The integration of functional imaging in the management of head and neck cancer

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Head and Neck
PET Imaging Research Program

- Clinical research program assessing the utility of functional (PET/CT) imaging in the evaluation of the neck following radiotherapy in head and neck cancer

- Incorporation of the findings into the routine management of head and neck cancer
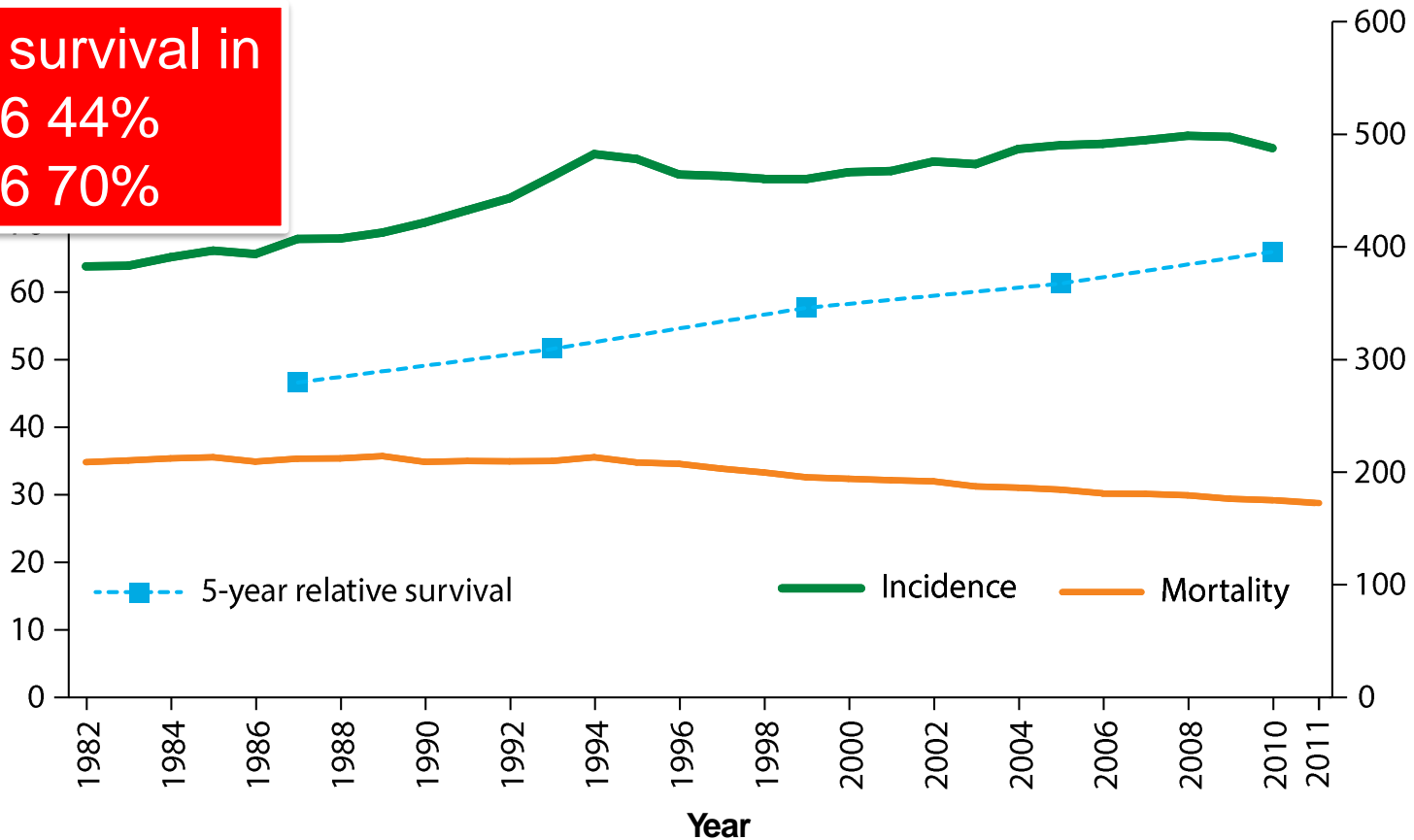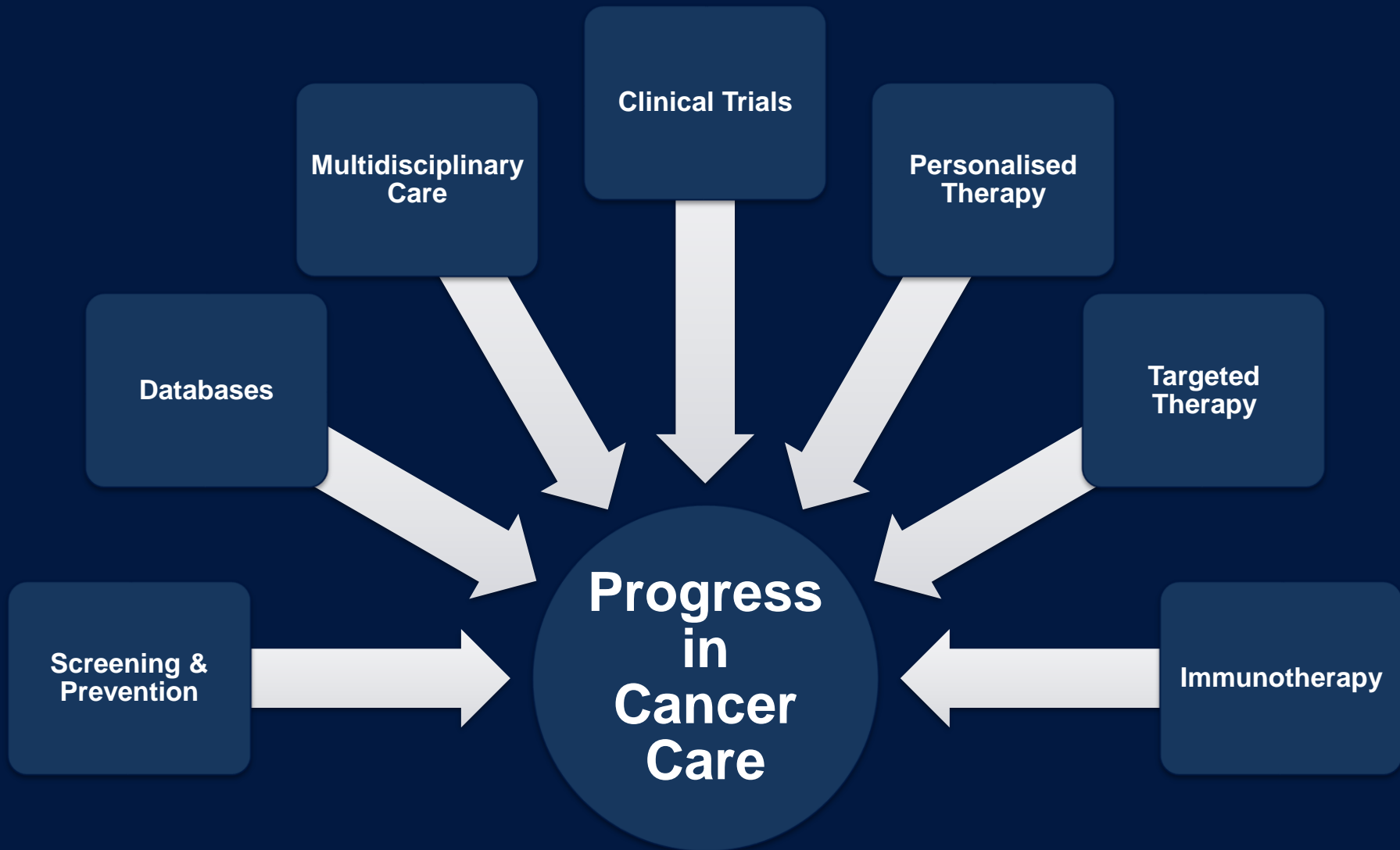
Australian cancer incidence & mortality

Multidisciplinary Care

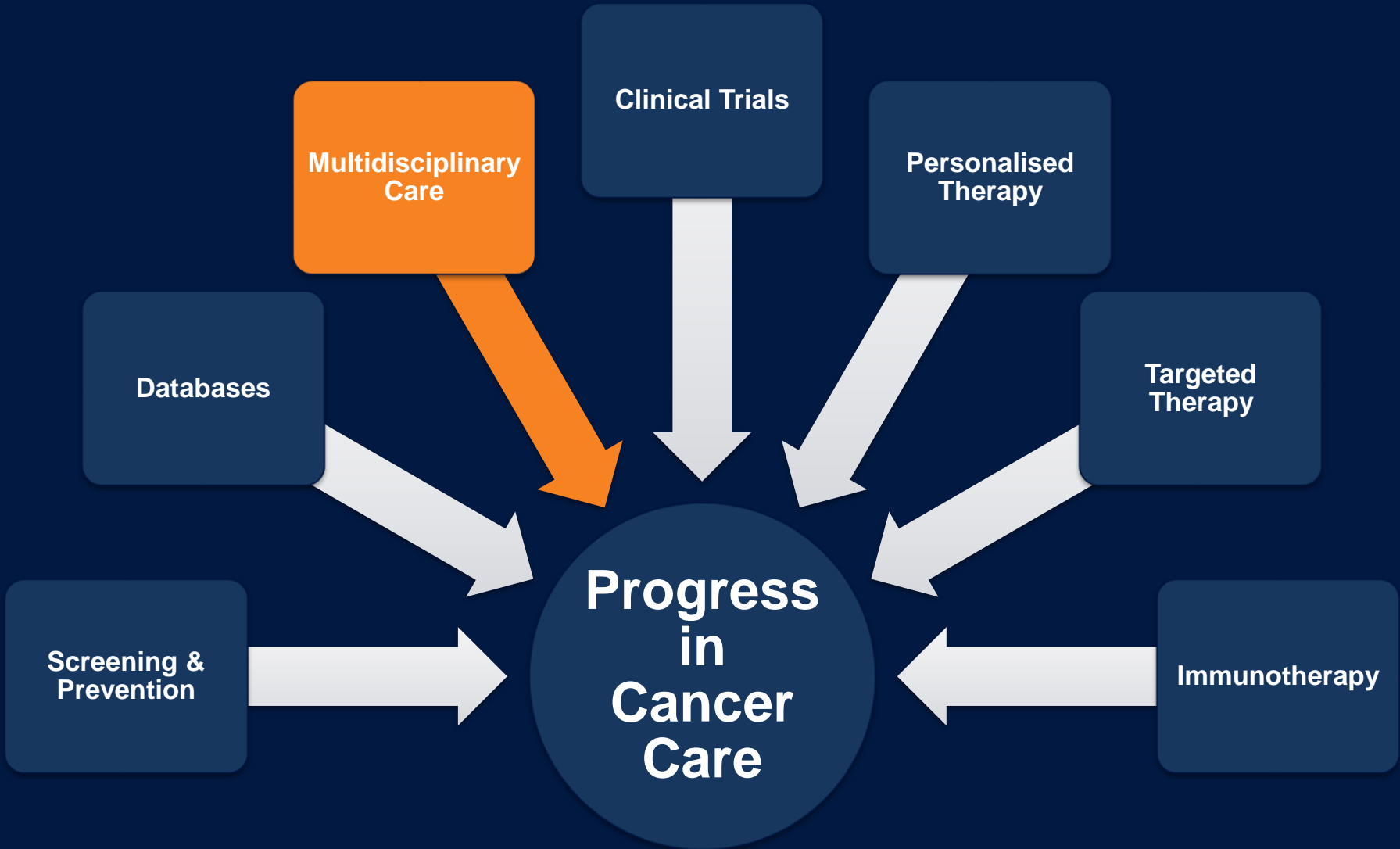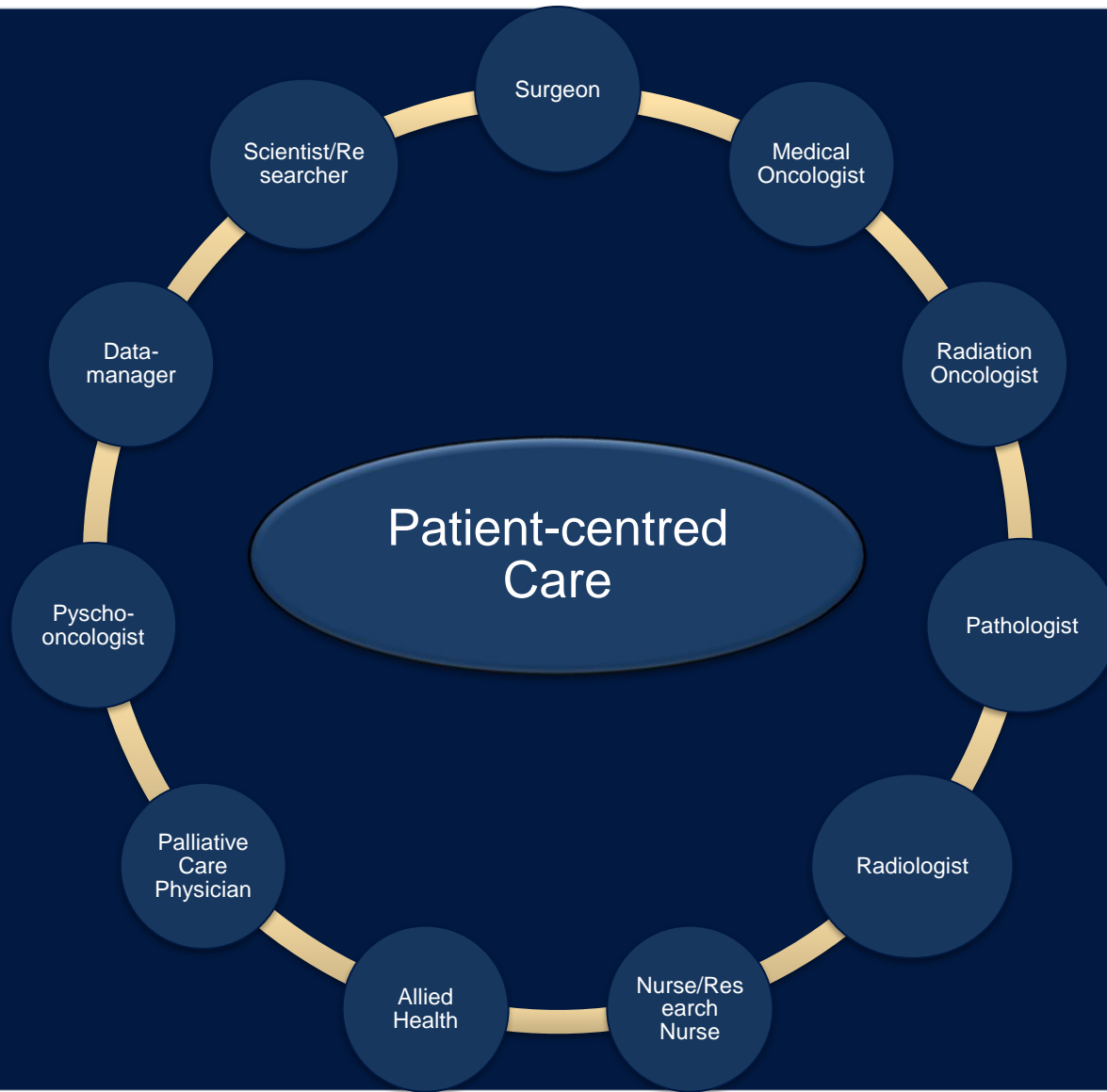# Multidisciplinary Care
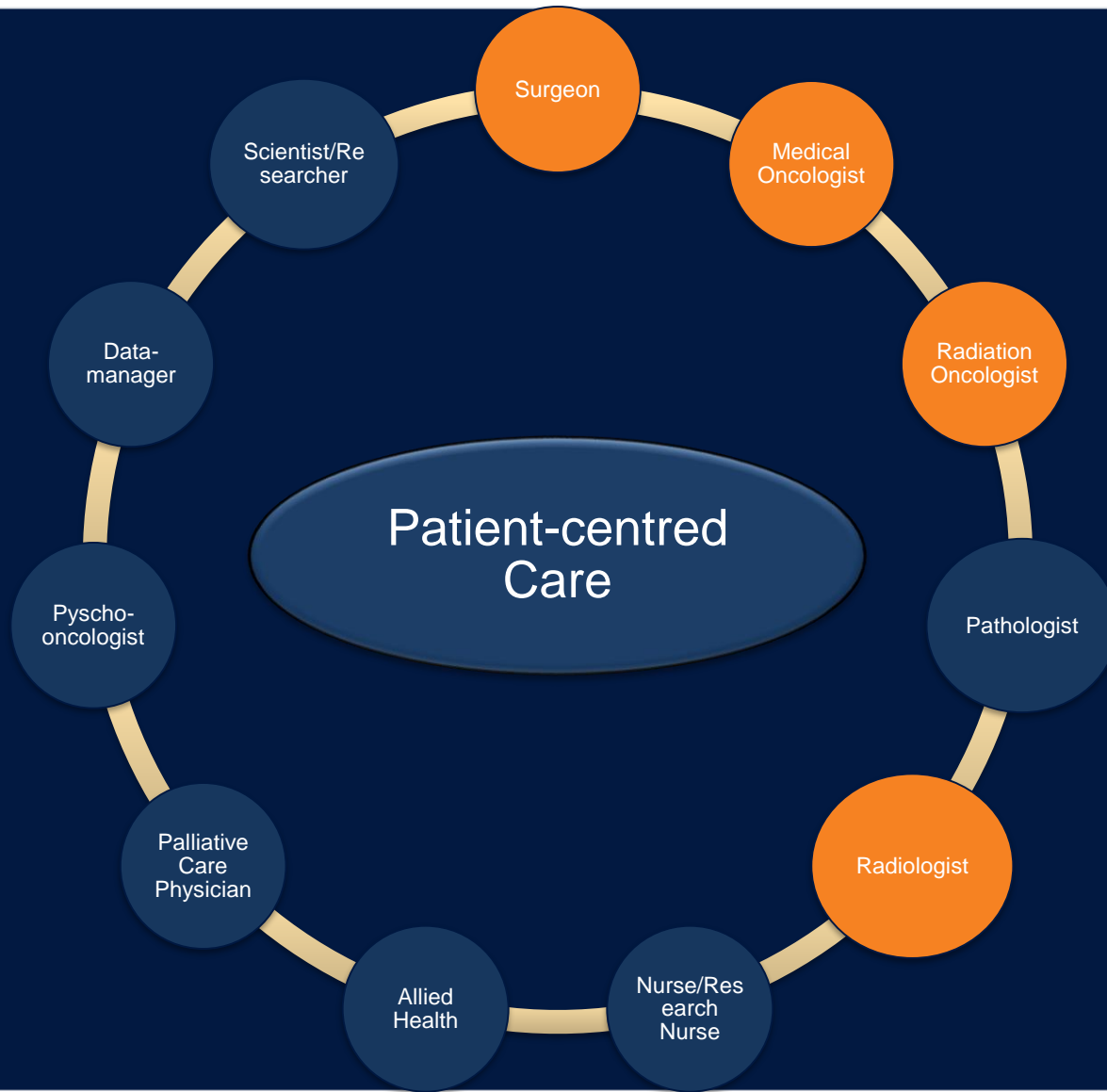
Mucosal Head and Neck Cancer
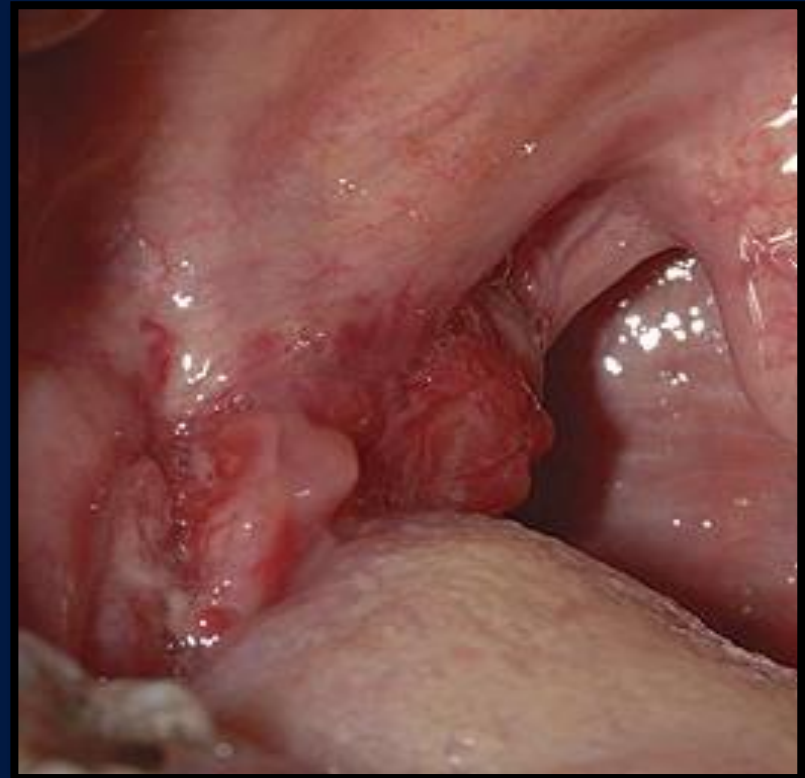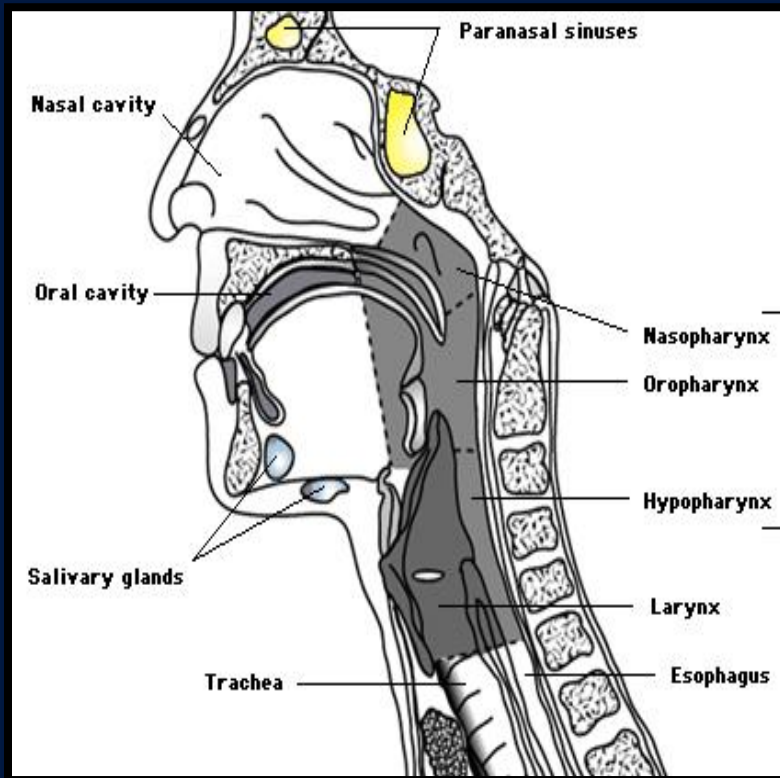
Head and Neck Cancer

- 4-6% of all cancers
- 5% of cancer-related deaths
- Commonly Squamous Cell Carcinoma
- Smoking related

AIHW 2008
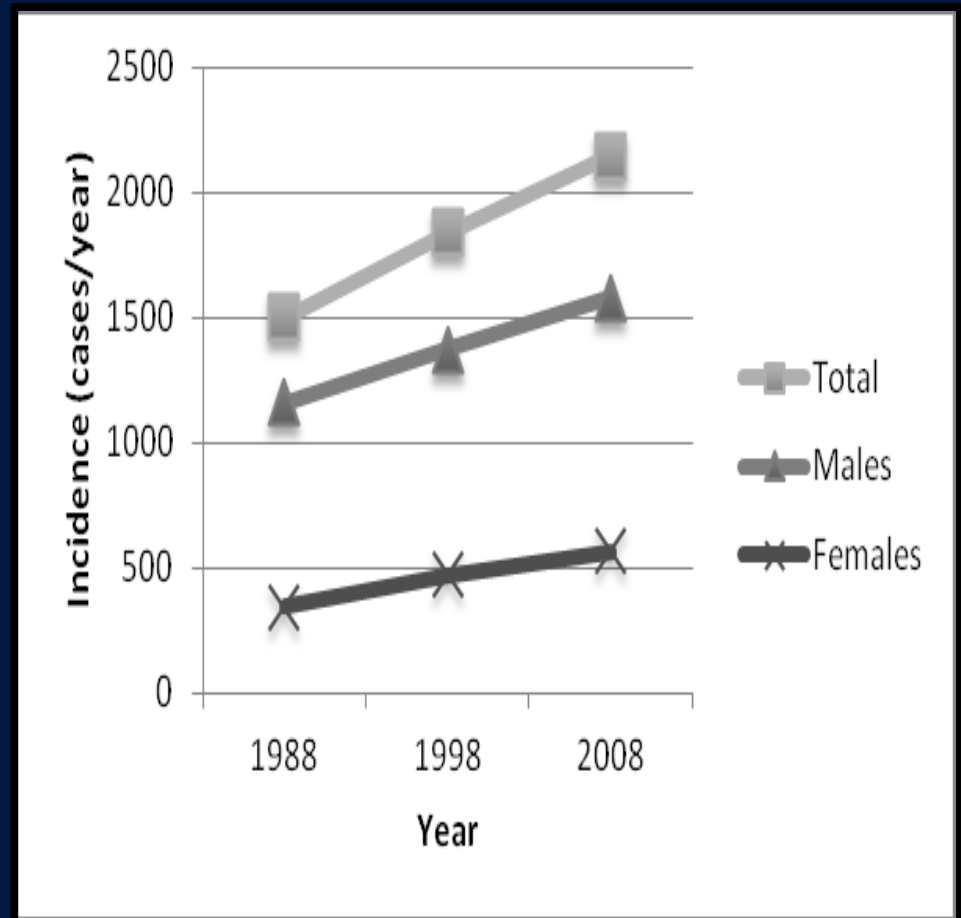
Falling rates of smoking
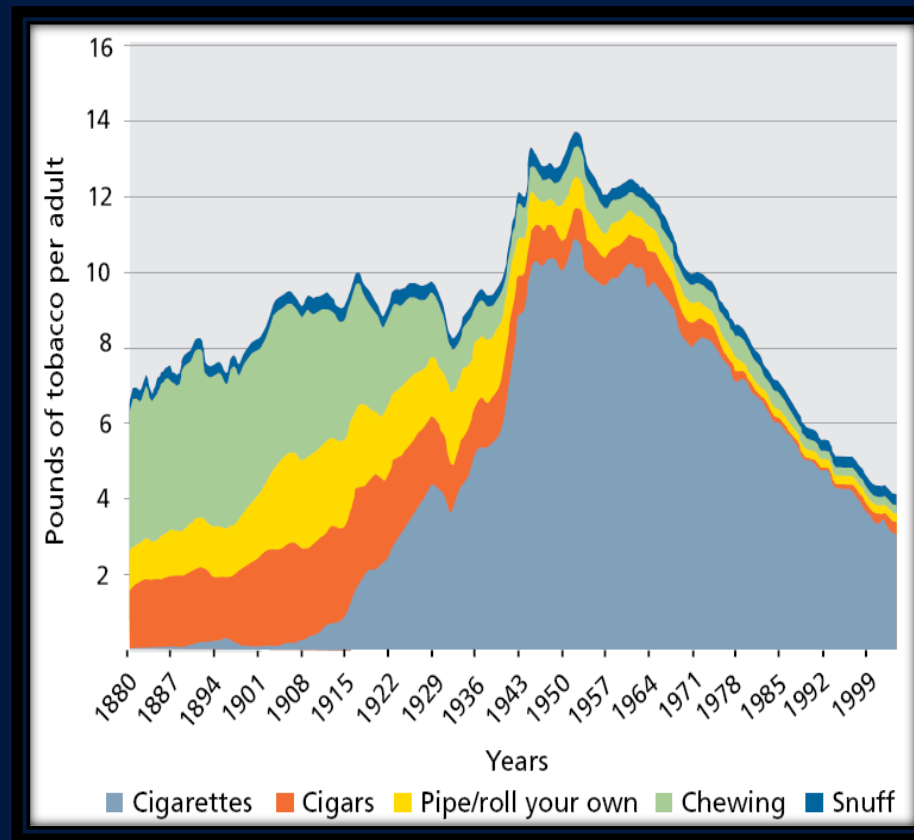
Rising incidence of Oropharyngeal SCC

Fig. 3. The incidence of laryngeal and oropharyngeal carcinomas in Denmark 1977–2007.

Larsen P. Radiother Oncol 2010
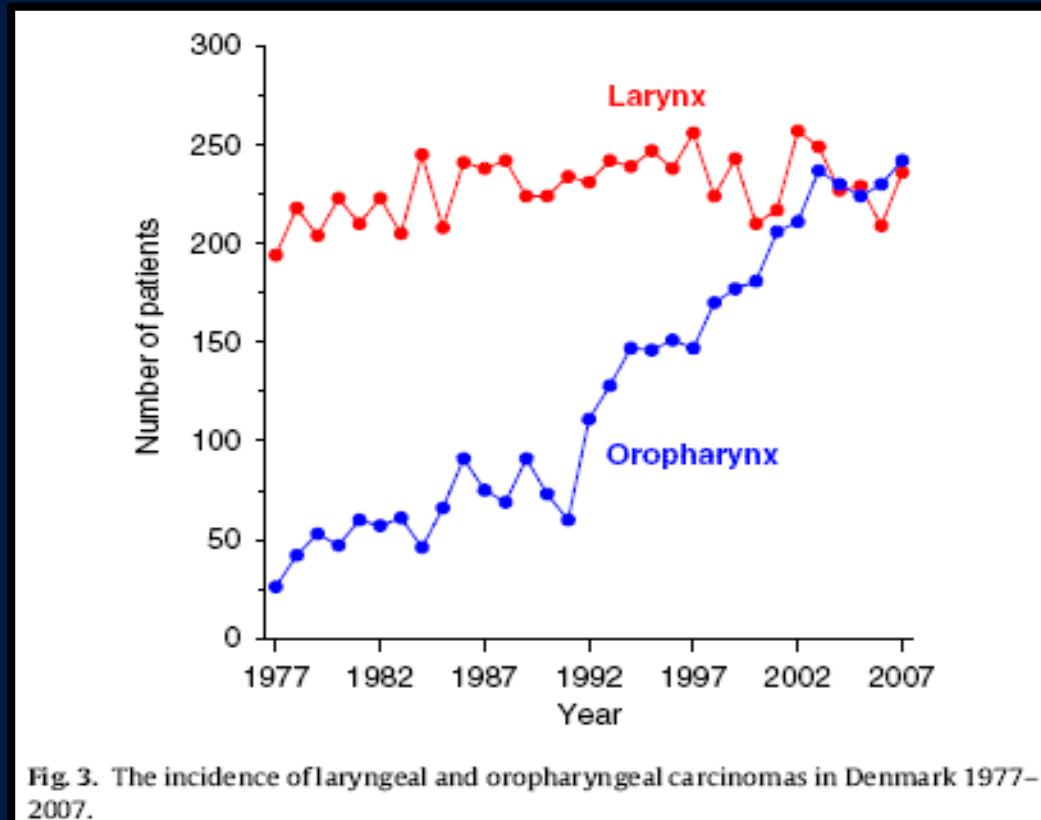
Rising incidence or HPV associated Oropharyngeal Ca
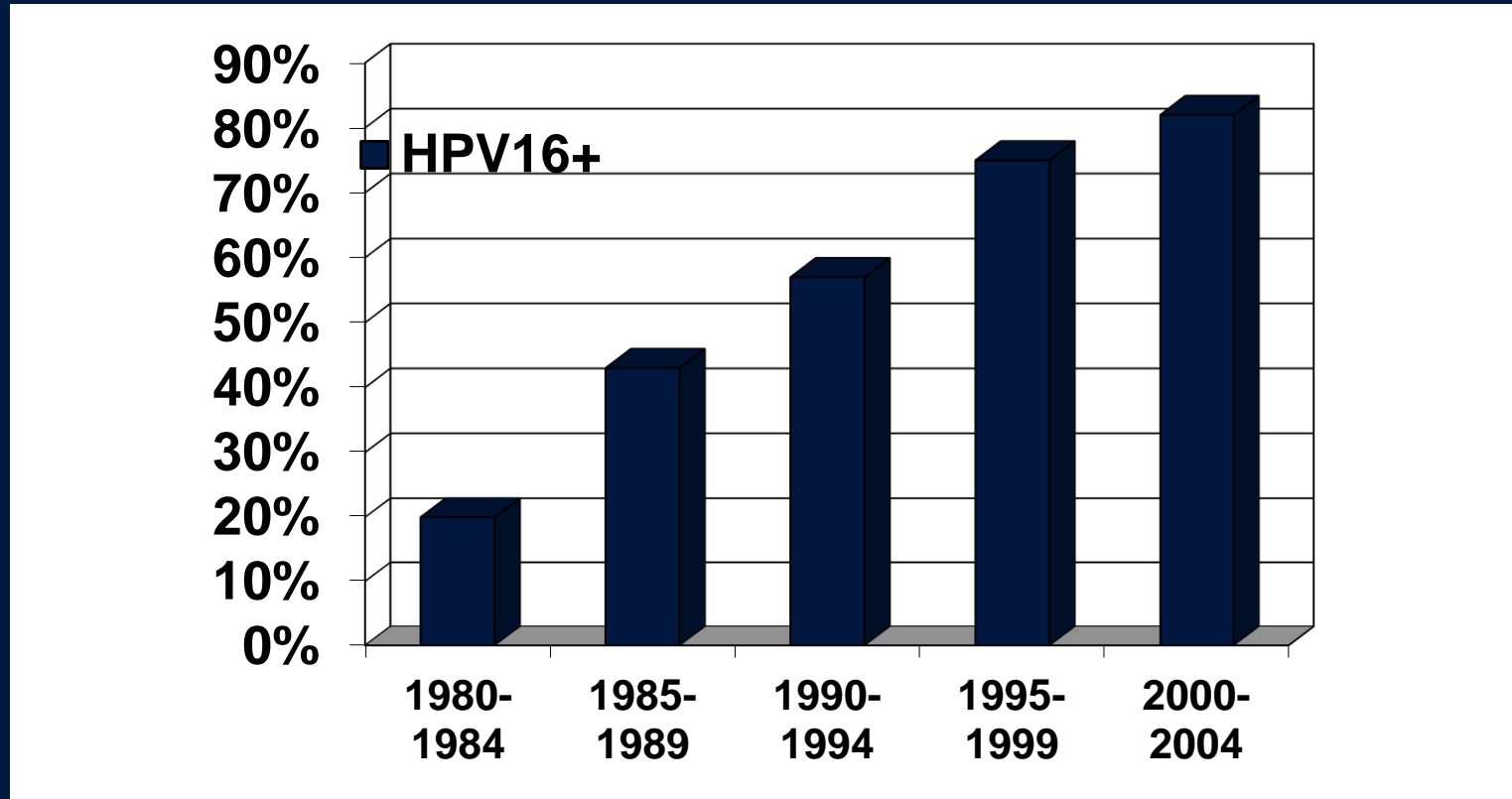
SEER Registry

Treatment
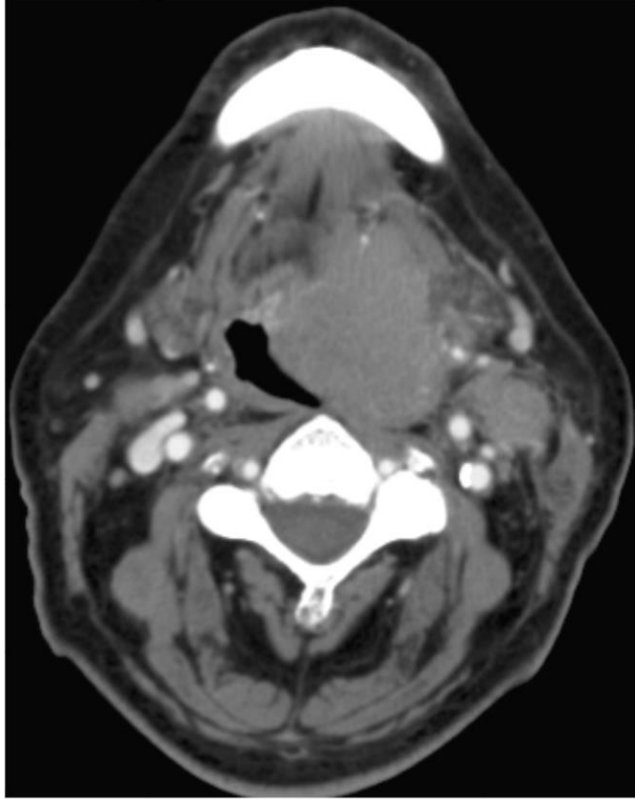
Base of Tongue SCC

Options

- Surgery/post-operative radiotherapy
- Chemo-radiotherapy
- No randomised comparisons

Outcomes

- 40-60% 3yr overall survival
- (85% 3yr OS HPV+ disease)

Curative chemo-radiotherapy
Node positive head & neck cancer

- 7 weeks of XRT & concurrent cisplatin
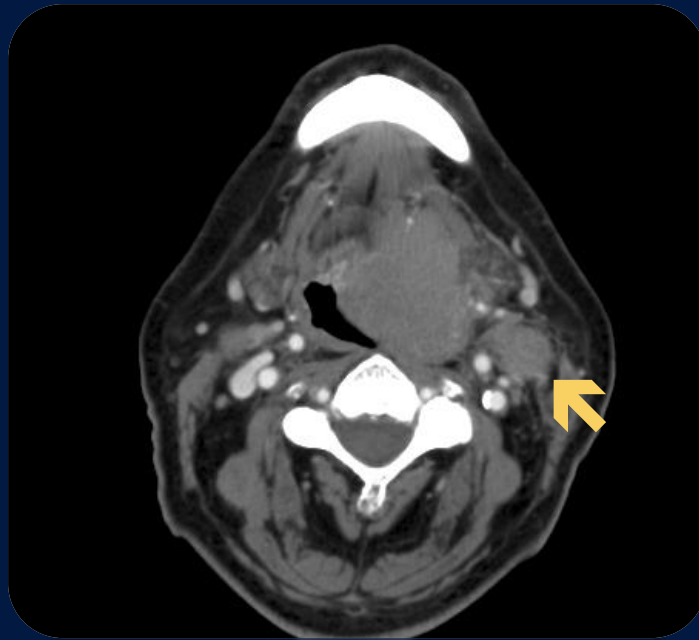
Pre-therapy
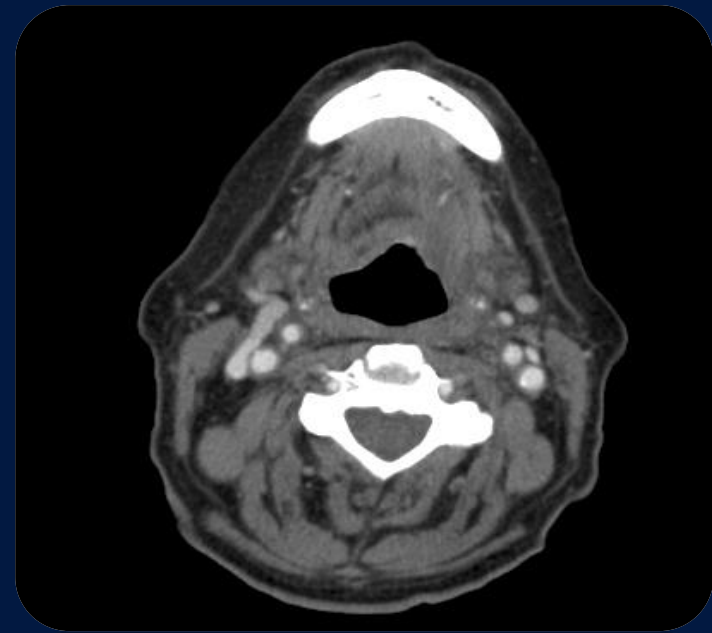
Post-therapy

Icarus effect

Residual nodal dilemma following radio(chemo)therapy

- 40-50% of patients with node positive Head & Neck SCC will have a residual nodal abnormality after radiotherapy

Management of the neck following Radiation Therapy and a complete response at the primary site

- Following a complete response in the neck - isolated nodal recurrence is uncommon ($\leq$ 5%) therefore observe the neck

- Patients with a residual nodal mass in the neck have a ~30-40% risk of having pathologically positive residual disease (non-HPV oropharyngeal cancer)

- Post radiotherapy biopsy of the residual neck mass is unreliable to guide the need for neck dissection

- Therefore perform neck dissection in patients with residual nodal abnormality

- Some advocate for ND in all patients presenting with nodal disease regardless of response (planned neck dissection)

Post-therapy neck dissection
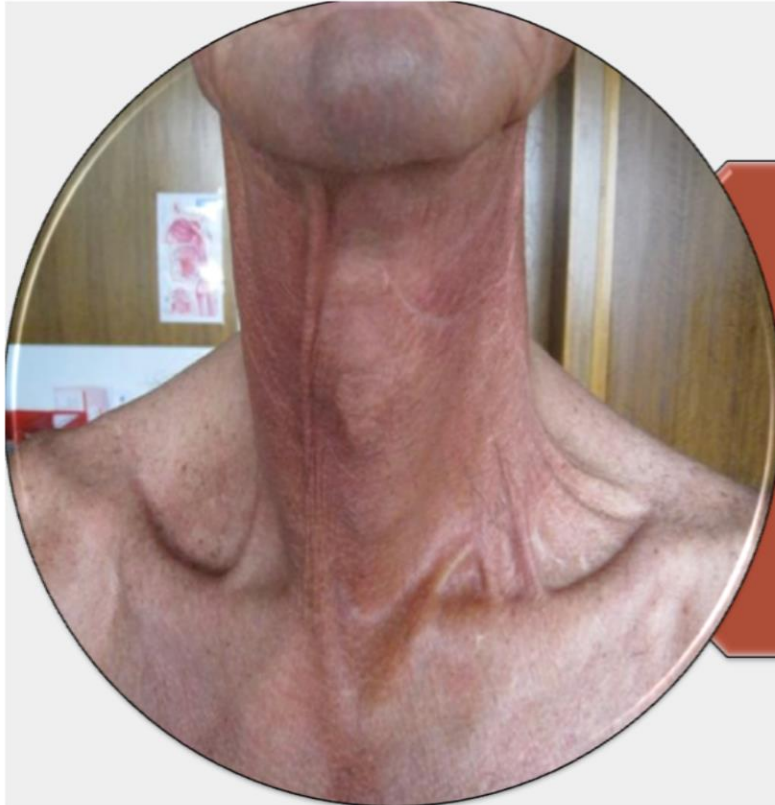
Increased late effects (fibrosis)

Macthay M et al JCO 08

Diminished quality of life

Donatelli-Lassig et al Oto laryng HN Surg 08

More selective approach to choosing patients for neck dissection would be advantageous

PET imaging of the neck

Improving the predictive value of post-therapy imaging for residual nodal disease through functional imaging (FDG PET-CT)
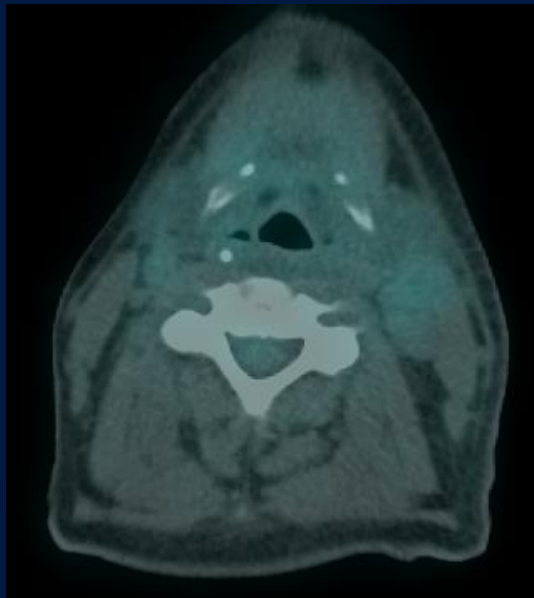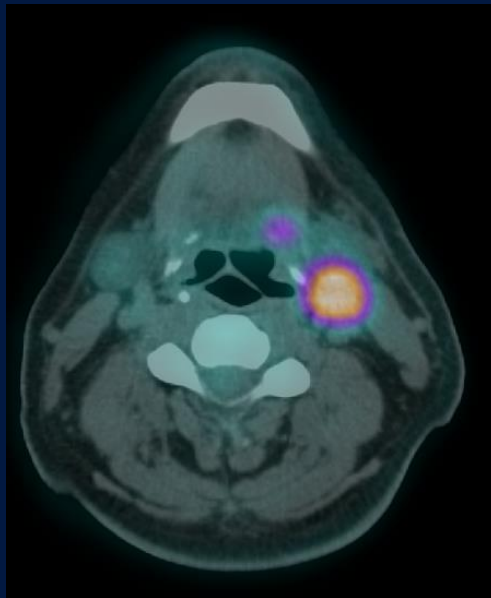
Utility of PET for the detection of residual neck nodes after radiotherapy in Head and Neck cancer

- 39 patients with node positive HNC who had a complete response at the primary site and a residual neck mass on CT after radiotherapy

- PET performed 12 weeks post therapy

- 32 pts with a residual neck mass were PET negative in the neck
    - 5 neck dissection - all pathologically negative
    - 27 patients observed with one neck failure
    - Negative Predictive value 97%

- 7 patients were PET positive in the neck
    - all had a neck dissection
    - Positive Predictive value 71%

Utility of PET for the detection of residual neck nodes after radiotherapy in Head and neck cancer

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Porceddu S et al Head Neck 2005

Prospective study of PET-directed management of the neck in node positive (N+) head and neck cancer following definitive radiotherapy with or without systemic therapy

SV. PORCEDDU, D. PRYOR, E. BURMEISTER, B. BURMEISTER, M. POULSEN, M. FOOTE, B. PANIZZA, J. LOGAN, D. MCFARLANE,
S COMAN, W. COMAN

Purpose

- Can PET predict who could safely have the neck observed despite the presence of any residual nodal CT abnormality in patients who achieved a complete response at the primary site

Endpoint

- Assess the isolated nodal failure rate in patients who achieve a complete response at the primary site

PET-guided policy of the neck

Mucosal N+ HNSCC treated with RT+/-Chemo
Complete response at primary site
12 week re-staging FDG-PET/CT
Synchronous diagnostic CT scan

PET
Neck Negative
Observed^

PET
Neck Equivocal
Repeat 4-6 weeks

PET
Neck Positive
Neck dissection

^ Regardless of any residual nodal abnormality on re-staging CT scan

Outcomes

123 patients treated during the study period (Jan05- Apr 09)

112 (91%) patients achieved a complete response at the primary site by 12 weeks

Oropharyngeal 83 (74%)

p16+ 59 (53%)

Median FU 28 (12-60) months

Outcomes in the neck

12 week nodal response	Patient No. n=112	Post-therapy treatment	Outcome (median FU 28m)
CT no residual PET Negative	62 (55%)	Observed	Isolated nodal failures = 0
CT Residual PET Negative	41 (37%)	Observed	Isolated nodal failures = 0
CT Residual PET Positive	9 (8%)	8 ND (7%)	Isolated nodal failures = 3 (2.7%)

^ Residual node defined as abnormality >10mm or necrotic of any size on CT

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Utility of PET for the detection of disease in patients with a residual structural nodal abnormality following radio(chemo)therapy in node positive head and neck cancer

– Negative Predictive Value = 98%

– Positive Predictive Value = 78%

Porceddu S et al Head Neck 2011

Conclusion

- PET-guided policy of the neck in node positive HNSCC following a complete response at the primary site results in a very low isolated nodal failure rate following definitive RT

- This policy appropriately spares a neck dissection in patients who are PET negative regardless of the presence of a residual CT nodal abnormality

T1N2bM0 oropharyngeal SCC
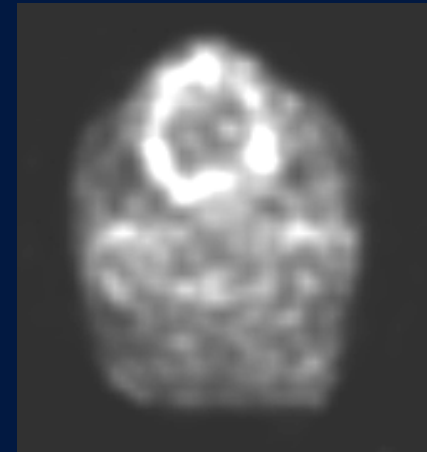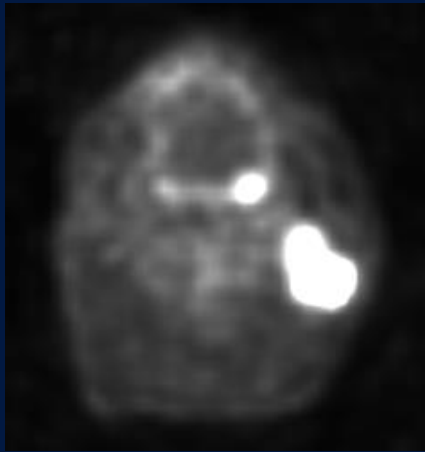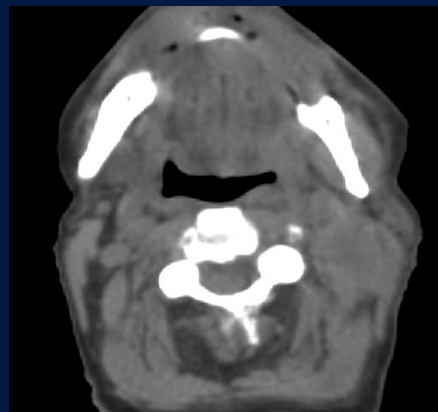
Pre-therapy   12 weeks   12 months

Impact of PET on neck dissection rate

Neck Dissection Policy	Neck Dissection rate
Planned Surgery for N2-3 (excluding N1)	101 (90%)
Neck surgery for residual CT abnormality (>10mm or necrotic)	50 (45%)
PET-directed Policy	8 (7%) For an isolated nodal failure rate of 2.7% (FU 28mths)

Median FU 62 months total nodal failures 4%   Sjovall J et al Oral Oncology 2015

Economic analysis of FDG-PET–guided management of the neck after primary chemoradiotherapy for node-positive head and neck squamous cell carcinoma

David I. Pryor, MBBS, FRANZCR,[1,2]* Sandro V. Porceddu, MBBS, MD, FRANZCR,[1,2] Paul A. Scuffham, BA, PhD,[3] Jennifer A. Whitty, BPharm, PhD,[3] Paul A. Thomas, BMed, FRACP,[2,4] Bryan H. Burmeister, MBChB, MD, FRANZCR[1,2]

[1]Division of Cancer Services, Princess Alexandra Hospital, Brisbane, Australia, [2]School of Medicine, Faculty of Health Sciences, University of Queensland, Brisbane, Australia, [3]Centre for Applied Health Economics, School of Medicine, Griffith Health Institute, Griffith University, Brisbane, Australia, [4]Queensland PET Service, Royal Brisbane and Women's Hospital, Brisbane, Australia.

ORIGINAL ARTICLE

PET-CT Surveillance versus Neck Dissection in Advanced Head and Neck Cancer

Hisham Mehanna, Ph.D., Wai-Lup Wong, F.R.C.R.,
Christopher C. McConkey, Ph.D., Joy K. Rahman, M.Sc.,
Max Robinson, Ph.D., Andrew G.J. Hartley, F.R.C.R., Christopher Nutting, Ph.D.,
Ned Powell, Ph.D., Hoda Al-Booz, F.R.C.R., Martin Robinson, F.R.C.R.,
Elizabeth Junor, F.R.C.R., Mohammed Rizwanullah, F.R.C.R.,
Sandra V. von Zeidler, Ph.D., Hulya Wieshmann, F.R.C.R., Claire Hulme, Ph.D.,
Alison F. Smith, M.Sc., Peter Hall, Ph.D., Janet Dunn, Ph.D.,
for the PET-NECK Trial Management Group*

PET-Neck Trial schema   Pragmatic non-inferiority trial

Eligible and consenting patient

Randomised 1:1

Stratified by:
- Centre
- T stage (T1-T2, T3-T4)
- N stage (N2a-N2b, N2c-N3)
- Disease site
- Chemotherapy schedule
- Timing of neck dissection (before or after CRT)

PET-CT guided 'active surveillance'

CRT

PET-CT & Assessment 9-13 weeks after CRT completion

If CR primary: is neck +ve or equivocal on PET-CT?

Yes → Neck dissection within 4 weeks

No

Standard treatment 'planned ND'

CRT

ND before or after CRT

CT & Assessment 9-13 weeks after CRT completion

Clinical Follow up: Year 1- monthly; Year 2-two monthly

PRESENTED AT: ASCO Annual '15 Meeting

Overall survival
(Primary Endpoint)
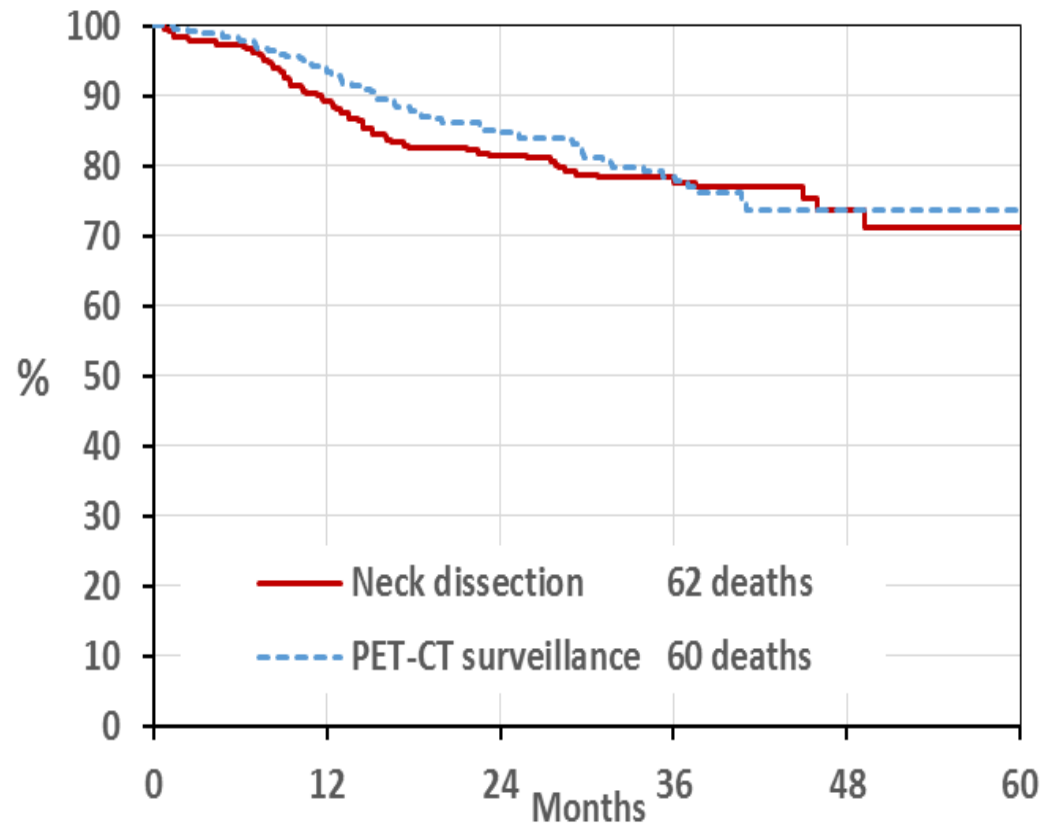
Loco-regional Control

	Neck dissection arm			Surveillance
	Intended pre CRT	Intended post CRT	Overall	
Total	77	205	282	282
2-year loco-regional control	94.8%	92.0%	92.6%	91.9%
2-year recurrence-free	85.7%	83.5%	84.0%	85.6%
Nodal recurrence			0.7%	2.3%
Node only recurrence			0.4%	1.1%

NCCN Guidelines

(POST CHEMORADIATION OR RT NECK EVALUATION)[1]

Persistent disease or progression → CT and/or MRI with contrast (4-8 weeks) Consider PET/CT scan → If diagnosis confirmed or progression → Neck dissection

After chemo/RT or RT → 4-8 weeks clinical assessment as appropriate

If response → or

PET/CT[2] (including CT + IV contrast) at minimum 12 weeks

- No lymph node or node <1 cm; PET/CT negative[3] → Observe

- Lymph node <1 cm; PET/CT positive[4] → Individual decision: Observe or Neck dissection Consider ultrasound FNA

- Observe or Neck dissection: Consider ultrasound FNA
  - Patient/surgeon decision
  - Consider amount of nodal regression

- Lymph node >1 cm; PET/CT negative[3] →

- Lymph node >1 cm; PET/CT positive[4] → Neck dissection

CT and/or MRI with contrast at 8-12 weeks

- Imaging positive → Neck dissection or Consider PET imaging at 12 weeks

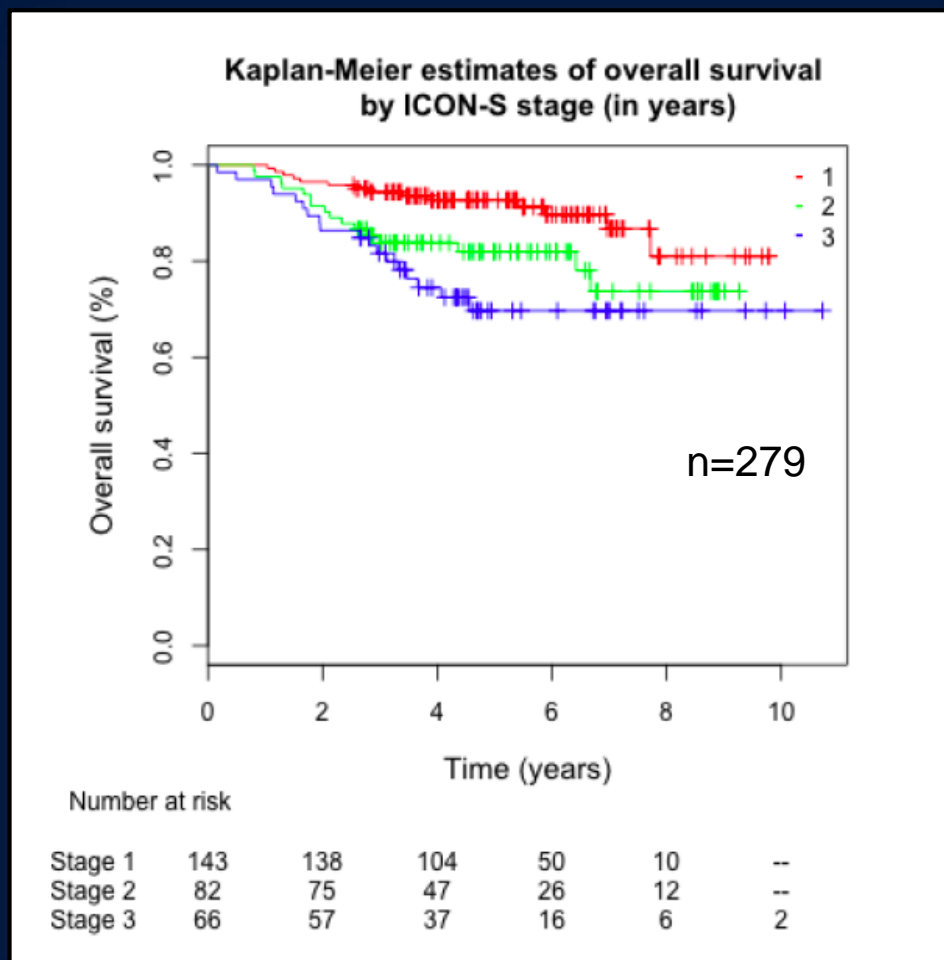- Imaging negative → Observe

Validation of the ICON-S staging for HPV-associated oropharyngeal carcinoma using a pre-defined treatment policy

Sandro V Porceddu [a,b,*], Rob Milne [b], Elizabeth Brown [a,c], Anne Bernard [d], Reza Rahbari [a], Bena Cartmill [a], Matthew Foote [a,b], Margaret McGrath [a], Jermaine Coward [a,b], Benedict Panizza [b,e]

Recommended guidelines for risk-adapted management of node positive HNSCC post-RT

Porceddu SV & Weber R *Uptodate 2016*
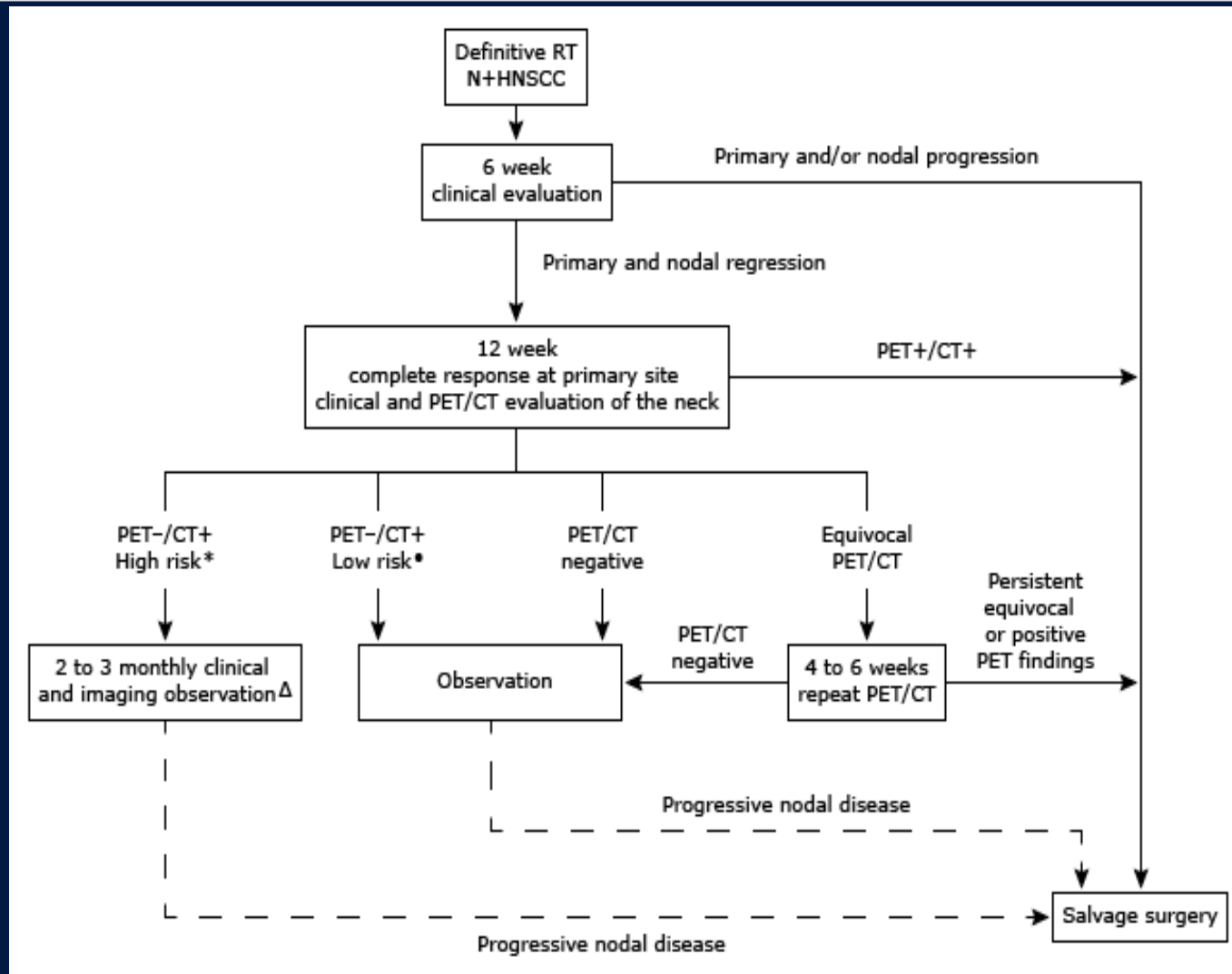
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Chris Perry
Scott Coman
James Bowman
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Howard Liu

IMAGINE 2017