



LIVERPOOL  
HOSPITAL

# Estimating population benefits of optimal radiotherapy use

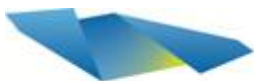
## Modelling Demand for Radiotherapy

**Dr Timothy P Hanna MD MSc FRCPC**

**Dr Jesmin Shafiq MBBS MCN MPH**

**Prof MB Barton MBBS MD FRANZCR Thesis Supervisor**

**Prof GP Delaney MBBS MD PhD FRANZCR Thesis co-Supervisor**



Ingham Institute  
Applied Medical Research



Health  
South Western Sydney  
Local Health District

# Background

- Clinical outcomes data refer to specific subgroups of cancer patients

## **Conservative Management of T1-T2N0 Supraglottic Cancer: A Retrospective Study**

*Giuseppe Spriano, MD, Paolo Antognoni, MD, Renato Piantanida, MD, Diego Varinelli, MD, Roberto Luraghi, MD, Lorenzo Cerizza, MD, and Michele Tordiglione, MD*

## **Functional organ preservation with definitive chemoradiotherapy for T4 laryngeal squamous cell carcinoma**

B. R. Knab<sup>1</sup>, J. K. Salama<sup>1,2\*</sup>, A. Solanki<sup>3</sup>, K. M. Stenson<sup>4</sup>, E. E. Cohen<sup>2,5</sup>, M. E. Witt<sup>1</sup>, D. J. Haraf<sup>1,2</sup> & E. E. Vokes<sup>1,2,5</sup>

# Background

- What would the benefits of radiotherapy be for the entire population of cancer patients, *if clinical practice guidelines were followed?*
- Important to know for economic analysis, advocacy, and planning, yet unknown

# Overview

- Background & rationale
- Method
- Results
- Strengths & limitations

# Rationale: Economic Analysis

- Cost-effectiveness of radiotherapy to population:
  - Need population-based benefit information
  - Need cost information
    - Per fraction, per course

# Rationale: Advocacy for Sufficient Services and Service Utilisation

- Underutilization of radiotherapy exists,  
and it matters *because...*

# Rationale: Planning

## *Targeting system improvement*

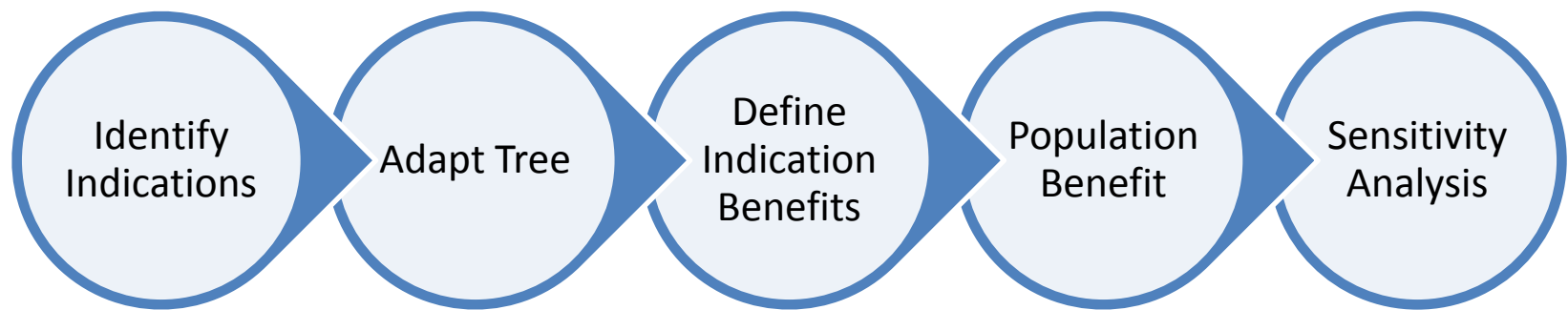
- Impact on outcome varies with case mix
  - Shortfall in adjuvant post-mastectomy RT
  - Shortfall in palliative bone radiation
  - Shortfall in radical cervix cancer treatment
  - Shortfall in use of concurrent chemo with radical cervix cancer tx
- To model impact, need info on benefit of optimal treatment and shortfall by indication

# Method

- Population: Australian cancer population (2008)
- Benefits of interest were:
  - XRT benefit: Absolute benefit of radiotherapy over
    - No treatment (Radical Radiotherapy)
    - Surgery alone (Adjuvant Radiotherapy)
  - CRT benefit: Benefit of chemoradiation over XRT
- Endpoints estimated:
  - Local control (at 5-yrs)
  - Overall survival (2-yr and 5-yr)



# Method: Model Development Process

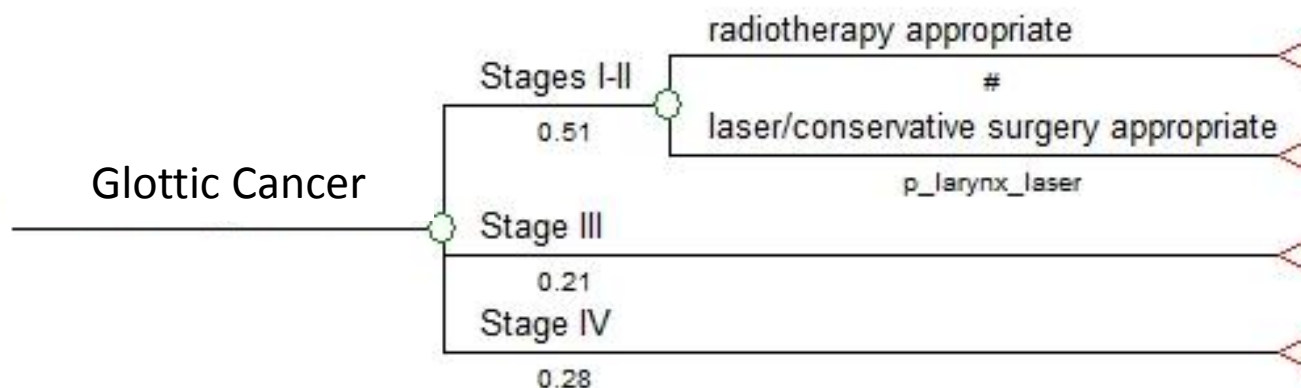


# Method

- TPH thesis
  - Gynae, Head and Neck, Genitourinary, Central Nervous System, Unknown Primary
- JS thesis
  - Lung, Haem, Gastrointestinal, Melanoma
- MBB supervisor, GPD co-supervisor for both

# Method: Identifying Indications

- Groups requiring radiotherapy already defined in previous models by Delaney et al
- TreeAge software



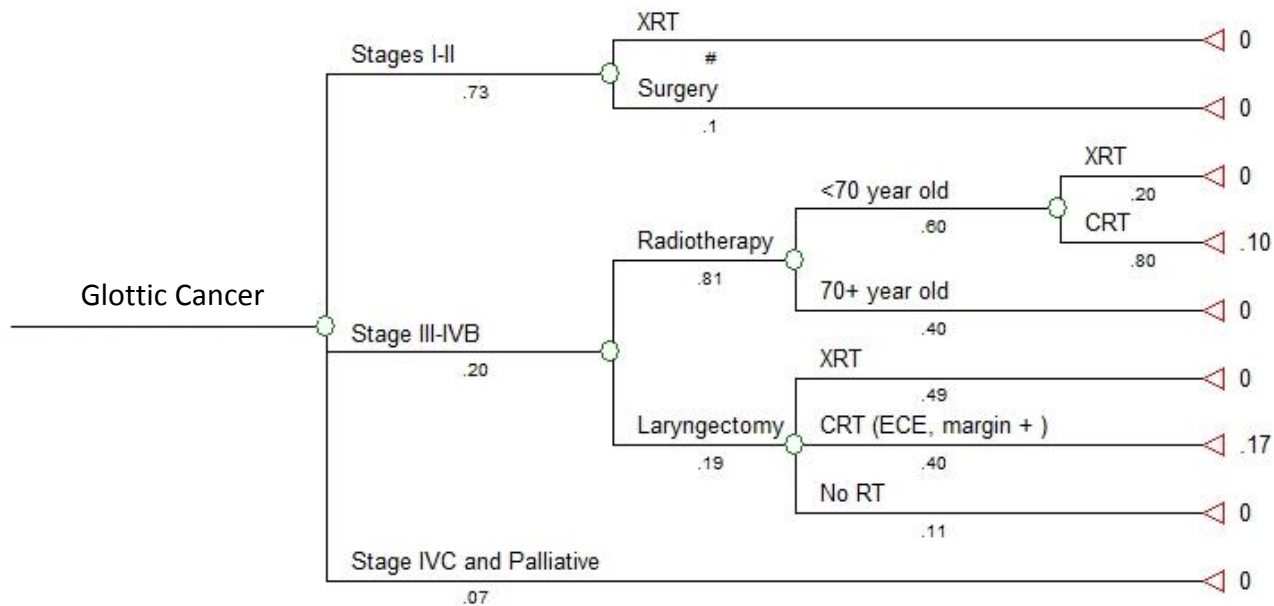
Delaney et al. Cancer 2005;104(6):1129-37

# Method: Identifying Indications

- Guideline review to separate into subgroups with different indications or benefits
  - Eg Stage III-IV Glottic Larynx cancer includes:
    - Radical CRT and XRT benefit
    - Adjuvant CRT and XRT benefit
    - Small group of palliative/metastatic pts without benefit

# Method: Adapting the tree

- Prevalence of characteristics defining subgroups using highest level of epi data



# Method:

## Estimating Indication Benefit

- Systematic review
- Electronic citation databases:
  - Medline, Embase, Cochrane
- Highest level of evidence according to NHMRC criteria
- Meta-analysis if multiple sources of same level identified

# Results: ENT and Gyne Cancer

- Mixed cancer population chosen for demonstration purposes

# Results:

## ENT and Gyne Cancer

- 23 relevant guidelines
- Population with indications
  - 37% of all patients had adjuvant or radical radiotherapy indications
    - 65% of all ENT
    - 22% of all Gyne
  - 35% of patients with radiotherapy indications had an indication for concurrent chemotherapy



# Results:

## ENT and Gyne Cancer

- Defining Indication Benefits
  - 79 relevant studies utilized:
    - 6 meta-analysis
    - 12 randomized trial
    - 61 comparative series or outcome reports
  - 1 publicly available population database
- Additional meta-analyses performed for thesis

# Results: Interpretation

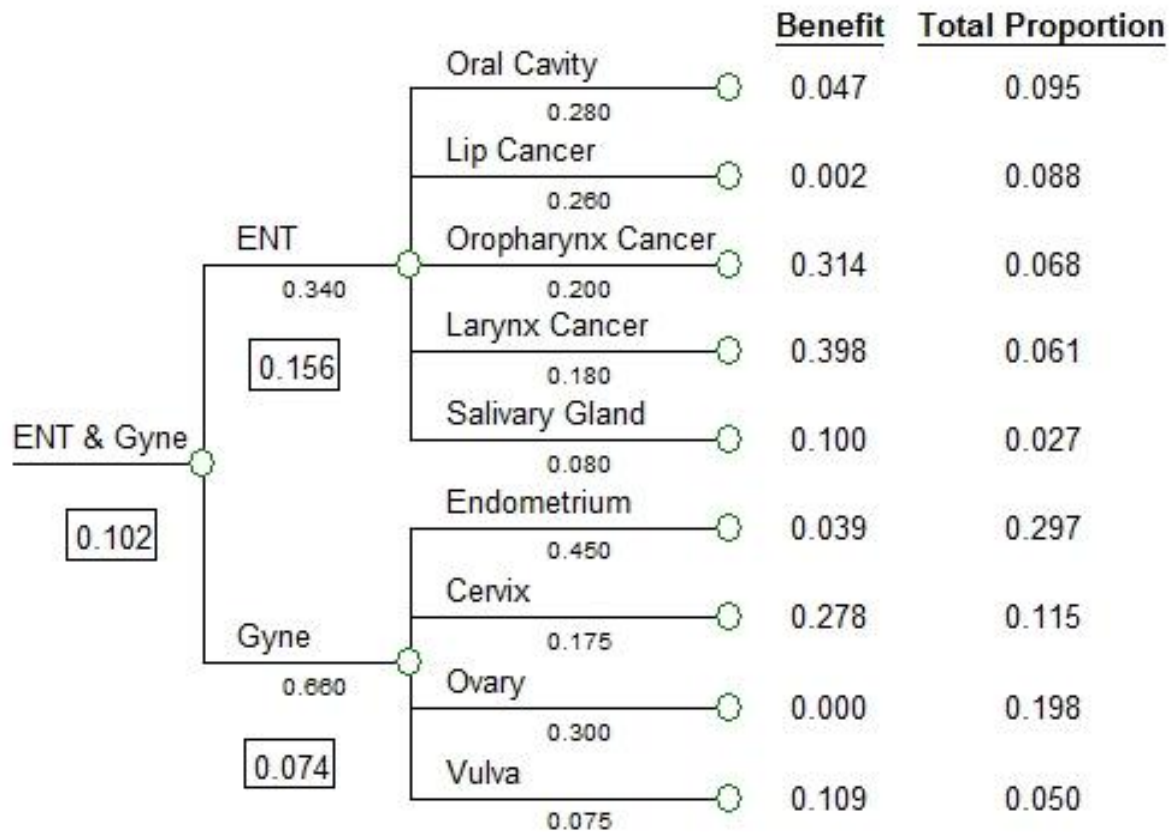
- What does a 10% 5-year overall survival XRT benefit mean?
  - Compared with no XRT, use of guideline-based XRT would achieve 5-year survival in an additional 10% of all Australian ENT & Gyne cancers

## Status at 5 years

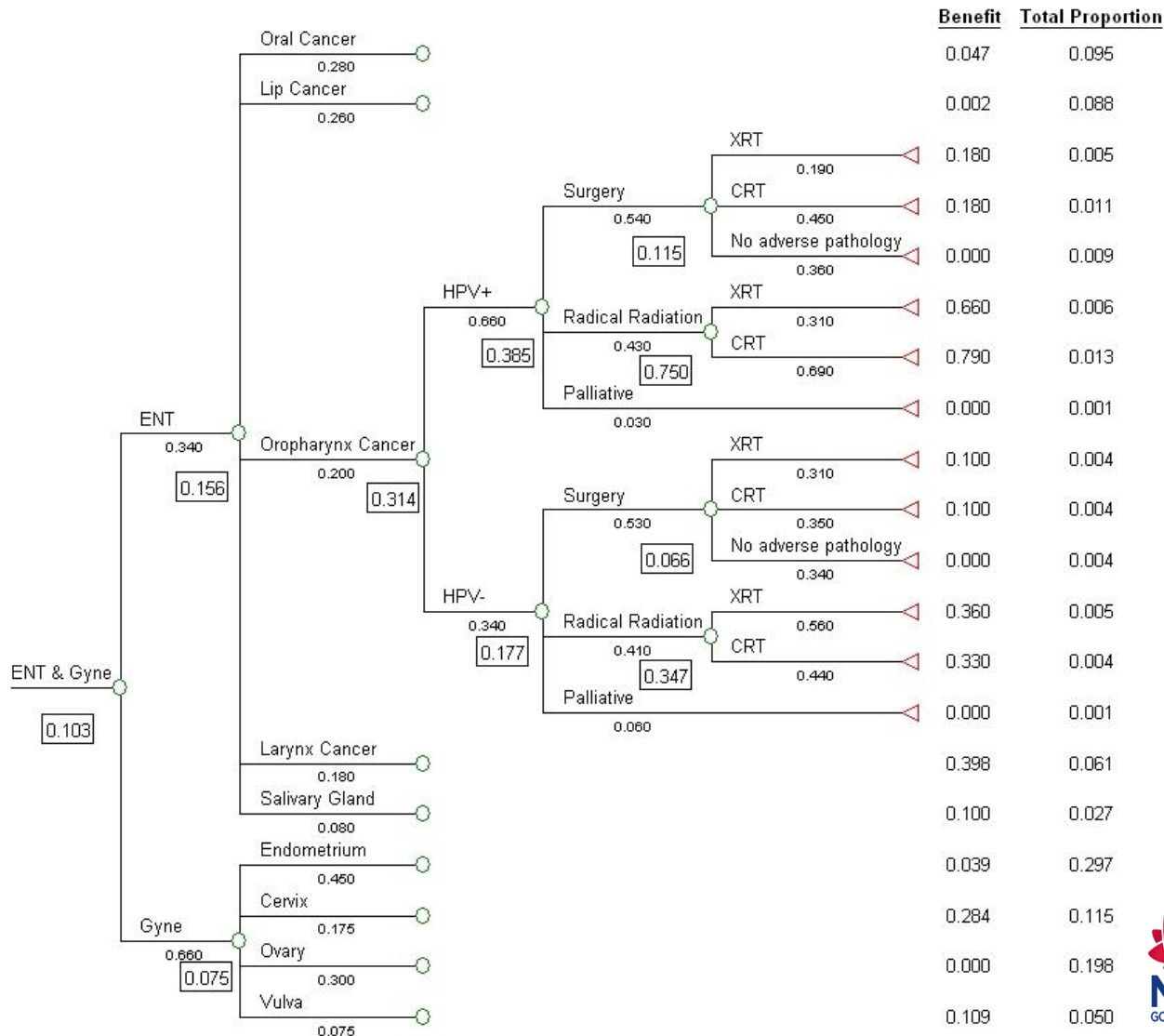


- Alive due to guideline-based XRT use
- Dead from cancer, Dead from other cause, Alive due to surgery/chemo

# Results: ENT and Gyne 5-yr XRT Overall Survival



# Results: ENT and Gyne 5-yr XRT Overall Survival- Oropharynx Expanded



# Epid Evidence Underlying Oropharynx Model

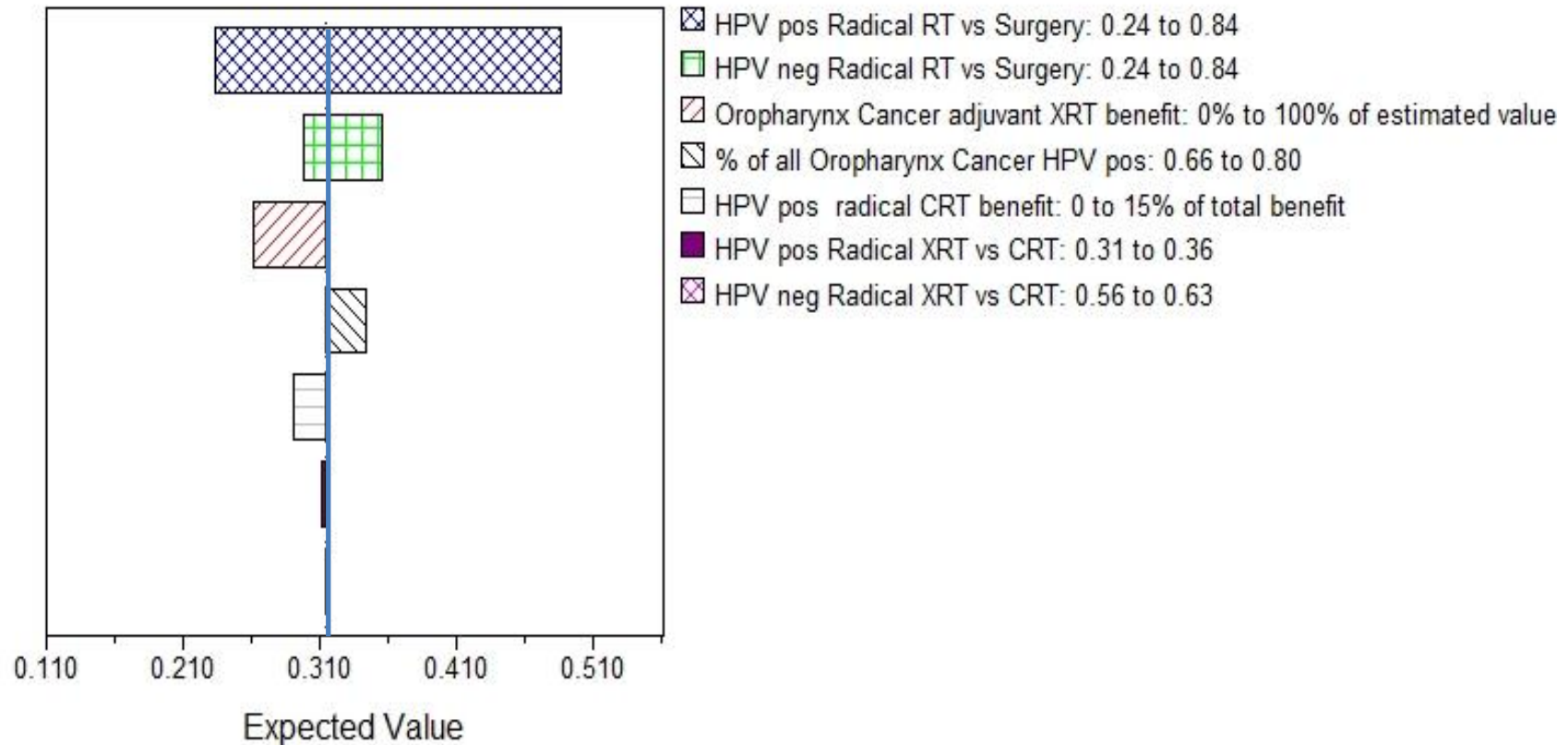
Key	Population or subpopulation of interest	Attribute	Proportion of population with this attribute\$	Quality of information	References
A	Oropharyngeal Cancer	HPV-positive	66%	$\theta$	Hong et al [9]
B	HPV-positive oropharyngeal cancer	Treated with surgery plus or minus adjuvant radiation	54%	$\gamma$	SEER [14]
C	HPV-negative oropharyngeal cancer	Treated with surgery plus or minus adjuvant radiation	53%	$\gamma$	SEER [14]
D	HPV-positive oropharyngeal cancer	Palliative treatment	3%	$\zeta$	Straetmans et al [17]
E	HPV-negative oropharyngeal cancer	Palliative treatment	6%	$\zeta$	Straetmans et al [17]
F	HPV-positive oropharyngeal cancer, radical radiation	Radiation alone	31%	$\zeta$	O'Sullivan et al [20]
G	HPV-negative oropharyngeal cancer, radical radiation	Radiation alone	56%	$\zeta$ $\zeta$ $\zeta$ $\gamma$	O'Sullivan et al [20] Huang et al [22, 23] O'Sullivan [21] AIHW [24]
H	HPV-positive oropharyngeal cancer, surgically excised	XRT indication CRT indication	19% 45%	$\gamma$ $\epsilon$ $\zeta$	SEER [14] Haughey et al [26] Walvekar et al [28]
I	HPV-negative oropharyngeal cancer, surgically excised	XRT indication CRT indication	31% 35%	$\zeta$ $\zeta$ $\Lambda$ $\lambda$	McMahon et al [29] Walvekar et al [28] Li et al [30] Zelevsky et al [31]

# Indication Benefit Data Underlying Oropharynx Model

Population of interest	Clinical Attribute	Proportion of all Oropharynx Cases	Tx Indication	Local control		2-year Overall Survival		5-year Overall Survival		Level of evidence XRT/CRT	References XRT/CRT	Notes
				(SE)*	(SE)*	(SE)*	(SE)*					
				XRT	CRT	XRT	CRT	XRT	CRT			
Oropharyngeal Cancer, p16 positive	Surgery, adjuvant XRT	.07	IA	16% (5.8)	0%	12% (5.8)	0%	18% (5.8)	0%	III-2/NA	[26]/NA	3
Oropharyngeal Cancer, p16 positive	Surgery, adjuvant CRT	.16	IA	16% (5.8)	0%	12% (5.8)	0%	18% (5.8)	0%	III-2/NA	[26]/NA	3
Oropharyngeal Cancer, p16 positive	Radical XRT	.09	IC/RC	87%** (3.1)	0%	82% (3.2)	0%	66% (4.3)	0%	IV/NA	[20]/NA	1
Oropharyngeal Cancer, p16 positive	Radical CRT	.20	IC/RC	85% (8.9)	0%	89% (2.0)	0%	79% (2.8)	0%	IV/ NA	[25, 32]/NA	2
Oropharyngeal Cancer, p16 negative	Surgery, adjuvant XRT	.06	IA	25% (8.4)	0%	7% (2.2)	0%	10% (3.3)	0%	III-2/NA	[33-35]/NA	3
Oropharyngeal Cancer, p16 negative	Surgery, adjuvant CRT	.06	IA	51% (95% CI 34,58)***	17% (4.6)	7% (2.2)	12% (3.9)	10% (3.3)	13% (4.5)	III-2/I	[33, 34, 36]/[37]	3
Oropharyngeal Cancer, p16 negative	Radical XRT	.08	IC/RC	54%** (7.1)	0%	51% (6.6)	0%	36% (6.8)	0%	IV/NA	[20]/NA	1
Oropharyngeal Cancer, p16 negative	Radical CRT	.06	IC/RC	39% (11.0)	11% (1.1)	53% (4.4)	7% (0.8)	33% (4.7)	8% (0.9)	IV/I	[25, 32]/[38]	2

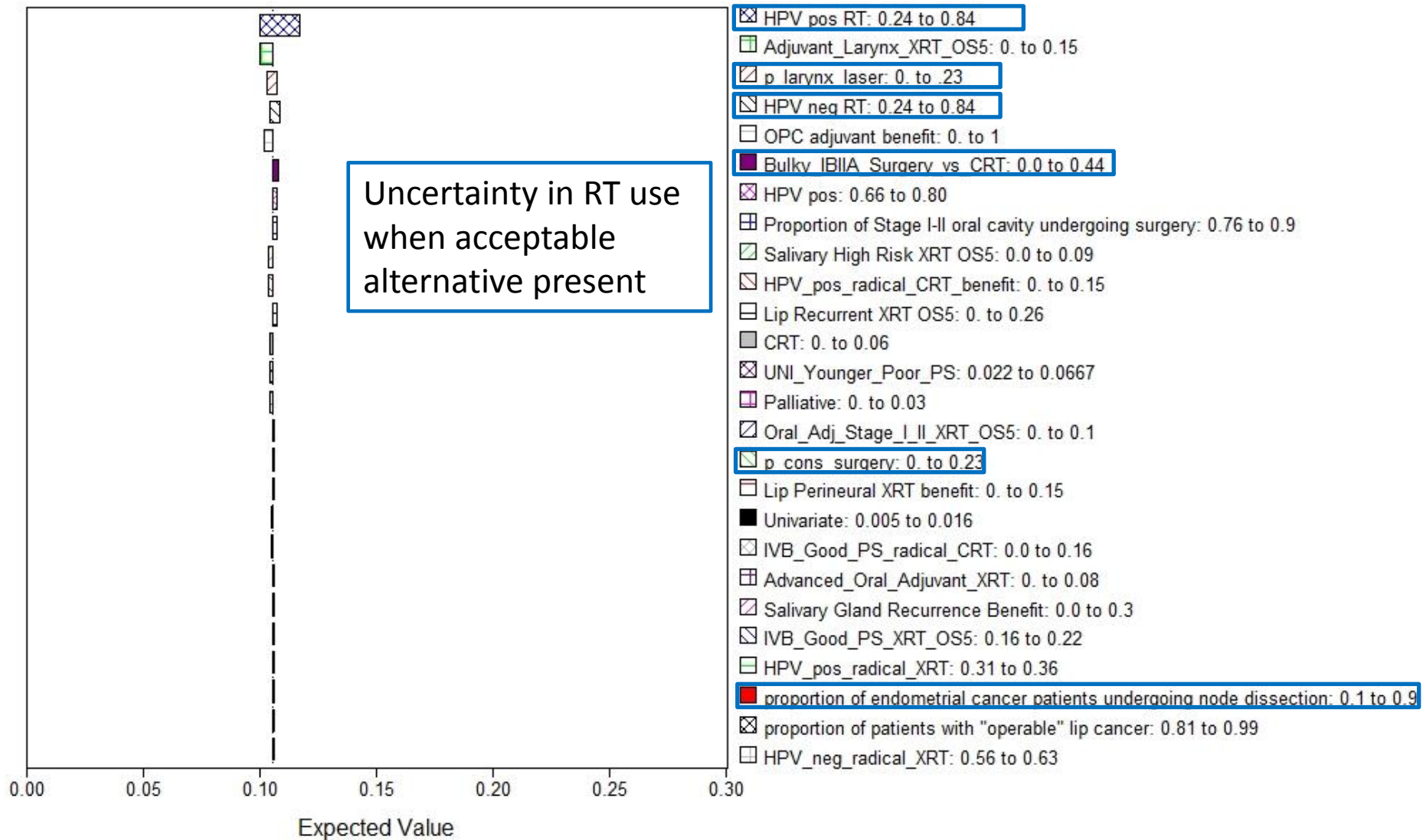
# Oropharynx Univariate Sensitivity Analysis

Tornado Diagram at  
Oropharynx Cancer XRT 5-yr OS Benefit



# All ENT & Gyne Sensitivity Analysis

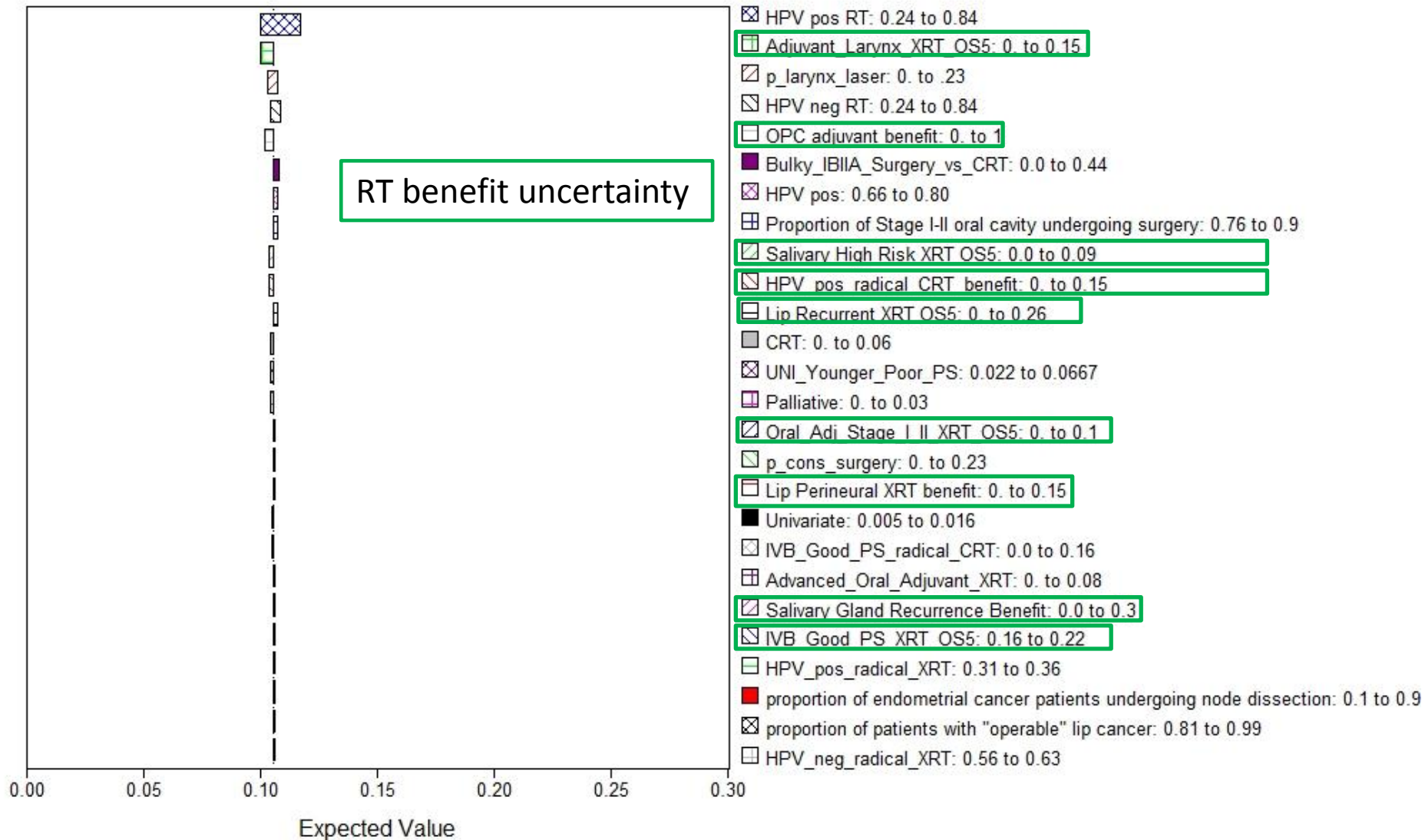
## XRT 5-year Overall Survival Benefit





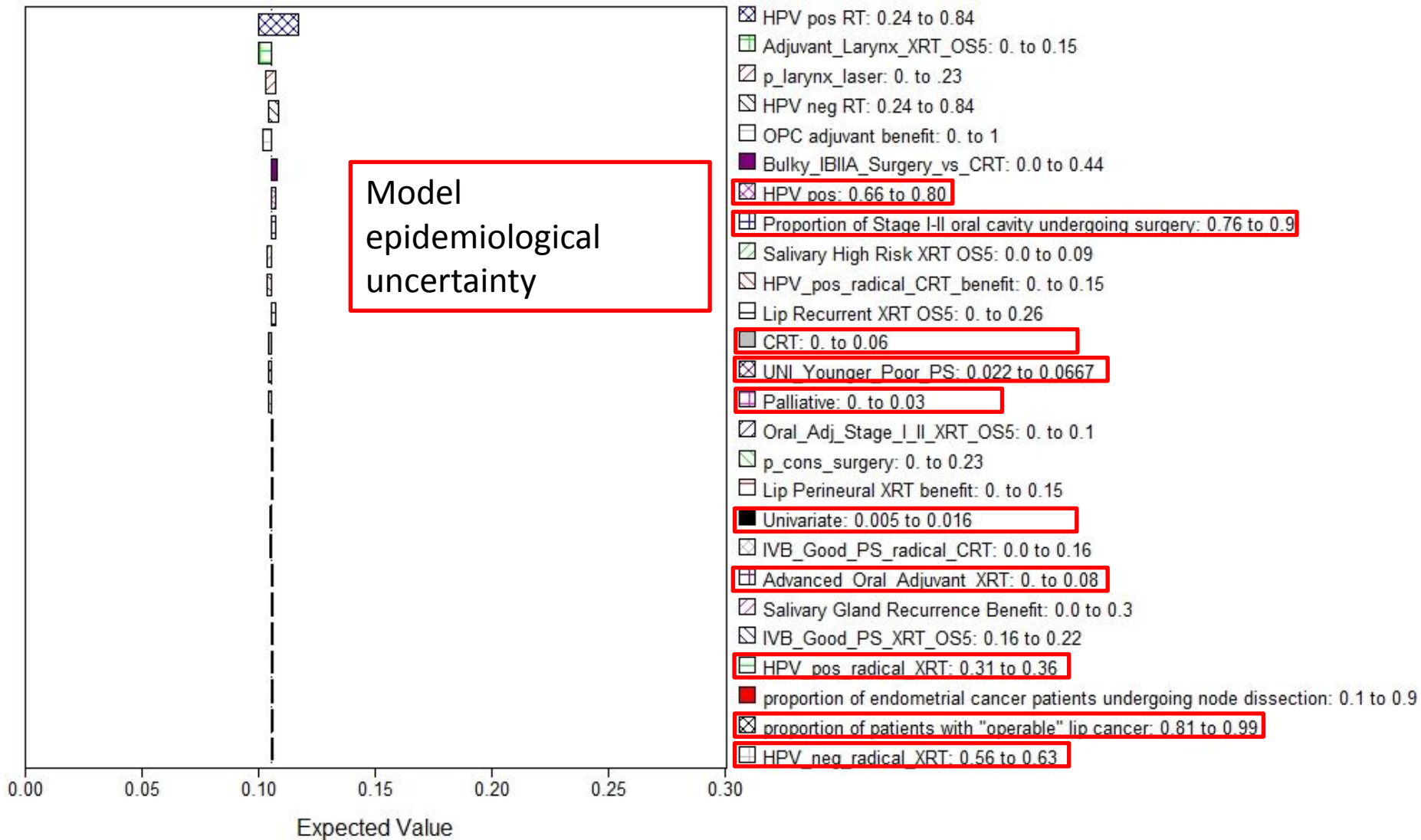
# All ENT & Gyne Sensitivity Analysis

## XRT 5-year Overall Survival Benefit



# All ENT & Gyne Sensitivity Analysis

## XRT 5-year Overall Survival Benefit



# All ENT & Gyne :

## Multivariate Sensitivity Analysis

	Local control (95% CI)			5-yr Overall Survival (95% CI)		
	XRT	CRT	Total	XRT	CRT	Total
All ENT & Gyne Cancer	16%(14,17)	1%(1,2)	17%	10%(9,11)	1%(1,1)	11%
If zero ENT Adjuvant XRT benefit	13%(11,14)	1%(1,2)	14%	10%(9,11)	1%(1,1)	11%

# Strengths & Limitations

## Strengths

- Robust model
- Rapidly adaptable
- Method transparency
- Consequences of under-utilization can be estimated
- Benefit per fraction can be estimated

## Limitations

- Bias, confounding & generalizability of source data
  - e.g. functional status
- Labor intensive model
- Cases of limited data
  - Modeling preference
  - Uncommon indications
  - RT quality & outcomes
- Other modalities & endpoints

# Conclusion

- RT pop benefit for ENT and Gyne cancer estimable
  - Under the condition of optimal RT use
- The model is robust despite multiple uncertainties
  - Greatest impact: choice between surgery and RT
- Model is flexible, allowing adaption to other settings
- Next steps:
  - Apply model to all remaining cancers
  - Put the data to use as per rationale

