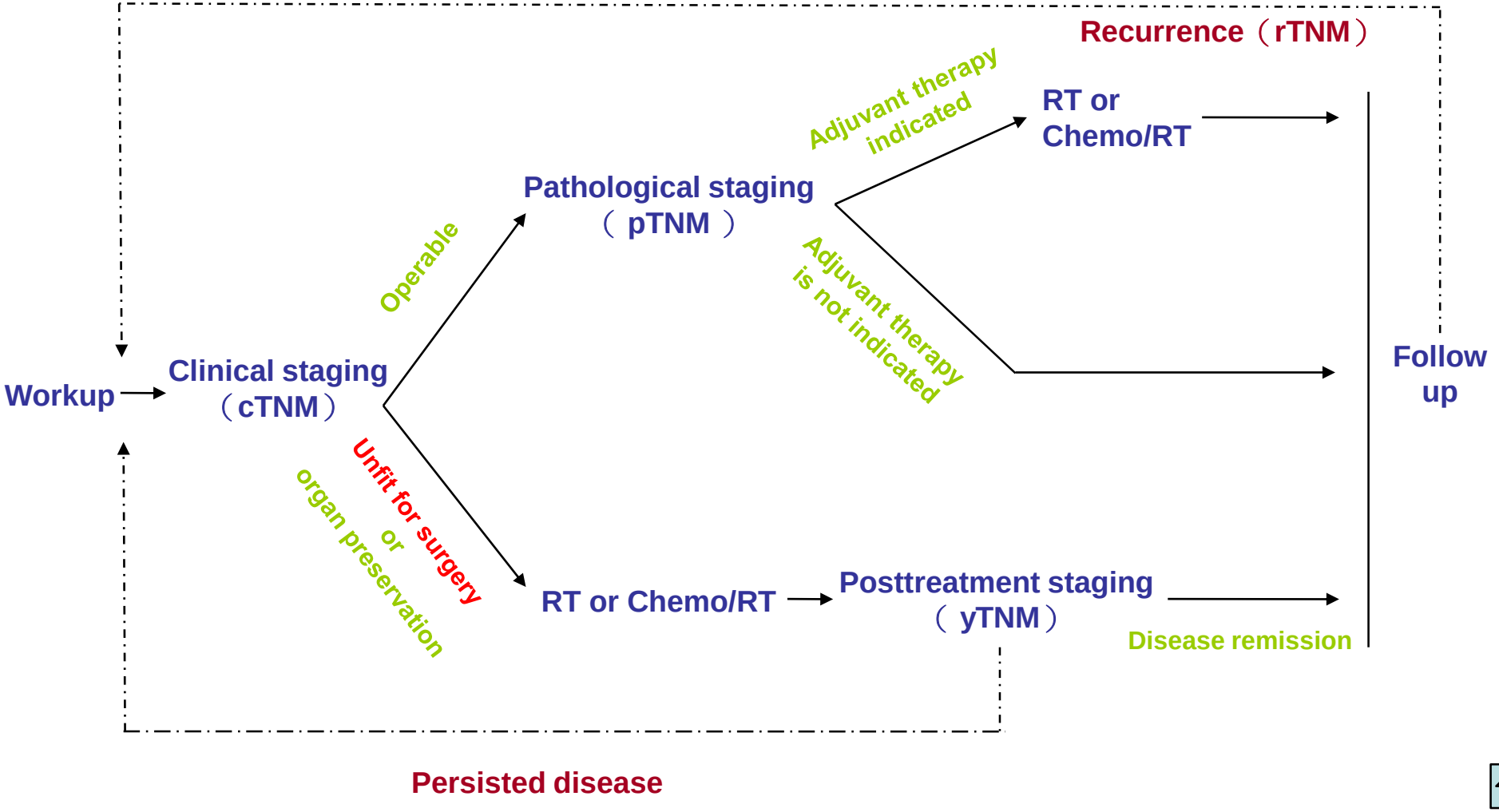
† 團隊召集人
¶ 副團隊召集人
§ 編輯委員

Pretreatment Workup

- **H&P**（under anesthesia if indicated）
- **Biopsy**（under anesthesia if indicated）
- **Primary site survey：Face CT / MRI[a]**
- **Metastasis survey：**
  - **Chest x-ray / CT[b]**
  - **Whole abdomen sonography**（optional for T1-2N0）
  - **Whole body bone scan**（optional for T1-2N0）
  - **PET/CT[c]**（optional for stage III-IV）
- **Dental/prosthodontic evaluation and prophylaxis[d]：**
  - **including Panoramic film**
- **ENT evaluation[e]：**
  - **endoscopic exam**
  - **speech and swallow evaluation**（optional）
- **Preanesthesia studies**
- **A multidisciplinary consultation as indicated[f]**
- **Establish of aggressive nutritional support[g]**

[a] MRI exam is recommended for primary sites located in tongue, mouth floor or category as T4b cases.
[b] Chest CT should be considered for patients at high risk for advanced nodal disease lung metastasis.
[c] PET/CT is an alternative systemic survey for metastasis.
[d] Dental prophylaxis including：full mouthultrasonic scaling, prophylactic extraction, fluoride carrier fabrication and oral hygiene instruction.
[e] Consult ENT for endoscopic examination of oropharyngeal extension or possible second primary lesion.
[f] Propose to “Head and Neck Cancer Combined Conference” under following situation: difficult to make diagnosis and treatment plan cases.
[g] Nasogastric or gastrostomy feeding tube if body weight loss more than 10%

Flow Chart of Treatment Sequence



TNM Staging System：UICC/AJCC 2017 8th Edition

Primary Tumor（T）

Tx：Primary tumor cannot be assessed

Tis：Carcinoma *in situ*

T1：Tumor ≤ 2cm in greatest dimension ＆ DOI[a] ≤ 5mm

T2：Tumor ≤ 2cm in greatest dimension ＆ DOI[a] > 5mm
or Tumor > 2cm but ≤ 4cm in greatest dimension ＆ DOI[a] ≤ 10mm

T3：Tumor > 2cm but ≤ 4cm in greatest dimension ＆ DOI[a] > 10mm
or Tumor > 4cm in greatest dimension ＆ DOI[a] ≤ 10mm

T4：Moderately advanced or very advanced local disease

T4a：Moderately advanced local disease
Tumor > 4cm in greatest dimension ＆ DOI[a] > 10mm
（Lip）：tumor invade through cortical bone, inferior alveolar nerve, floor of mouth, or skin of the face（ie, chin or nose）
（Oral cavity）：tumor invade adjacent structure（eg, through cortical bone of the mandible or maxilla, maxillary sinus, skin of face）

T4b：Very advanced local disease.
Tumor invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery

• **Note：Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify as T4.**
[a] **DOI is depth of invasion and not tumor thickness**

TNM Staging System：UICC/AJCC 2017 8th Edition

Clinical N Category　　Regional Lymph Nodes（N）

Nx：Regional lymph nodes cannot be assessed

N0：No regional lymph nodes metastasis

N1：Metastasis in a single ipsilateral lymph node, ≤ 3cm, ENE（-）

N2：Metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）
or metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）
or in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2a：Metastasis in single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）

N2b：Metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2c：Metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N3：Metastasis in a lymph node > 6 cm in greatest dimension, ENE（-）
or metastasis in any lymph node(s) and clinically overt ENE（+）

N3a：Metastasis in a lymph node > 6 cm in greatest dimension, ENE（-）

N3b：Metastasis in any lymph node(s) and clinically overt ENE（+）

*** Note：A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L).**
Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+).

Distant Metastasis（M）

M0：No distant metastasis（no pathological M0; use clinical M to complete stage group）

M1：Distant metastasis

TNM Staging System：UICC/AJCC 2017 8th Edition

Pathological N Category　Regional Lymph Nodes（N）

Nx：Regional lymph nodes cannot be assessed

N0：No regional lymph nodes metastasis

N1：Metastasis in a single ipsilateral lymph node, ≤ 3cm, ENE（-）

N2：Metastasis in a single ipsilateral or contralateral lymph node, ≤ 3cm, ENE（+）
or metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）
or metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）
or metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2a：Metastasis in a single ipsilateral or contralateral lymph node, ≤ 3cm, ENE（+）
Metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）

N2b：Metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2c：Metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N3：Metastasis in a lymph node > 6 cm in greatest dimension, ENE（-）
or metastasis in a single ipsilateral node, > 3cm in greatest dimension, ENE（+）
or metastasis in multiple ipsilateral, bilateral or contralateral lymph nodes, ENE（+）

N3a：Metastasis in lymph node > 6 cm in greatest dimension, ENE（-）

N3b：Metastasis in a single ipsilateral node, > 3cm in greatest dimension, ENE（+）
Metastasis in multiple ipsilateral, bilateral or contralateral lymph nodes, ENE（+）

***Note：A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L).**
Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+).

Distant Metastasis（M）

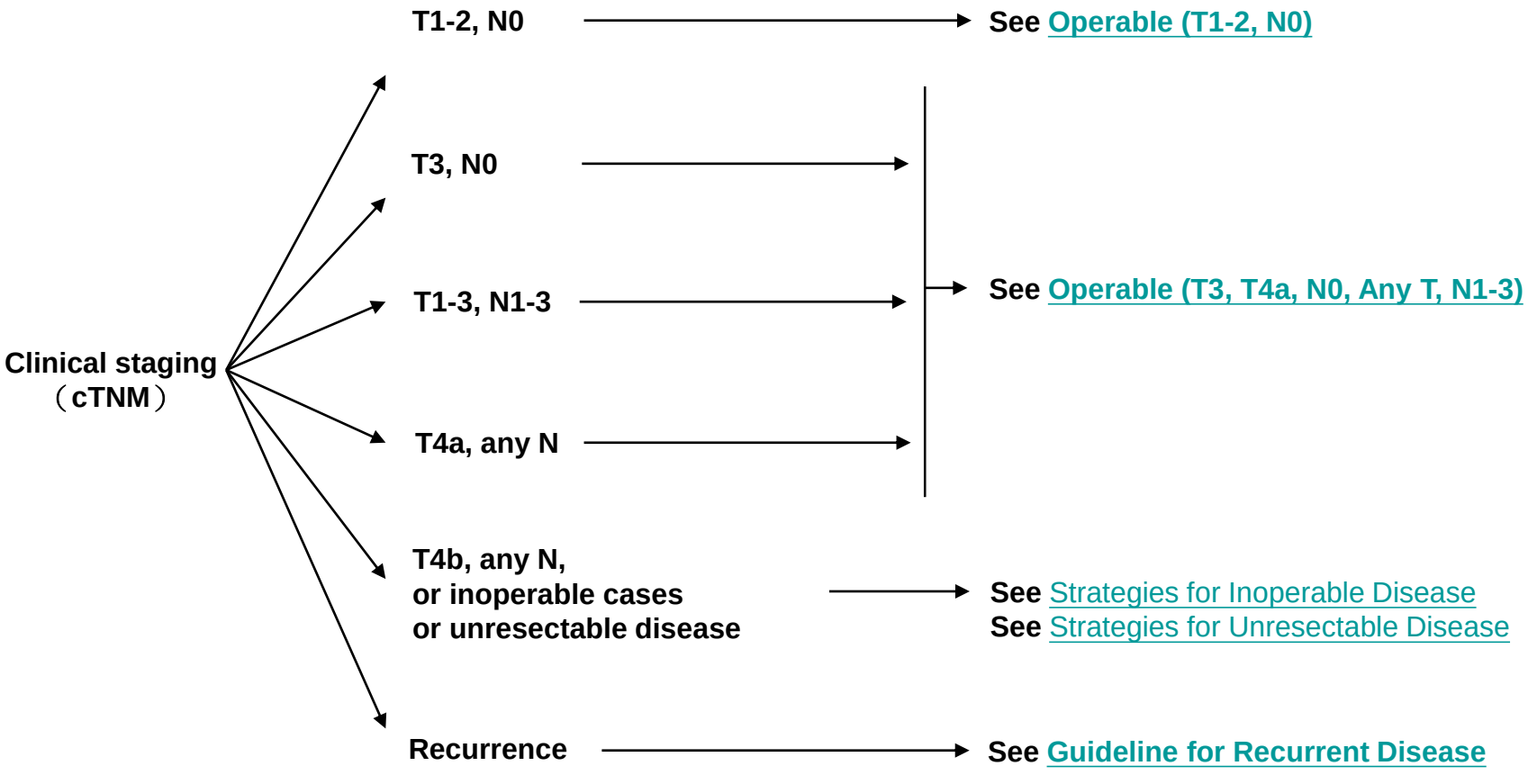
M0：No distant metastasis（no pathological M0; use clinical M to complete stage group）

M1：Distant metastasis

TNM Staging System：UICC/AJCC 2017 8th Edition
Stage Grouping of M0 Disease（M1 disease as Stage IVC）

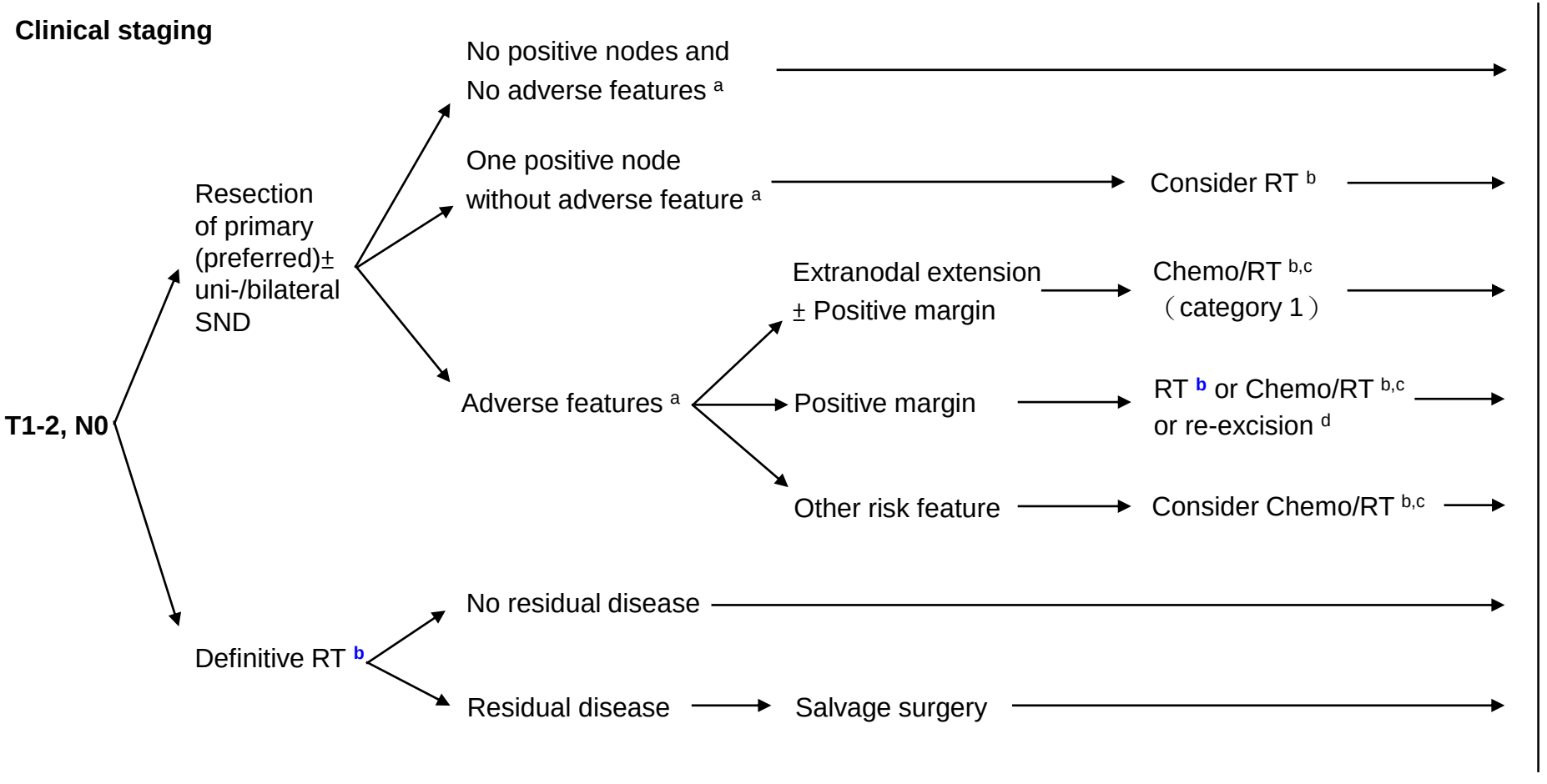
	T1	T2	T3	T4a	T4b
N0	I	II	III	IVA	IVB
N1	III	III	III	IVA	IVB
N2	IVA	IVA	IVA	IVA	IVB
N3	IVB	IVB	IVB	IVB	IVB

Treatment Stratification



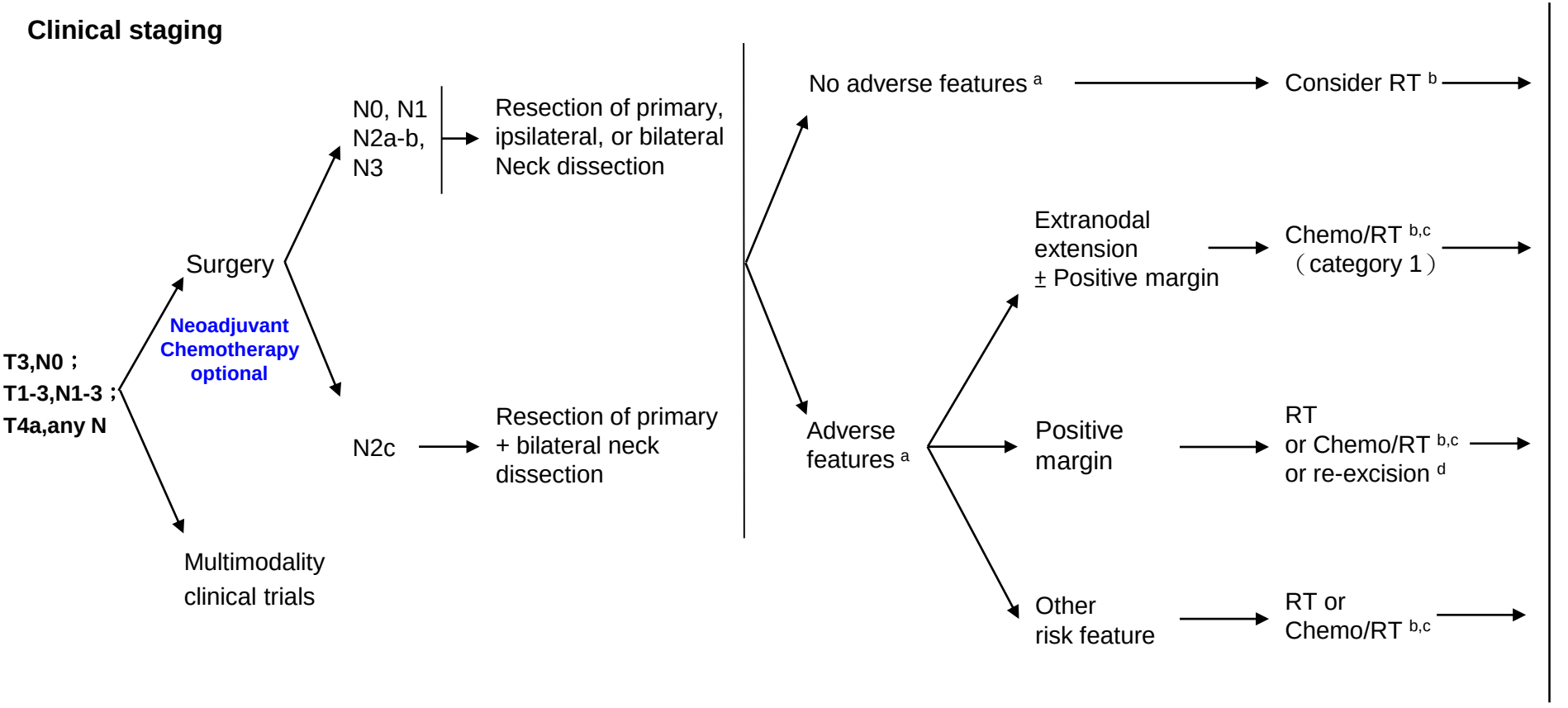
[a] In cases of high risk for surgical intervention or those who refuse surgery（not mentioned as unresectable）

Guidelines for Operable Cases



[a] Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.
[b] See Principles of Radiation Therapy.
[c] See Principles of Systemic Therapy.
[d] Consider re-resection to achieve negative margin is optional if initial positive margin noted.

Guidelines for Operable Cases



[a] Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.

[b] See Principles of Radiation Therapy.

[c] See Principles of Systemic Therapy.

[d] Consider re-resection to achieve negative margin is optional if initial positive margin noted.

TNM Staging System：UICC/AJCC 2017 8th Edition

Primary Tumor（T）

T0：No primary identified

T1：Tumor 2 cm or smaller in greatest dimension

T2：Tumor more than 2 cm but not more than 4 cm in greatest dimension

T3：Tumor more 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*

*** Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of larynx**

TNM Staging System：UICC/AJCC 2017 8th Edition

Clinical N Category

Regional Lymph Nodes（N）

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

Pathological N Category

Regional Lymph Nodes（N）

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

Distant Metastasis（M）

M0：No distant metastasis（no pathological M0; use clinical M to complete stage group）
M1：Distant metastasis

TNM Staging System：UICC/AJCC 2017 8th Edition
Stage Grouping of M0 Disease（M1 disease as Stage IV）

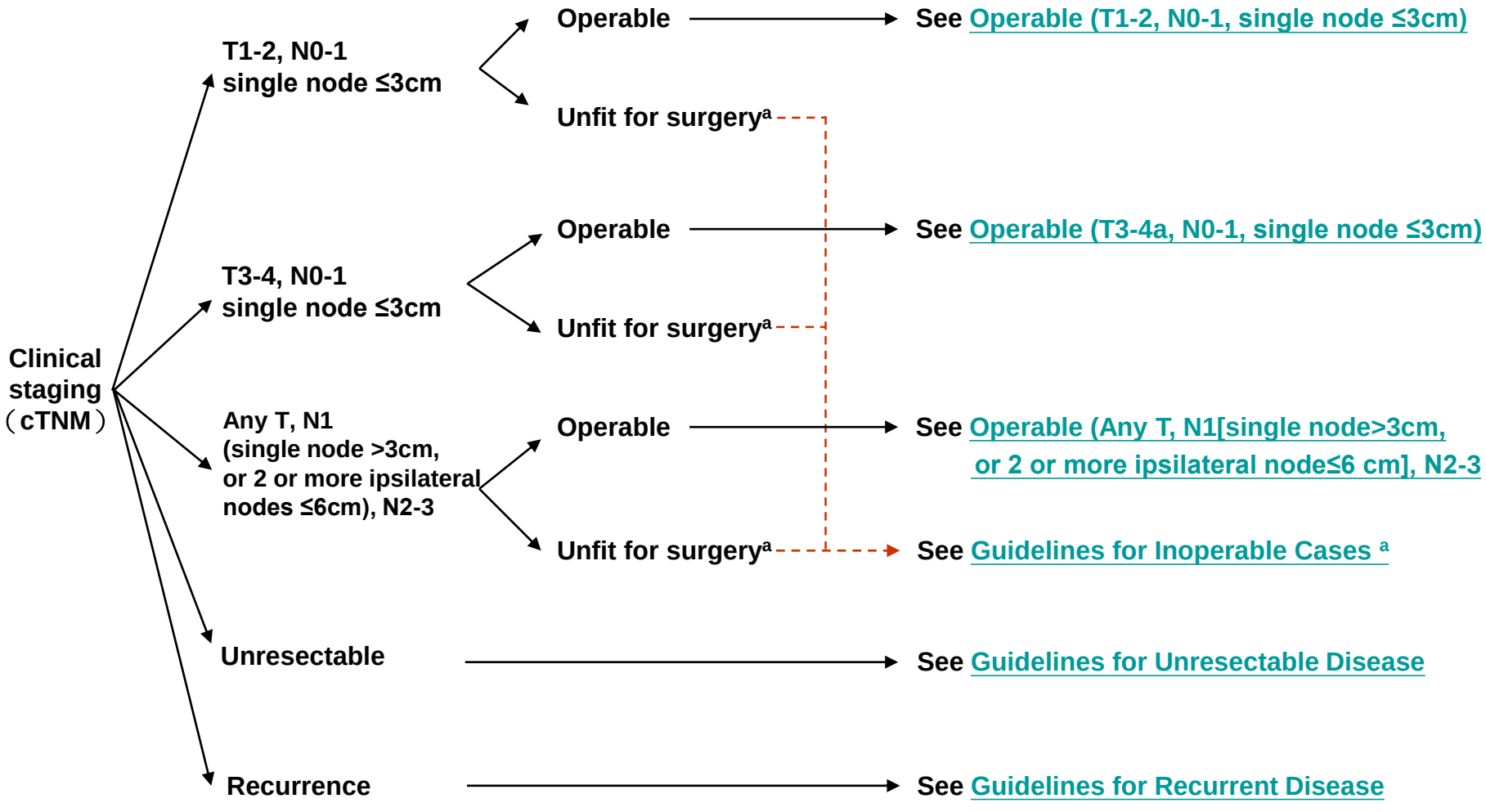
Clinical Stage Groups

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

Pathological Stage Groups

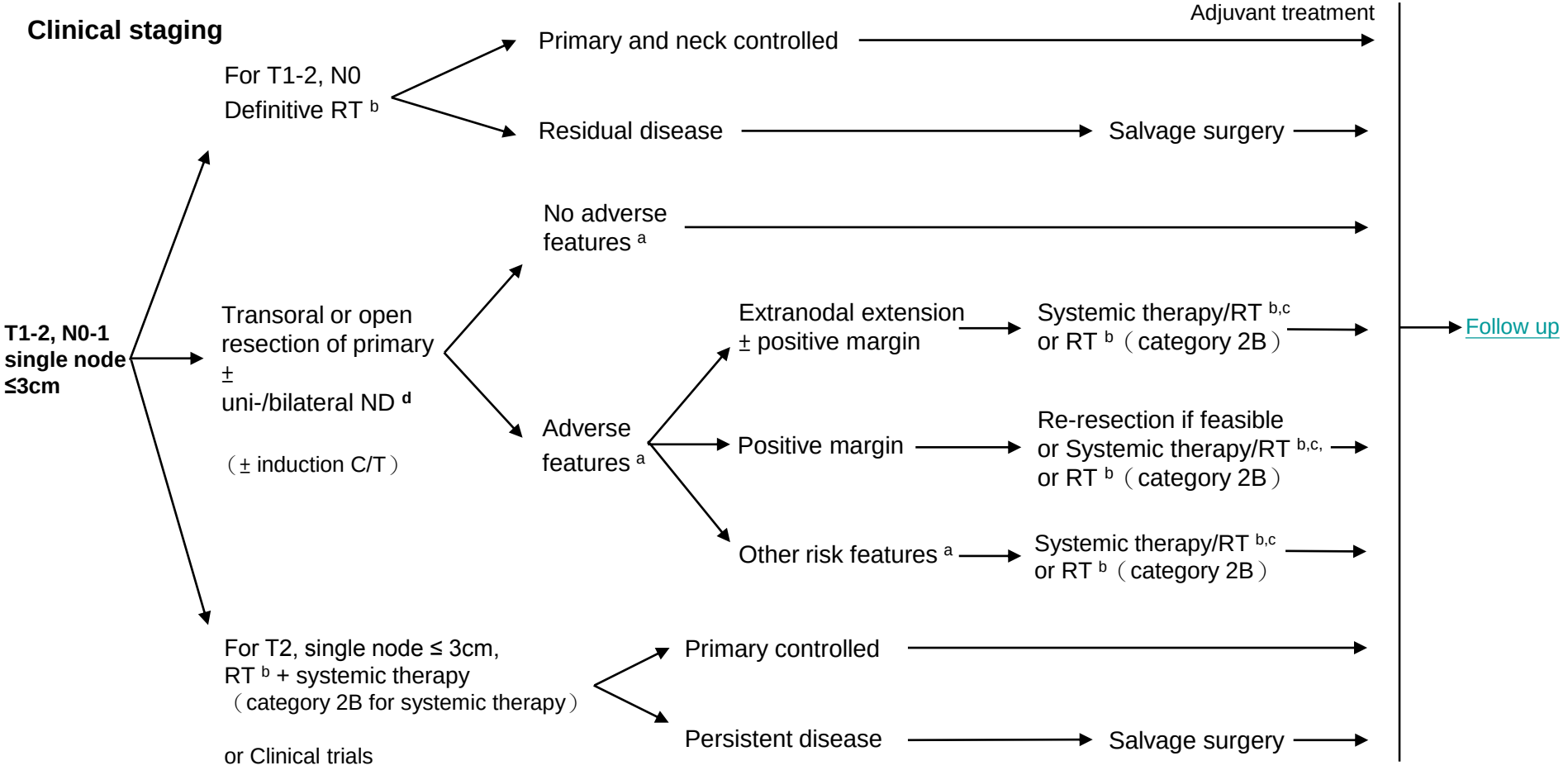
	T0	T1	T2	T3	T4
N0	NA	I	I	II	II
N1	I	I	I	II	II
N2	II	II	II	III	III

Treatment Stratification



[a] In cases of high risk for surgical intervention or those who refuse surgery（not mentioned as unresectable）

Operable（T1-2, N0-1, single node ≤3cm）



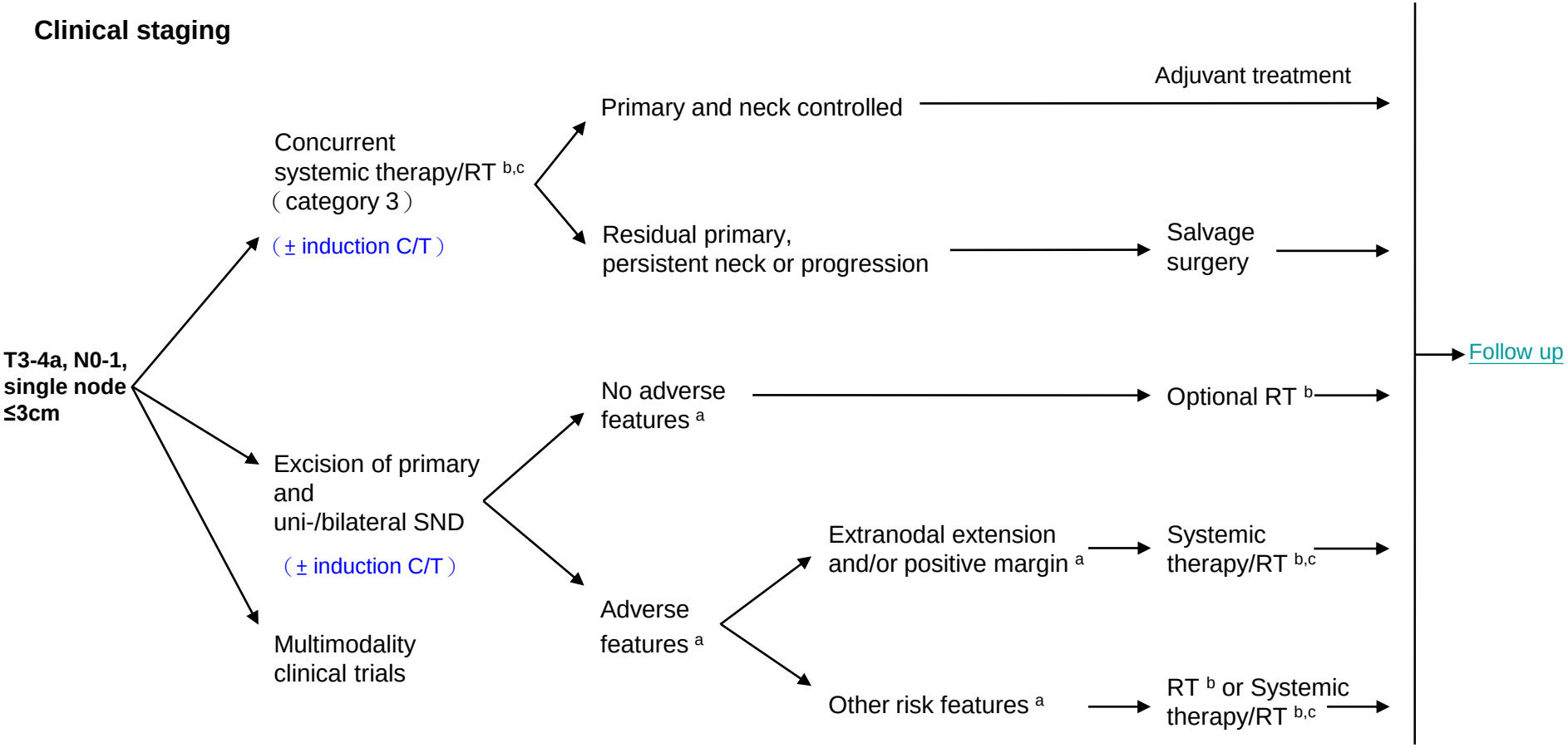
[a] **Adverse features：Extranodal extension, positive margins, nodal disease in levels IV or V, perineural invasion, lymphovascular invasion, tumor emboli.**
The definition of an adverse feature in the context of HPV+ disease is an area of active research.

[b] **See Principles of Radiation Therapy.**

[c] **See Principles of Systemic Therapy.**

[d] **Not including tonsillectomy or biopsy cases.**

Operable（T3-4, N0-1, single node ≤3cm）



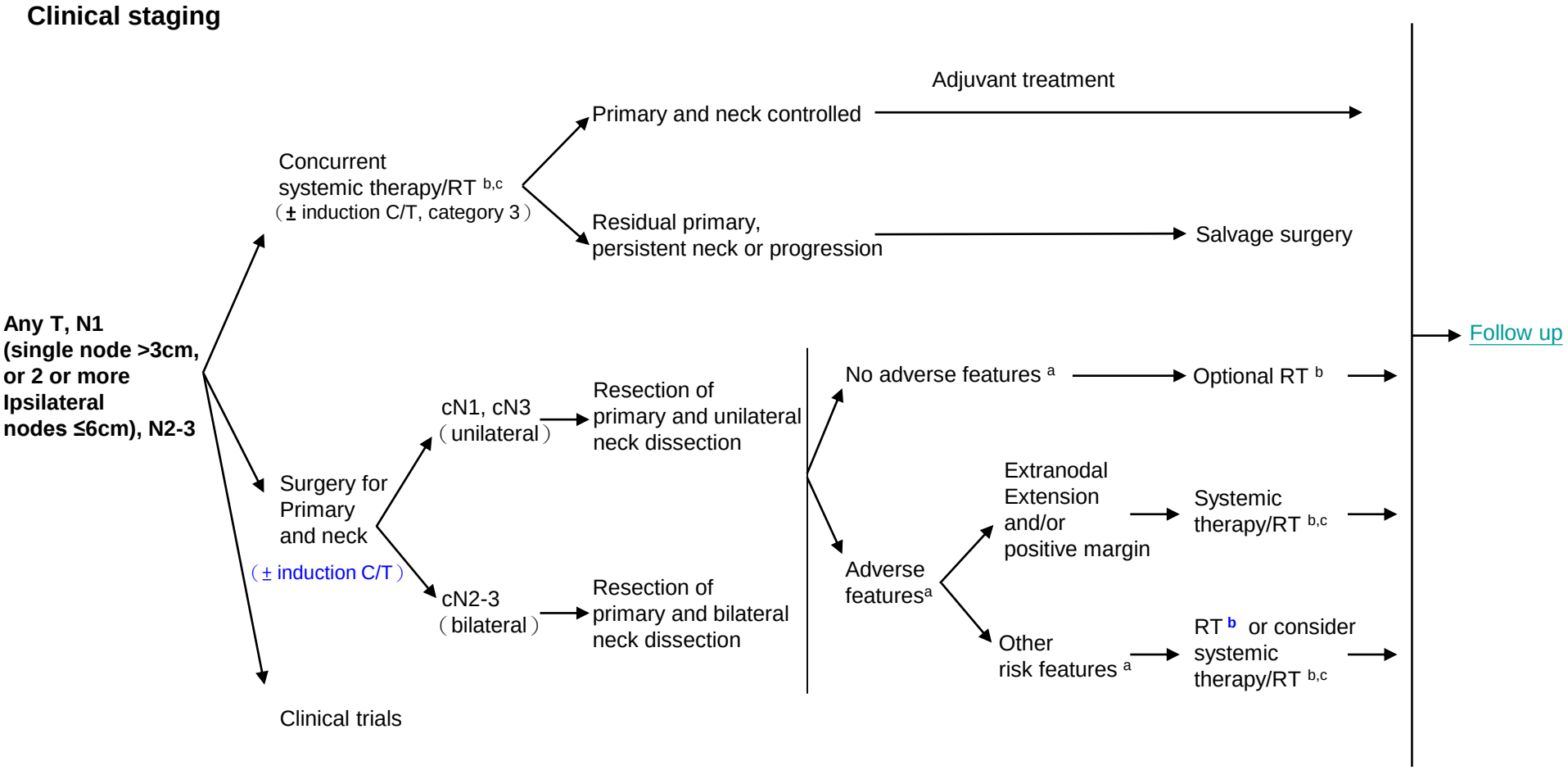
[a] **Adverse features：Extranodal extension, positive margins, nodal disease in levels IV or V, perineural invasion, lymphovascular invasion, tumor emboli.**
The definition of an adverse feature in the context of HPV+ disease is an area of active research.

[b] **See Principles of Radiation Therapy.**

[c] **See Principles of Systemic Therapy.**

[d] **Not including tonsillectomy or biopsy cases.**

Operable（Any T, N1 (single node >3cm, or 2 or more ipsilateral nodes≤6cm), N2-3）



[a] Adverse features：Extranodal extension, positive margins, nodal disease in levels IV or V, perineural invasion, lymphovascular invasion, tumor emboli.
The definition of an adverse feature in the context of HPV+ disease is an area of active research.

[b] See Principles of Radiation Therapy.

[c] See Principles of Systemic Therapy.

[d] Not including tonsillectomy or biopsy cases.

TNM Staging System：UICC/AJCC 2017 8th Edition

Primary Tumor（T）

Tx：Primary tumor cannot be assessed

Tis：Carcinoma in situ

T1：Tumor 2 cm or smaller in greatest dimension

T2：Tumor more than 2 cm but not more than 4 cm in greatest dimension

T3：Tumor more than 4 cm in greatest dimension or
extension to lingual surface of epiglottis

T4a：moderately advanced local disease
Tumor invades the larynx, extrinsic muscle of tongue, medial petrygoid, hard palate, or mandible*

T4b：very advanced local disease
Tumor invades lateral petrygoid muscle, petrygoid plates, lateral nasopharynx, or skull base or encases carotid artery.

*** Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of larynx**

TNM Staging System：UICC/AJCC 2017 8th Edition

Clinical N Category

Regional Lymph Nodes（N）

Nx：Regional lymph nodes cannot be assessed

N0：No regional lymph nodes metastasis

N1：Metastasis in a single ipsilateral lymph node, ≤ 3cm, ENE（-）

N2：Metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）
or metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）
or metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2a：Metastasis in single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）

N2b：Metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2c：Metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N3：Metastasis in a lymph node >6 cm in greatest dimension, ENE（-）
or metastasis in any lymph node(s) and clinically overt ENE（+）

N3a：Metastasis in a lymph node >6 cm in greatest dimension, ENE（-）

N3b：Metastasis in any lymph node(s) and clinically overt ENE（+）

*** Note：A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L).**
Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+).

Distant Metastasis（M）

M0：No distant metastasis（no pathological M0; use clinical M to complete stage group）

M1：Distant metastasis

TNM Staging System：UICC/AJCC 2017 8th Edition

Pathological N Category　Regional Lymph Nodes（N）

Nx：Regional lymph nodes cannot be assessed

N0：No regional lymph nodes metastasis

N1：Metastasis in a single ipsilateral lymph node, ≤ 3cm, ENE（-）

N2：Metastasis in a single ipsilateral or contralateral lymph node, ≤ 3cm, ENE（+）
or metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）
or metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）
or metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2a：Metastasis in a single ipsilateral or contralateral lymph node, ≤ 3cm, ENE（+）
Metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）

N2b：Metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2c：Metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N3：Metastasis in a lymph node >6 cm in greatest dimension, ENE（-）
or metastasis in a single ipsilateral node, > 3cm in greatest dimension, ENE（+）
or metastasis in multiple ipsilateral, bilateral or contralateral lymph nodes, ENE（+）

N3a：Metastasis in lymph node >6 cm in greatest dimension, ENE（-）

N3b：Metastasis in a single ipsilateral node, > 3cm in greatest dimension, ENE（+）
Metastasis in multiple ipsilateral, bilateral or contralateral lymph nodes, ENE（+）

*** Note：A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L).**
Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+).

Distant Metastasis（M）

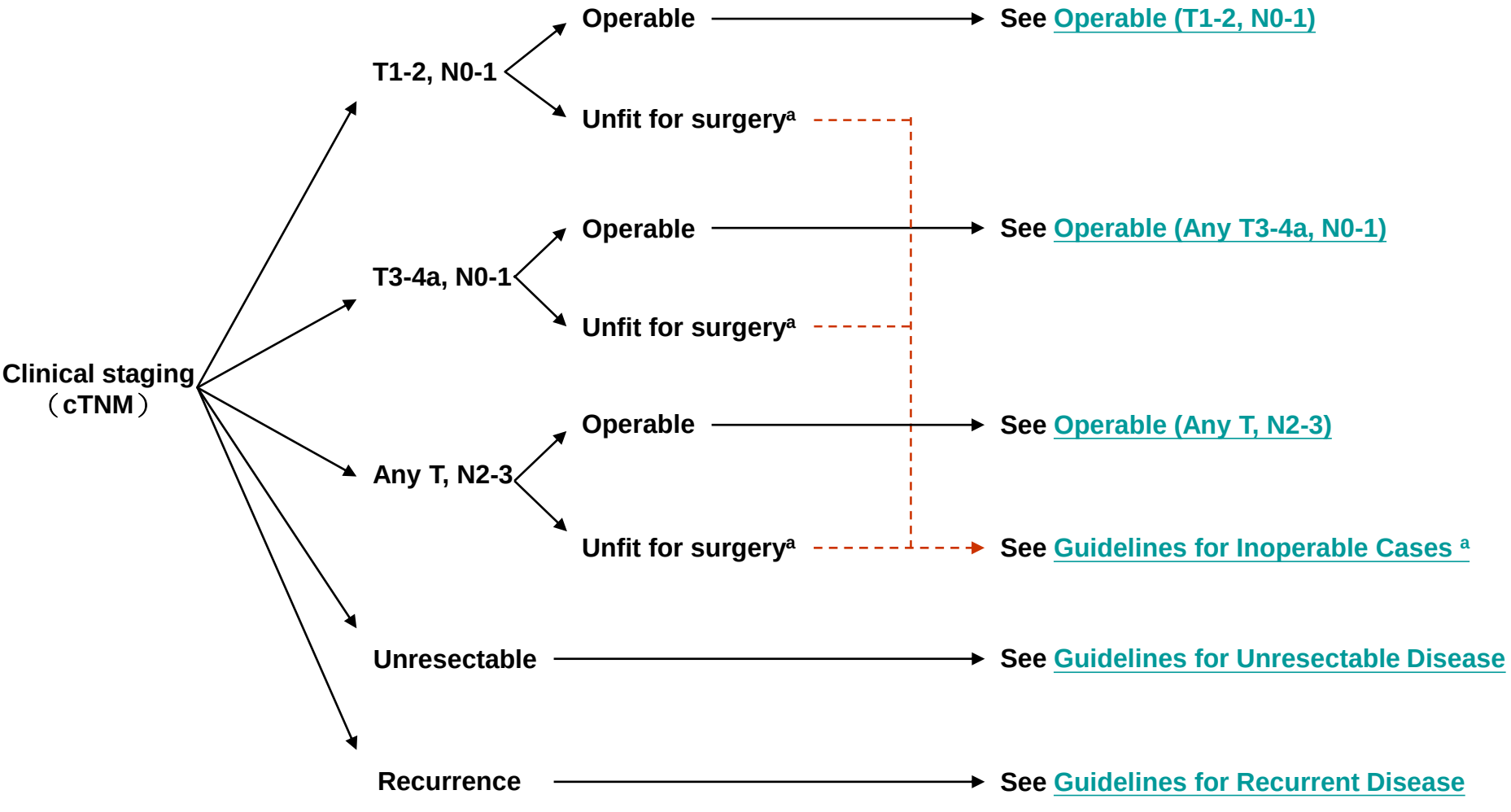
M0：No distant metastasis（no pathological M0; use clinical M to complete stage group）

M1：Distant metastasis

TNM Staging System：UICC/AJCC 2017 8th Edition
Stage Grouping of M0 Disease（M1 disease as Stage IVC）

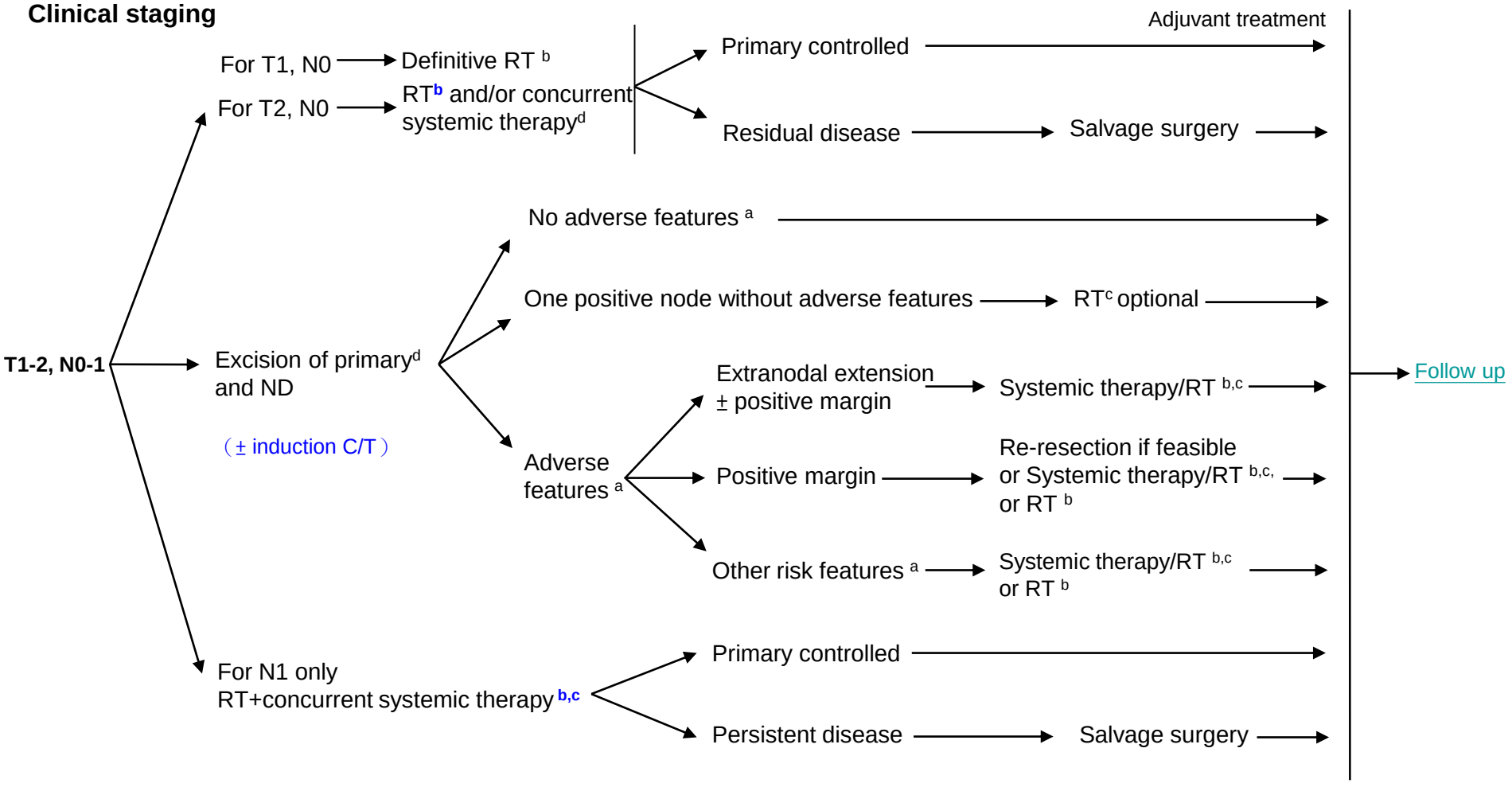
	T1	T2	T3	T4a	T4b
N0	I	II	III	IVA	IVB
N1	III	III	III	IVA	IVB
N2	IVA	IVA	IVA	IVA	IVB
N3	IVB	IVB	IVB	IVB	IVB

Treatment Stratification



[a] In cases of high risk for surgical intervention or those who refuse surgery（not mentioned as unresectable）

Operable（T1-2, N0-1）



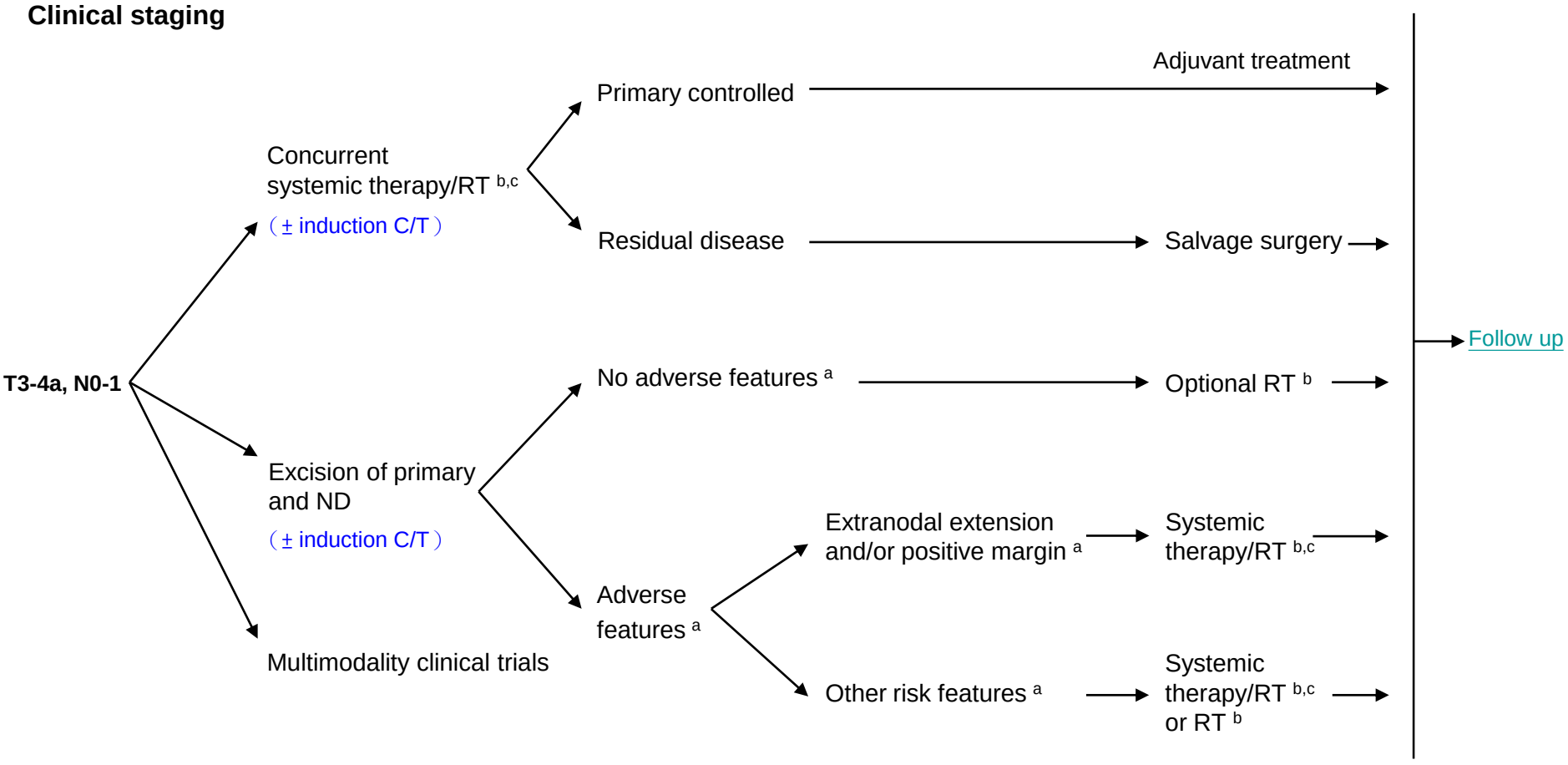
[a] **Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.**

[b] **See Principles of Radiation Therapy.**

[c] **See Principles of Systemic Therapy.**

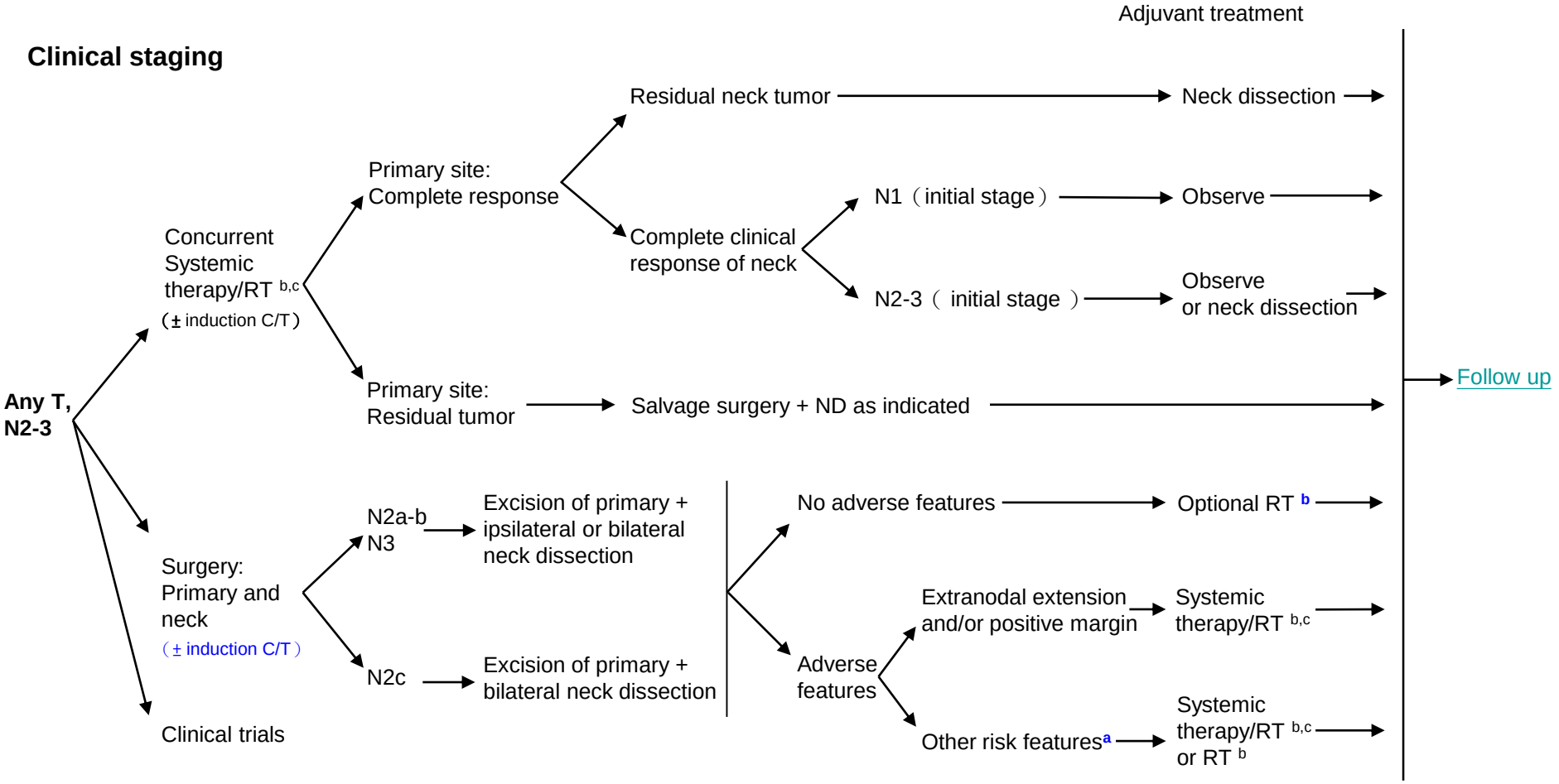
[d] **Consider re-resection to achieve negative margin is optional if initial positive margin noted.**

Operable（T3-4, N0-1）



[a] Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.
[b] See Principles of Radiation Therapy.
[c] See Principles of Systemic Therapy.
[d] Consider re-resection to achieve negative margin is optional if initial positive margin noted.

Operable（Any T, N2-3）



[a] Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.

[b] See Principles of Radiation Therapy.

[c] See Principles of Systemic Therapy.

[d] Consider re-resection to achieve negative margin is optional if initial positive margin noted.

TNM Staging System：UICC/AJCC 2017 8th Edition

Primary Tumor（T）

Tx：Primary tumor cannot be assessed

Tis：Carcinoma *in situ*

T1：Tumor limited to one subsite of hypopharynx and/or 2 cm or smaller in greatest dimension

T2：Tumor invades more than one subsite of hypopharynx or an adjacent site, or measures larger than 2 cm but not larger than 4 cm in greatest diameter without fixation of hemilarynx

T3：Tumor larger than 4 cm in greatest dimension or with fixation of hemilarynx or extension to esophagus

T4：Moderately advanced or very advanced local disease

- **T4a**：Moderately advanced local disease
  Tumor invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, or central compartment soft tissue*
- **T4b**：Very advanced local disease
  Tumor invades prevertebral fascia, encases carotid artery, or involves mediastinal structures

*** Central compartment soft tissue included prelaryngeal strap muscles and subcutaneous fat**

TNM Staging System：UICC/AJCC 2017 8th Edition

Clinical N Category

Regional Lymph Nodes（N）

Nx：Regional lymph nodes cannot be assessed

N0：No regional lymph nodes metastasis

N1：Metastasis in a single ipsilateral lymph node, ≤ 3cm, ENE（-）

N2：Metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）
or metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）
or metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2a：Metastasis in single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）

N2b：Metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2c：Metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N3：Metastasis in a lymph node >6 cm in greatest dimension, ENE（-）
or metastasis in any lymph node(s) and clinically overt ENE（+）

N3a：Metastasis in a lymph node >6 cm in greatest dimension, ENE（-）

N3b：Metastasis in any lymph node(s) and clinically overt ENE（+）

*** Metastases at level VII are considered regional lymph node metastases**

Distant Metastasis（M）

M0：No distant metastasis（no pathological M0; use clinical M to complete stage group）

M1：Distant metastasis

TNM Staging System：UICC/AJCC 2017 8th Edition

Pathological N Category　Regional Lymph Nodes（N）

Nx：Regional lymph nodes cannot be assessed

N0：No regional lymph nodes metastasis

N1：Metastasis in a single ipsilateral lymph node, ≤ 3cm, ENE（-）

N2：Metastasis in a single ipsilateral or contralateral lymph node, ≤ 3cm, ENE（+）
or metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）
or metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）
or metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2a：Metastasis in a single ipsilateral or contralateral lymph node, ≤ 3cm, ENE（+）
Metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）

N2b：Metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2c：Metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N3：Metastasis in a lymph node >6 cm in greatest dimension, ENE（-）
or metastasis in a single ipsilateral node, > 3cm in greatest dimension, ENE（+）
or metastasis in multiple ipsilateral, bilateral or contralateral lymph nodes, ENE（+）

N3a：Metastasis in lymph node >6 cm in greatest dimension, ENE（-）

N3b：Metastasis in a single ipsilateral node, > 3cm in greatest dimension, ENE（+）
Metastasis in multiple ipsilateral, bilateral or contralateral lymph nodes, ENE（+）

*** Metastases at level VII are considered regional lymph node metastases**

Distant Metastasis（M）

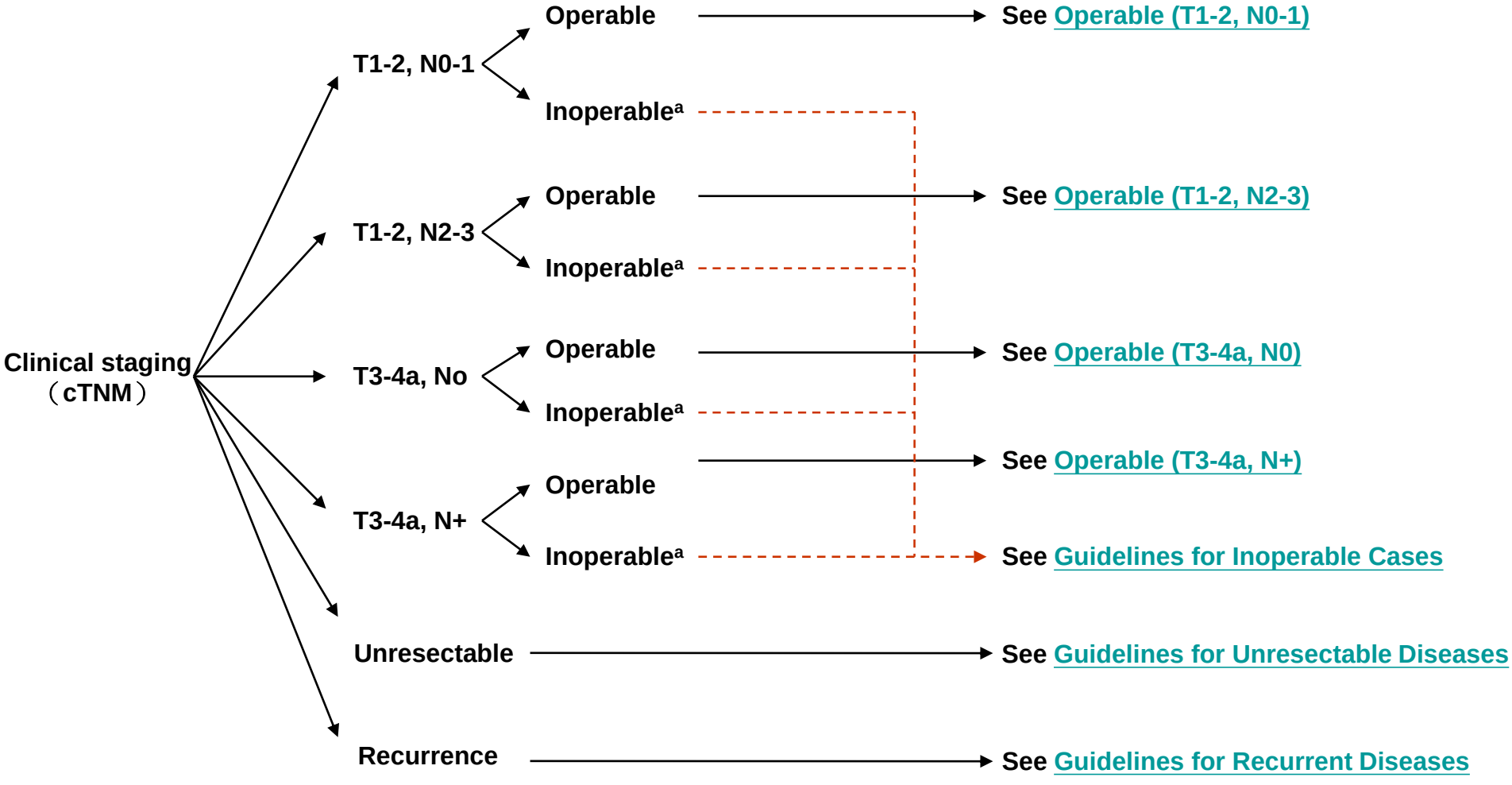
M0：No distant metastasis（no pathological M0; use clinical M to complete stage group）

M1：Distant metastasis

TNM Staging System：UICC/AJCC 2017 8th Edition
Stage Grouping of M0 Disease（M1 disease as Stage IVC）

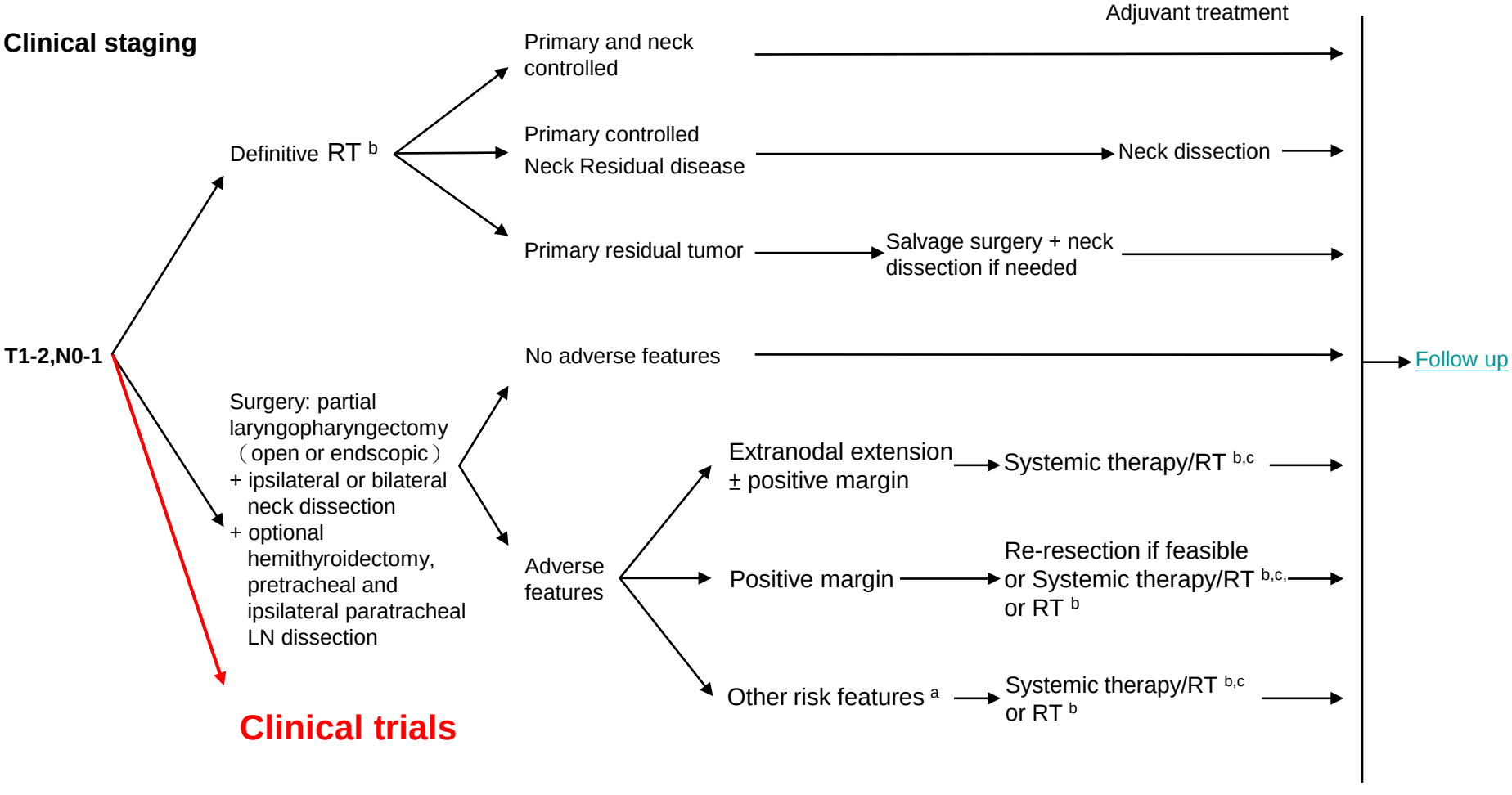
	T1	T2	T3	T4a	T4b
N0	I	II	III	IVA	IVB
N1	III	III	III	IVA	IVB
N2	IVA	IVA	IVA	IVA	IVB
N3	IVB	IVB	IVB	IVB	IVB

Treatment Stratification



[a] In cases of high risk for surgical intervention or those who refuse surgery（not mentioned as unresectable）

Operable（T1-2, N0-1）

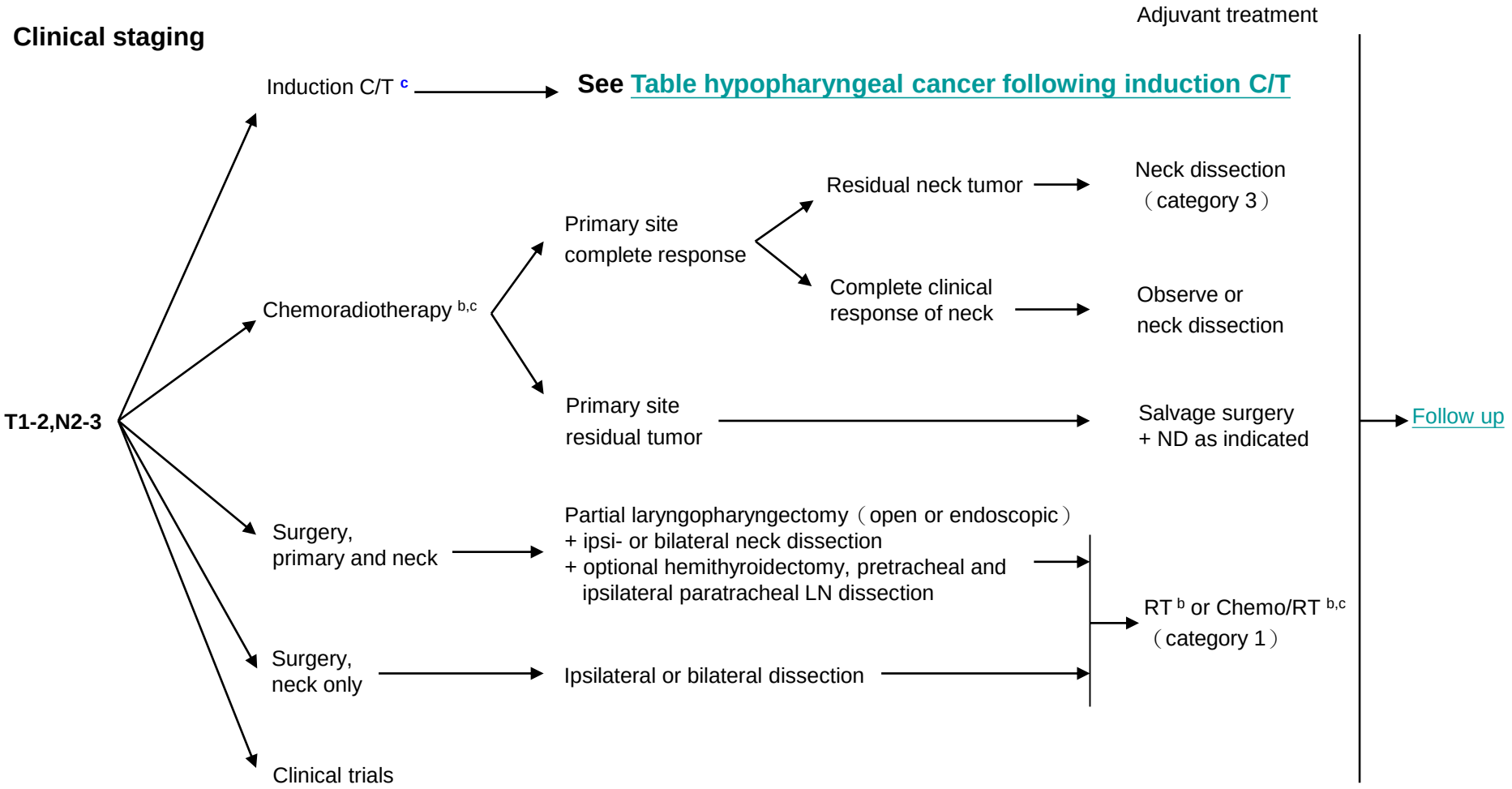


[a] **Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.**

[b] **See Principles of Radiation Therapy.**

[c] **See Principles of Systemic Therapy.**

Operable（T1-2, N2-3）

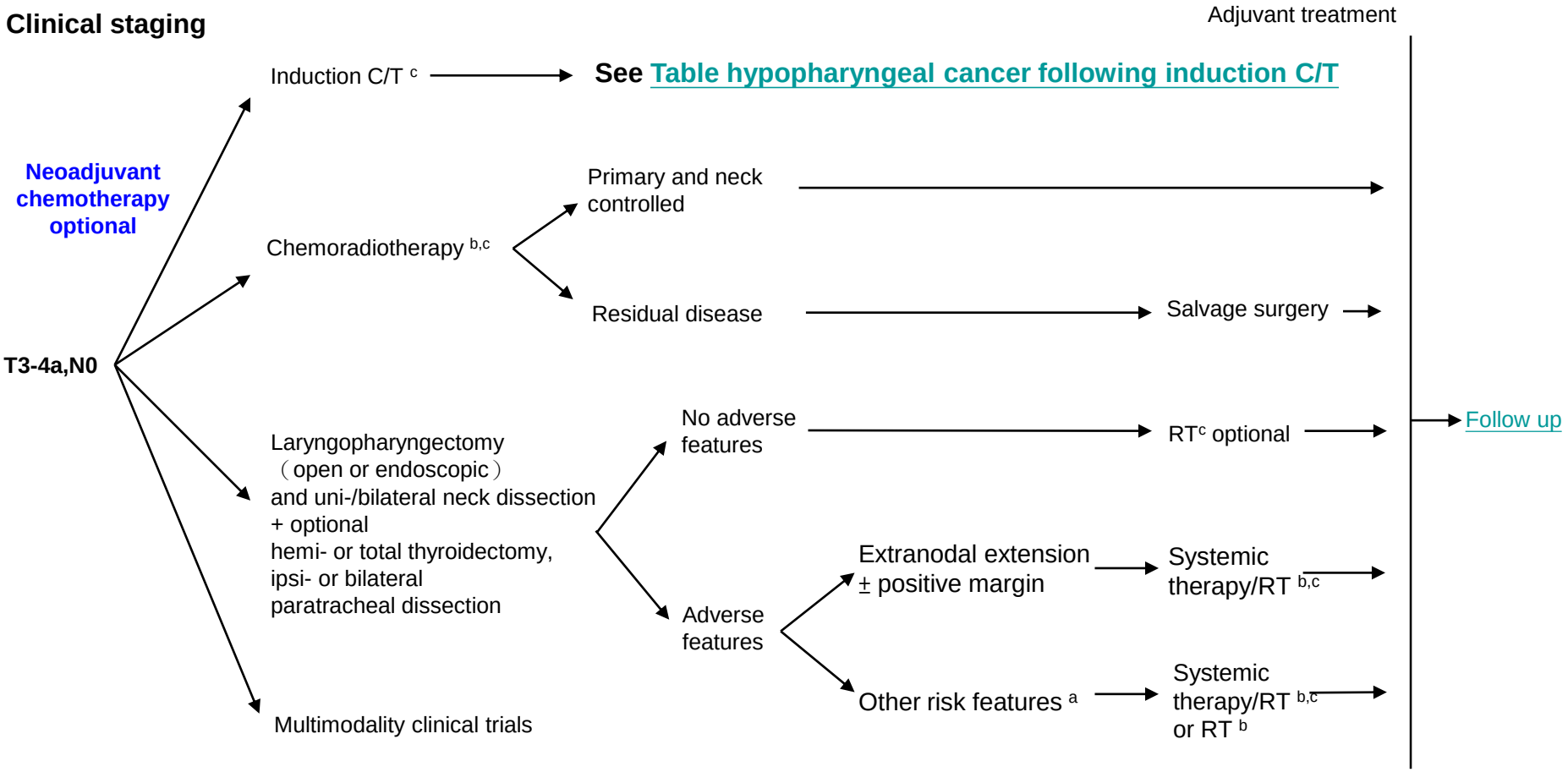


[a] **Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.**

[b] **See Principles of Radiation Therapy.**

[c] **See Principles of Systemic Therapy.**

Operable（T3-4a, N0）

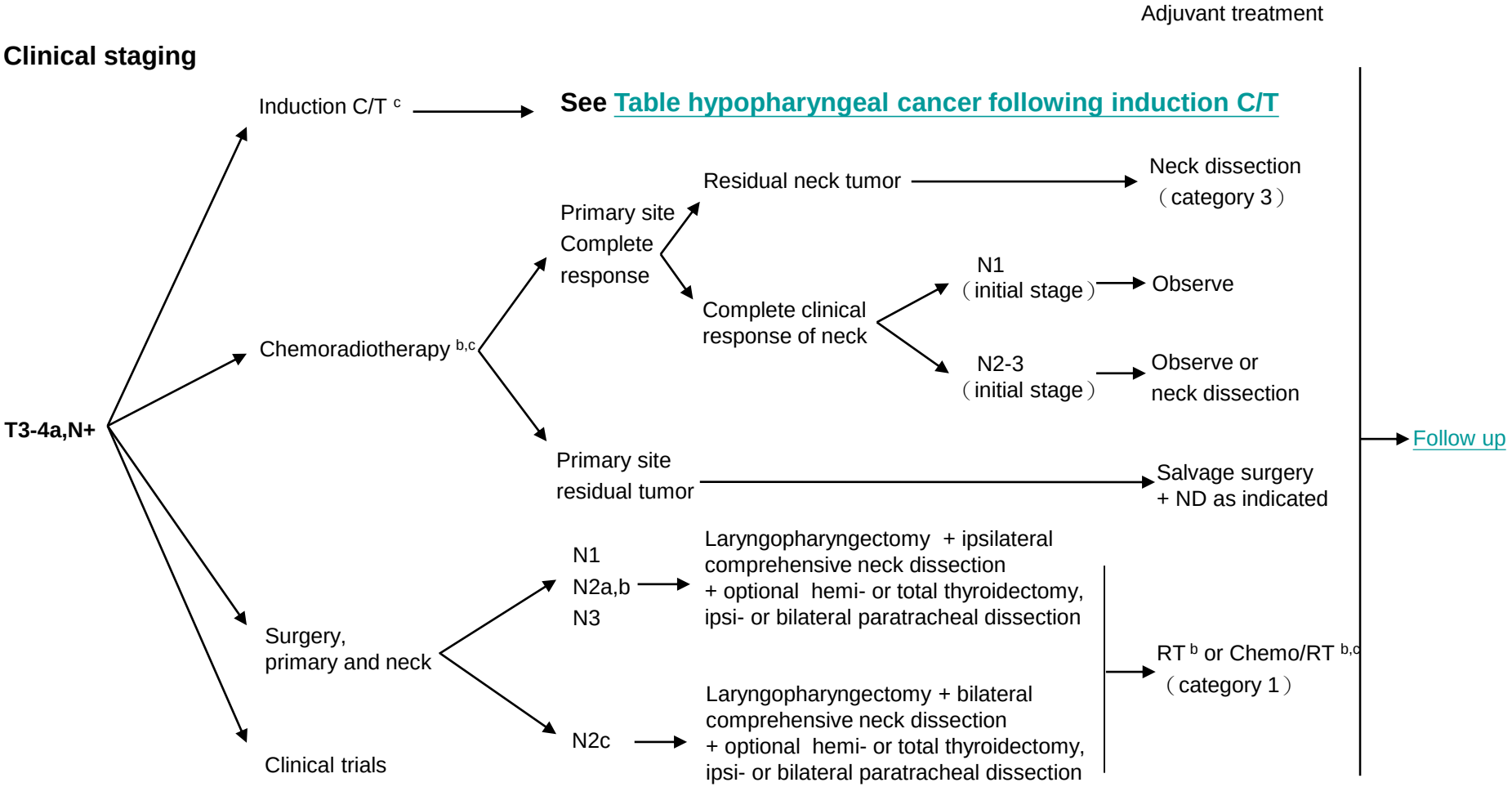


[a] **Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.**

[b] **See Principles of Radiation Therapy.**

[c] **See Principles of Systemic Therapy.**

Operable（T3-4a, N+）

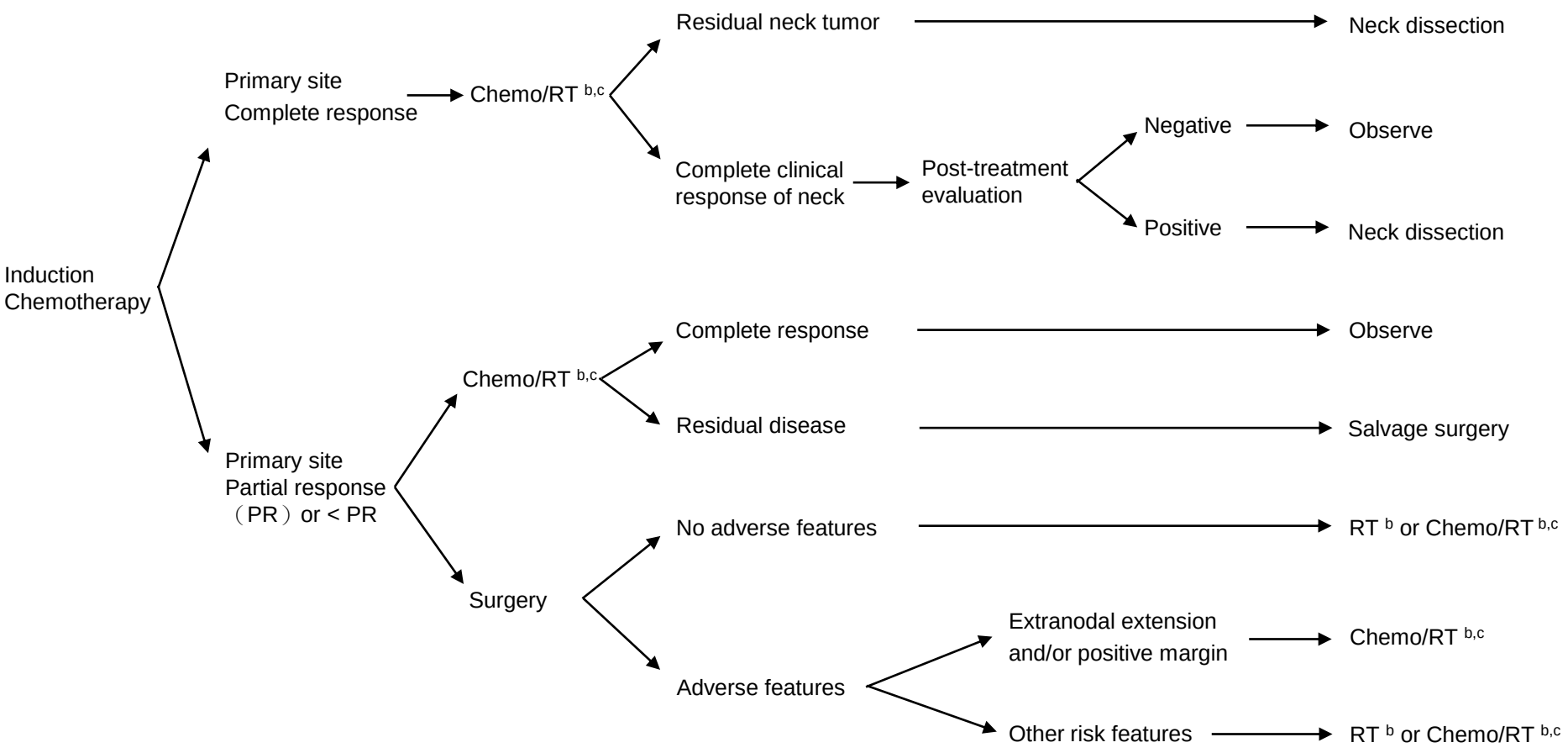


[a] **Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.**

[b] **See Principles of Radiation Therapy.**

[c] **See Principles of Systemic Therapy.**

Hypopharyngeal cancer following induction C/T

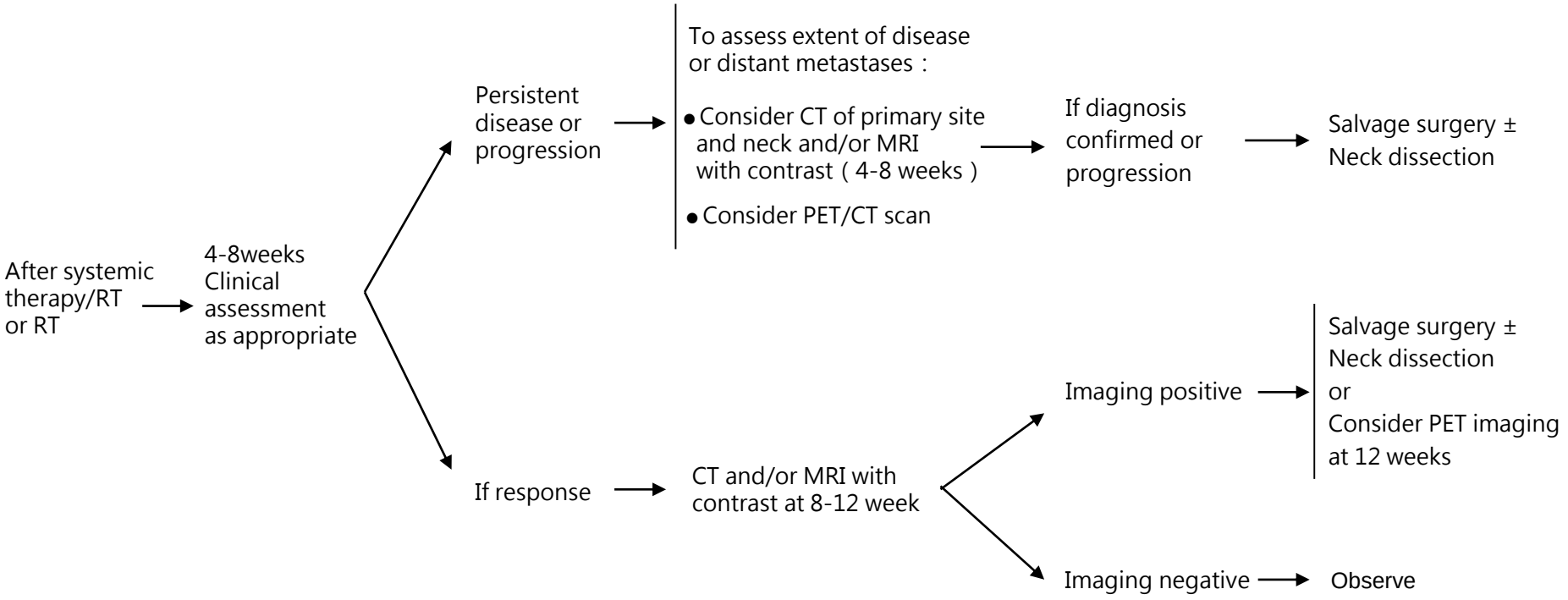


[a] **Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.**

[b] **See Principles of Radiation Therapy.**

[c] **See Principles of Systemic Therapy.**

Hypopharyngeal cancer following CRT/RT



[a] **Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.**

[b] **See Principles of Radiation Therapy.**

[c] **See Principles of Systemic Therapy.**

TNM Staging System：UICC/AJCC 2017 8th Edition

Primary Tumor（T）

Tx：Primary tumor cannot be assessed

~~**T0**：No evidence of primary tumor~~

Tis：Carcinoma *in situ*

Supraglottis

T1：Tumor limited to one subsite of supraglottis with normal vocal cord mobility

T2：Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis（e.g., mucosa of base of tongue, vallecula, medial wall of pyriform sinus）without fixation of the larynx

T3：Tumor limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, pre-epiglottic tissues, paraglottic space, and/or inner cortex of thyroid cartilage

T4a：moderately advanced local disease
Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx

T4b：very advanced local disease
Tumor invades prevertebral space, encases carotid artery, or involves mediastinal structures

TNM Staging System：UICC/AJCC 2017 8th Edition

Primary Tumor（T）

Tx：Primary tumor cannot be assessed
~~T0：No evidence of primary tumor~~
Tis：Carcinoma *in situ*

Glottis

T1：Tumor limited to the vocal cord（s）（may involve anterior or posterior commissure）with normal mobility
T1a：Tumor limited to one vocal cord
T1b：Tumor involves both vocal cords
T2：Tumor extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility
T3：Tumor limited to the larynx with vocal cord fixation and/or invades paraglottic space, and/or inner cortex of the thyroid cartilage
T4a：Tumor invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx
T4b：Tumor invades prevertebral space, encases carotid artery, or involves mediastinal structures

Subglottis

T1：Tumor limited to the subglottis
T2：Tumor extends to vocal cord（s）with normal or impaired mobility
T3：Tumor limited to larynx with vocal cord fixation and/or invades paraglottic space, and/or inner cortex of the thyroid cartilage
T4a：Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx
T4b：Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

TNM Staging System：UICC/AJCC 2017 8th Edition

Clinical N Category

Regional Lymph Nodes（N）

Nx：Regional lymph nodes cannot be assessed

N0：No regional lymph nodes metastasis

N1：Metastasis in a single ipsilateral lymph node, ≤ 3cm, ENE（-）

N2：Metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）
or metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）
or in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2a：Metastasis in single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）

N2b：Metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2c：Metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N3：Metastasis in a lymph node >6 cm in greatest dimension, ENE（-）
or metastasis in any lymph node(s) and clinically overt ENE（+）

N3a：Metastasis in a lymph node >6 cm in greatest dimension, ENE（-）

N3b：Metastasis in any lymph node(s) and clinically overt ENE（+）

*** Metastases at level VII are considered regional lymph node metastases**

Distant Metastasis（M）

M0：No distant metastasis（no pathological M0; use clinical M to complete stage group）

M1：Distant metastasis

TNM Staging System：UICC/AJCC 2017 8th Edition

Pathological N Category　Regional Lymph Nodes（N）

Nx：Regional lymph nodes cannot be assessed

N0：No regional lymph nodes metastasis

N1：Metastasis in a single ipsilateral lymph node, ≤ 3cm, ENE（-）

N2：Metastasis in a single ipsilateral or contralateral lymph node, ≤ 3cm, ENE（+）
or metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）
or metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）
or metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2a：Metastasis in a single ipsilateral or contralateral lymph node, ≤ 3cm, ENE（+）
Metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）

N2b：Metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2c：Metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N3：Metastasis in a lymph node >6 cm in greatest dimension, ENE（-）
or metastasis in a single ipsilateral node, > 3cm in greatest dimension, ENE（+）
or metastasis in multiple ipsilateral, bilateral or contralateral lymph nodes, ENE（+）

N3a：Metastasis in lymph node >6 cm in greatest dimension, ENE（-）

N3b：Metastasis in a single ipsilateral node, > 3cm in greatest dimension, ENE（+）
Metastasis in multiple ipsilateral, bilateral or contralateral lymph nodes, ENE（+）

*** Metastases at level VII are considered regional lymph node metastases**

Distant Metastasis（M）

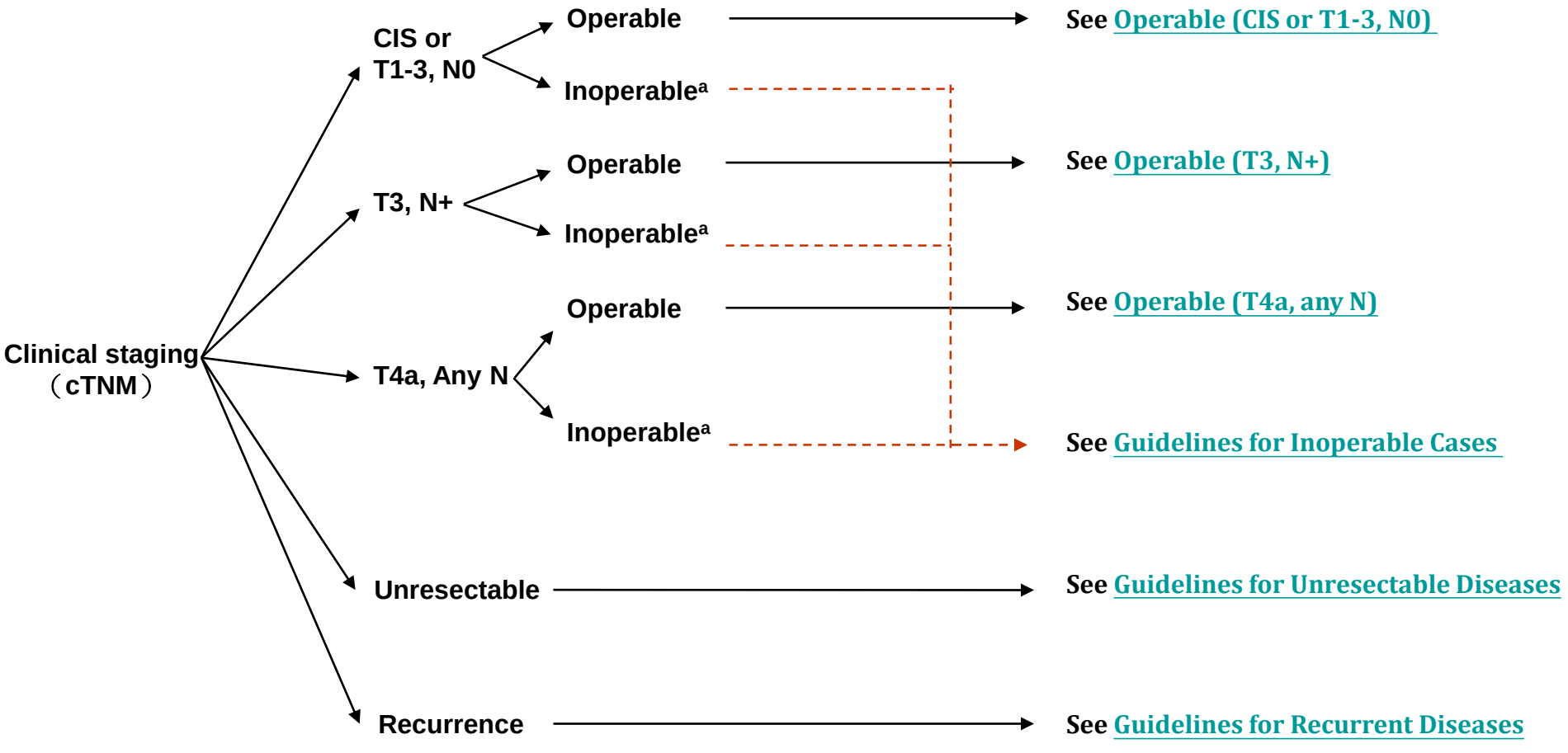
M0：No distant metastasis（no pathological M0; use clinical M to complete stage group）

M1：Distant metastasis

TNM Staging System：UICC/AJCC 2017 8th Edition
Stage Grouping of M0 Disease（M1 disease as Stage IVC）

	T1	T2	T3	T4a	T4b
N0	I	II	III	IVA	IVB
N1	III	III	III	IVA	IVB
N2	IVA	IVA	IVA	IVA	IVB
N3	IVB	IVB	IVB	IVB	IVB

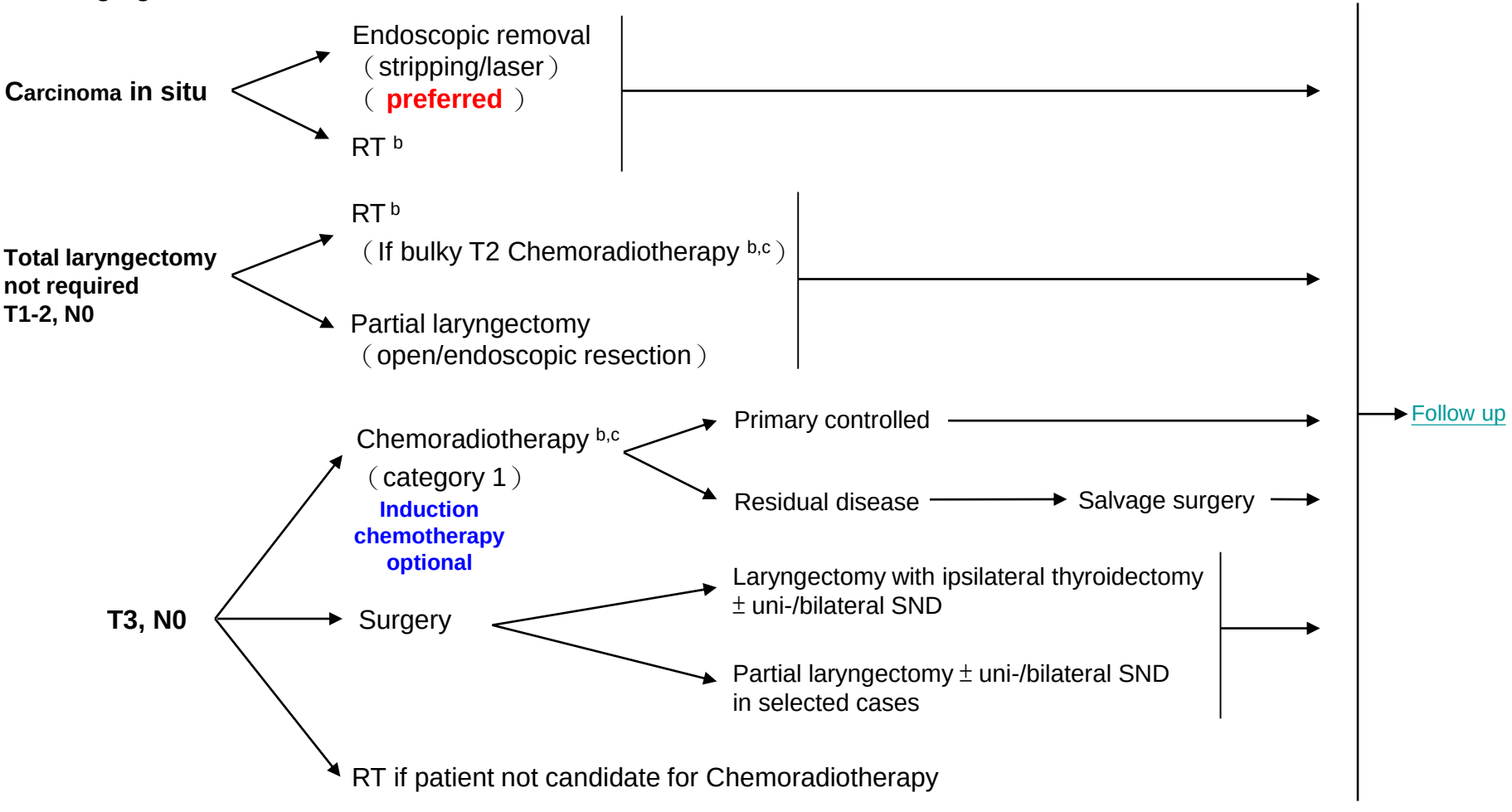
Treatment Stratification



[a] In cases of high risk for surgical intervention or those who refuse surgery（not mentioned as unresectable）

Operable（CIS or T1-3 N0）

Clinical staging

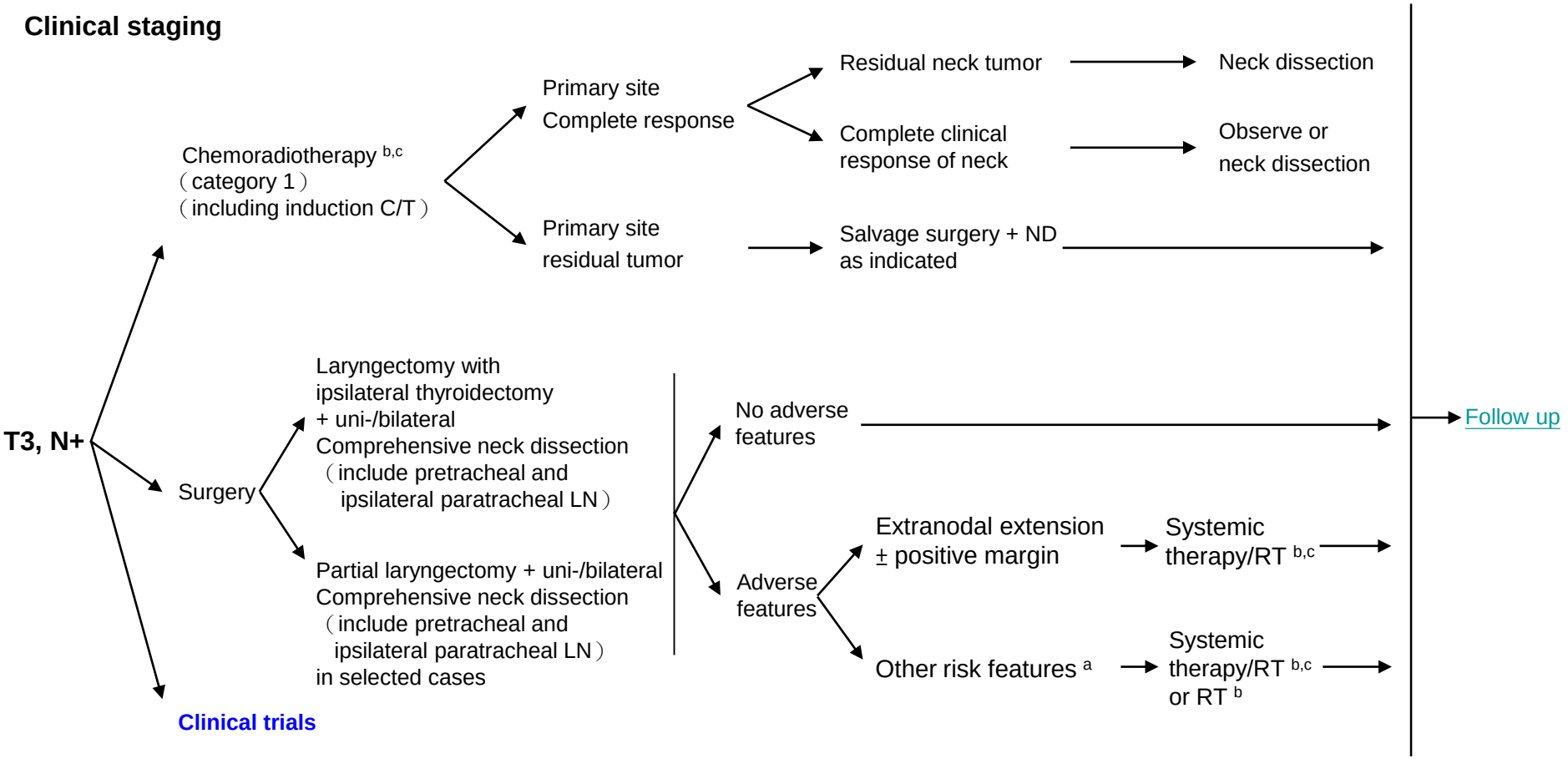


[a] **Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.**

[b] **See Principles of Radiation Therapy.**

[c] **See Principles of Systemic Therapy.**

Operable（T3 N+）

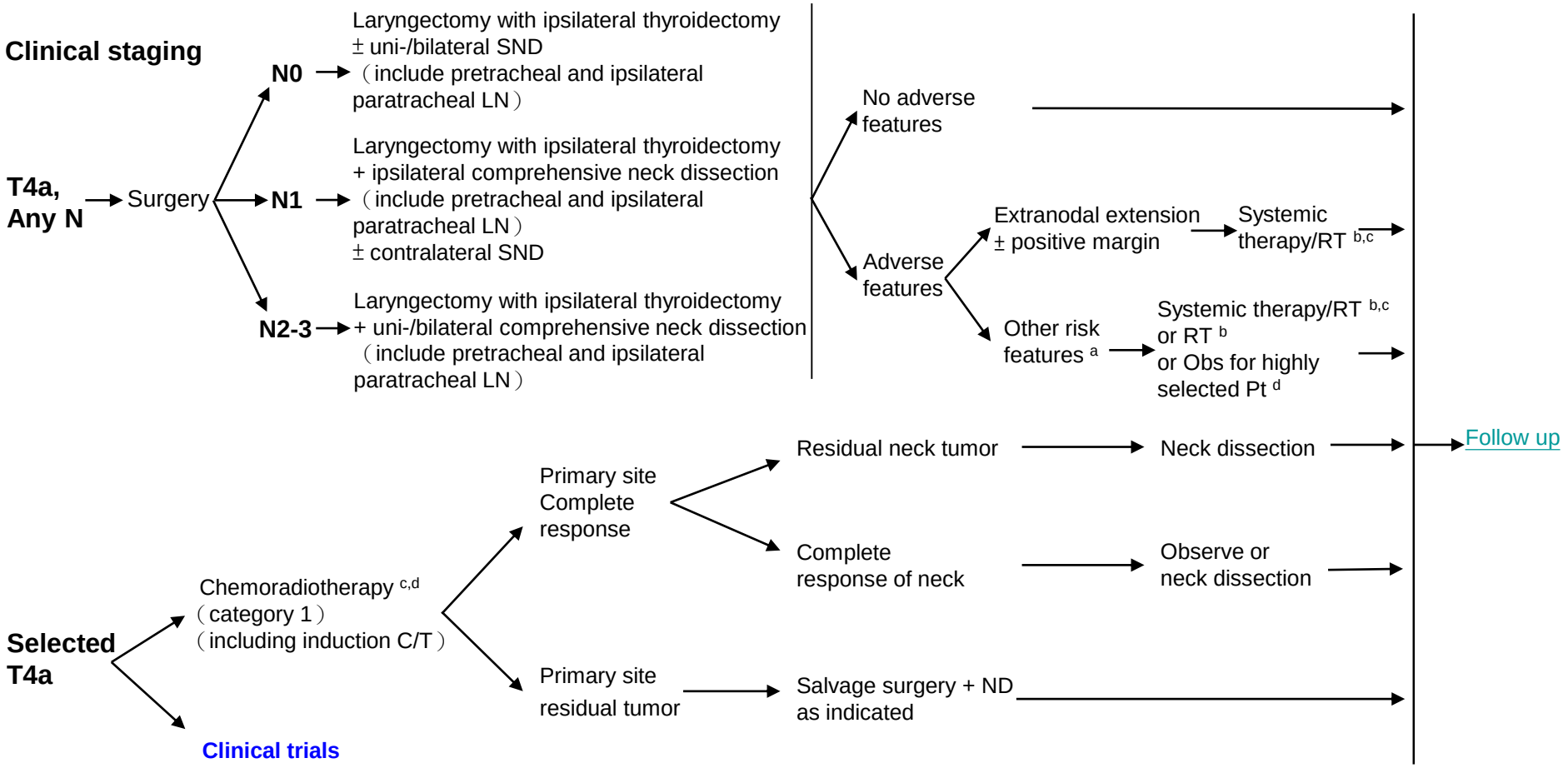


[a] **Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.**

[b] **See Principles of Radiation Therapy.**

[c] **See Principles of Systemic Therapy.**

Operable（T4a any N）



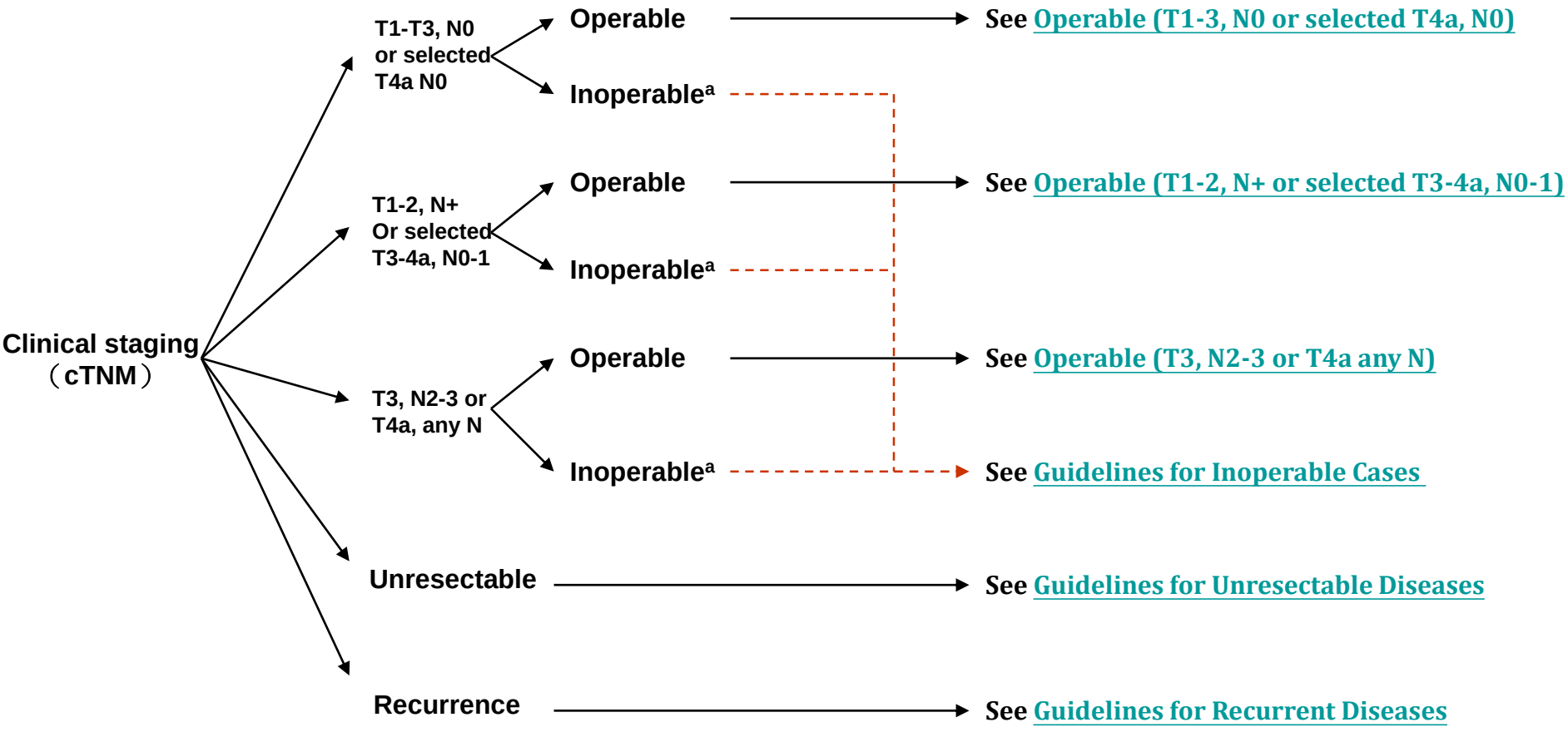
[a] Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.

[b] See Principles of Radiation Therapy.

[c] See Principles of Systemic Therapy.

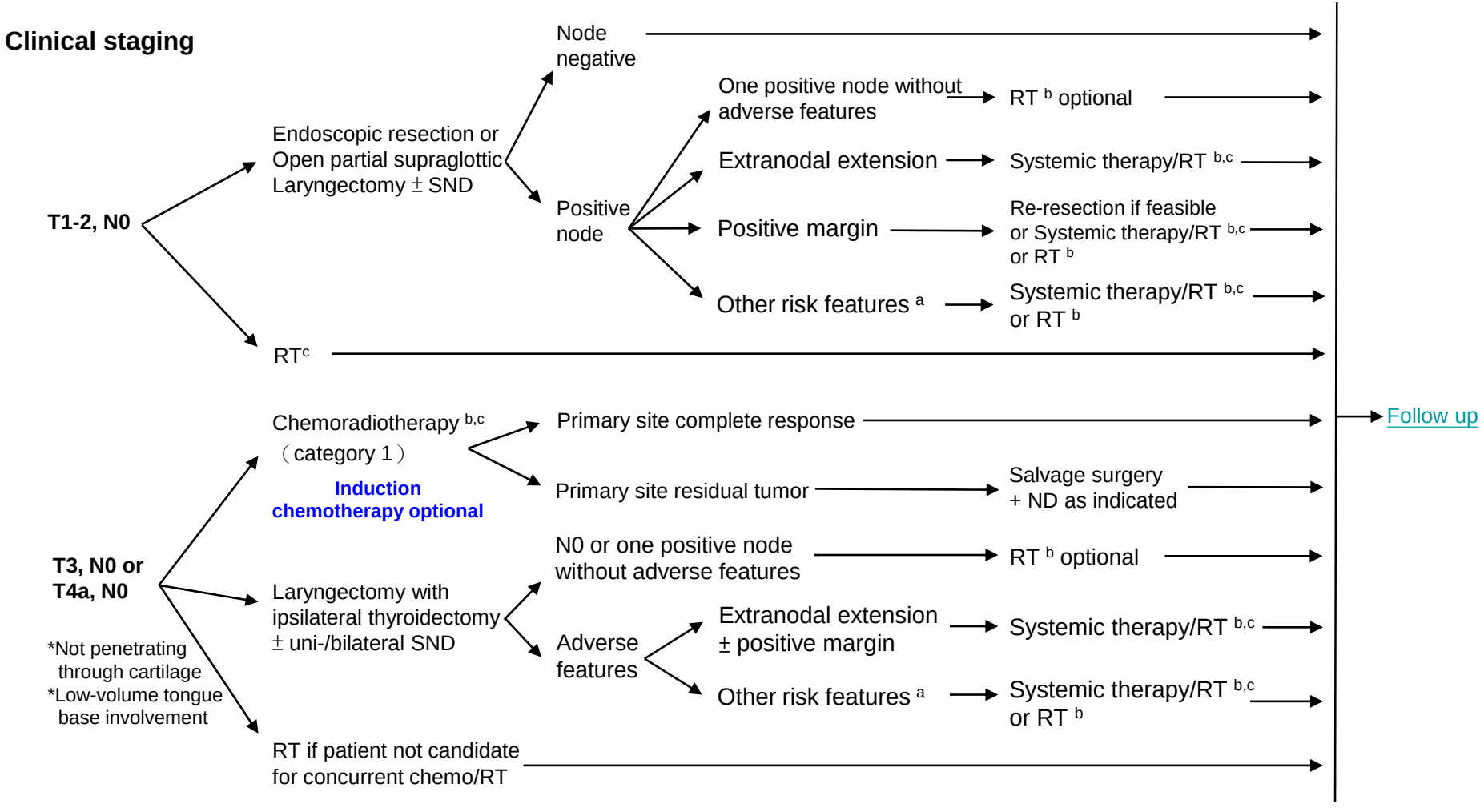
[d] Good risk features: 1. papillary variant of SCC, verrucous carcinoma, 2. negative margins, pN0 (esp Lv VI) w/o PNI/LVI, 3. low volume disease with microscopic extralaryngeal extension and negative margin, 4. pN0, subglottic extension < 1cm

Treatment Stratification



[a] In cases of high risk for surgical intervention or those who refuse surgery（not mentioned as unresectable）

Operable（T1-T3 N0 or selected T4a N0）

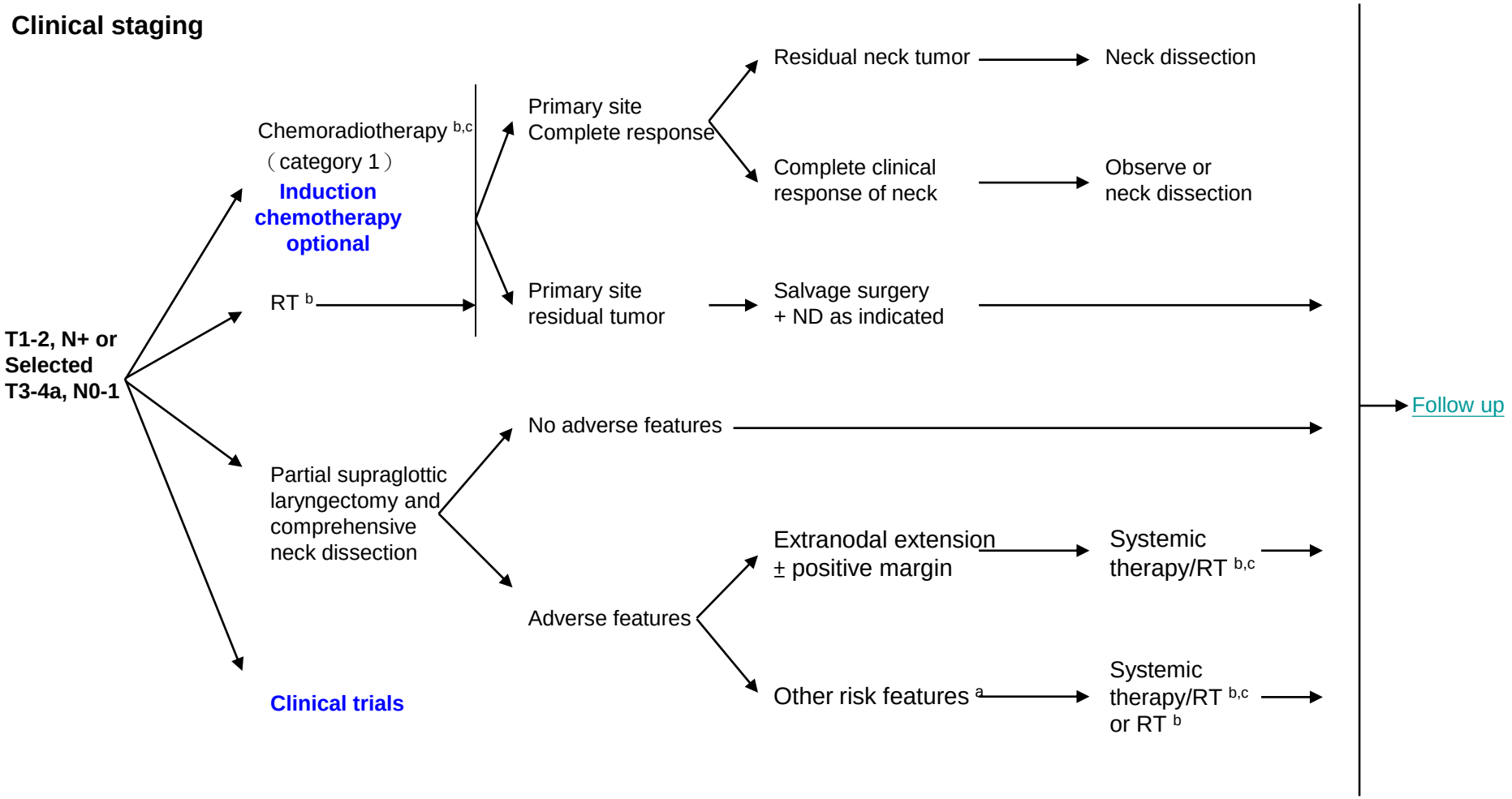


[a] **Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.**

[b] **See Principles of Radiation Therapy.**

[c] **See Principles of Systemic Therapy.**

Operable（T1-2 N+ or selected T3-4a N0-1）

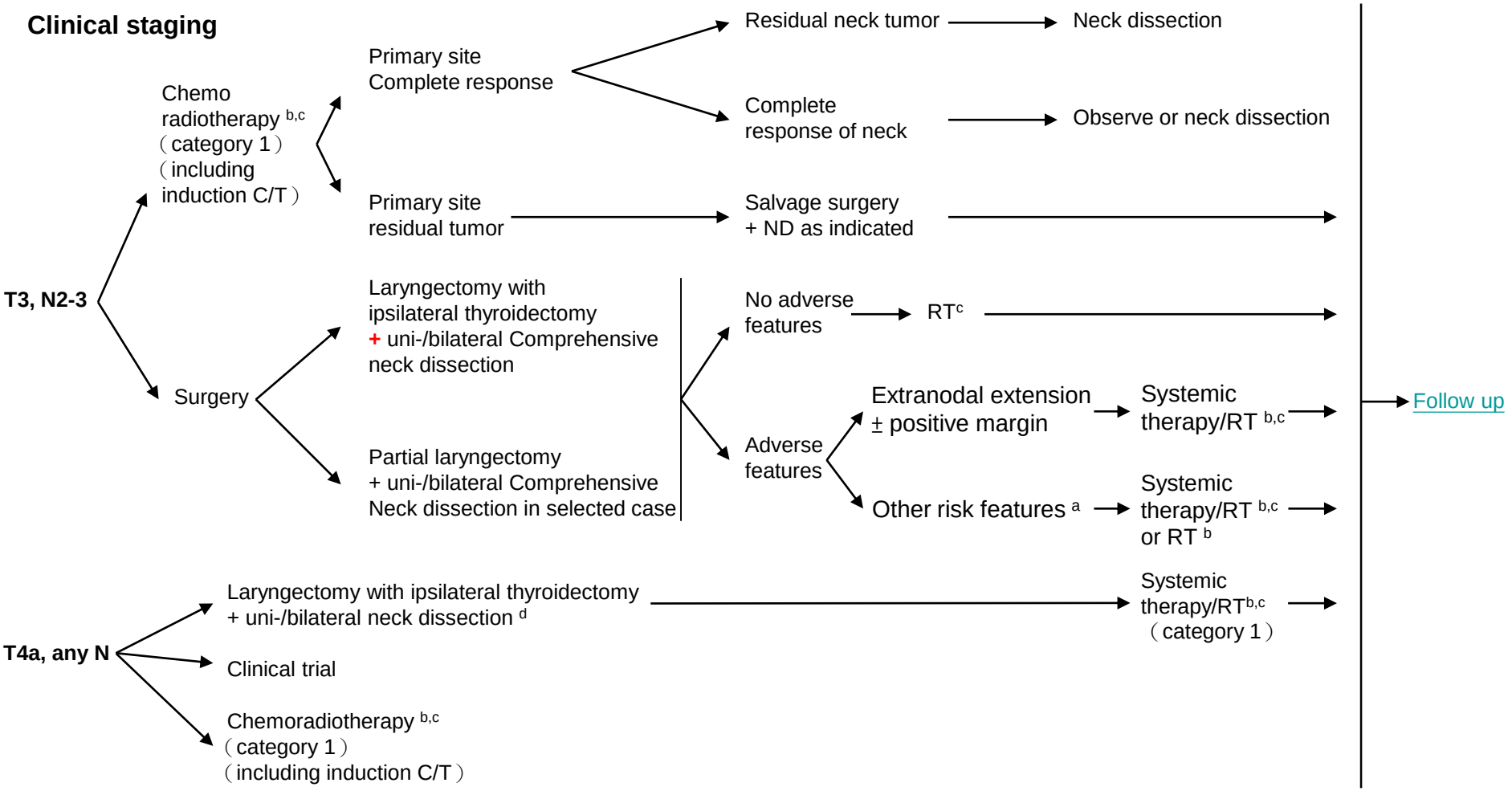


[a] Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.

[b] See Principles of Radiation Therapy.

[c] See Principles of Systemic Therapy.

Operable（T3 N2-3 or T4a any N）



[a] **Adverse risk features：Extranodal extension, positive margins; upstage as pT3 or T4 primary; N2 or N3 nodal disease, nodal disease in levels IV or V; perineural invasion, lymphovascular invasion, tumor emboli.**

[b] **See Principles of Radiation Therapy.**

[c] **See Principles of Systemic Therapy.**

[d] **Cartilage destruction, Skin involvement, Massive tongue base invasion.**

TNM Staging System：UICC/AJCC 2017 8th Edition

Primary Tumor（T）

Tx：Primary tumor cannot be assessed

T0：No evidence of primary tumor

Tis : Carcinoma *in situ*

T1：Tumor 2 cm or smaller in greatest dimension without extraparenchymal extension*

T2：Tumor more than 2 cm but not more than 4 cm in greatest dimension without extraparenchymal extension*

T3：Tumor more than 4 cm and/or tumor having extraparenchymal extension*

T4：Moderately advanced or very advanced local disease

T4a：Moderately advanced disease
Tumor invades skin, mandible, ear canal, and/or facial nerve

T4b：Very advanced disease
Tumor invades skull base and/or pterygoid plates and/or encases carotid artery

*Note：Extraparenchymal extension is clinical or macroscopic evidence of invasion of soft tissues. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes.

TNM Staging System：UICC/AJCC 2017 8th Edition

Clinical N Category

Regional Lymph Nodes（N）

Nx：Regional lymph nodes cannot be assessed

N0：No regional lymph nodes metastasis

N1：Metastasis in a single ipsilateral lymph node, ≤ 3cm, ENE（-）

N2：Metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）
or metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）
or in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2a：Metastasis in single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）

N2b：Metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2c：Metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N3：Metastasis in a lymph node >6 cm in greatest dimension, ENE（-）
or metastasis in any lymph node(s) and clinically overt ENE（+）

N3a：Metastasis in a lymph node >6 cm in greatest dimension, ENE（-）

N3b：Metastasis in any lymph node(s) and clinically overt ENE（+）

***Note：A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L).**
Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+).

Distant Metastasis（M）

M0：No distant metastasis（no pathological M0; use clinical M to complete stage group）

M1：Distant metastasis

TNM Staging System：UICC/AJCC 2017 8th Edition

Pathological N Category　Regional Lymph Nodes（N）

Nx：Regional lymph nodes cannot be assessed

N0：No regional lymph nodes metastasis

N1：Metastasis in a single ipsilateral lymph node, ≤ 3cm, ENE（-）

N2：Metastasis in a single ipsilateral or contralateral lymph node, ≤ 3cm, ENE（+）
or metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）
or metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）
or metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2a：Metastasis in a single ipsilateral or contralateral lymph node, ≤ 3cm, ENE（+）
Metastasis in a single ipsilateral lymph node, > 3cm, but ≤ 6cm in greatest dimension, ENE（-）

N2b：Metastasis in multiple ipsilateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N2c：Metastasis in bilateral or contralateral lymph nodes, ≤ 6cm in greatest dimension, ENE（-）

N3：Metastasis in a lymph node >6 cm in greatest dimension, ENE（-）
or metastasis in a single ipsilateral node, > 3cm in greatest dimension, ENE（+）
or metastasis in multiple ipsilateral, bilateral or contralateral lymph nodes, ENE（+）

N3a：Metastasis in lymph node >6 cm in greatest dimension, ENE（-）

N3b：Metastasis in a single ipsilateral node, > 3cm in greatest dimension, ENE（+）
Metastasis in multiple ipsilateral, bilateral or contralateral lymph nodes, ENE（+）

***Note：A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L).**
Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+).

Distant Metastasis（M）

M0：No distant metastasis（no pathological M0; use clinical M to complete stage group）

M1：Distant metastasis

TNM Staging System：UICC/AJCC 2017 8th Edition
Stage Grouping of M0 Disease（M1 disease as Stage IVC）

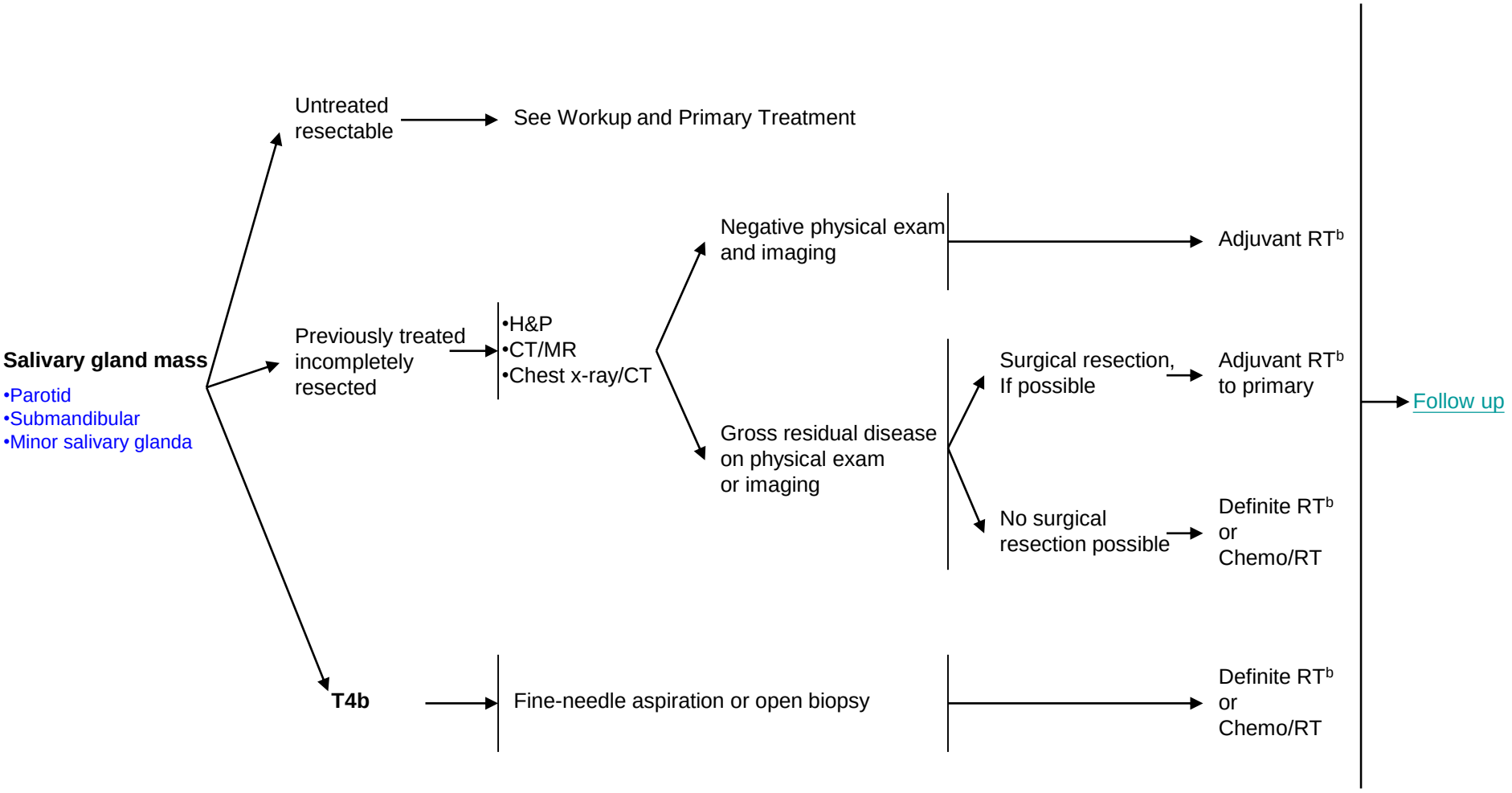
	T0	T1	T2	T3	T4a	T4b
N0	NA	I	II	III	IVA	IVB
N1	III	III	III	III	IVA	IVB
N2	IVA	IVA	IVA	IVA	IVA	IVB
N3	IVB	IVB	IVB	IVB	IVB	IVB

Salivary Gland Tumors

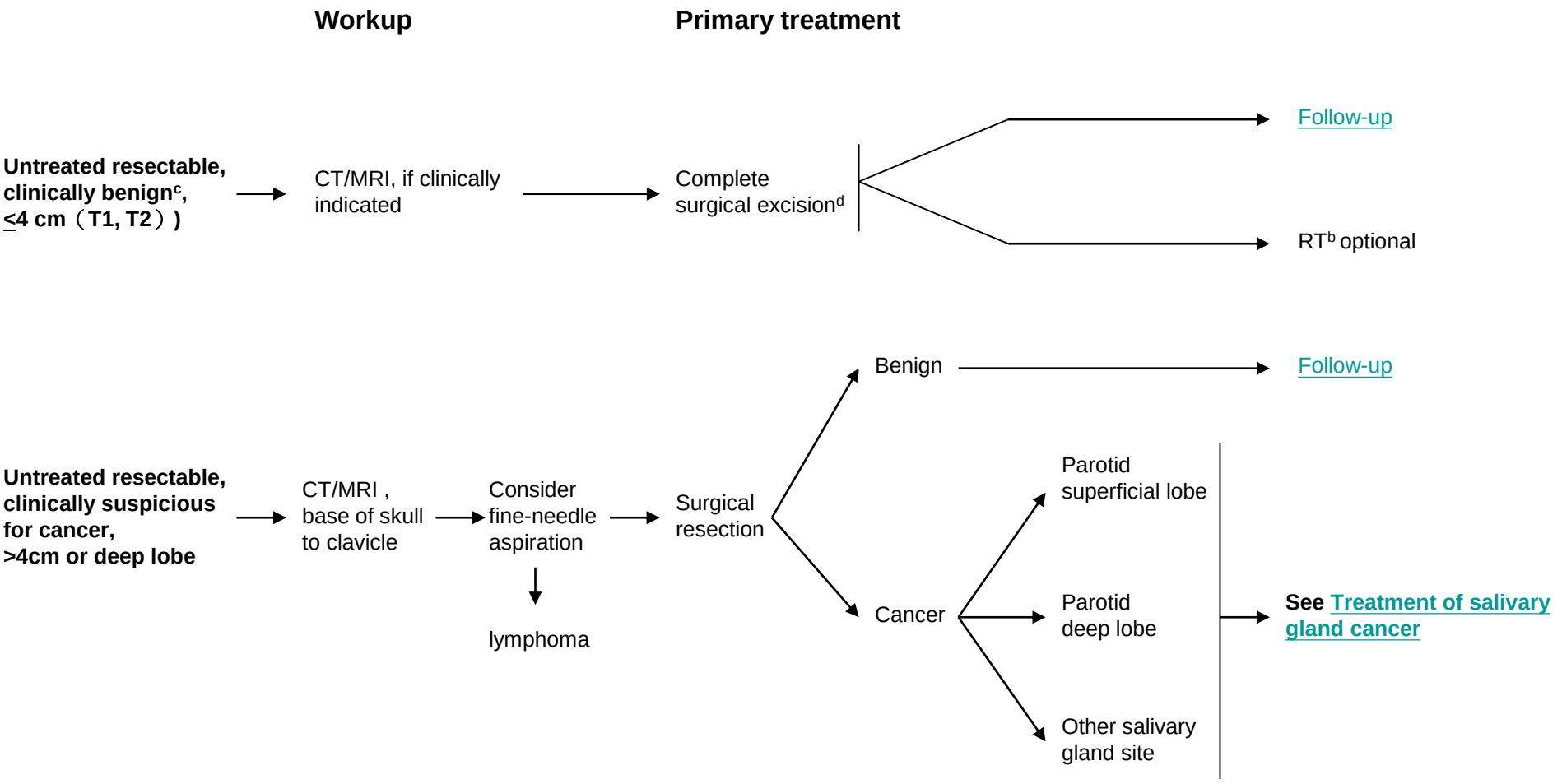
Clinical presentation

Workup

Treatment



[a] **Site and stage determine therapeutic approaches.**
[b] **See Principles of Radiation Therapy**



[b] See Principles of Radiation Therapy.
[C] Characteristics of benign tumor include mobile superficial lobe, slow growth, painless, VII intact, and no neck nodes.
[d] Surgical excision of clinically benign tumor: no enucleation of lateral lobe, intraoperative communication with pathologist if indicated.

Untreated resectable, clinically suspicious for cancer, >4cm or deep lobe

Treatment

- Parotid superficial lobe
  - Clinical N0 → Parotidectomy
  - Clinical N+ → Parotidectomy + neck dissection
- Parotid deep lobe
  - Clinical N0 → Total parotidectomy
  - Clinical N+ → Total parotidectomy + neck dissection
- Other salivary gland sites
  - Clinical N0 → Complete gland excision
  - Clinical N+ → Complete gland excision and neck dissection

- Completely excised
  - No adverse characteristics → **See follow-up**
  - Adenoid cystic → RT [b]
  - • Intermediate or high grade
    • Close or positive margins
    • Neural/perineural invasion
    • Lymph node metastases
    • Lymphatic/vascular invasion
    • T3-4 tumors
    → Adjuvant RT [b] or Consider chemo/RT
- Incompletely excised gross residual disease
  No further surgical resection possible → Definitive RT [b] or Chemo/RT

[b] **See Principles of Radiation Therapy.**

Principles of Radiation Therapy（Salivary Gland Tumor）

- **Definitive RT（for unresectable or gross residual diseases）**
  - Photo/electron therapy or neutron therapy
  - Dose
    - High risk：

      Primary and involved lymph nodes ≥ 66Gy（1.8~2Gy/day）[1]
    - Low to intermediate risk：

      Sites of suspected subclinical spread 44~63Gy（1.6~2Gy/day ）[1]
- **Postoperative RT**
  - Photo/electron therapy or neutron therapy
  - Dose
    - High risk：Adverse features such as positive margin 60~66Gy（2Gy/day）
    - Low to intermediate risk：

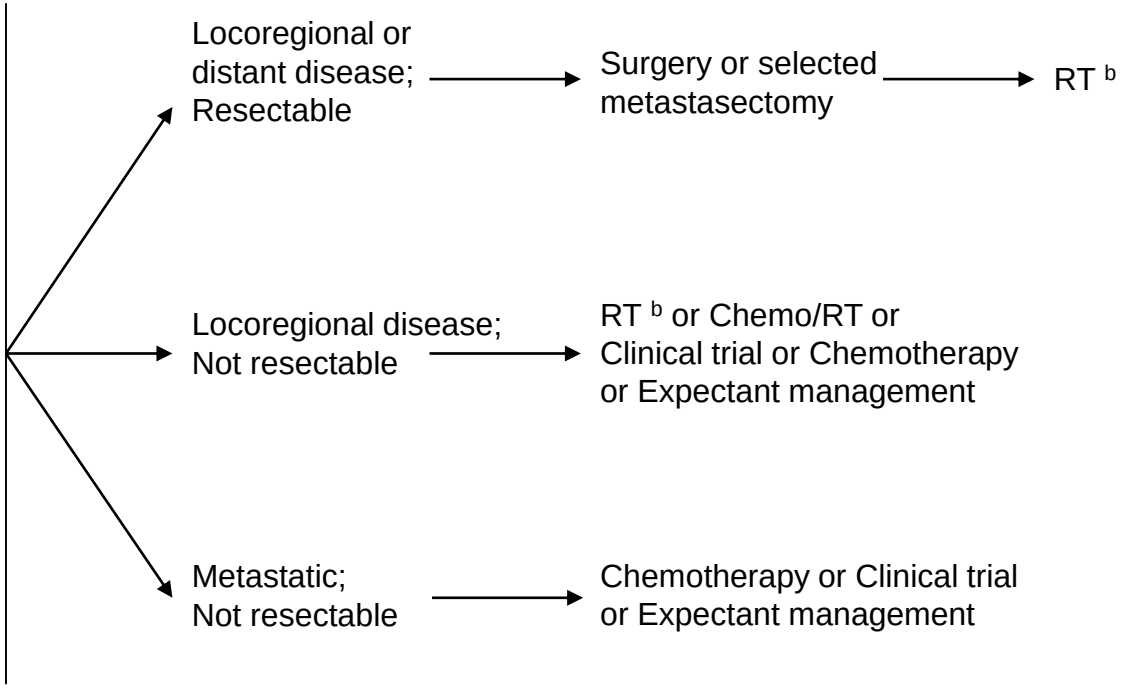
      Sites of suspected subclinical spread 44~63Gy（1.6~2Gy/day ）[1]

[1] **Range based on grade/natural history of the disease（eg. 1.8Gy fraction may be use for slower glowing tumors）**

Follow-up

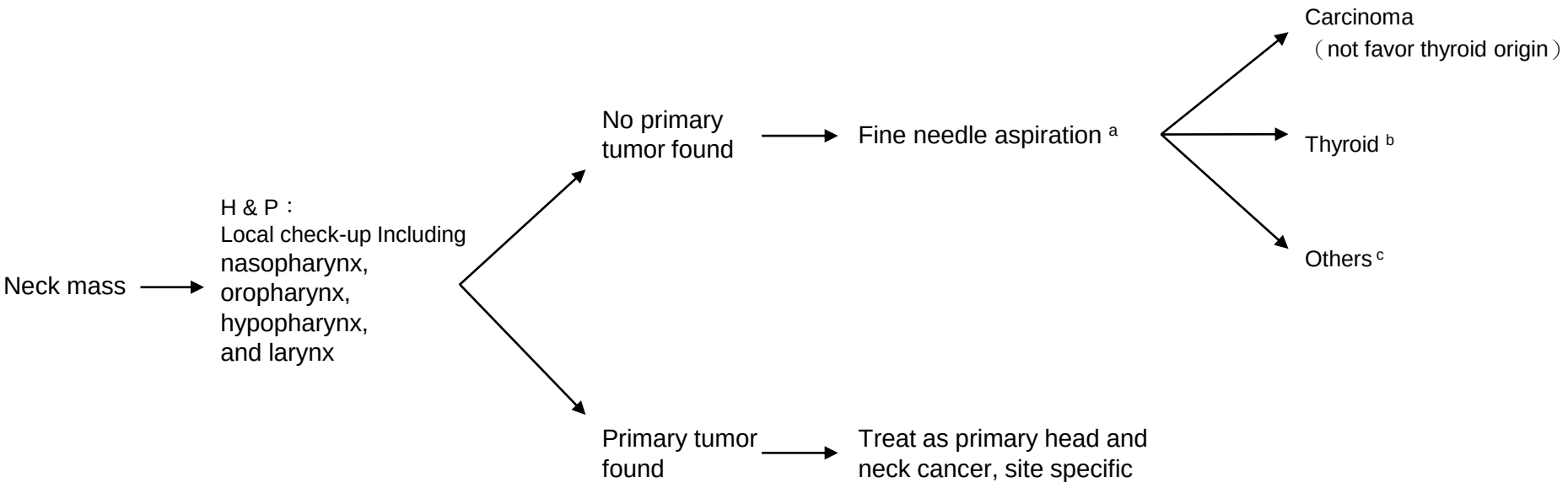
- Physical exam：
  - > Year 1, every 1-3 mo
  - > Year 2, every 2-4 mo
  - > Years 3-5, every 4-6 mo
  - > 5yr, every 6-12 mo
- Chest x-ray/ CT as clinically indicated
- TSH every 6-12 mo, if neck irradiated

Recurrence



[b] See Principles of Radiation Therapy.

Occult primary of neck

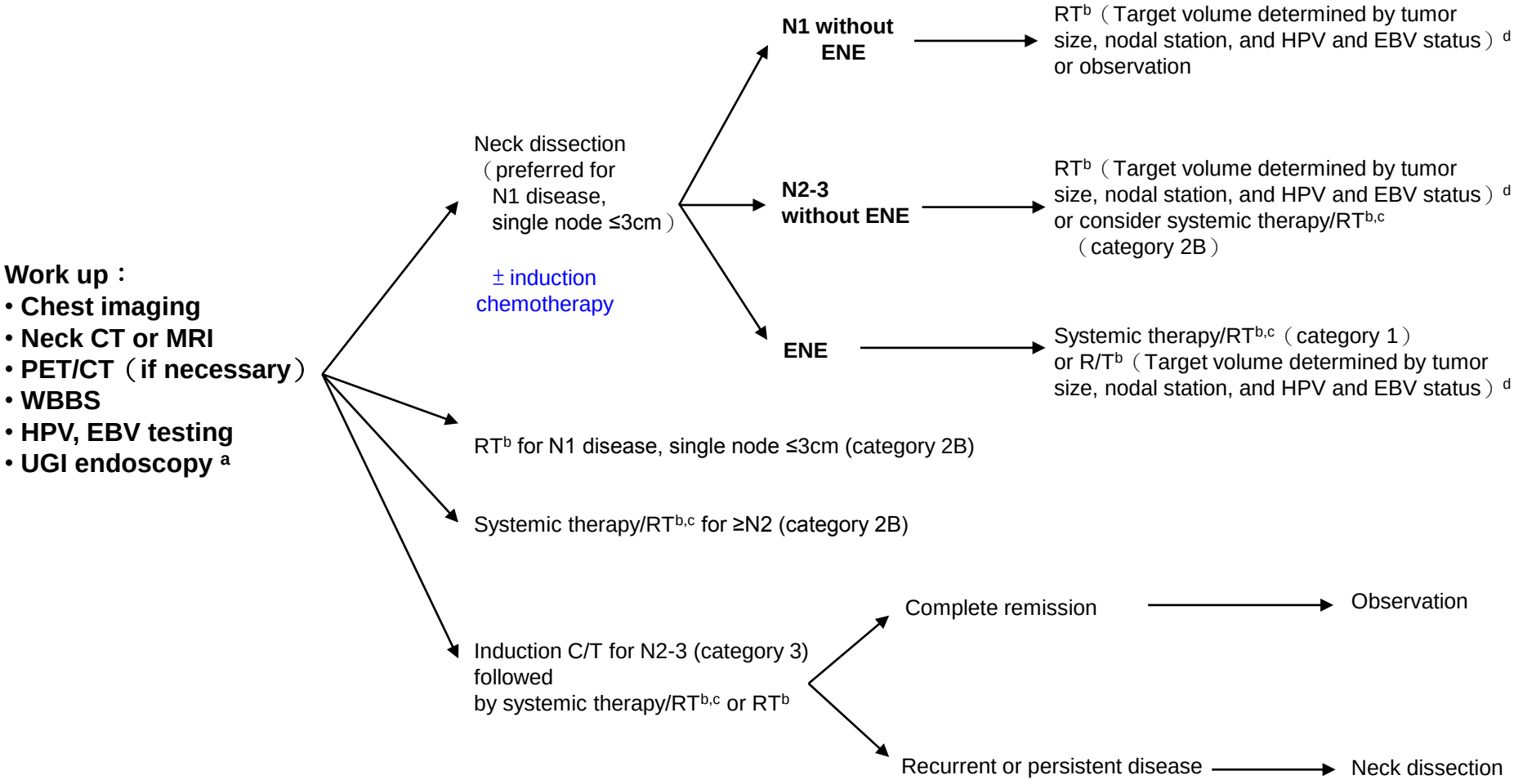


[a] Repeat FNA, core, or open biopsy may be necessary for uncertain or non-diagnostic histologies. Patient should be prepared for neck dissection at time of open biopsy, if indicated. Tonsillectomy could be considered in node level I, II, III, upper IV

[b] According to thyroid ca. treatment guideline

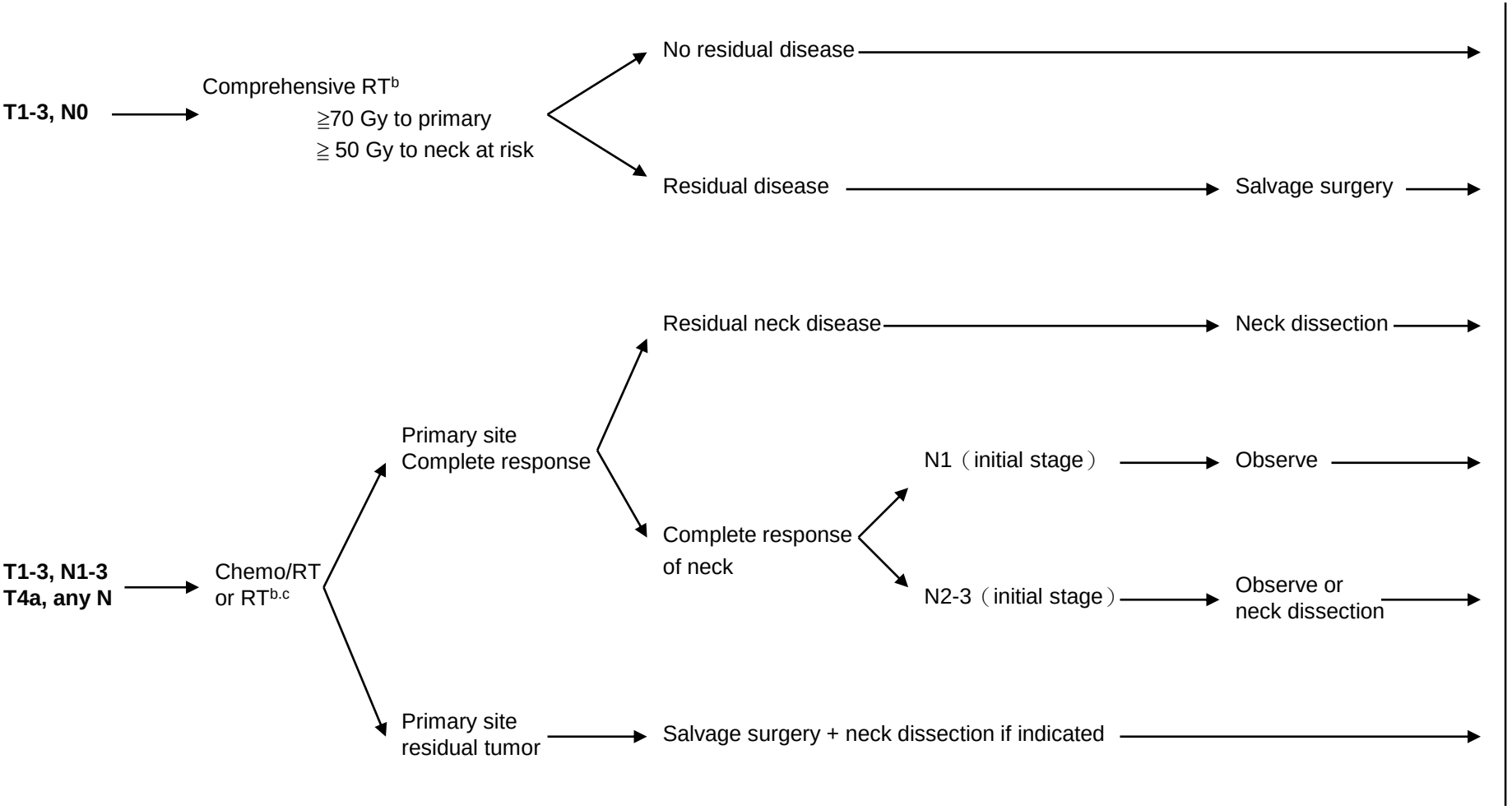
[c] Other diseases should be treated according to their guidelines individually, such as lymphoma, melanoma etc.

Occult primary of neck



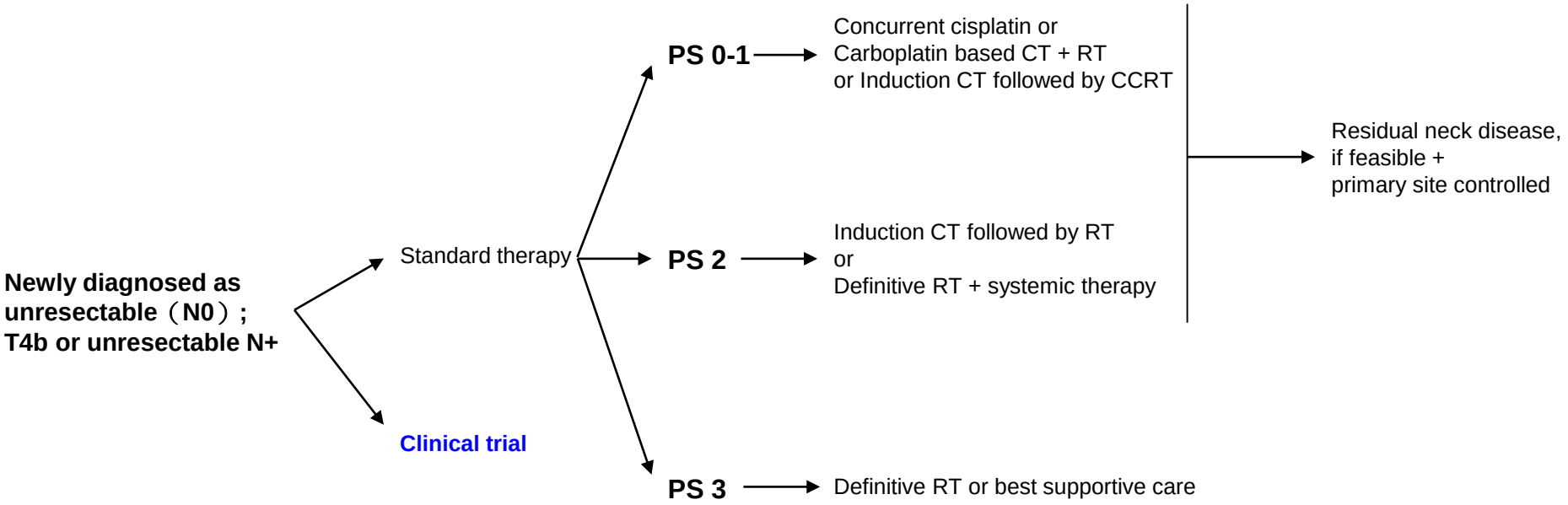
[a] Considered in node level IV or lower V
[b] See Principles of Radiation Therapy.
[c] See Principles of Systemic Therapy.
[d] Whether HPV or EBV positive status may help to define the radiation fields is being investigated.

Guidelines for Inoperable Cases [a]



[a] In cases of high risk for surgical intervention or those who refuse surgery（not mentioned as unresectable）.
[b] See Principles of Radiation Therapy.
[C] See Principles of Systemic Therapy.

Strategies for Unresectable Diseases



ECOG performance status（*Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982*）：

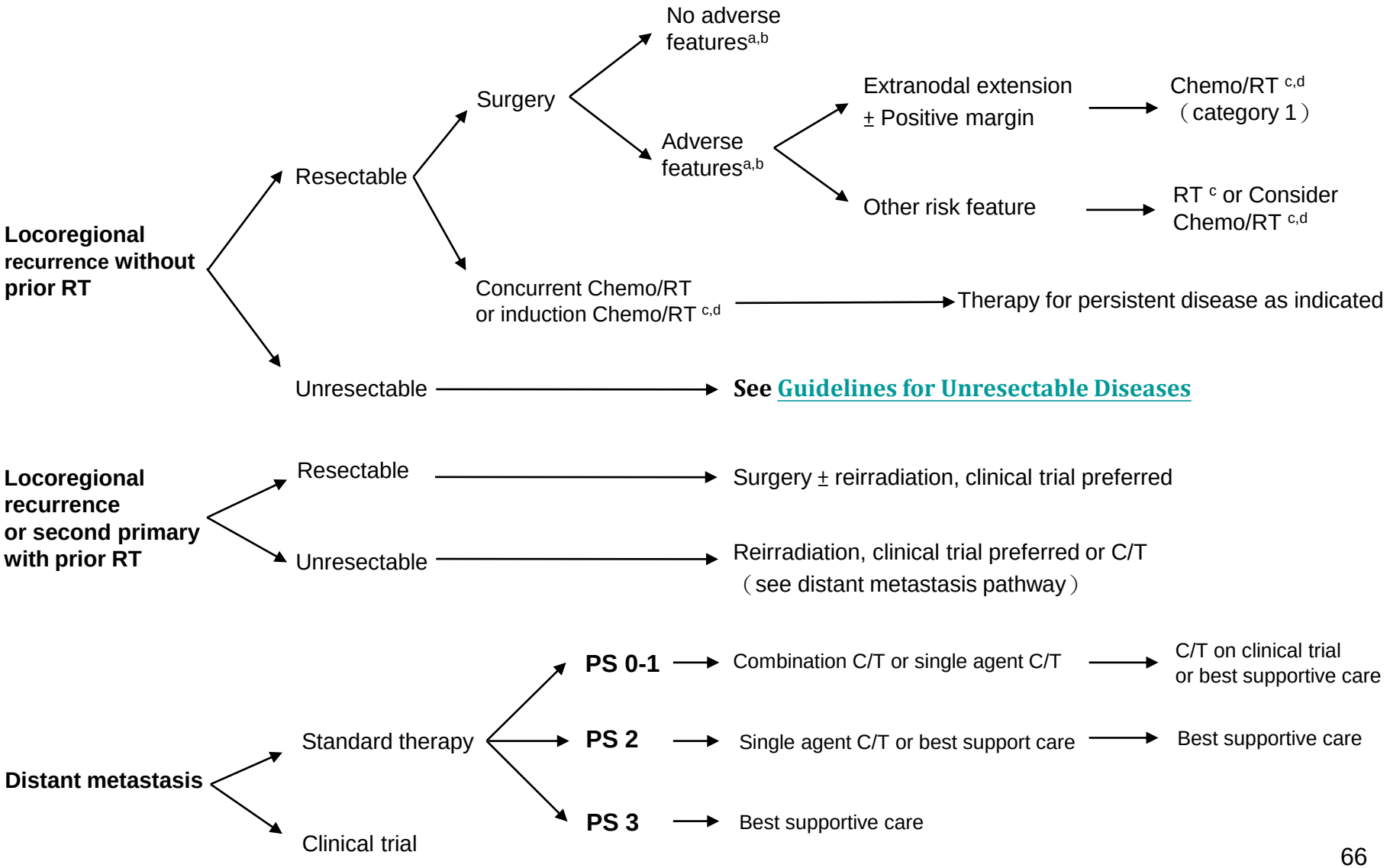
0 Fully active, able to carry on all pre-disease performance without restriction

1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g. light housework

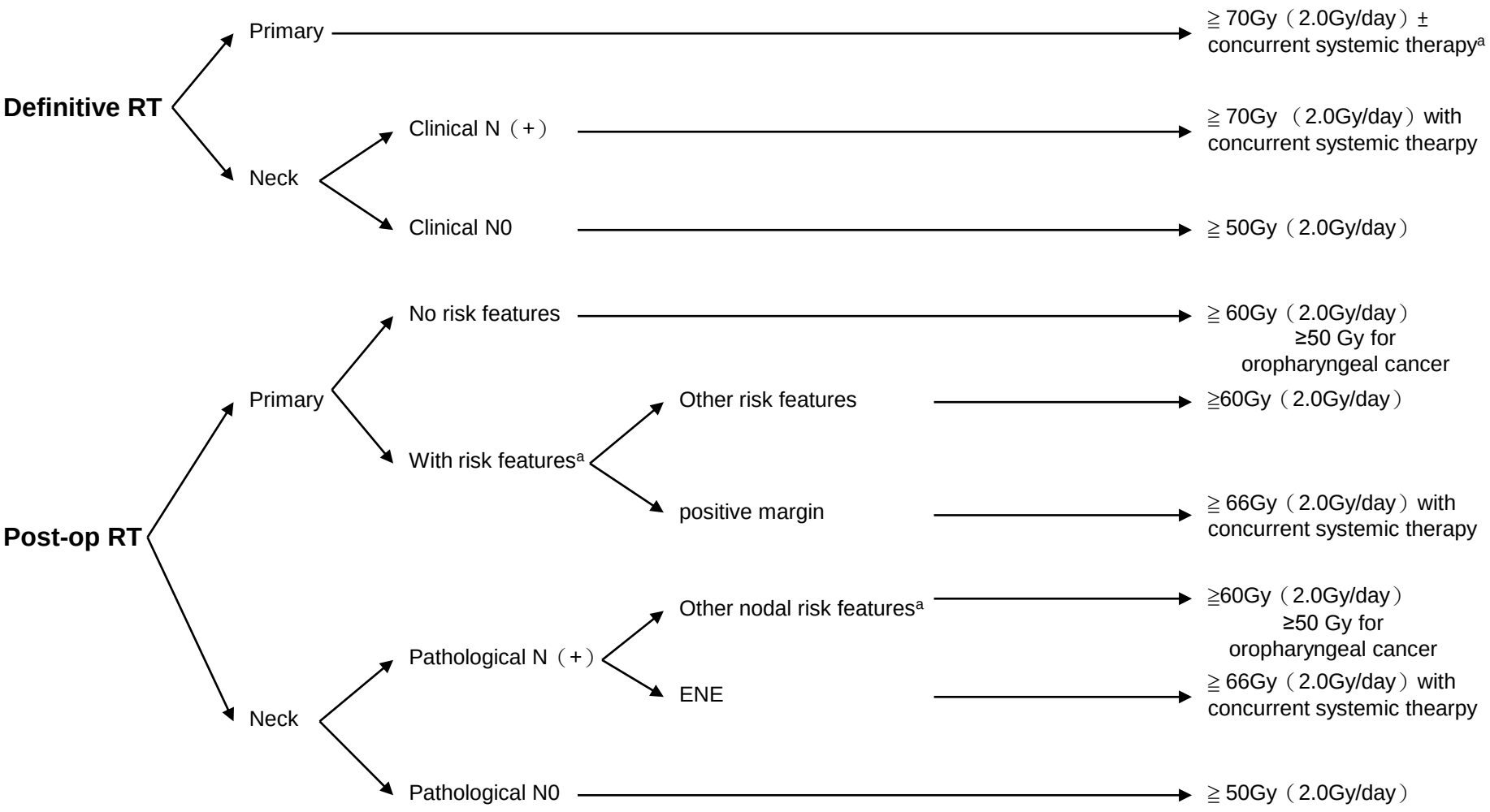
2 Ambulatory and capable of self care but unable to carry out any work activities：up and about more than 50% of waking hours

3 Capable of only limited self care, confined to bed or chair more than 50% of waking hours

Strategies for Recurrence Disease



Principles of Radiation Therapy



[a] **Adverse features：extranodal extension, positive margins, pT3 or pT4 primary, N2 or N3 nodal disease, nodal disease in levels IV or V, perineural invasion, lymphovascular invasion, lymphatic invasion.**
The definition of an adverse feature in the context of HPV+ disease is an area of active research.

Definition of oral cavity cancer:

Cancers arising from the lips, the buccal mucosa, the front two thirds of the tongue, the upper and lower gingiva, the floor of the mouth under the tongue, the hard palate, and the retromolar trigone.

Indications of radiation therapy

- **Definitive radiotherapy**
  - Early stage（T1-2N0）disease
  - Clinical trial for other stages
- **Adjuvant radiotherapy**
  - Risk factors: positive surgical margin（< 5 mm）, extracapsular spreading（ECS）of metastatic lymphadenopthy, perineural invasion, vascular embolism, lymphovascular permeation, pT3 or pT4 primary, N2 or N3 nodal disease, nodal disease in levels IV or V.

Principles of patient simulation

- Patients must have an immobilization device（e.g., aquaplast mask）made prior to treatment planning CT scan.
- Shoulder fixation is recommended, esp. with IMRT technique.
- A cork or tongue depressor can be used to depress the tongue for tongue, floor of mouth or hard palate cancer.
- The treatment planning CT scan should be performed with IV contrast so that the major vessels of the neck are easily visualized. The treatment planning CT scan must be performed with the immobilization device and in the treatment position. Slice thickness should be at most 0.5 cm.

Principles of Radiation Therapy

- **Radiation technique：**

– **Intensity-Modulated Radiotherapy（IMRT）**

IMRT has been shown to be useful in reducing long-term toxicity in oropharyngeal, paranasal sinus, and nasopharyngeal cancers by reducing the dose to salivary glands, temporal lobes, auditory structures（including cochlea）, and optic structures. The application of IMRT to other sites（eg, oral cavity, larynx, hypopharynx, salivary glands）is evolving and may be used at the discretion of treating physicians.

– **IMRT and Fractionation**

A number of ways exist to integrate IMRT, target volume dosing, and fractionation. The **Simultaneous Integrated Boost（SIB）**technique uses differential "dose painting"（66-74 Gy to gross disease; 50-60 Gy to subclinical disease）for each fraction of treatment throughout the entire course of radiation. SIB is commonly used in conventional（5 fractions/week）and the "6 fractions/week accelerated" schedule. The **Sequential（SEQ）**IMRT technique typically delivers the initial（lower dose）phase（weeks 1-5）followed by the high-dose boost volume phase（weeks 6-7）using 2-3 separate dose plans, and is commonly applied in standard fractionation and hyperfractionation.

Principles of Radiation Therapy

- **Definitive radiotherapy**
  - Primary and gross adenopathy：
    - Conventional fractionation：66-74 Gy（2.0-2.2 Gy/fraction; daily）
    - Altered fractionation：
      - 6 fractions/week accelerated：
        66-74 Gy to gross disease, 44-60 Gy to subclinical disease.
      - Concomitant boost accelerated RT：
        72 Gy/6 weeks（1.8 Gy/fraction, large field; 1.5 Gy boost as second daily fraction during last 12 treatment days）
      - Hyperfractionation：
        81.6 Gy/7 weeks（1.2 Gy/fraction, twice daily）
  - Neck
    - Uninvolved nodal stations：44-60 Gy（1.6-2.0 Gy/fraction）

Principles of Radiation Therapy

- **Postoperative radiotherapy**
  - Preferred interval between resection and postoperative RT is 6 weeks.
  - Primary：60 Gy（2.0 Gy/fraction）for free margins;

    66 Gy（2.0 Gy/fraction）for positive or close margins.
  - Neck
    - Involved nodal stations：60-66 Gy（2.0-2.2 Gy/fraction）
    - Uninvolved nodal stations：44-60 Gy（1.6-2.0 Gy/fraction）

Principles of Target volume delineation

- **Gross Target Volume（GTV）delineation**
  - defined as tumor detected on physical examination or imaging studies. In postoperative cases, the GTV was defined as the preoperative gross tumor volume.
- **Clinical Target Volume（CTV）delineation**
  - included all potential areas at risk for microscopic tumor involvement by either direct extension or nodal spread.
  - Including volumes 4-5 mm around GTV.
- **Planning Target Volume（PTV）delineation**
  - including a margin for patient motion and setup errors.
  - 3 to 5 mm margin is usually added to CTV.

Contouring guideline

- Image registration of CT and MRI/PET（if available）should be done for GTV delineation.
- Adequate coverage of infratemporal fossa is necessary for upper gingival or retromolar trigone cancer.
- For oral cavity cancer, adjacent level Ia and Ib of neck are usually included, except for early retromolar trigone tumors（only Ib）. Level II to V should be covered for LN（+）cases.
- Lateral retropharyngeal LN（of Rouviere, level VIIb）are rarely involved by oral cavity cancer.（Only few case reports exist）.
- The following lymph nodes are not included：
  - **Level VIa**：Lymph nodes in the prelaryngeal area of the neck.
  - **Level VIb**：Lymph nodes in the paratracheal area of the neck and upper mediastinum.

CTV: unilateral or bilateral neck?

- For early-stage buccal, gingival, retromolar and hard palate cancer, usually unilateral neck is treated.
- For tongue and floor of mouth cancer（midline position）, bilateral neck is usually treated.
- Locally advanced primary disease, multi-involvement of ipsilateral neck nodes, high pathological grading are associated with contralateral neck lymph node metastasis.
- For salvage irradiation after local（regional）recurrence, contralateral neck treatment is recommended for patients with extracapsular spreading.

Principles of Radiation Therapy

- **Radiation technique：**

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Principles of Radiation Therapy

- **Definitive radiotherapy**
  - Primary and gross adenopathy in the neck：
    - Conventional fractionation：
      66-70 Gy（2.0-2.2 Gy/fraction; daily）in 6 to 7 weeks
    - Altered fractionation：
      - 6 fractions/week accelerated：
        66-70 Gy to gross disease, 44-60 Gy to subclinical disease.
      - Concomitant boost accelerated RT：
        72 Gy/6 weeks（1.8 Gy/fraction, large field; 1.5 Gy boost as second daily fraction during last 12 treatment days）
      - Hyperfractionation：81.6 Gy/7 weeks（1.2 Gy/fraction, twice daily）
  - Neck
    - Intermediate risk（adjacent to gross adenopathy）：
      54 to 63 Gy（1.8 to 2.0 Gy/ fraction）
    - Uninvolved nodal stations：44-50 Gy（1.6-2.0 Gy/fraction）

Principles of Radiation Therapy

- **Postoperative radiotherapy**
  - Preferred interval between resection and postoperative RT is less than 6 weeks.
  - Primary：60 to 66 Gy（2.0-2.2 Gy/fraction）in 6 to 6.5 weeks.
    >50 Gy for those without risk features
  - Neck
    - Involved nodal stations: 54-66 Gy（1.8-2.2Gy/fraction ）
      >50 Gy for those without risk features
    - Uninvolved nodal stations: 44-60 Gy（1.6-2.0 Gy/fraction ）

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Principles of Radiation Therapy

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Principles of Radiation Therapy

- **Definitive radiotherapy**
  - Primary and gross adenopathy in the neck：
    - Conventional fractionation：
      66-70 Gy（2.0-2.2 Gy/fraction; daily）in 6 to 7 weeks.
    - Altered fractionation：
      - 6 fractions/week accelerated：
        66-70 Gy to gross disease, 44-60 Gy to subclinical disease.
      - Concomitant boost accelerated RT：
        72 Gy/6 weeks（1.8 Gy/fraction, large field; 1.5 Gy boost as second daily fraction during last 12 treatment days）
      - Hyperfractionation：81.6 Gy/7 weeks（1.2 Gy/fraction, twice daily）
  - Neck
    - Intermediate risk（adjacent to gross adenopathy）：
      54 to 63 Gy（1.8 to 2.0 Gy/ fraction)
    - Uninvolved nodal stations：44-50 Gy（1.6-2.0 Gy/fraction）

Principles of Radiation Therapy

- **Postoperative radiotherapy**
  - Preferred interval between resection and postoperative RT is less than 6 weeks.
  - Primary：
    60 to 66 Gy（2.0-2.2 Gy/fraction）in 6 to 6.5 weeks
  - Neck
    - Involved nodal stations：
      54-66 Gy（1.8-2.2Gy/fraction）
    - Uninvolved nodal stations：
      44-60 Gy（1.6-2.0 Gy/fraction）

Principles of Target volume delineation

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  - defined as tumor detected on physical examination or imaging studies. In postoperative cases, the GTV was defined as the preoperative gross tumor volume.
- **Clinical Target Volume（CTV）delineation**
  - included all potential areas at risk for microscopic tumor involvement by either direct extension or nodal spread.
  - Including volumes 4-5 mm around GTV.
- **Planning Target Volume（PTV）delineation**
  - including a margin for patient motion and setup errors.
  - 3 to 5 mm margin is usually added to CTV.

Regimens for Induction Chemotherapy

TPF（Q3W）x 2~3 cycles

- Docetaxel 60 mg/m^2 infusion for 3 hours
- Cisplatin 75 mg/m^2 infusion for 3 hours
- 5-FU **750 mg/m^2** per 24 hours as a 96-hour continuous infusion

4-day PFL（Q3W）x 2~3 cycles

- Cisplatin 80 mg/m^2 infusion for 3 hours
- 5-FU 600 mg/m^2 per 24 hours as a 96-hour continuous infusion
- Leucovorin 90 mg/m^2 per 24 hours as a 96-hour continuous infusion

Cisplatin + DeGramount（Q2W）x 3 cycles

- Cisplatin 50 mg/m2 infusion for 3 hours
- Leucovorin 200 mg/m2 infusion for 2 hours per day for 2 days
- 5-FU 400 mg/m2 infusion for 30 minutes per day for 2 days
- 5-FU 600 mg/m2 per 24 hours as a 48-hour continuous infusion

DCU（every 21 days a cycle）x 2 cycles

- Docetaxel（Taxotere）36 mg/m2 IVD for 2hr on D1 and D8
- Cisplatin （CDDP） 30 mg/m2 IVD for 2hr on D1 and D8
- UFUR 300mg/m2 x 14days

* Cetuximab can be used as combination by the physician's judgment, however, it is not suggested the combination of cetuximab and cisplatin without docetaxel.
* Other drugs combined with cisplatin such as paclitaxel or UFUR could be considered according to the specific patients' condition and agreed after discussing in the committee.
* Carboplatin should only be considered unless patients' Ccr < 40 or other inevitable reasons that cisplatin cannot be used after discussing in the committee.

Regimens for Definitive Concurrent Chemoradiation Therapy

CFHx（Q3W）x 2 cycles

- Cisplatin 20 mg/m^2 per 3 hours as a 96-hour continuous infusion
- 5-FU 600 mg/m^2 per 20 hours as a 96-hour continuous infusion
- Hydroxyurea 500 mg po stat and bid x 11 doses

4-day PFL with reduced 5FU dose（Q4W）x 2 cycles

- Cisplatin 80 mg/m2 infusion for 3 hours
- 5-FU 400 mg/m2 per 21 hours as a 96-hour continuous infusion
- Leucovorin 90 mg/m2 per 21 hours as a 96-hour continuous infusion

Weekly Cisplatin（QW）x 7 cycles

- Cisplatin 35 mg/m2 infusion for 3 hours

Cetuximab（Q3W）x 7 cycles

- Cetuximab 400 mg/m2 infusion for 2 hours 1 wk before RT
- Cetuximab 200 mg/m2 infusion for 1 hours every wk during RT

TFHx（Q3W）x 2 cycles

- Hydroxyurea 500 mg po stat and bid x 11 doses
- Paclitaxel 20 mg/m2 infusion for 1 hours, QD for 5days
- 5-FU 600 mg/m2 per 24 hours as a 96-hour continuous infusion

Regimens for Definitive Concurrent Chemoradiation Therapy

Weekly Cetuximab and Cisplatin x 7 cycles

- Cisplatin 35 mg/m^2 infusion for 1 hour every week during Radiotherapy
- Cetuximab 400 mg/m^2 infusion for 2 hours 1 week before Radiotherapy
- Cetuximab 250 mg/m^2 infusion for 1 hour every week during Radiotherapy

Weekly Cisplatin and Paclitaxel（QW）x 7 cycles

- Cisplatin 25 mg/m2 infusion for 1 hour
- Paclitaxel 50 mg/m2 infusion for 1 hour

Q3W Cisplatin（Q3W）x 3 cycles

- Cisplatin 80 mg/m2 infusion for 3 hours

***Other drugs such as paclitaxel, tegafur/uracil, mitomycin, epirubicin, etc. could be considered according to the specific patients' condition and agreed after discussing in the committee.**
***Cetuximab is only suggested as monotherapy in concurrent chemoradiation currently.**
***If patient use docetaxel as induction chemotherapy, the followed concurrent chemoradiation suggests the use of paclitaxel.**

Regimens for Adjuvant Concurrent Chemoradiation Therapy

Weekly Cisplatin（QW）with Tegafur-Uracil x 7 cycles

- Cisplatin 25~30 mg/m^2 infusion for 2~4 hours
- UFUR 2# bid（or 1# tid）till completion of radiation

PM +Tegafur-Uracil x 2 cycles followed by 5-FU x 4 cycles

- D1： Cisplatin 70mg/m2 iv 3 hours
  + mitomycin C 7mg/m2 iv 30 min, q 4 weeks x 2 cycles
- Tegafur-Uracil 1# tid, po qd continuous until 5-FU complete
- 5-FU 1000mg/m2, iv weekly x 4 cycles after 4 weeks complete R/T

Regimens for Recurrent and Metastatic Setting

* No single preferred chemotherapeutic regimen, salvage surgery or radiotherapy is also indicated if feasible.
* Platinum based therapy is suggested for the first line treatment.
* Cetuximab could be added according to the physician's judgement.
* 5-FU, taxanes, methotrexate, ifosfamide, bleomycin, gemcitabine, etc. le therapy according to the physician's judgement and agreed after discussing in the committee.

Follow-Up

- **Physical examination and endoscopy**
  - 1st year, every 4-6 weeks
  - 2nd year, every 2-3 months
  - 3rd ~5th year, every 3~6 months
- **Image studies：**
  - CXR：every 6-12 months
  - Face CT/MRI：every 6-12 months
  - PET/CT（optional）
    - 1st year, every 3-4 months
    - 2nd year, every 6-12 months
- **Thyroid function：**
  - Every 6~12 months if neck irradiated
- **Liver function、renal function、CBC：**
  - Every 6 months post chemotherapy or radiotherapy
- **Dental care:** every 6 months
- **Speech and swallow evaluation（optional）**

Manuscript

- **Incidence and Etiology**

Cancer of the oral cavity is the 6th leading malignancy in Taiwan. According to the report from the Department of Health, approximately 4,435 new cases of oral cancer were estimated to occur in 2003 and about 2,200 death occurred in 2006. This accounts for about 7.09% of new cancer cases in Taiwan. Alcohol, betel quid and tobacco abuse are common etiologic factors in cancers of the oral cavity.

The oropharynx includes the base of the tongue, tonsils, soft palate, and posterior pharyngeal wall. The oropharynx is extremely rich in lymphatics. Depending on the subsite involved, 15% to 75% of patients with oropharyngeal cancer present with lymph node involvement. Alcohol, betel quid and tobacco abuse are common etiologic factors in cancers of the oropharynx.

The hypopharynx extends from the superior border of the hyoid bone to the lower border of the cricoid cartilage and is essentially a muscular, lined tube extending from the oropharynx to the cervical esophagus. Prognosis for hypopharyngeal cancer is unfavorable compared with other head and neck cancers owing to the tendency of advanced presentation, submucosal extension, early cervical lymph node metastasis and the propensity for distant metastasis.
Alcohol, betel quid and tobacco abuse are common etiologic factors in cancers of the oral cavity, oropharynx and hypopharynx. By the theory of “field cancerization”, patients with cancer of hypopharynx are at risk for developing second primary neoplasms of the upper aerodigestive tract.

Manuscript

- **Staging**

  Stage at diagnosis is the most predictive factor of survival. The 2010 AJCC staging classification was used as a basis for the treatment guideline of oral cancer. Generally, stage I or stage II disease defines a relatively small primary tumor with no nodal involvement. Stage III and stage IV cancers include large primary tumors, which may invade underlying structures and/or spread to regional neck lymph nodes. Distant metastases are uncommon at presentation.

- **Anatomical Considerations**：

  This guideline is applicable to the following anatomical sites（ICD-O-3-T Codes）

  Oral Cavity
  - Lip
  - Buccal mucosa
  - Anterior tongue
  - Alveolar ridge
  - Floor of mouth
  - Retromolar trigone
  - Hard palate

  Oropharynx
  - Posterior pharyngeal wall
  - Tonsillar fossa & pillar
  - Base of tongue
  - Soft palate & uvula Lip

  Hypopharynx
  - Pyriform sinus
  - Post-cricoid area
  - Posterior pharyngeal wall

Manuscript

- **Pathological Considerations**：

  This guideline is applicable to the lesions pathologically diagnosed as **squamous cell carcinoma**. It is not applicable to other pathological entities, such as sarcoma, lymphoma ..etc. Special considerations should be provided for malignant salivary gland tumor.

- **Definition of Unresectable Disease**：

  “unresectable”: if surgeons doubt their ability to remove all gross tumor on anatomic grounds or if they are certain local control will not be achieved after an operation（even with the addition of radiotherapy to the treatment approach）.

  Conditions not classified as unresectable disease：

  - Patients refuse surgical management.
  - The locoregional disease may be surgically treatable, but patients with distant metastases. The patient choice or a doctor‘s expectations regarding cure and morbidity will influence or determine treatment.
  - Patients with resectable tumors who can be adequately treated without an operation（the disease is usually less extensive that may represent an equivalent outcome by definitive treatment with radiation therapy alone or RT combined with chemotherapy）.

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