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# Risk of lymphedema following contemporary treatment for breast cancer: an analysis of 7,426 patients from a multidisciplinary perspective

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# Introduction

- **Secondary lymphedema** is the most dreaded complication of breast cancer treatment.
- Incurable, progressive, and disabling



# Introduction

## De-escalation strategies for breast cancer

Surgery

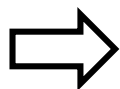
Sentinel LN  
biopsy

Systemic Tx

Oncotype DX  
MammaPrint

Radiotherapy

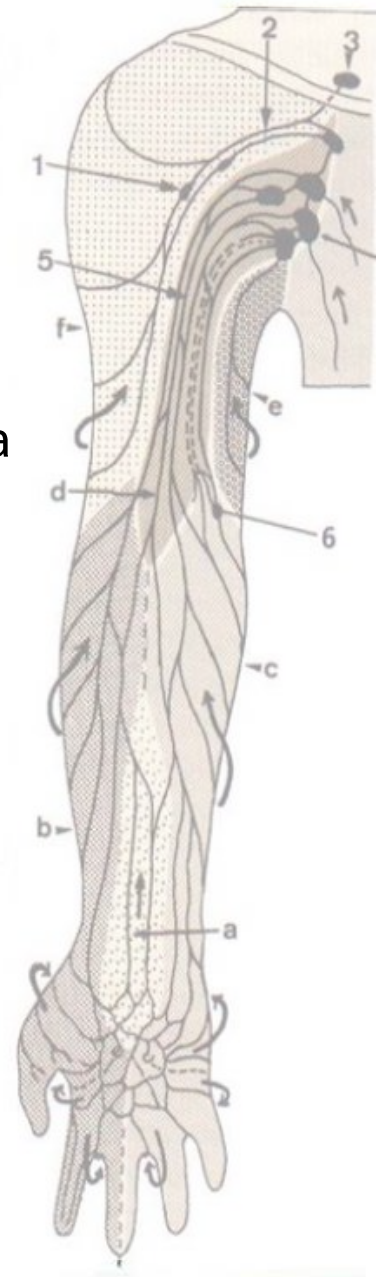
HypoFx  
Regional field



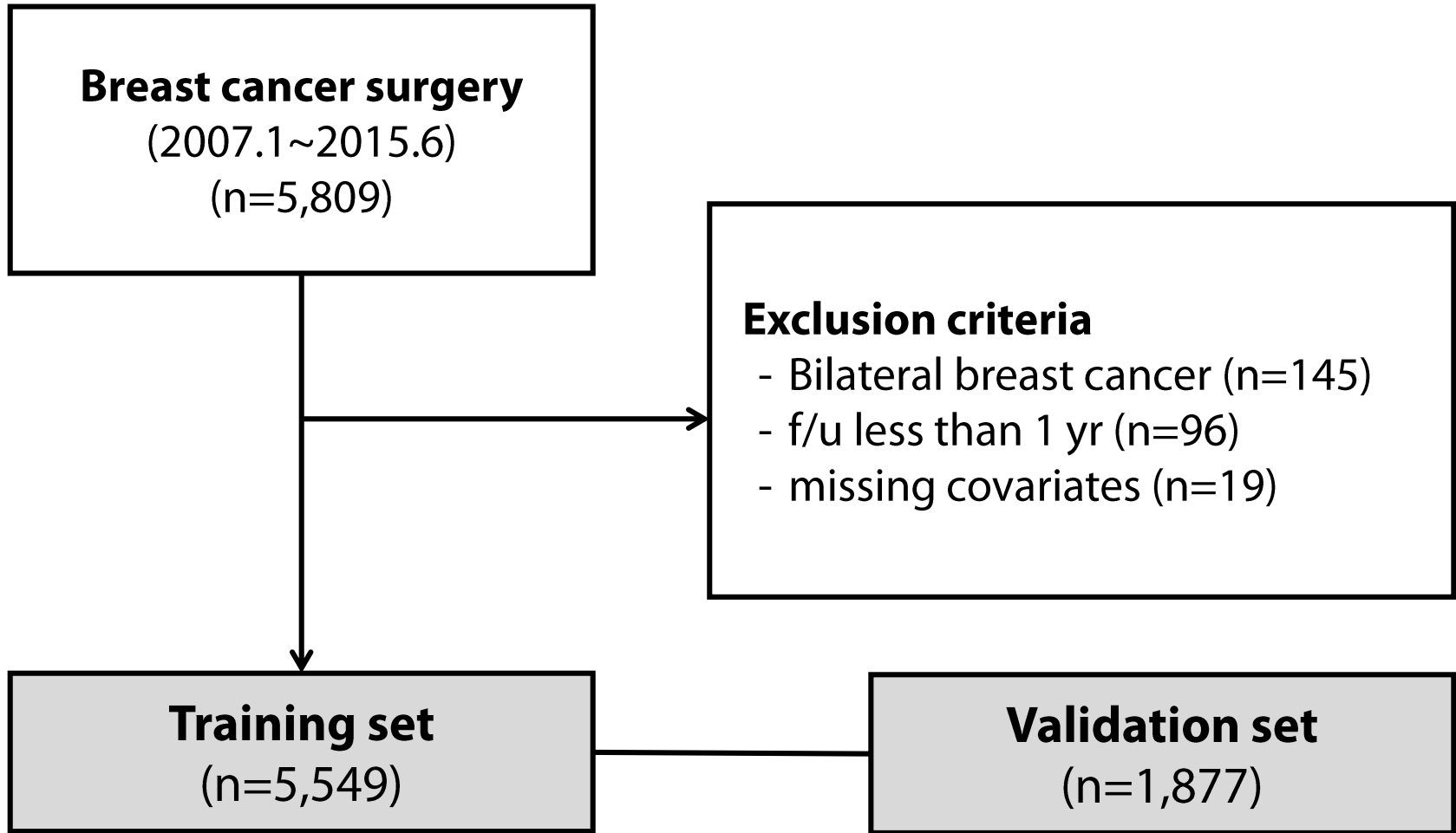
**The impact of new practice patterns on lymphedema**

# Purpose

- To identify the comprehensive risk factors of lymphedema including **hypofractionation** and **regional irradiation field**.



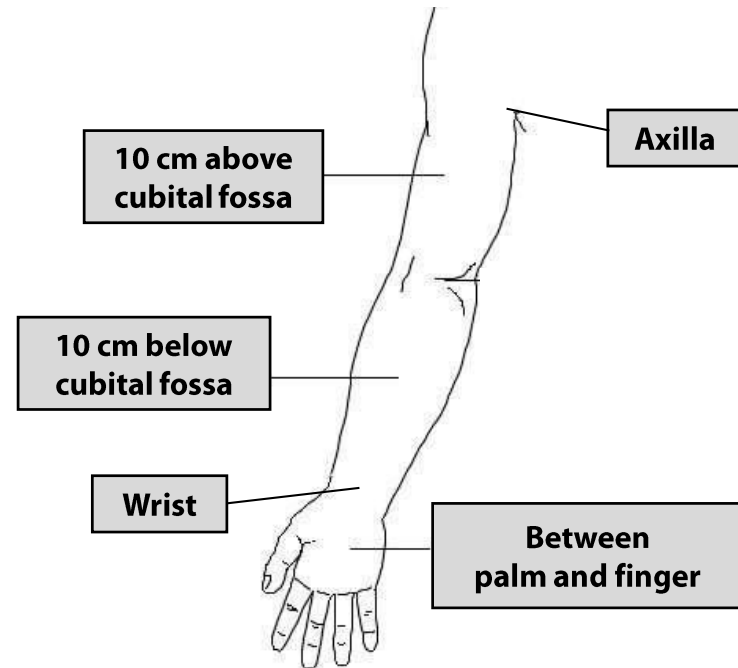
# Methods: Flowchart of patient selection



# Methods: Endpoint

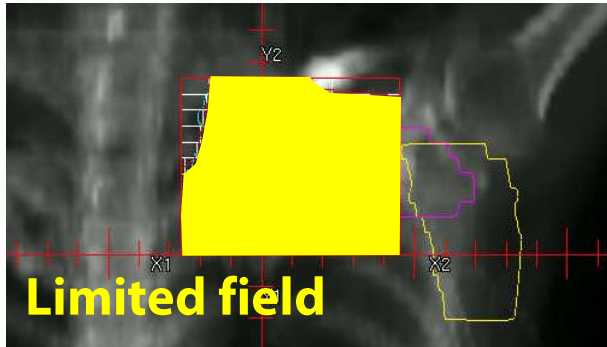
- **Patients with lymphedema**

- Difference in arm circumference  $\geq 2$  cm
- Patient perception of arm edema assessed by rehabilitation physicians.

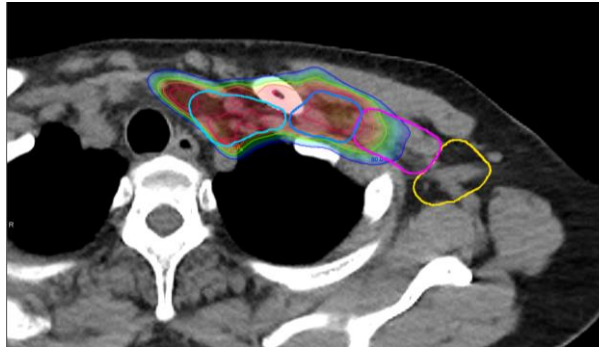


# Methods: Regional field

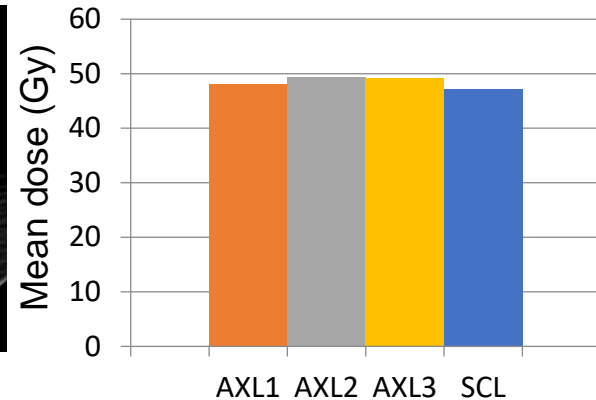
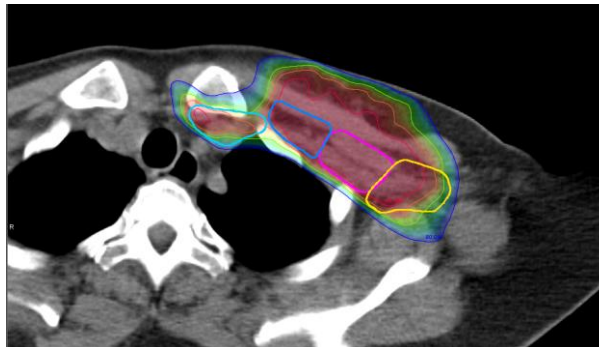
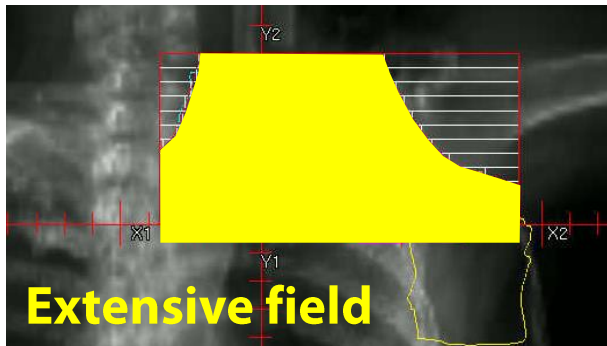
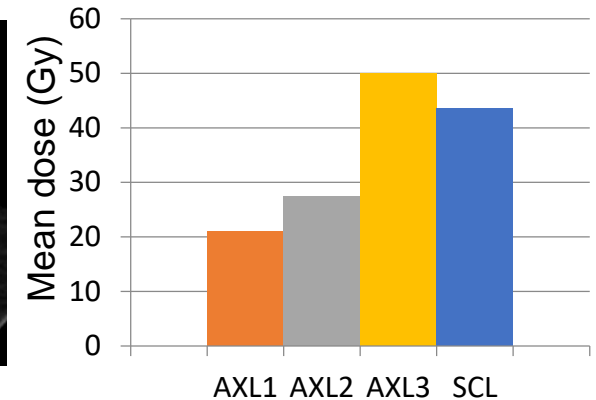
3D-CRT



IMRT



Representative Cases (n = 5)



# Results:

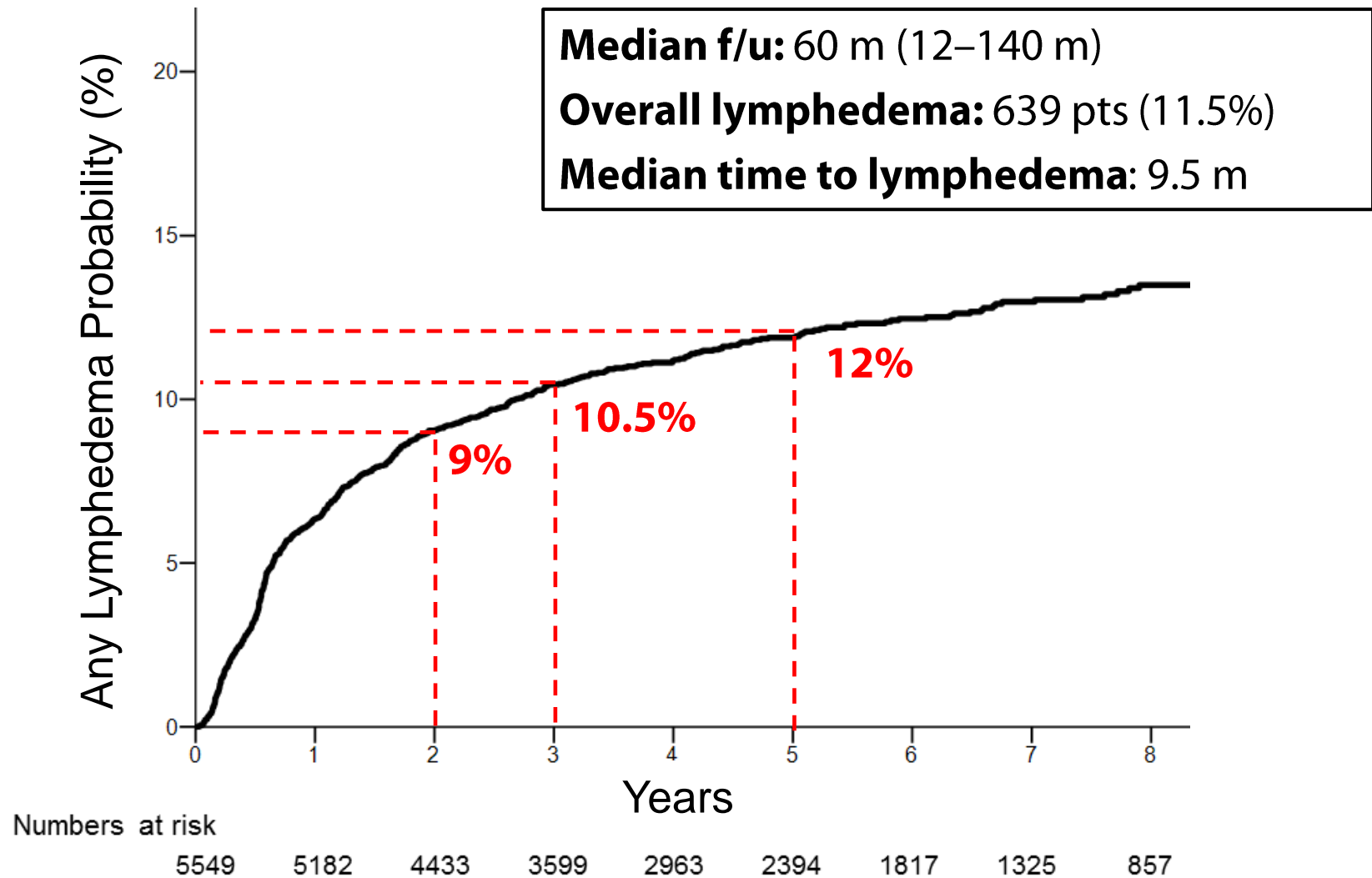
## Patients characteristics (n = 5,549)

	N or median	% or IQR
Age, years	50.5	44.3–58.5
BMI, kg/m <sup>2</sup>	23.0	21.1–25.3
Use of adjuvant RT		
No	1522	27.4
Yes	4027	72.6
RT field		
B/CW	2447	60.8
SCL+Lv.3	478	11.9
SCL+Lv.1-3	1102	27.4
RT fractionation		
Hypofractionated	927	23.0
Conventional	3100	77.0

	N or median	% or IQR
Type of surgery		
Partial mastectomy	3215	57.9
Total mastectomy	2334	42.1
Reconstruction	247	10.6
No. of positive nodes	0	0–1
No. of dissected nodes	6	3–12
Chemotherapy	3173	57.2
Neoadjuvant	822	25.9
Adjuvant	2612	82.3
Antracyclin-based	2919	92.0
Taxane-based	1698	53.5
Herceptin-based	674	21.2



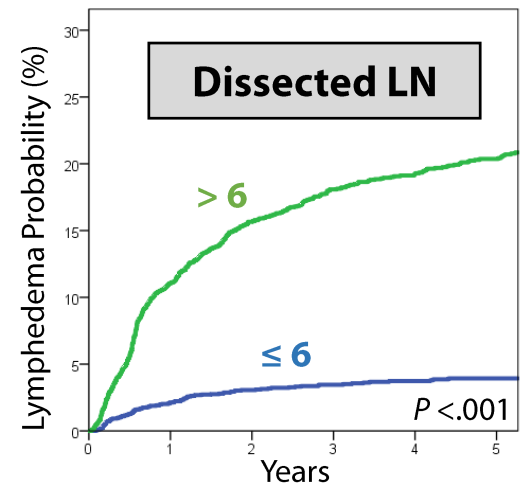
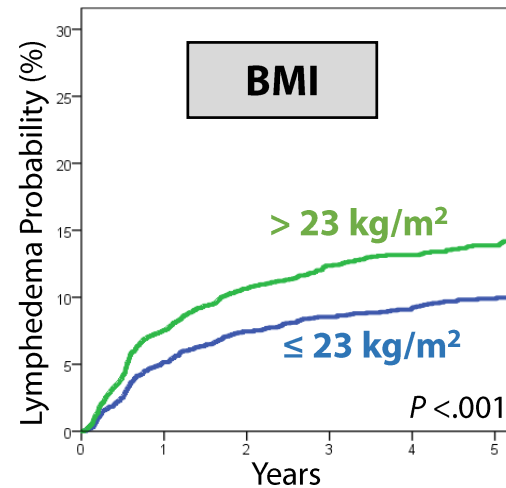
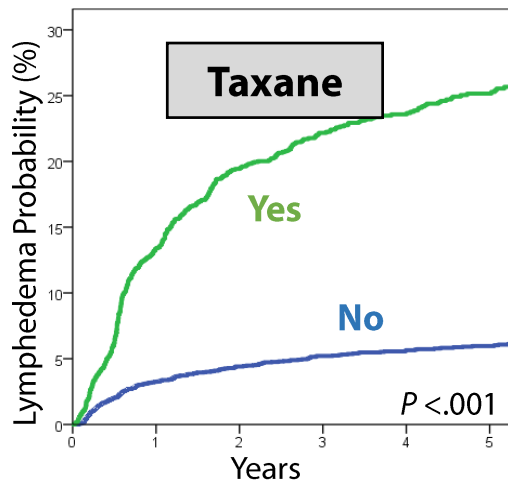
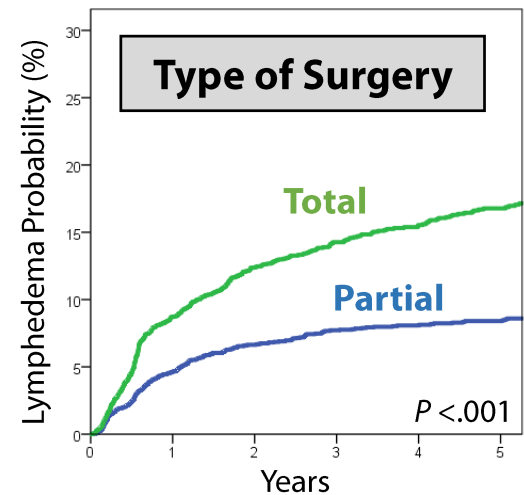
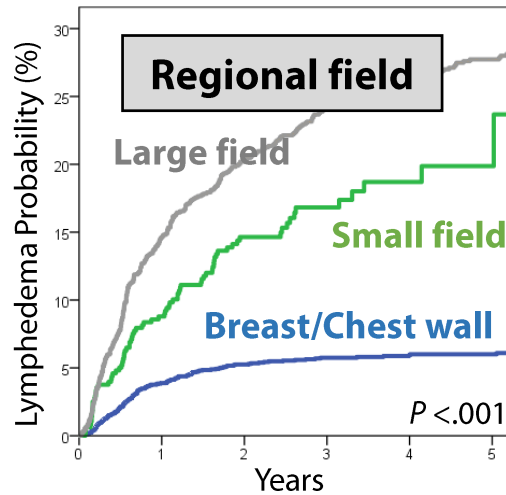
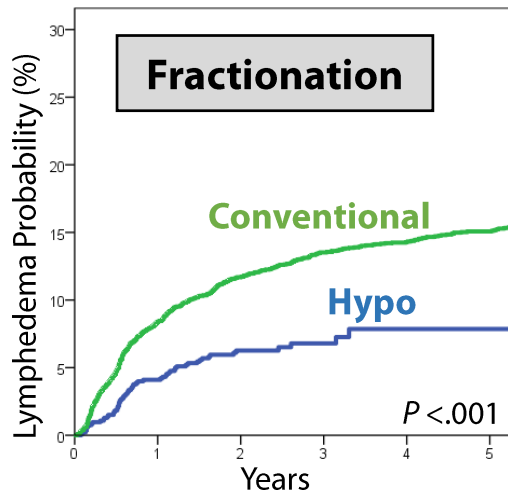
# Results: Lymphedema probability



# Results: Univariate & Multivariate analysis

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age, years	0.99 (0.99–1.00)	.082		
BMI, kg/m <sup>2</sup>	1.06 (1.04–1.09)	<.001	1.05 (1.03–1.07)	<.001
Antracyclin-based chemotherapy (Yes vs. No)	2.60 (2.18–3.10)	<.001		
Taxane-based chemotherapy (Yes vs. No)	4.68 (3.97–5.51)	<.001	2.16 (1.77–2.64)	<.001
Herceptin (Yes vs. No)	1.87 (1.53–2.28)	<.001		
Hormonal therapy (Yes vs. No)	0.75 (0.64–0.89)	.001		
No. of positive nodes	1.09 (1.07–1.10)	<.001		
No. of dissected nodes	1.08 (1.07–1.08)	<.001	1.04 (1.03–1.05)	<.001
Type of surgery (Total vs. Partial mastectomy)	2.01 (1.72–2.35)	<.001	1.65 (1.35–2.02)	<.001
Immediate reconstruction (Yes vs. No)	1.61 (1.18–2.22)	.003		
Regional RT field				
(Excluding AXL 1-2 vs. No regional RT)	3.23 (2.50–4.17)	<.001	1.36 (1.02–1.80)	.037
(Including AXL 1-2 vs. No regional RT)	4.84 (4.10–5.72)	<.001	1.73 (1.35–2.21)	<.001
RT fractionation (Hypo vs. Conventional)	0.51 (0.40–0.67)	<.001	0.74 (0.63–0.85)	<.001

# Results: Univariate analyses



# Results: Multivariate analysis

**BMI** (5% ↑ per kg/m<sup>2</sup>)

**Patients'  
perspective**

**Dissected LN** (4% ↑ per 1 node)

**Removed breast tissue**

(x1.7 Total vs. Partial)

**Surgical  
perspective**

**Taxane-based chemotherapy**

(x2.2 Yes vs. No)

**Systemic therapeutic  
perspective**

**Total radiation dose**

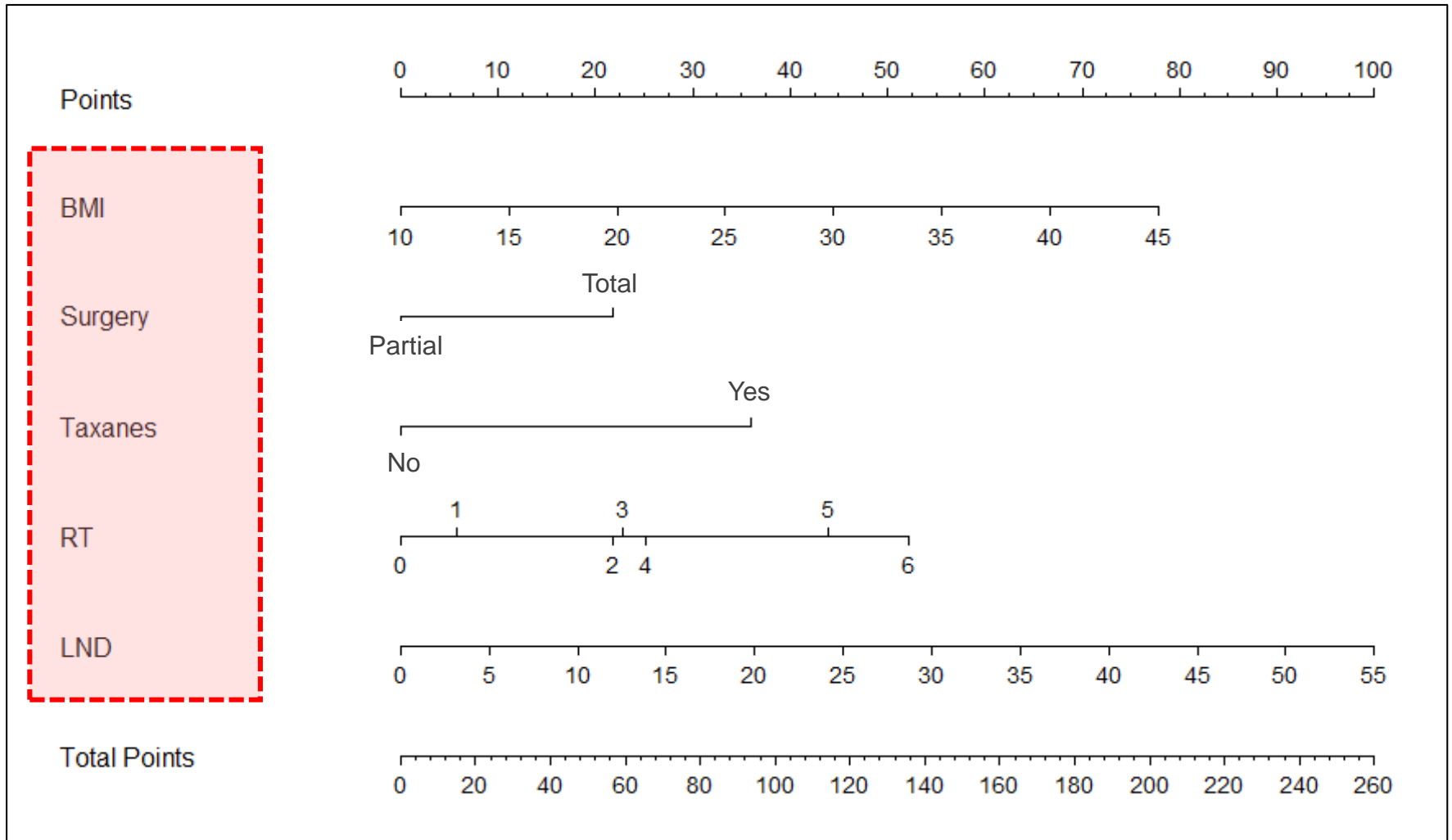
(36% ↓ Hypo vs. Conventional)

**Irradiated AXL volume**

(x1.7 Extensive vs. x1.4 Limited vs. No RNI)

**Radiotherapeutic  
perspective**

# Results: Nomogram

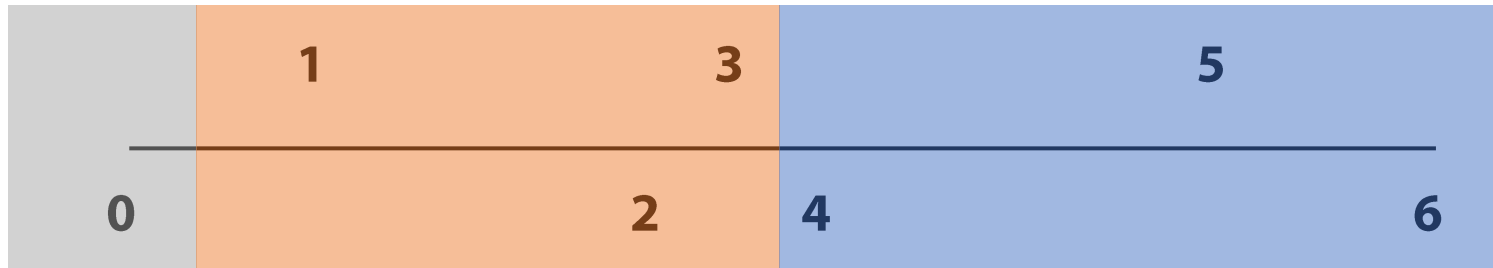


# Results: Nomogram

## Total radiation dose

No                      HypoFx                      Conventional Fx

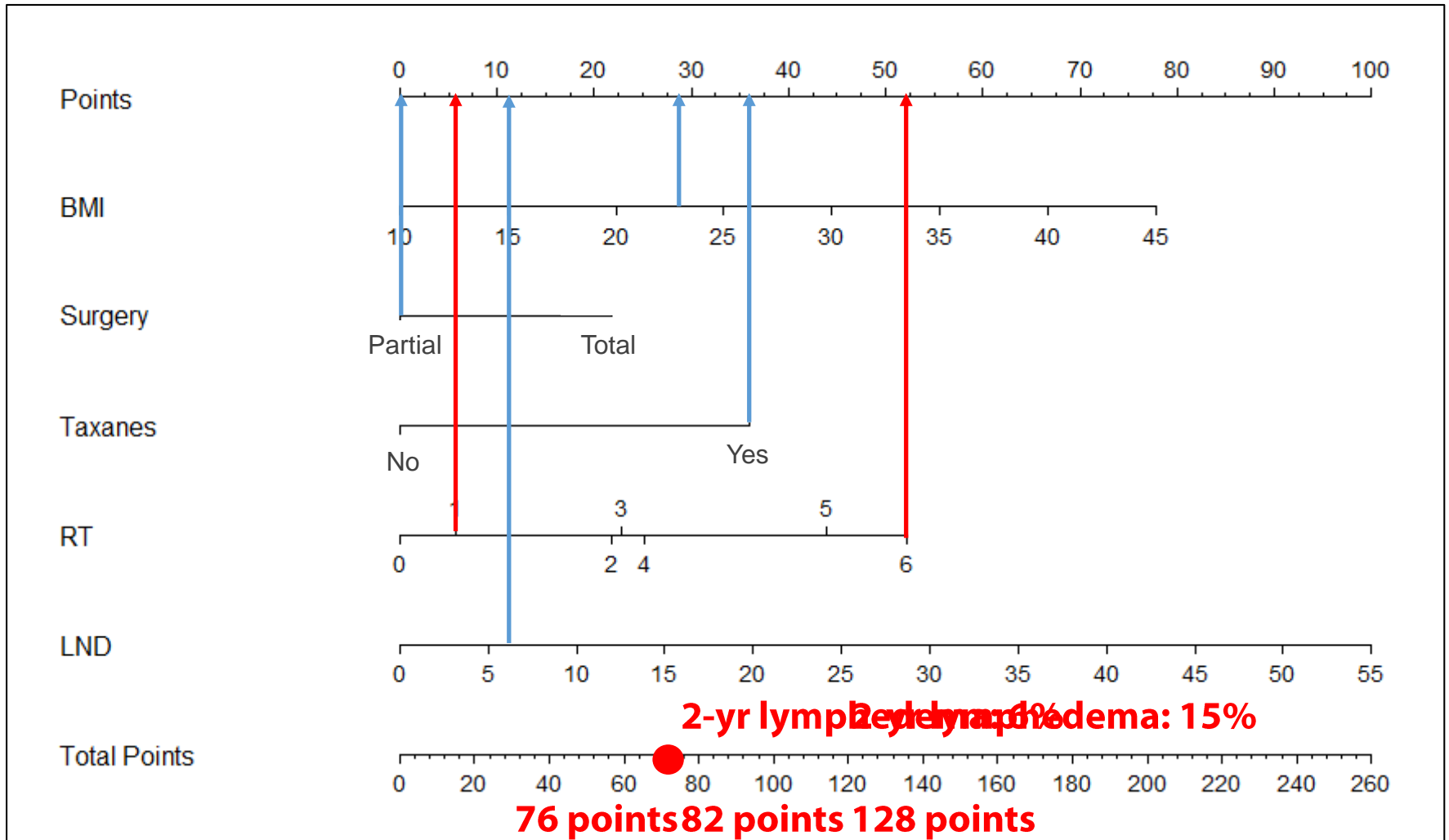
RT



No                      Limited    Extensive    No                      Limited    Extensive

## Irradiated AXL volume

# Results: Nomogram



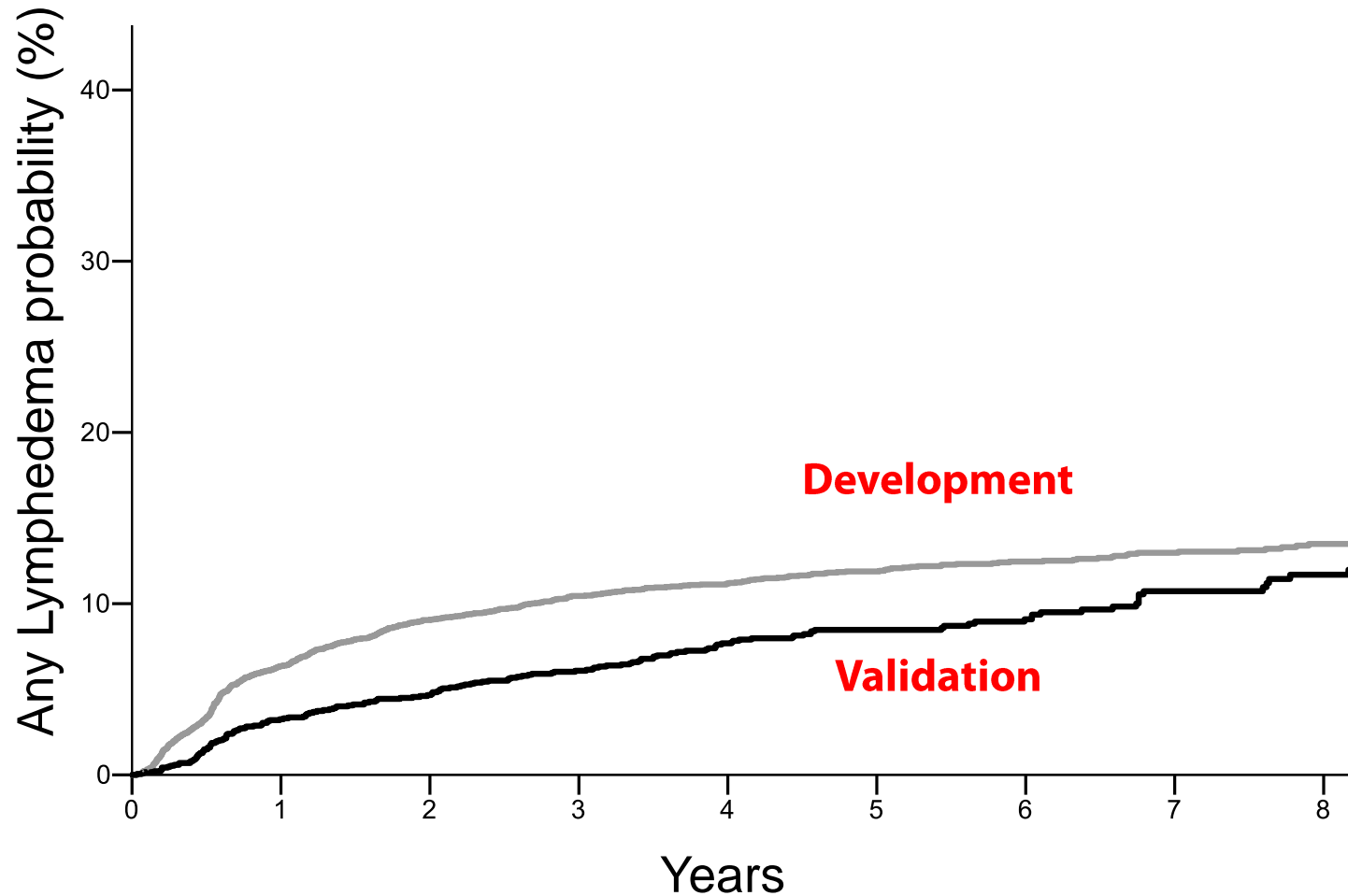
# Results: Patients characteristics

		Traning set N = 5549		Validation set N = 1877		
		N	%	N	%	P
<b>BMI</b>	<b>&lt;26 kg/m2</b>	4456	80.3	1547	82.4	0.044
	<b>≥26 kg/m2</b>	1093	19.7	330	17.6	
<b>No. of dissected nodes, median, range</b>		6	3–12	5	3–14	<.001
<b>Type of surgery</b>	<b>Partial mastectomy</b>	3215	57.9	886	47.2	<.001
	<b>Total mastectomy</b>	2334	42.1	991	52.8	
<b>Taxane-based chemotherapy</b>	<b>No</b>	3851	69.4	1457	77.6	<.001
	<b>Yes</b>	1698	30.6	420	22.4	
<b>RT</b>	<b>No</b>	1522	27.4	802	42.7	<.001
	<b>Yes</b>	4027	72.6	1075	57.3	
<b>RT dose/fractionation</b>	<b>Hypo</b>	927	23	0	0	<.001
	<b>Conventional</b>	3100	77	1075	100	
<b>RT field</b>	<b>No regional RT</b>	2447	60.8	735	68.4	<.001
	<b>Regional RT</b>	1580	39.2	340	31.6	



# Results

## Lymphedema for the development and validation set



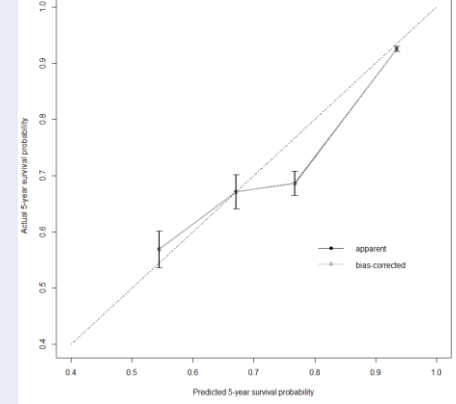
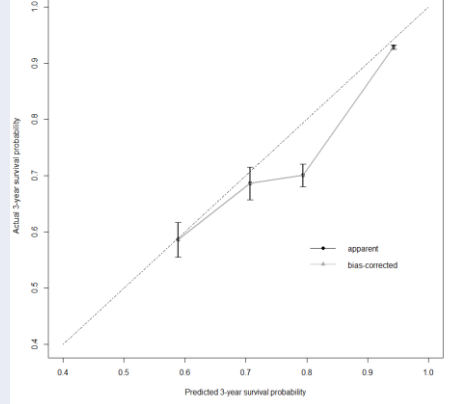
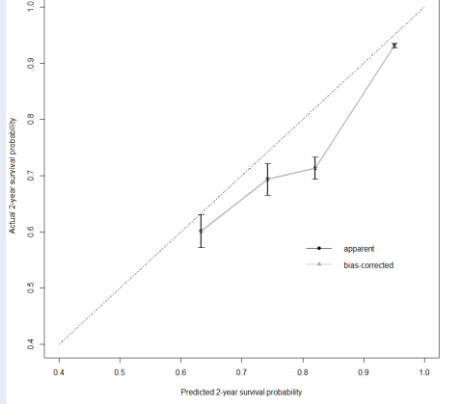
2 yr

3 yr

5 yr

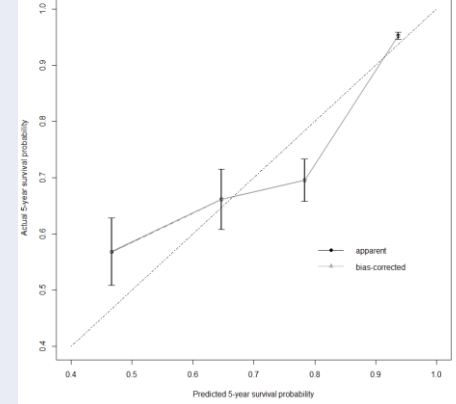
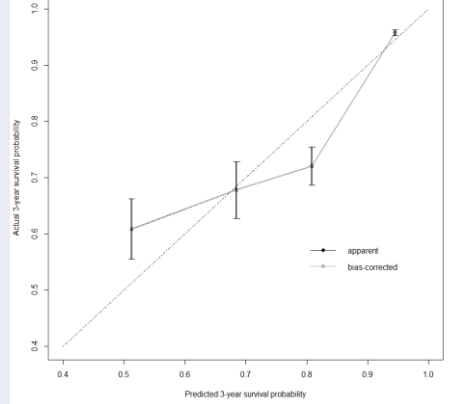
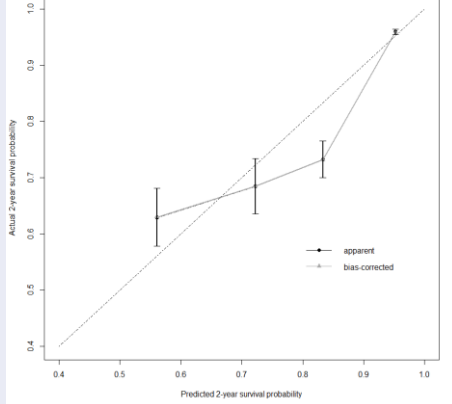
Internal

**1,000 bootstrap samples**



External

**1,877 external patients**



**C-index (95% CI)**

0.774 (0.756–0.790)

0.832 (0.806–0.856)

**iAUC (95% CI)**

0.750 (0.733–0.765)

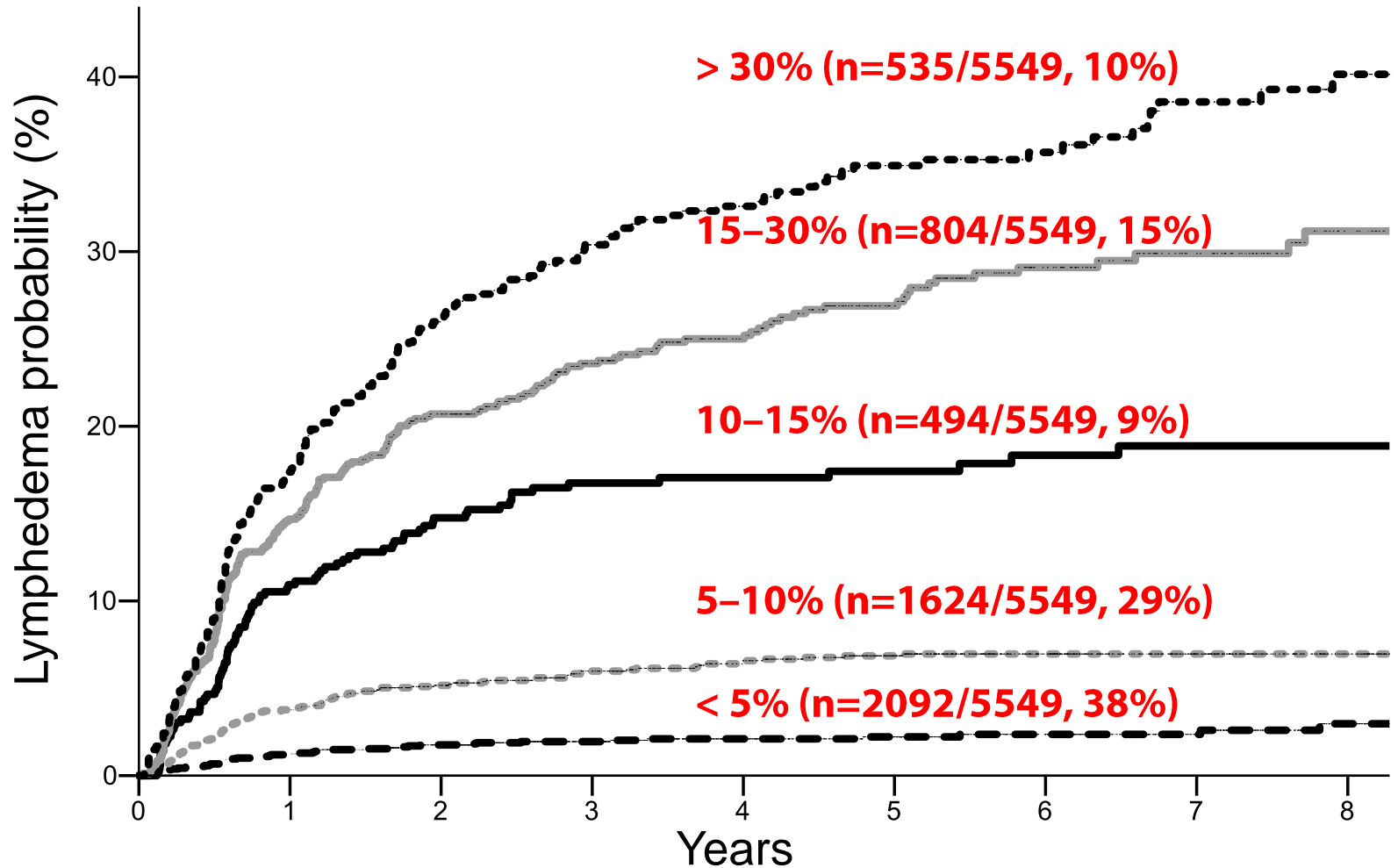
0.782 (0.754–0.810)

Internal

External

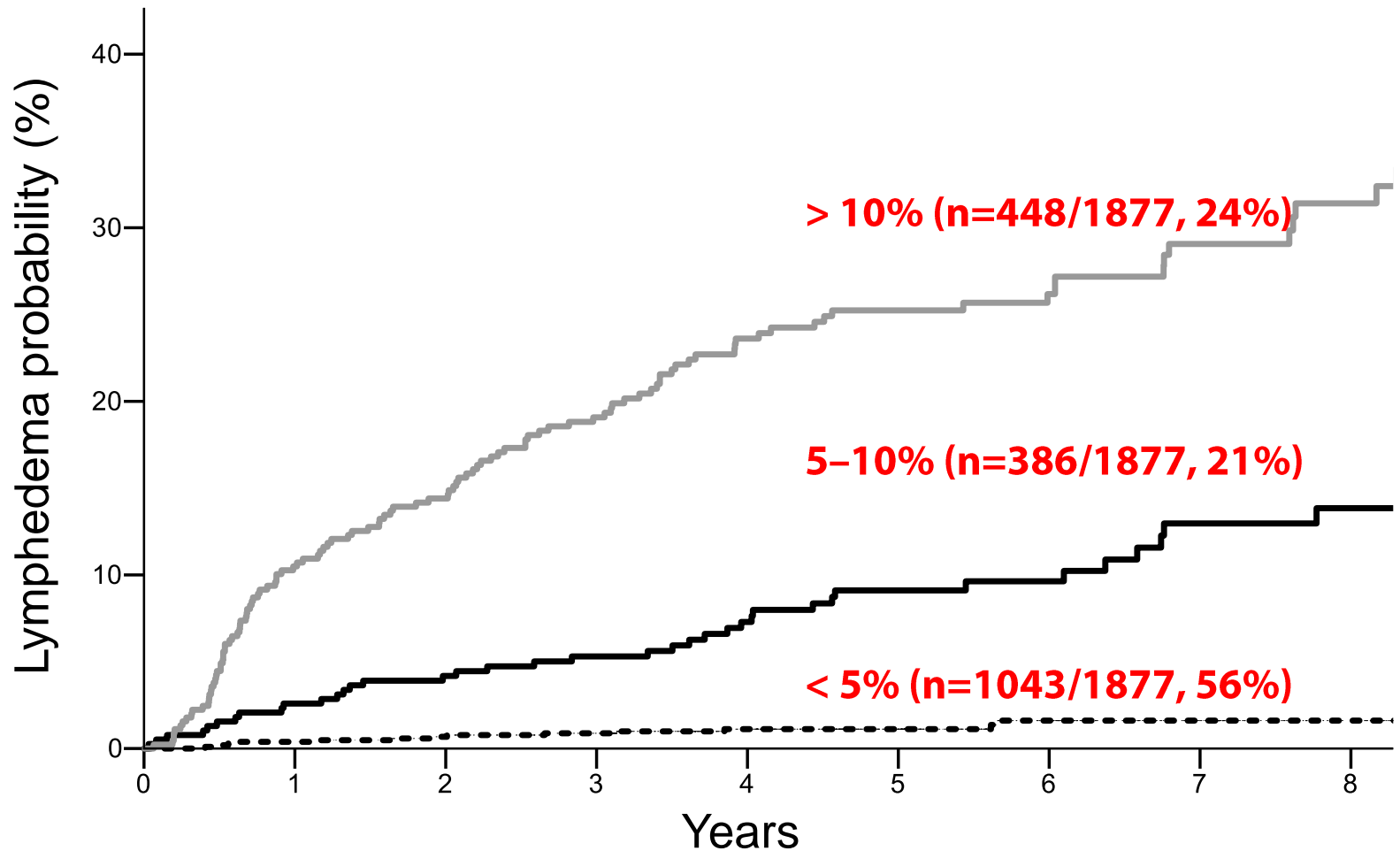
# Results

## Risk groups in the development set



# Results

## Risk groups in the validation set



# Summary

- Lymphedema for breast cancer has **multifactorial etiology**, and many interacting risk factors among **tri-modalities** are involved in its development.
  - BMI, Dissected LN, Total mastectomy
  - RNI field, RT dose, Taxane
- A **nomogram** to predict the individual risk of lymphedema was successfully built.
- The nomogram showed **excellent calibration and discrimination** internally (C-index: 0.774) and externally (0.832).

# Conclusion

- Efforts to decrease lymphedema risk by focusing on **modifying regional field** or **hypofractionation** are likely to have a major effect.
- **De-escalation strategy** to minimize lymphedema risk should be discussed in a multidisciplinary team.

*Severance*

**Thank you for your attention.**

