
No conflict of Interests



Memorial Sloan-Kettering
Cancer Center

TSH suppression increases the risk of osteoporosis without changing recurrence in non-high risk patients with differentiated thyroid carcinoma

Laura Y. Wang¹, Andrew W. Smith¹, Frank L. Palmer¹,
Azhar Mahrous², Snehal G. Patel¹, Ian Ganly¹,
R. Michael Tuttle², James A. Fagin², Laura Boucai²

¹ *Head and Neck Service, Department of Surgery*

² *Endocrinology Service, Department of Medicine*
Memorial Sloan-Kettering Cancer Center



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Background

- **Traditional treatment for WDTC**
 - **Total thyroidectomy +/- I-131 treatment + TSH suppression ¹**
- **TSH stimulates thyroid cell proliferation ²**
- **Removing this stimulus is believed to inhibit growth of residual neoplastic tissue ²**
- **No evidence-based consensus on the optimal TSH level**
 - **reduce tumor recurrences, while ensuring minimal adverse effects**

¹ Cooper DS, *et al.* *Thyroid*. 2009; 19:1167-214

² Balme HW, *et al.* *Lancet*. 1954; 266(6816):812-3



Objectives

To determine the effect of TSH suppression:

1. Benefit on recurrence

2. Risk of harm

- Composite outcome of harm
- Risk of Atrial Fibrillation
- Risk of Osteoporosis

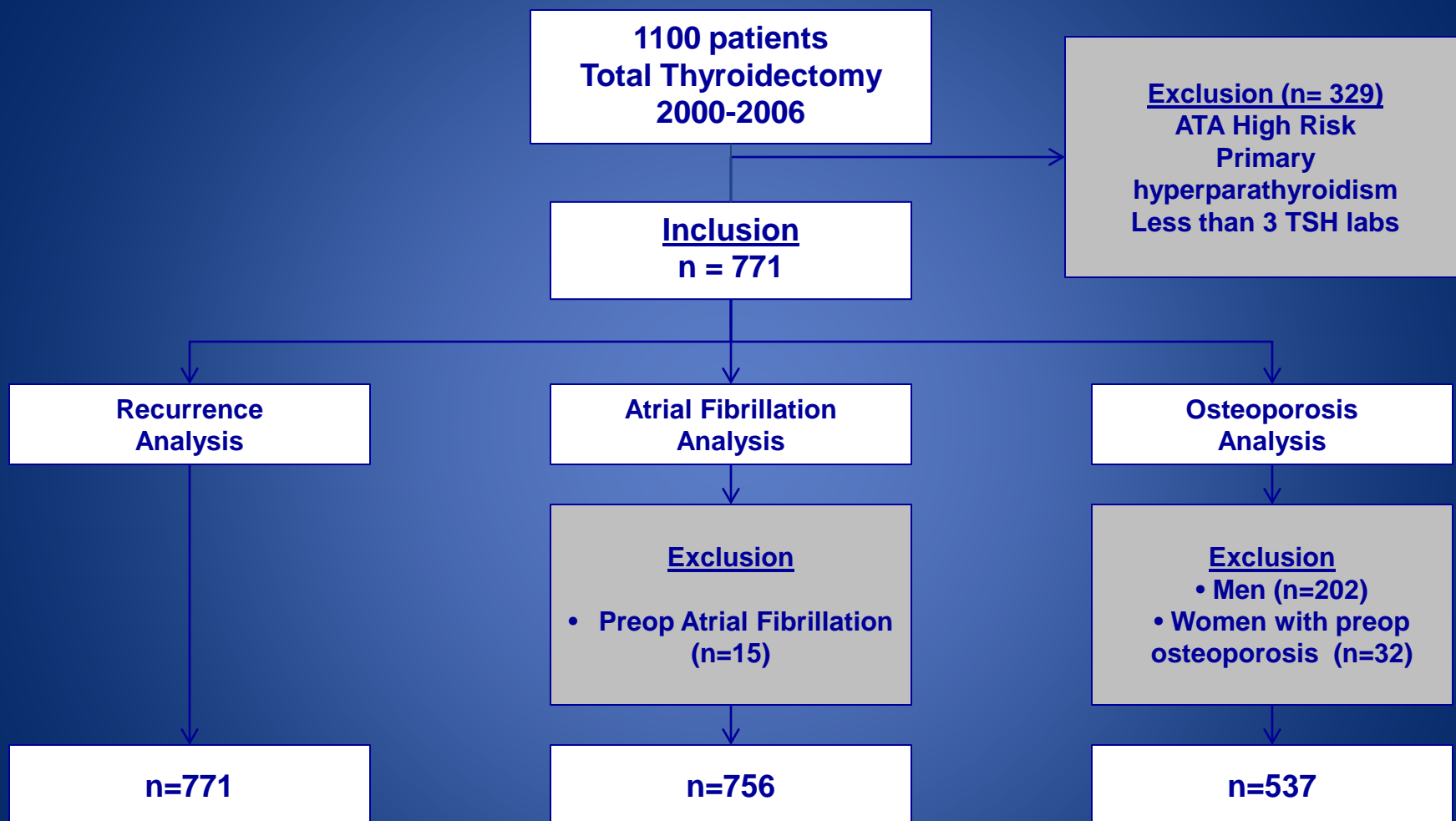


Methods

- **Total thyroidectomy at MSKCC**
 - 2000 - 2006
 - Institutional database
 - Median follow-up: 6.5 years.
- **Exclusion**
 - ATA High Risk
 - Primary hyperparathyroidism
 - Less than 3 postoperative TSH lab results
 - Pre-operative atrial fibrillation
 - Pre-operative osteoporosis



Methods



Definitions

- Recurrence
 - Locoregional – biopsy proven
 - Distant – imaging or biopsy proven
- Atrial Fibrillation
 - EKG proof of persistent arrhythmia OR
 - New documentation
- Osteoporosis
 - DEXA scan T-score ≤ -2.5 OR
 - New documentation OR
 - Bisphosphonate therapy in absence of another indication



Methods

- TSH Suppressed group
median TSH ≤ 0.4 mU/L
- TSH Not suppressed group
median TSH > 0.4 mU/L
- TSH labs were analyzed up to the date of
 - event OR
 - last follow-up
- Excluded TSH labs within 7 days of RAI



Statistical Methods

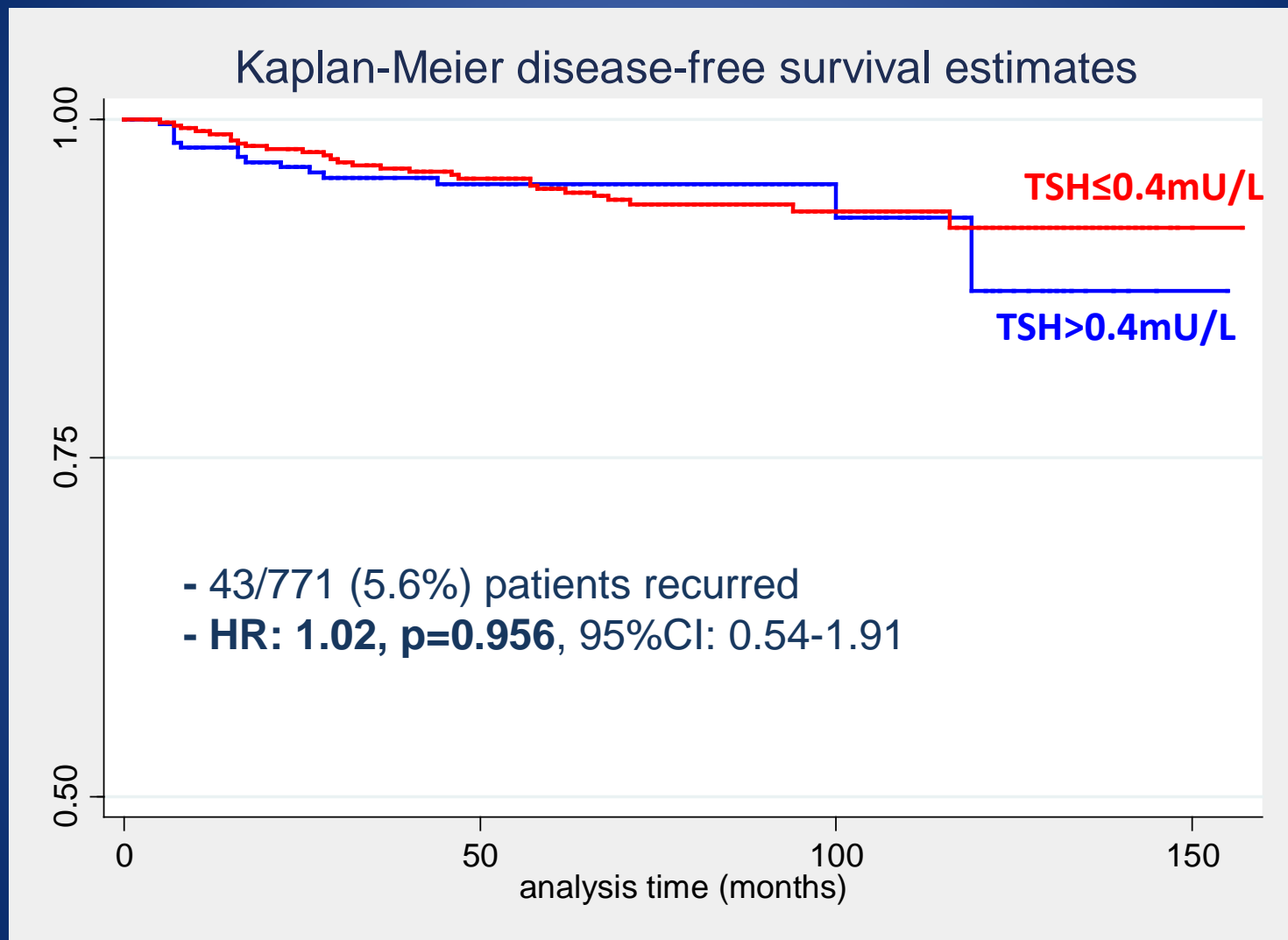
- **Kaplan-Meier survival estimates were employed to assess risk of**
 - **Recurrence (n=771)**
 - **Composite outcome of harm**
 - **Atrial Fibrillation (n=756)**
 - **Osteoporosis in women (n=537)**
- **Cox Proportional Hazards Models were built to allow for multivariate adjustment by**
 - **Age**
 - **Gender**
 - **ATA risk of recurrence**
 - **Administration of RAI**
- **Propensity Scores to adjust for indication bias**



Patient and Tumor Characteristics

Characteristics	Suppressed TSH ≤0.4mU/L (n=449)	Not Suppressed TSH>0.4mU/L(n=322)	p-value
Age , y (mean±SD)	46.3±13.8	50.1 ± 14.8	<0.01
Sex , females n (%)	342 (76%)	226 (70%)	0.06
Histology			
Microcarcinomas	51 (11%)	58 (13%)	0.01
Classical Type	150 (33%)	86 (27%)	0.06
Follicular variant	127 (28%)	87 (27%)	0.69
Tall cell variant	72 (16%)	44 (14%)	0.37
Other	49 (11%)	47 (14%)	0.21
Extrathyroidal extension	162 (36%)	92(29%)	0.04
Vascular invasion	11(2.5%)	15 (4.6%)	0.11
N stage			
N0	169 (38%)	134 (42%)	0.26
N1a	100 (22%)	55 (17%)	0.09
N1b	76 (17%)	40 (13%)	0.08
Nx	104 (23%)	93 (28%)	0.07
RAI therapy	335 (74%)	197 (61%)	<0.01
ATA Risk			<0.01
Low	179 (40%)	162 (50%)	
Intermediate	270 (60%)	160 (50%)	

Disease Free Survival



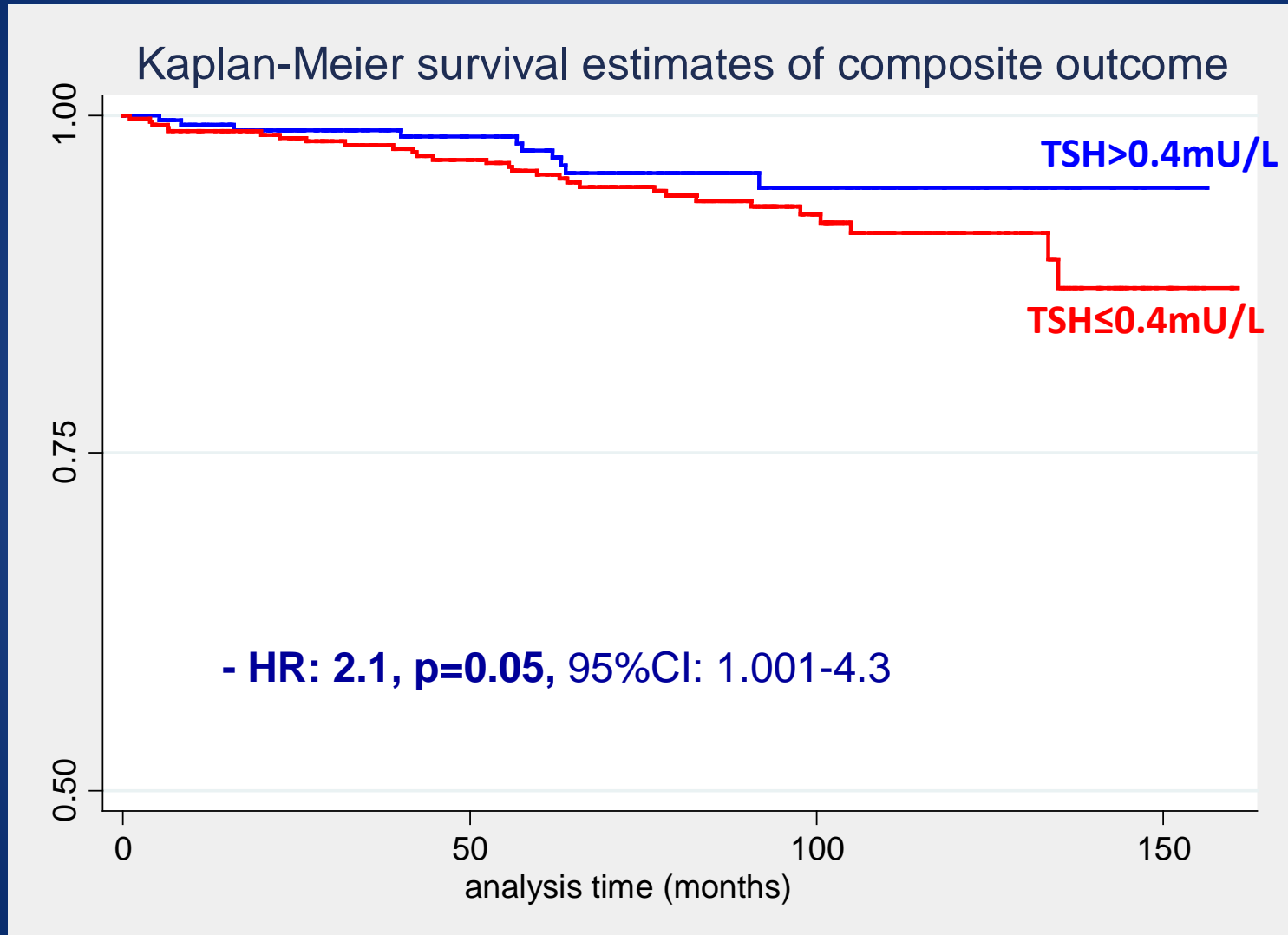
Multivariate analysis for Recurrence

Multivariate analysis	HR	95% CI	p-value
TSH suppression	0.88	0.46-1.66	0.692
Age	0.99	0.97-1.02	0.862
Sex	0.53	0.29-0.96	0.038
RAI therapy	1.5	0.55-3.94	0.437
ATA risk	6.5	2.2-19.3	0.001

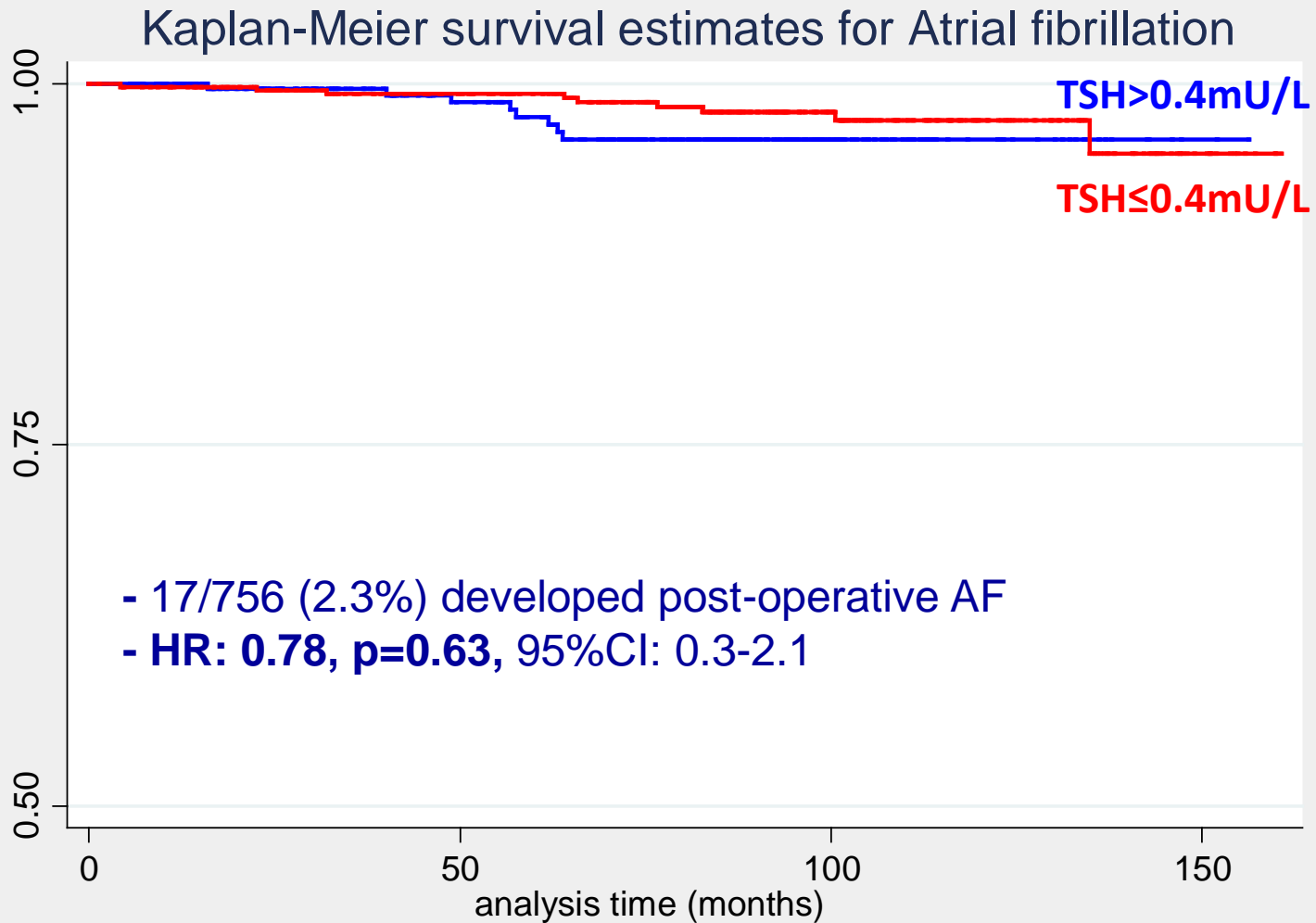
Using Propensity Scores	HR	95% CI	p-value
TSH suppression	1.08	0.45-2.63	0.856



Composite Outcome

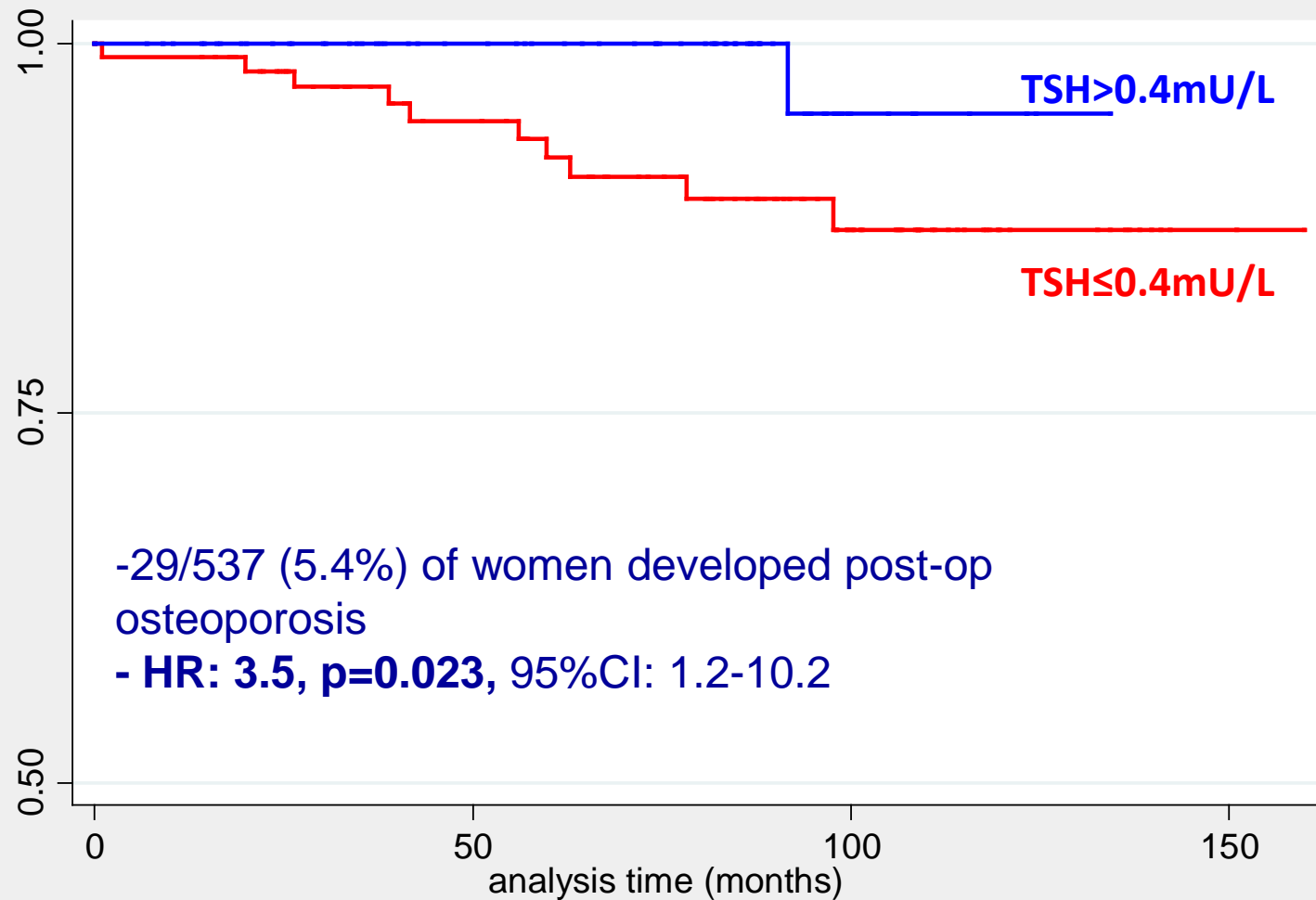


Atrial Fibrillation



Osteoporosis

Kaplan-Meier survival estimates for Osteoporosis

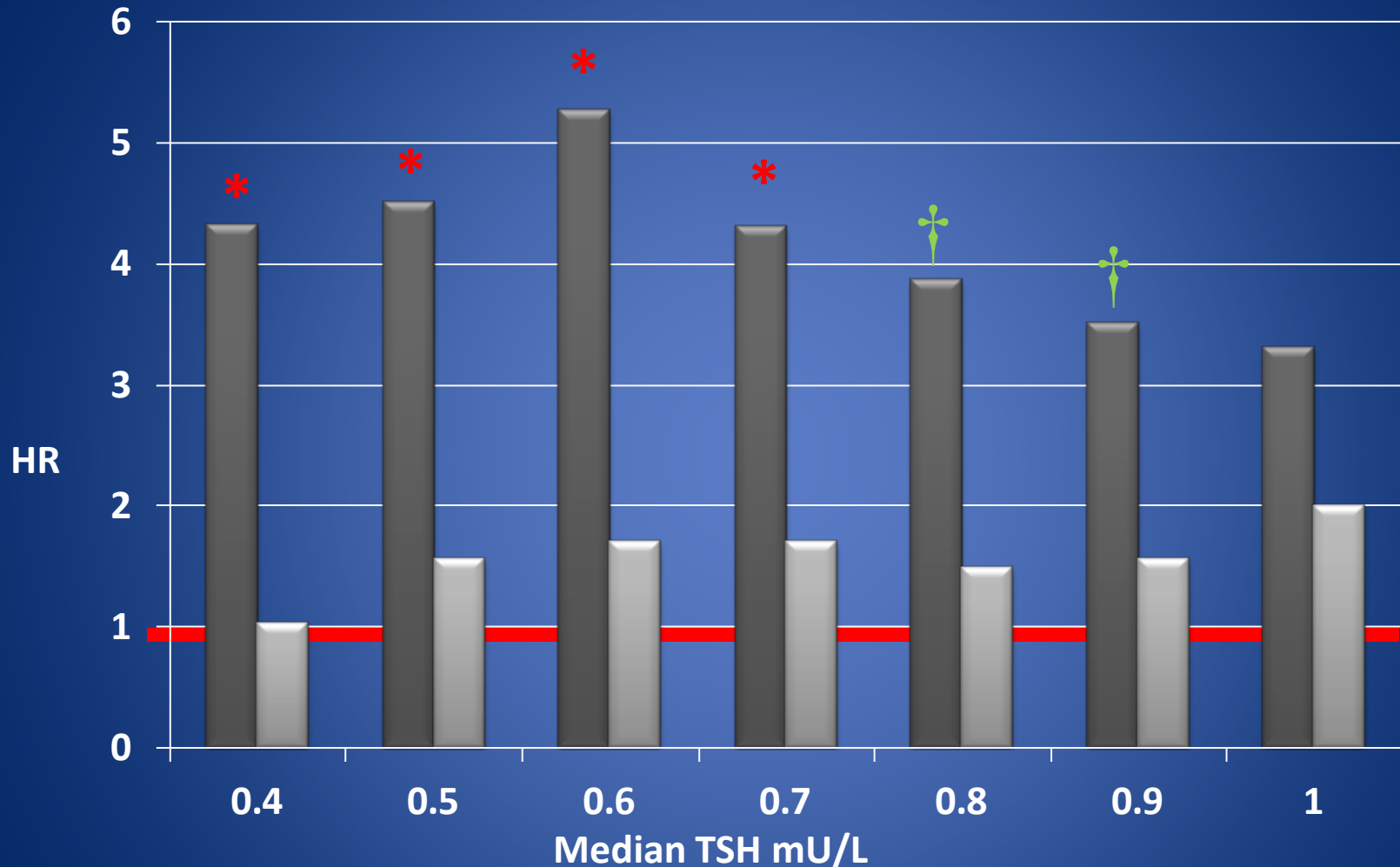


Multivariate analysis for Osteoporosis

Multivariate analysis	HR	95% CI	p-value
TSH suppression	4.32	1.45-12.85	0.009
Age	1.08	1.04-1.13	<0.001



What TSH level is optimal?



* $p < 0.05$



Osteoporosis HR



+ $p < 0.08$



Tumor Recurrence HR



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Summary

- No recurrence benefit of TSH suppression
- TSH suppression increases the risk of a composite outcome of harm
- No effect of TSH suppression on risk of postoperative Atrial Fibrillation
- TSH suppression increases the risk of osteoporosis in women, especially in older women



Limitations

- Retrospective study
- Indication bias
 - Higher risk patients more likely to be TSH suppressed and treated with RAI
 - Patients at higher preoperative risk of Atrial Fibrillation or Osteoporosis may have received less TSH suppression
 - Patients on TSH suppression possibly more likely to be investigated for Atrial Fibrillation or Osteoporosis
- Osteoporosis outcome measured in females only



Conclusions

- TSH suppression ≤ 0.4 mU/L increases the risk of osteoporosis without changing recurrence in thyroid cancer patients at low and intermediate-risk of recurrence
- Therapeutic efforts should focus on avoiding harm in indolent disease

