

P2:271: Impact of Estimated Radiation Dose to Immune Cells in Locally Advanced Non-Small Cell Lung Cancer: A Systematic Review, Meta-analysis and Institutional Validation

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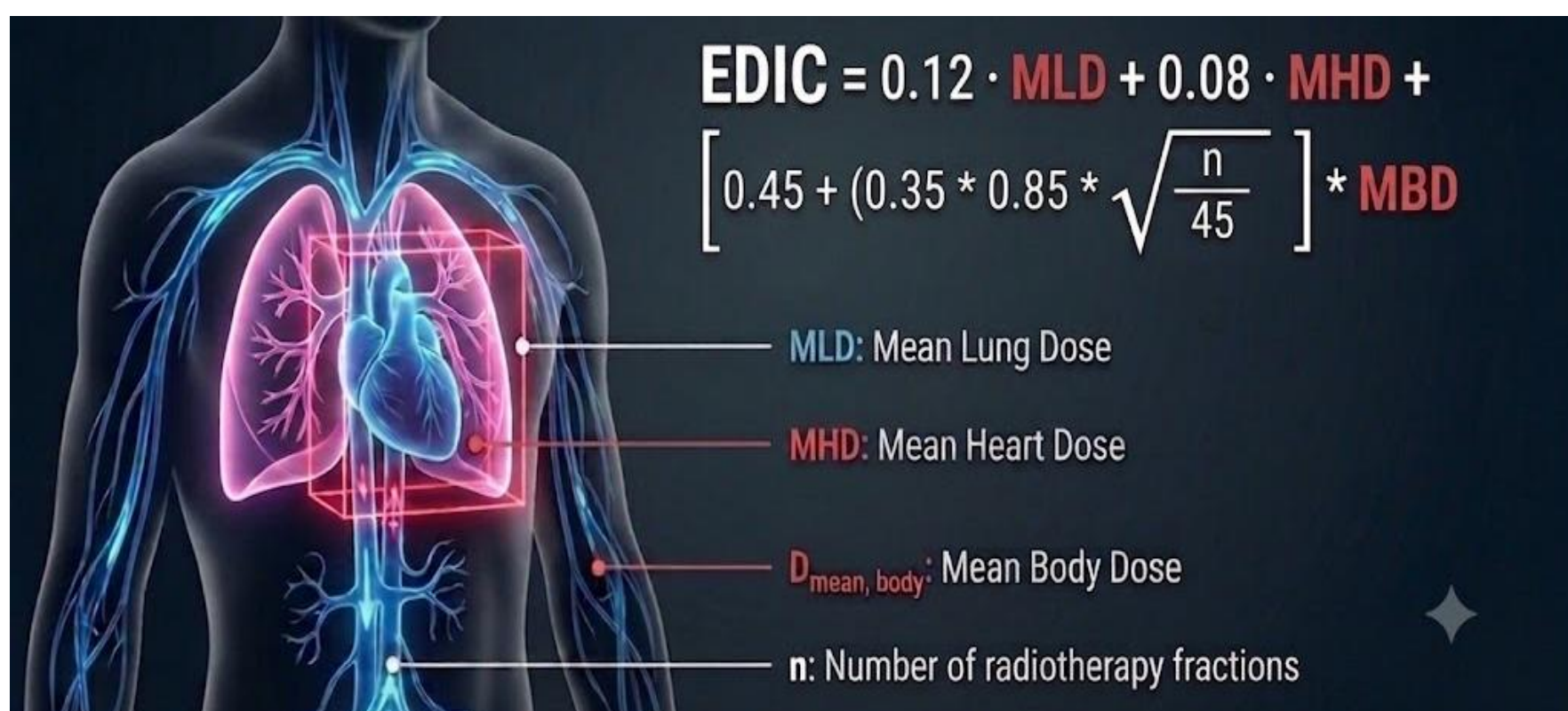
INTRODUCTION

Background

- PACIFIC trial established consolidation durvalumab following chemoradiotherapy as a standard of care for locally advanced non-small cell lung cancer (NSCLC).
- While radiation induces tumor antigen release and prime microenvironment for durvalumab-mediated T-cell activation, excessive radiation dose to the circulating lymphocytes may destroy the host immunity required for this synergy.

Objectives

- To quantify the **prognostic impact of estimated radiation dose to immune cells (EDIC) on survival outcomes** in locally advanced NSCLC treated with definitive chemoradiotherapy +/- immunotherapy.
- To evaluate the **association between EDIC, lymphocyte kinetic, survival, and toxicity outcomes** in a cohort treated using PACIFIC regimen.



METHODS

Systematic review and meta-analysis

- Databases: PubMed, Embase
- Risk of bias tool: Newcastle-Ottawa Scale
- Statistics: random-effects meta-analysis with prespecified subgroup analysis

Institutional cohort study (PACIFIC regimen)

- Ethics approval granted
- Comparison of baseline characteristics between low and high EDIC groups: Wilcoxon rank-sum (continuous) and Chi-square (categorical) tests
- Longitudinal changes in absolute lymphocyte counts (ALC) over time: repeated-measures mixed model
- Time-to-event outcomes: Cox proportional hazard regression with Kaplan-Meier estimation
- Binary outcomes: logistic regression

RESULTS

Systematic Review and Meta-analysis

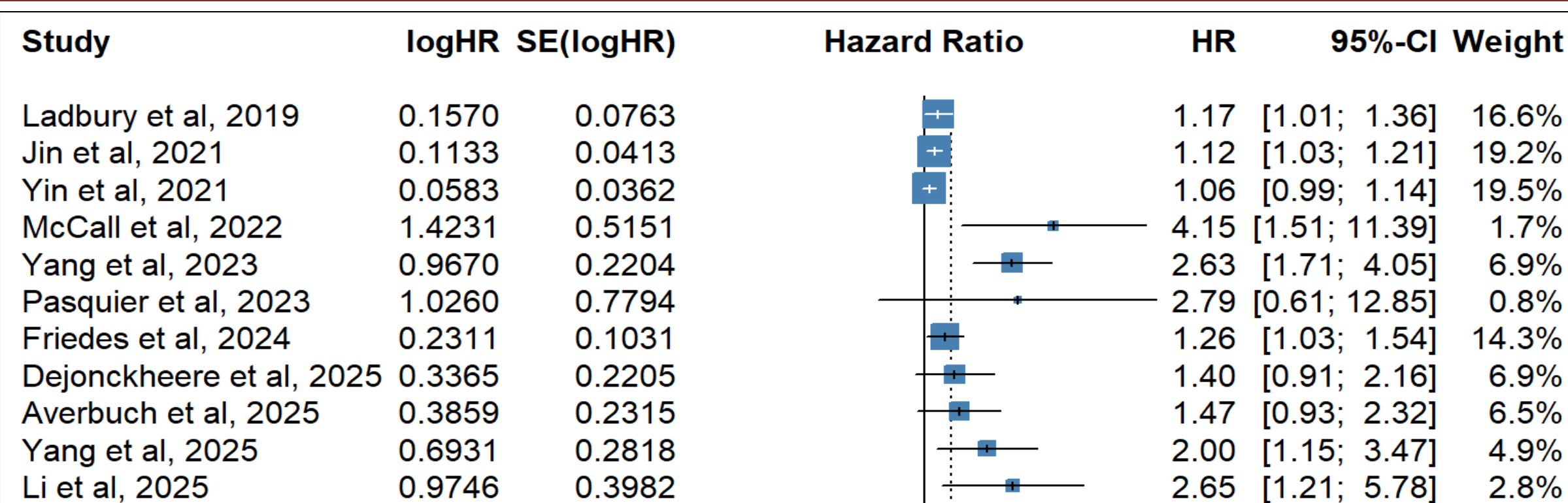
Study	Country	N	Stage	Immunotherapy	Cutoff selection	Cutoff (Gy)
Ladbury, 2019	USA	117	III	No	Median	6.1
Jin, 2021	USA	456	III	No	Continuous	Nil
Yin, 2021	China	201	III	No	Median	6.92
McCall, 2022	USA	100	II-III	Yes (consolidation)	Median/ continuous	6
Yang, 2023	Korea	517	I-III	Yes (consolidation)	Median	3.01
Pasquier, 2023	France	50	II-III	Yes (consolidation)	Previous study	6.3
Friedes, 2024	USA	786	II-III	30%(consolidation)	Median	4.7
Dejonckheere, 2025	German	153	II-III	No	Median	5.7
Averbuch, 2025	Israel	286	III	Yes (consolidation)	Median	9.57
Yang, 2025	China	139	II-III	Yes (consolidation)	Optimal cutoff	4.44
Li, 2025	China	104	III	Yes (concurrent)	Median	6.4

- Eleven studies with 2,909 patients
- Low risk of bias for all the included studies

Subgroup Analysis: Populations at Most Risk

Subgroup	Category	Hazard Ratio (HR)	95% Confidence Interval
Immunotherapy Use	Yes	1.97	1.40-2.77
	No	1.10	1.04-1.16
Median Age	≥ 65 years	1.63	1.23-2.16
	< 65 years	1.10	1.04-1.16

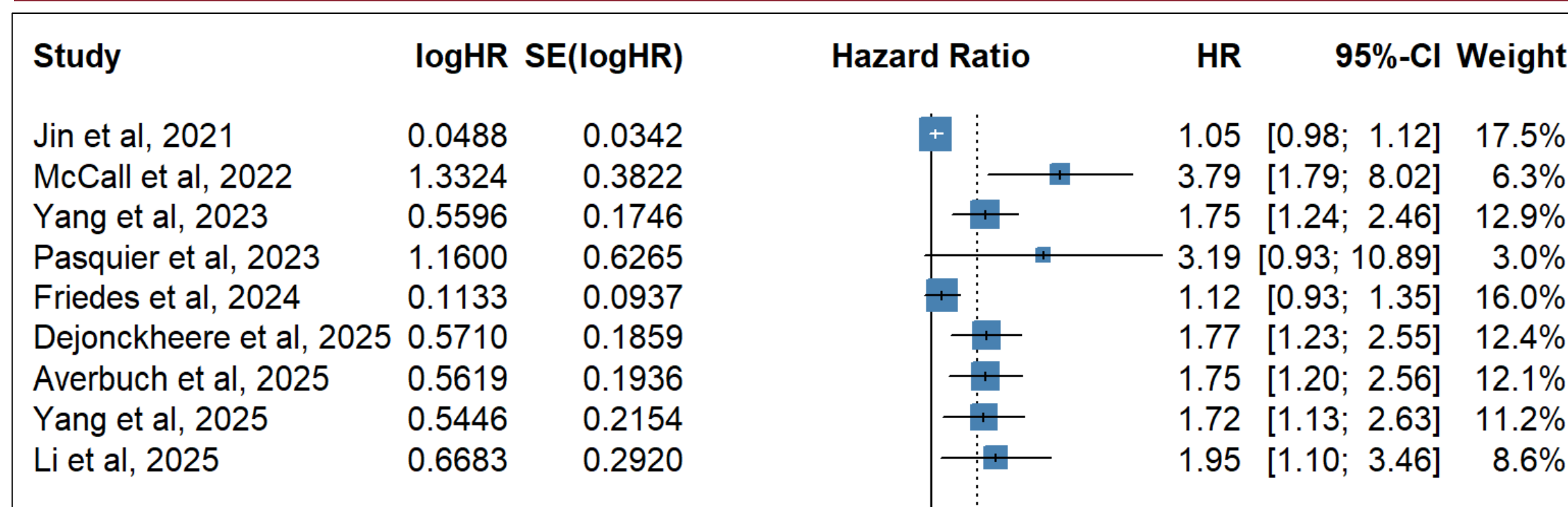
Impact of EDIC on OS



Random effects model

Heterogeneity: $I^2 = 73.5\%$, $\tau^2 = 0.0246$, $p < 0.0001$
P < 0.0001

Impact of EDIC on PFS



Random effects model

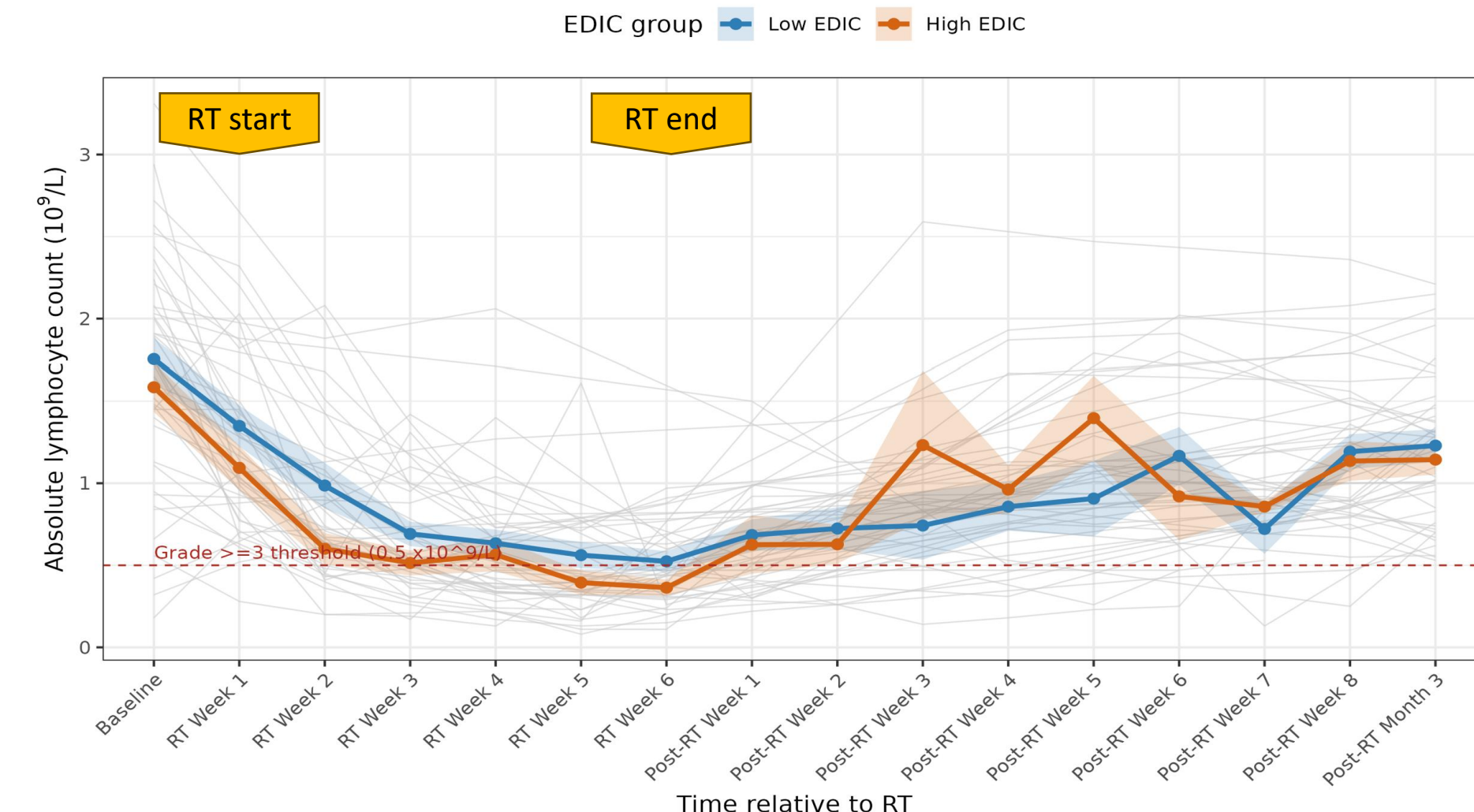
Heterogeneity: $I^2 = 80.9\%$, $\tau^2 = 0.0808$, $p < 0.0001$
P < 0.0001

Institutional Cohort Study

Longitudinal analysis of lymphocytes

Absolute lymphocyte count over time

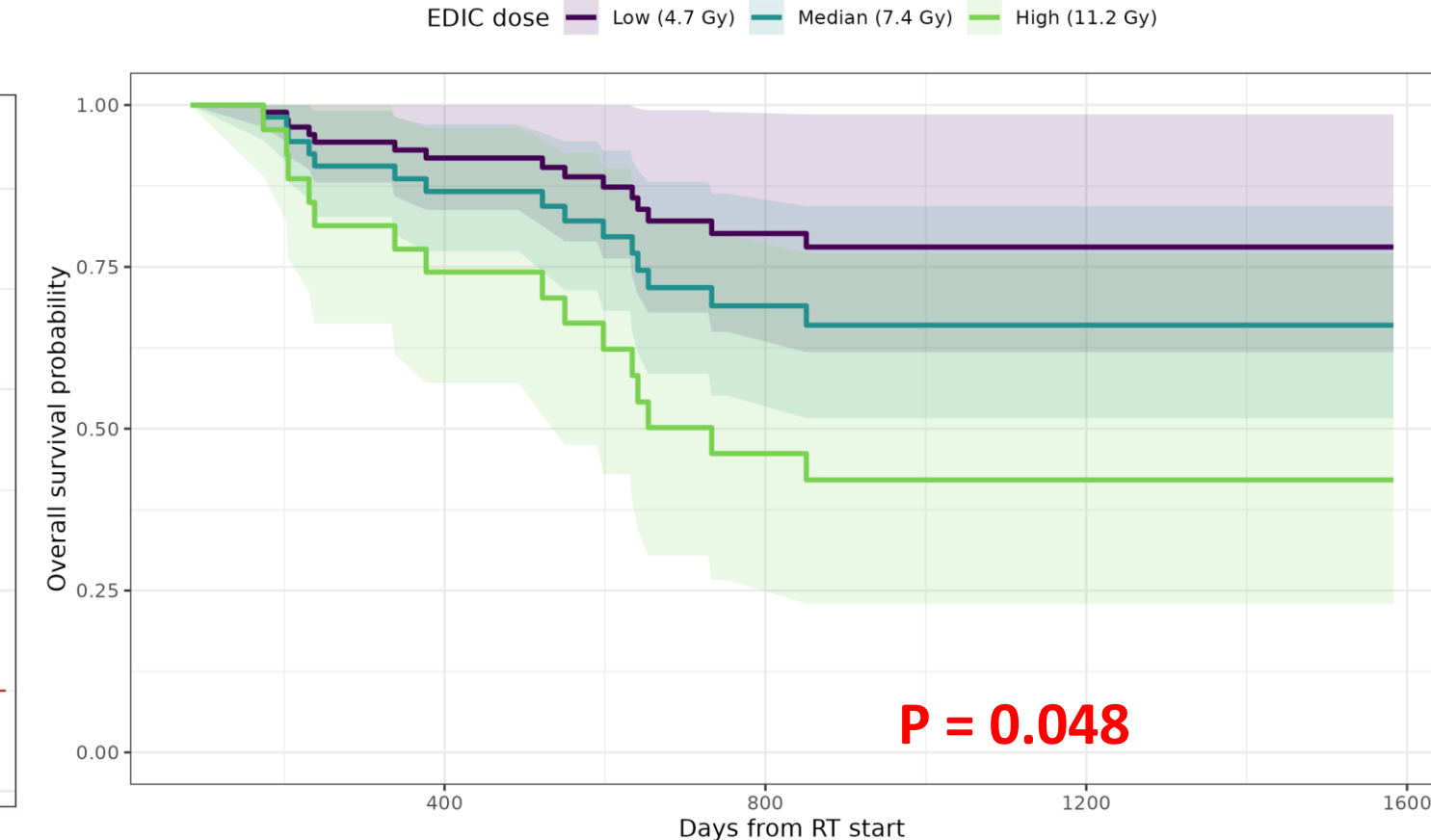
Individual trajectories (grey) with mean ± SE by EDIC group



OS

Overall survival by EDIC dose (continuous, Cox model)

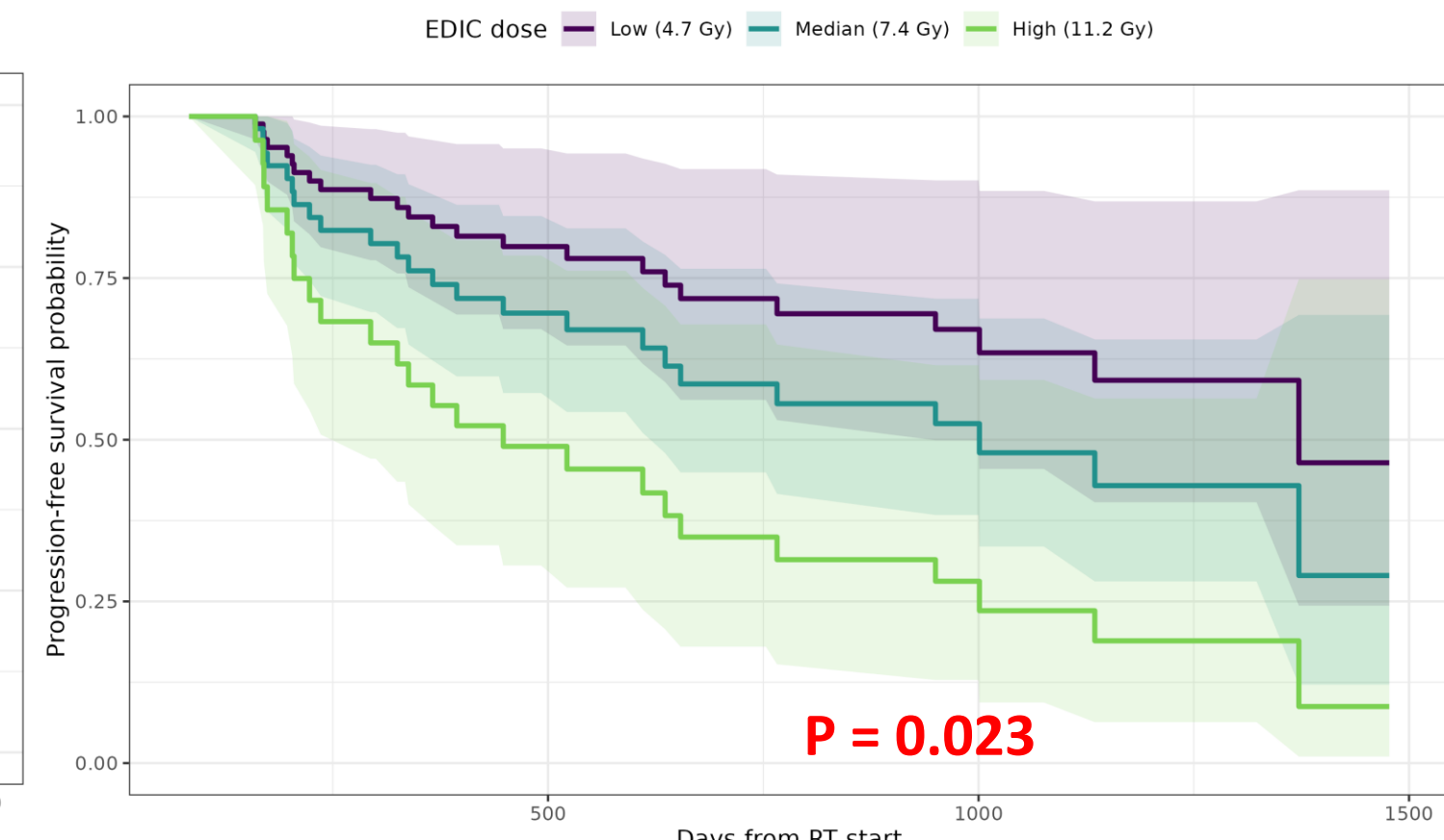
Cox model-predicted survival at representative EDIC doses (HR 1.21 per 1 Gy, p = 0.048)



PFS

Progression-free survival by EDIC dose (continuous, Cox model)

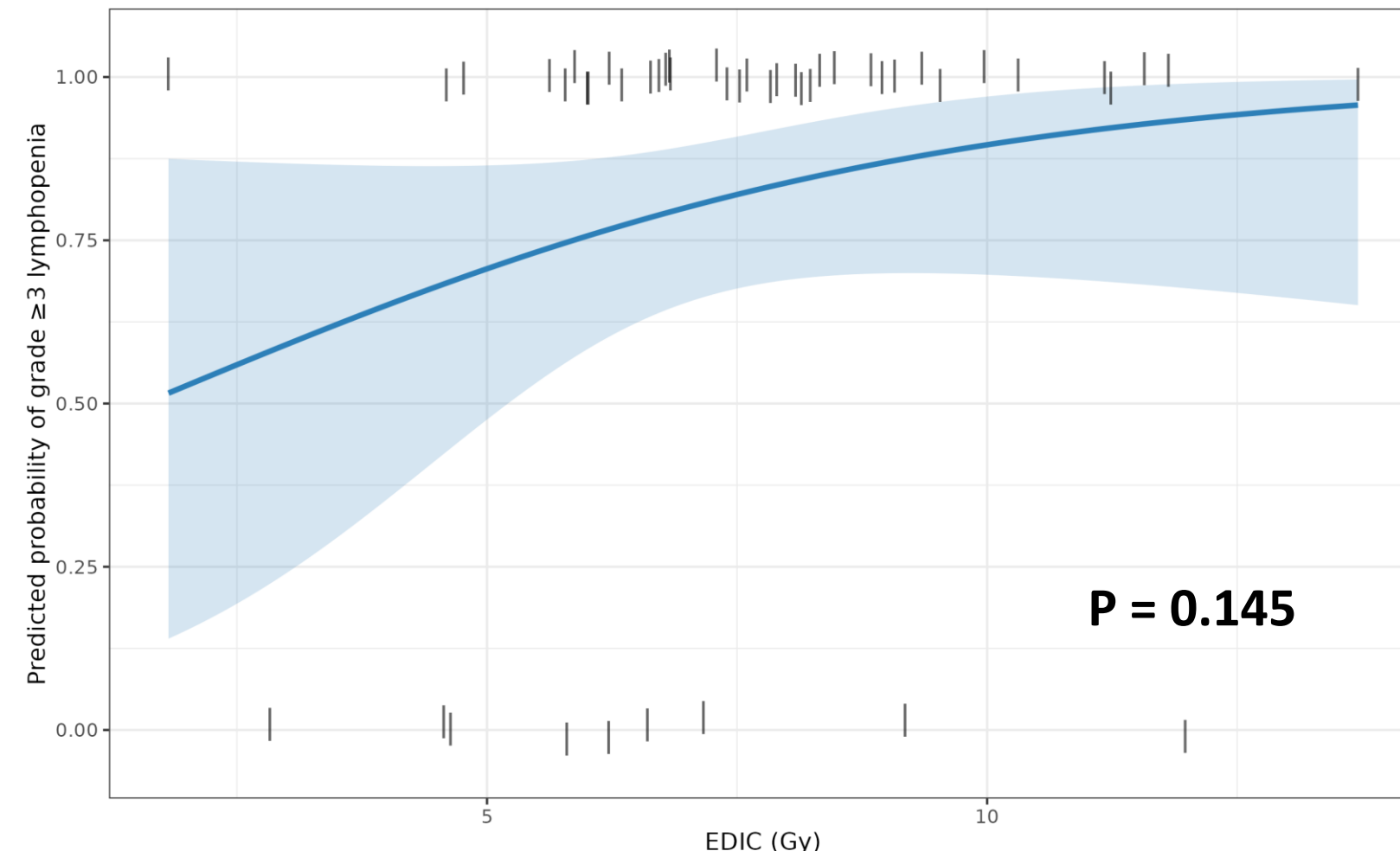
Cox model-predicted survival at representative EDIC doses (HR 1.20 per 1 Gy, p = 0.023)



Lymphopenia

Incidence of grade ≥3 lymphopenia by EDIC dose (continuous, logistic regression)

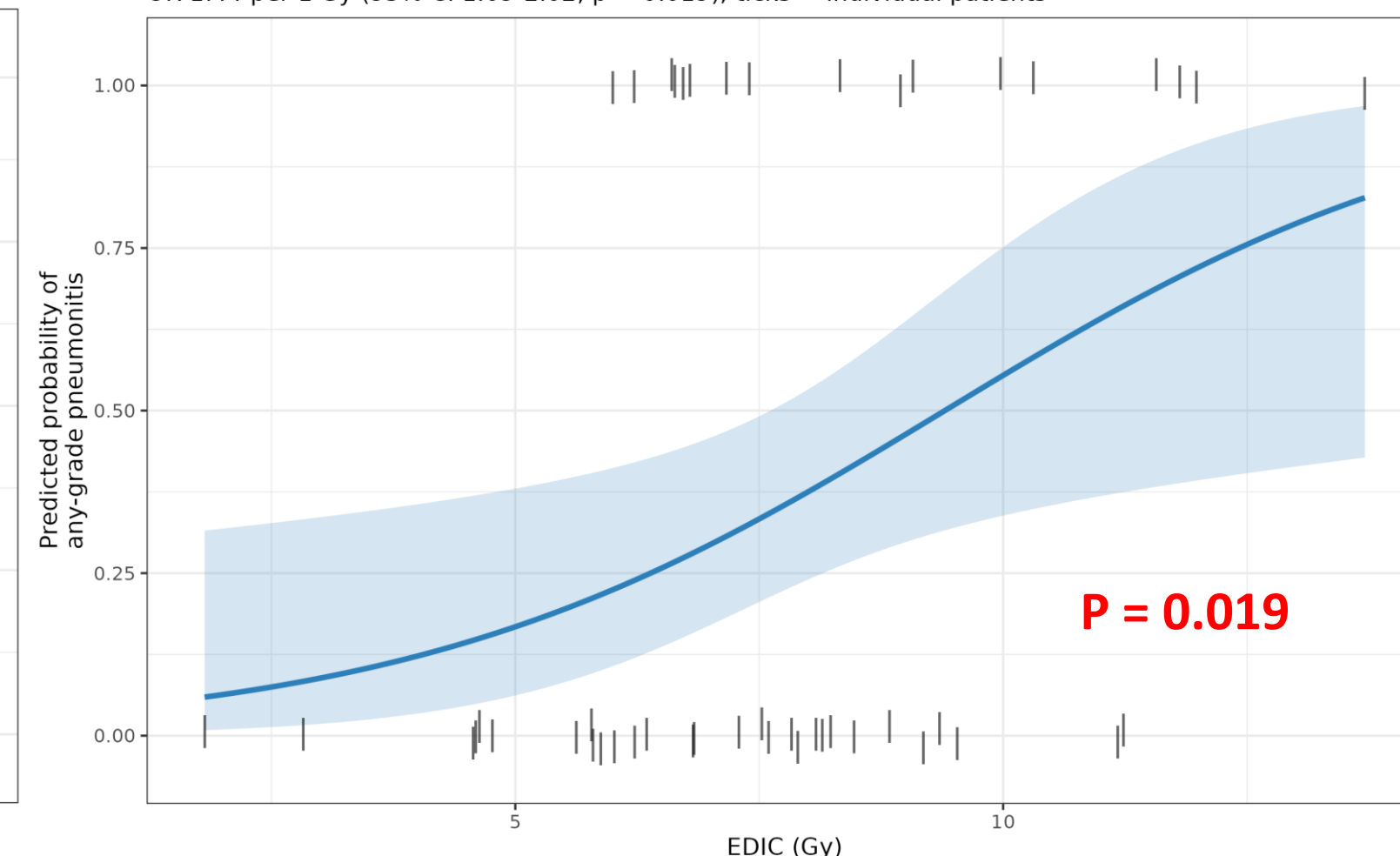
OR 1.29 per 1 Gy (95% CI 0.93-1.89, p = 0.145); ticks = individual patients



Pneumonitis

Any-grade pneumonitis by EDIC dose (continuous, logistic regression)

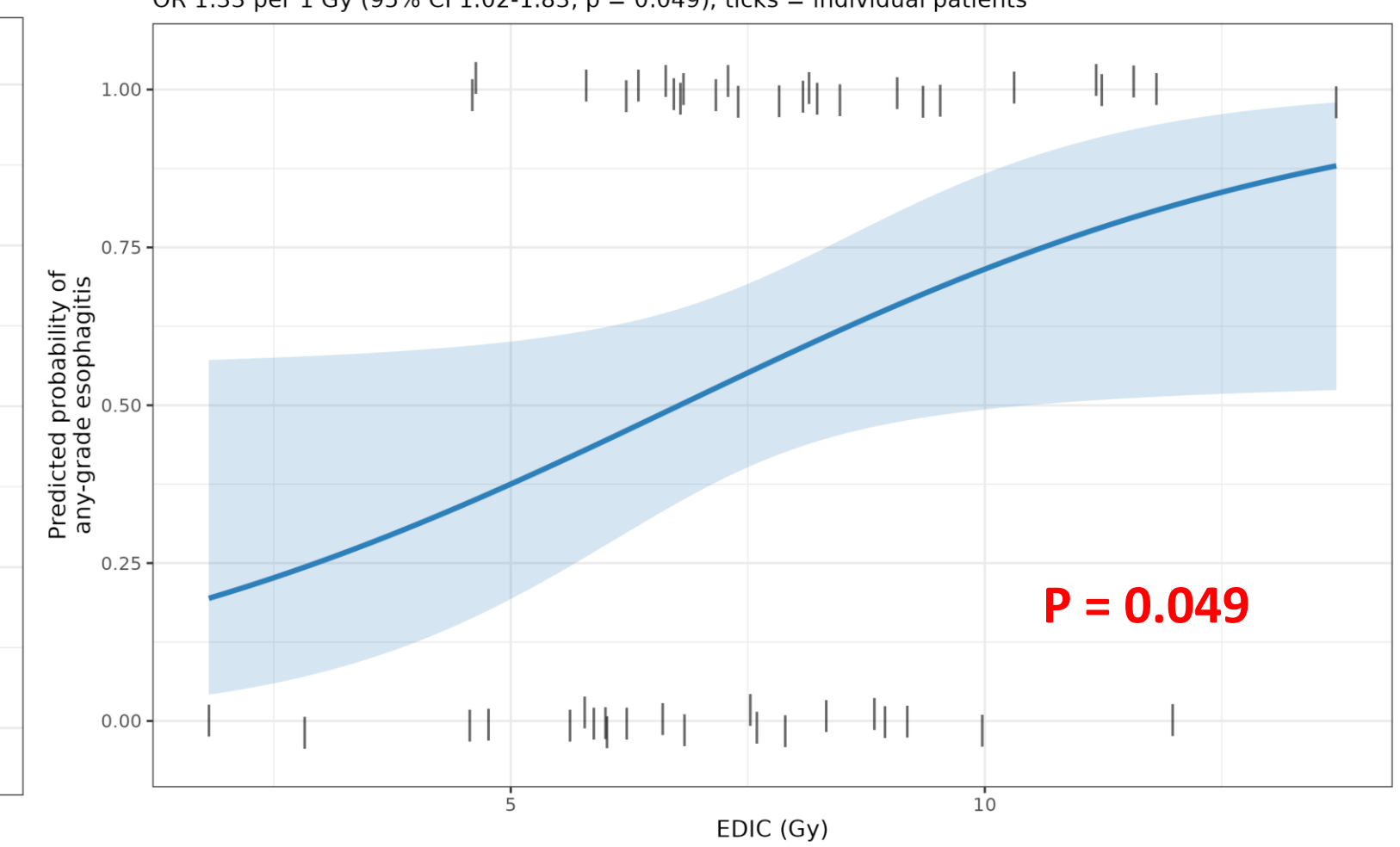
OR 1.44 per 1 Gy (95% CI 1.09-2.02, p = 0.019); ticks = individual patients



Esophagitis

Any-grade esophagitis by EDIC dose (continuous, logistic regression)

OR 1.33 per 1 Gy (95% CI 1.02-1.83, p = 0.049); ticks = individual patients



CONCLUSION

Meta-analysis demonstrates that a **higher EDIC is associated with worse PFS and OS**, with more pronounced effects in patients receiving immunotherapy and in older patients.

Institutional cohort study shows that a higher EDIC:

- Correlates with **large gross tumor volume**.
- Is associated with increased risk of **pneumonitis and esophagitis**.

Directions for Future Research

- An ongoing **dosimetric study** is evaluating if new radiation plans which reduce EDIC will meet other planning objectives.
- Validation of EDIC using **large clinical trial datasets** for further dosimetric and toxicity analyses.
- Prospective trials** comparing clinical outcomes of standard and EDIC-optimized radiotherapy plans.

ACKNOWLEDGEMENTS

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