

INTRODUCTION

Osimertinib is standard first-line therapy for advanced EGFR-mutated NSCLC.

While osimertinib is generally well tolerated, a subset of patients may undergo dose reductions or treatment breaks to mitigate side effects.

Randomized trials do not routinely capture the impact of such modifications on clinical outcomes, leaving clinicians and patients with limited evidence to guide treatment decisions.

STUDY OBJECTIVE

Evaluate impact of treatment modification within the first 6 months of osimertinib initiation on 1) time to treatment failure (TTF) and 2) overall survival (OS) among patients with advanced EGFR-mutated NSCLC.

METHODS

Study design/
setting

- Adult patients with Stage IV EGFR-mutated NSCLC prescribed ≥1 month of osimertinib
- Treated at Kaiser Permanente Northern California between 1/1/2018-6/30/2023 (followed until 12/31/2024)

Matching
procedures

- Patients with treatment modification were matched to patients on full-dose regimen
- Matched on age, sex, race/ethnicity, comorbidities, mutation type, and line of treatment

Outcomes

- Primary outcome (TTF):** defined as time until addition or switch to new systemic therapy, >60 days off osimertinib, or death
- Secondary outcome (OS):** Compared restricted mean survival times between exposure groups

Exposure definition

- Treatment modification: ≥14 days of dose <80 mg or treatment hold during first 6 months

Exclusion criteria

- Referred to hospice or died within 30 days
- Ever prescribed a dose higher than 80 mg
- Prescribed concurrent chemotherapy within 30 days after osimertinib start

KEY FINDINGS

- Patients with advanced/metastatic NSCLC prescribed osimertinib who underwent early treatment modification had **longer time to treatment failure** compared with patients on full dose, although the absolute differences were small.
- Survival rates were similar between the two groups.
- Treatment modifications within first six months do not appear to compromise clinical outcomes for patients prescribed osimertinib.

RESULTS

Table 1: Demographic characteristics

Characteristic	Early Treatment Modification		p-value
	No (N=645)	Yes (N=115)	
Age at osimertinib initiation, Median (IQR)	69 (61, 76)	75.0 (67, 82)	<0.001
Sex, n (%)			0.82
F	444 (68.8)	81 (70.4)	
M	201 (31.2)	34 (29.6)	
Race/Ethnicity, n (%)			0.47
White	236 (36.6)	47 (40.9)	
Asian/Pacific Islander	343 (53.2)	59 (51.3)	
Black or African American	22 (3.4)	5 (4.3)	
Other/Unknown	44 (6.8)	4 (3.5)	
Language, n (%)			0.75
English	525 (81.4)	97 (84.3)	
Non-English	120 (18.6)	18(15.7)	
Neighborhood Deprivation Index, n (%)			0.81
1 - least deprived	178 (27.6)	33 (28.7)	
2	208 (32.2)	40 (34.8)	
3	165 (25.6)	29 (25.2)	
4 - most deprived	94 (14.6)	13 (11.3)	
Cancer stage before osimertinib initiation, n (%)			0.012
Stage 4 or distant recurrence	533 (82.6)	83 (72.2)	
Early Stage (I-III)	112 (17.4)	32 (27.8)	
Time from cancer diagnosis to osimertinib initiation (in days), Median (IQR)	55.0 (35.0, 405.0)	161.0 (40.5, 865.5)	0.002
EGFR Status, n (%)			0.4
Unknown	163 (25.3)	36 (31.3)	
Classic	427 (66.2)	70 (60.9)	
Non-Classic	55 (8.5)	9 (7.8)	
Elixhauser Comorbidity Score, Median (IQR)	3 (2, 5)	4 (3, 6)	<0.001
Insurance status, n (%)			<0.001
Commercial only	226 (35.0)	22 (19.1)	
Medicaid only	11 (1.7)	3 (2.6)	
Medicare only	362 (56.1)	86 (74.8)	
Multiple/Other/Unknown	46 (7.1)	4 (3.5)	
Osimertinib line of treatment			0.32
First-line	507 (78.6)	85 (73.9)	

RESULTS

Table 2: Restricted mean survival times by treatment modification

Outcome	Treatment modification (months)	Full Dose (months)	Ratio (95% CI)
All treatment modifications			
TTF at 1 year of follow-up	10.04	9.16	1.10 (1.02-1.18)
TTF at 2 years of follow-up	16.03	15.26	1.05 (0.94-1.18)
OS at 2 years of follow-up	18.45	18.88	0.98 (0.90-1.06)
Dose reduction group only			
TTF at 1 year of follow-up	10.23	8.75	1.17 (1.07-1.27)
TTF at 2 years of follow-up	16.62	14.21	1.17 (1.03-1.33)
OS at 2 years of follow-up	18.96	17.92	1.06 (0.96-1.17)

Figure 1.
Restricted mean survival time for treatment failure-free survival (tau = 80 months)

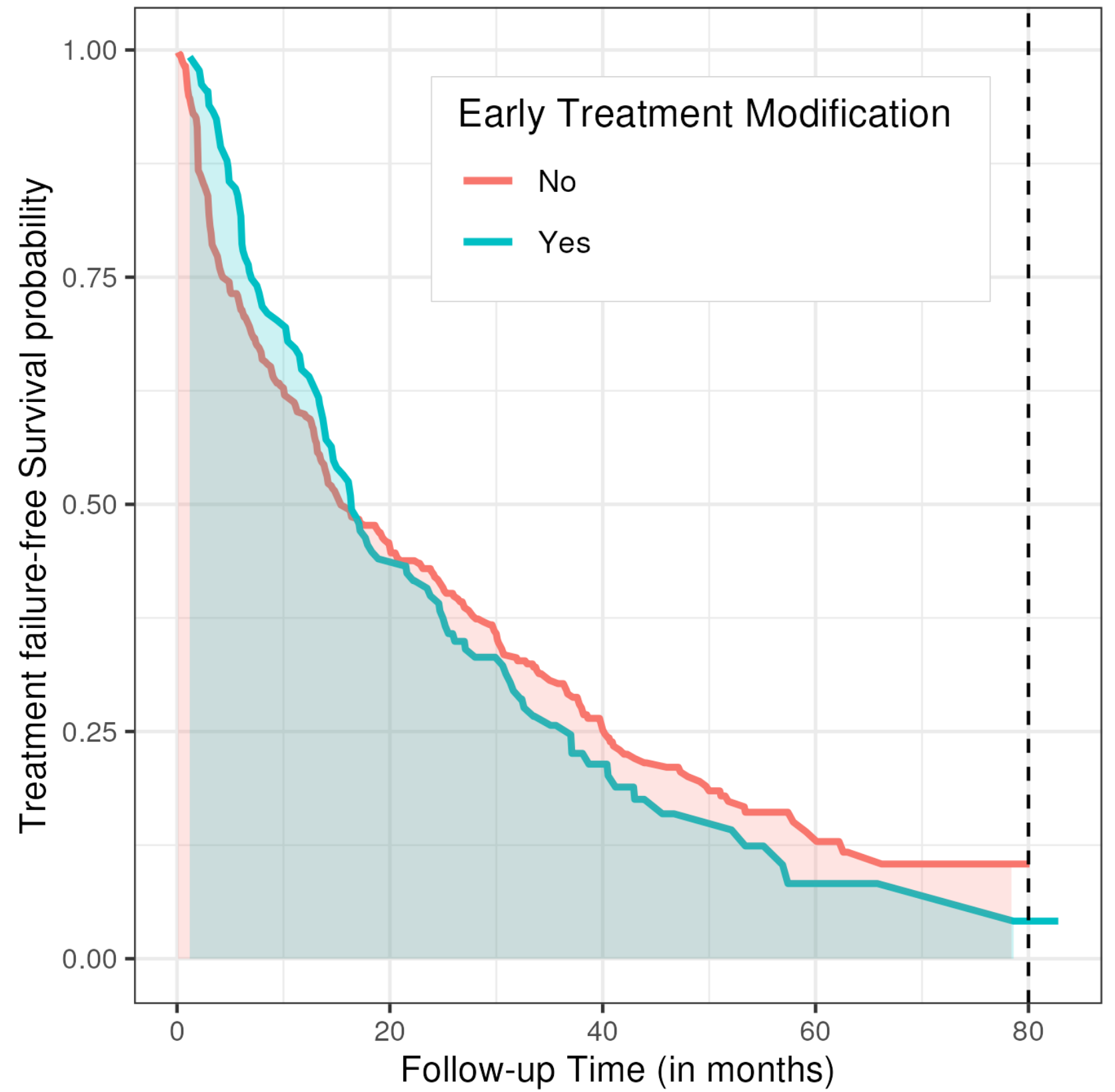
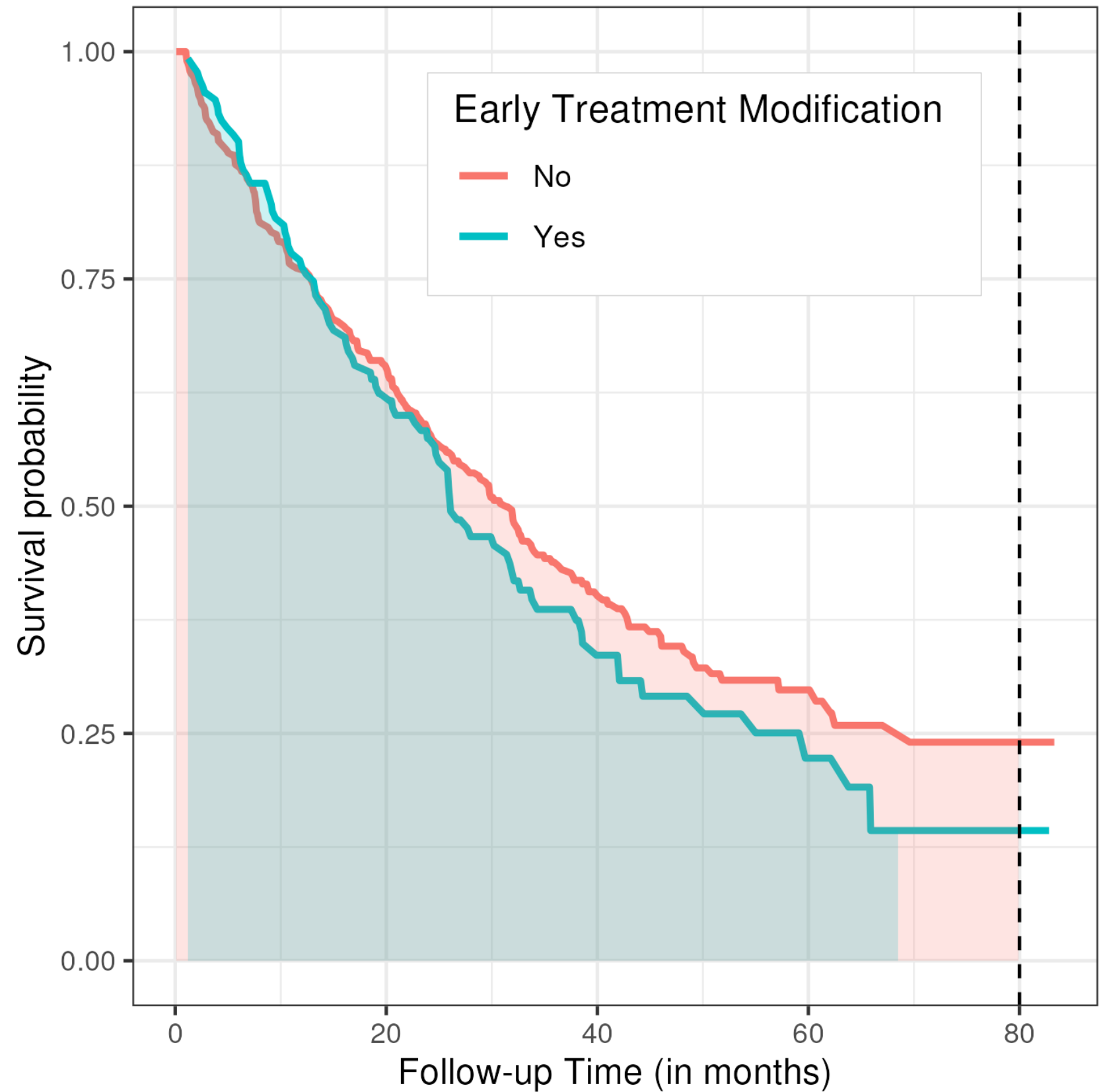


Figure 2.
Restricted mean survival time for overall survival (tau = 80 months)



ACKNOWLEDGMENTS

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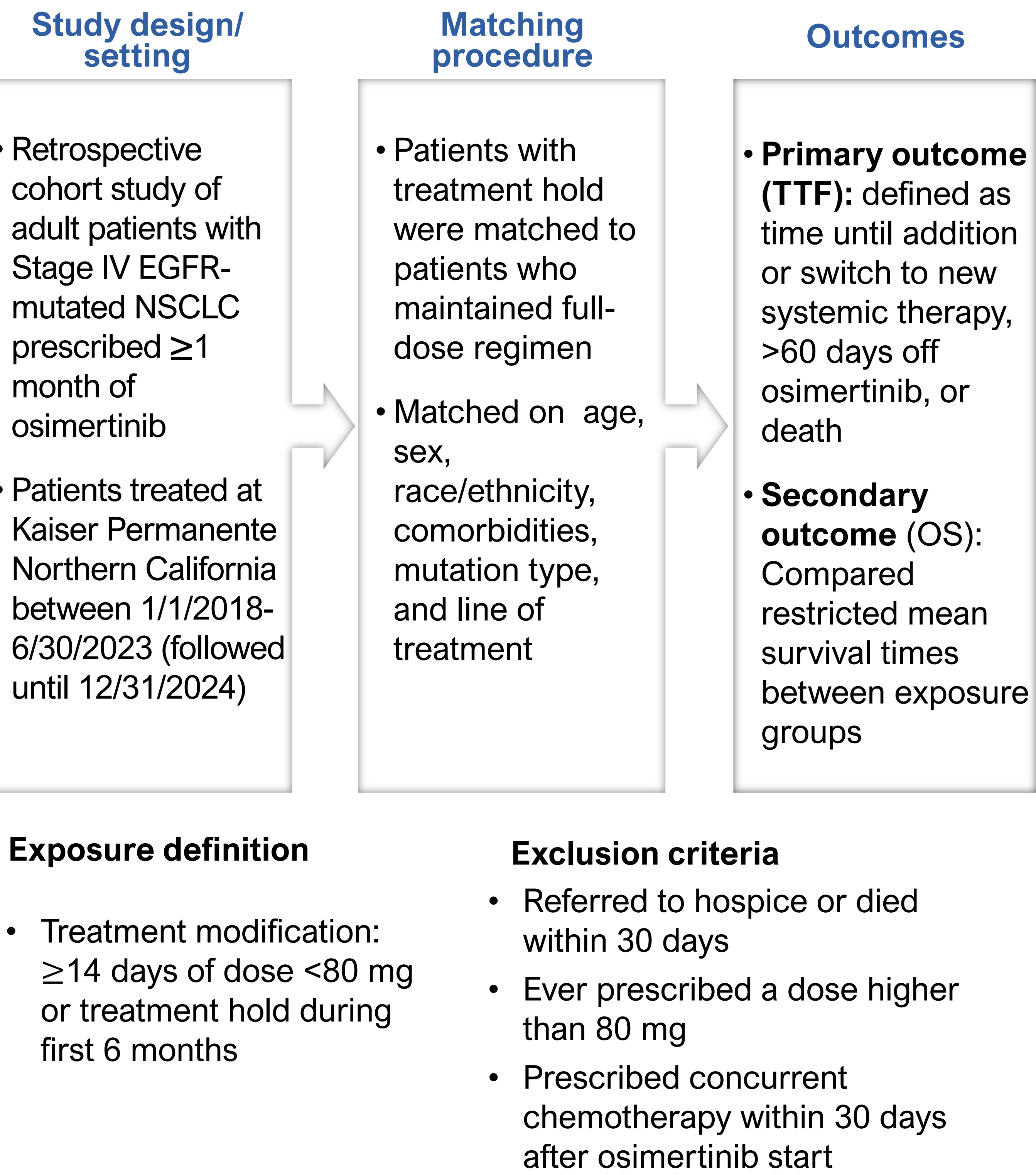
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Randomized trials do not routinely capture the impact of such modifications on clinical outcomes, leaving clinicians and patients with limited evidence to guide treatment decisions.

STUDY OBJECTIVE

Evaluate the impact of a treatment modification (dose reduction or treatment hold) within the first 6 months of osimertinib initiation on 1) time to treatment failure (TTF) and 2) overall survival (OS) among patients with advanced EGFR-mutated NSCLC.

METHODS



KEY FINDINGS

- Patients with advanced NSCLC prescribed osimertinib who underwent early treatment modification had **longer time to treatment failure** compared with patients on full dose, although absolute differences were small.
- Survival rates were similar between the two groups.
- Treatment modifications within first six months do not appear to compromise clinical outcomes for patients prescribed osimertinib.

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Multiple/Other/Unknown	46 (7.1)	4 (3.5)	
Osimertinib line of treatment			0.32
First-line	507 (78.6)	85 (73.9)	
Post first-line	138 (21.4)	30 (26.1)	
Baseline CNS involvement	302 (48.1)	54 (40.9)	0.16

RESULTS

Table 2: Restricted mean survival times by treatment modification

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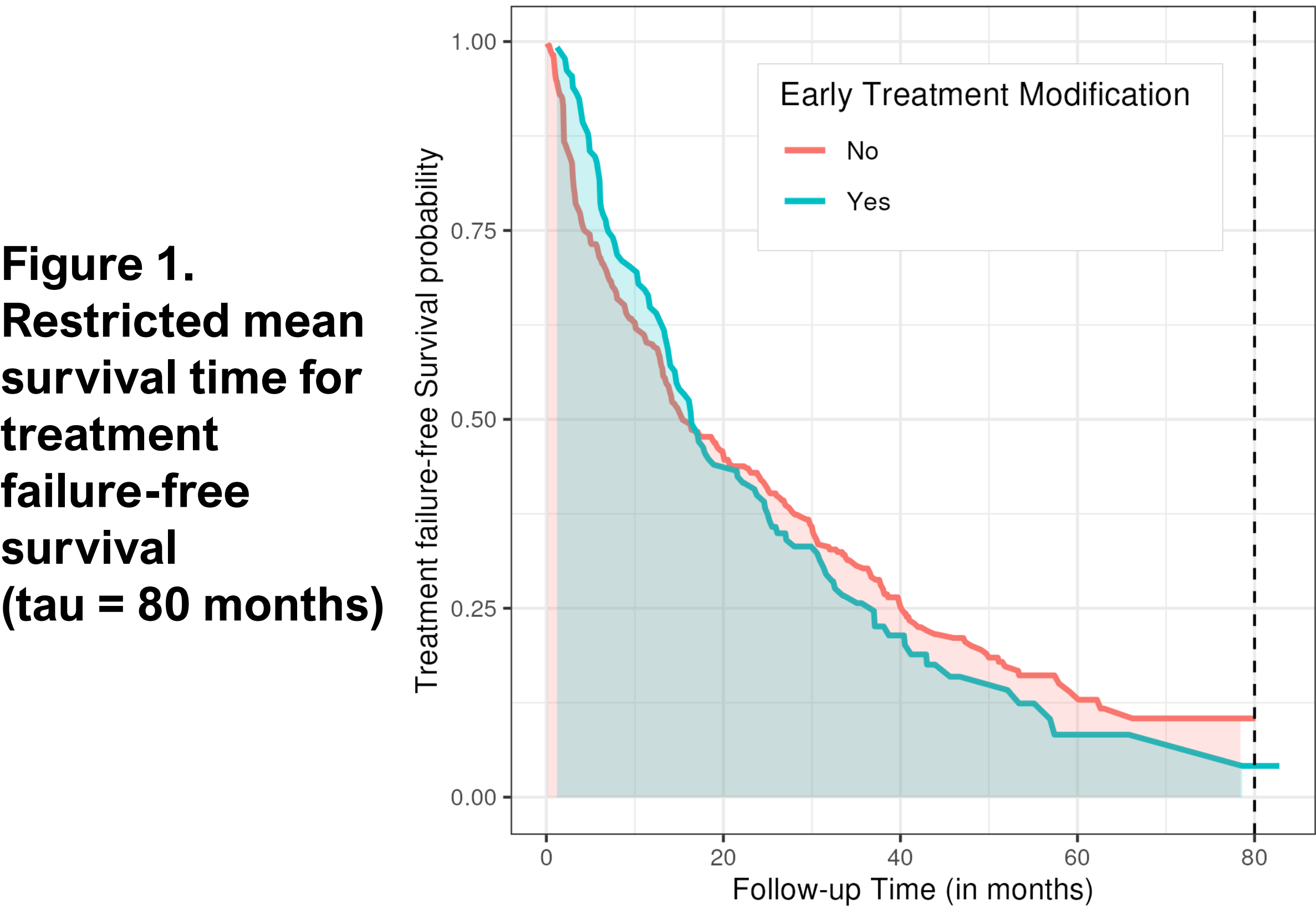


Figure 1.
Restricted mean survival time for treatment failure-free survival (tau = 80 months)

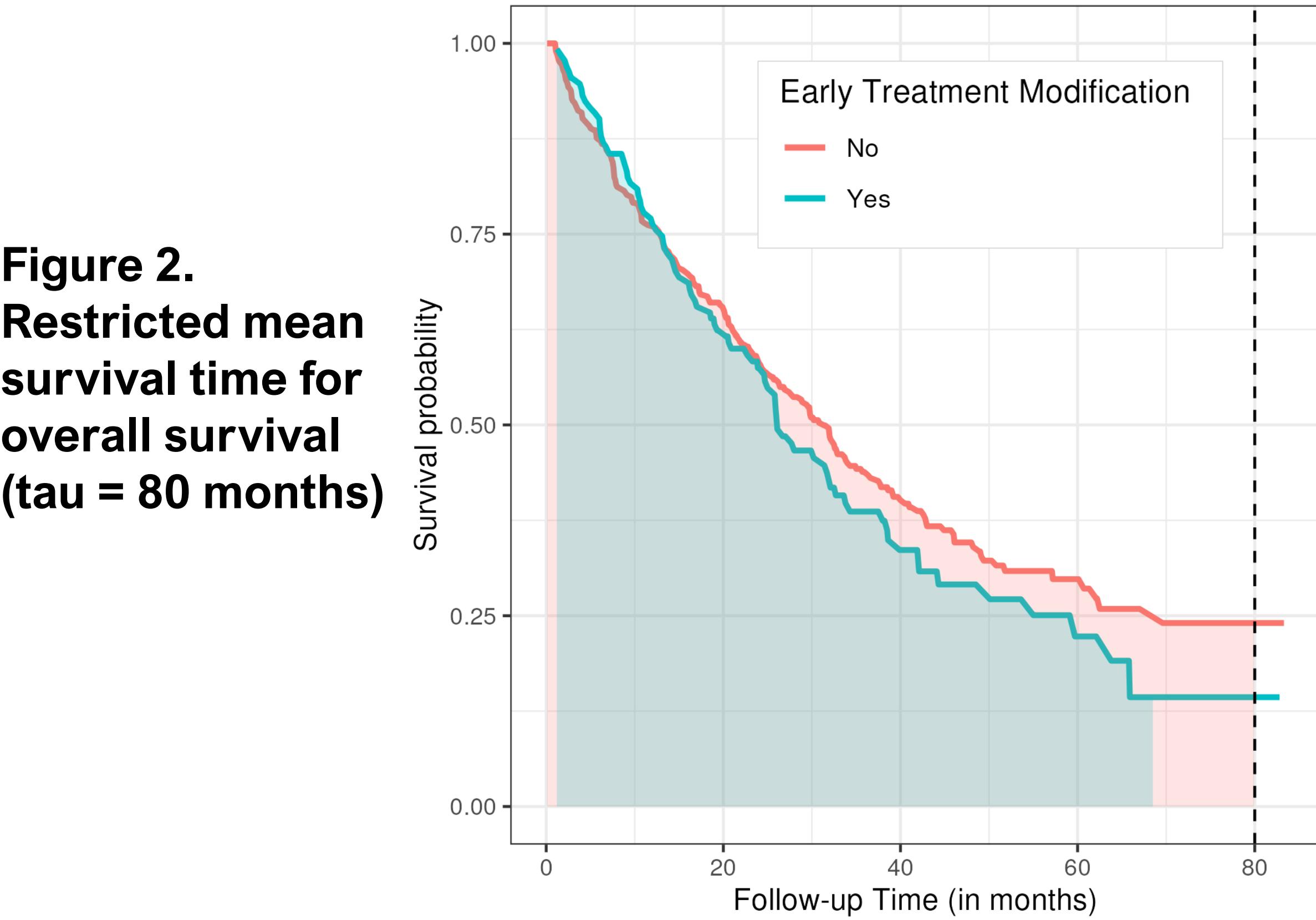


Figure 2.
Restricted mean survival time for overall survival (tau = 80 months)

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