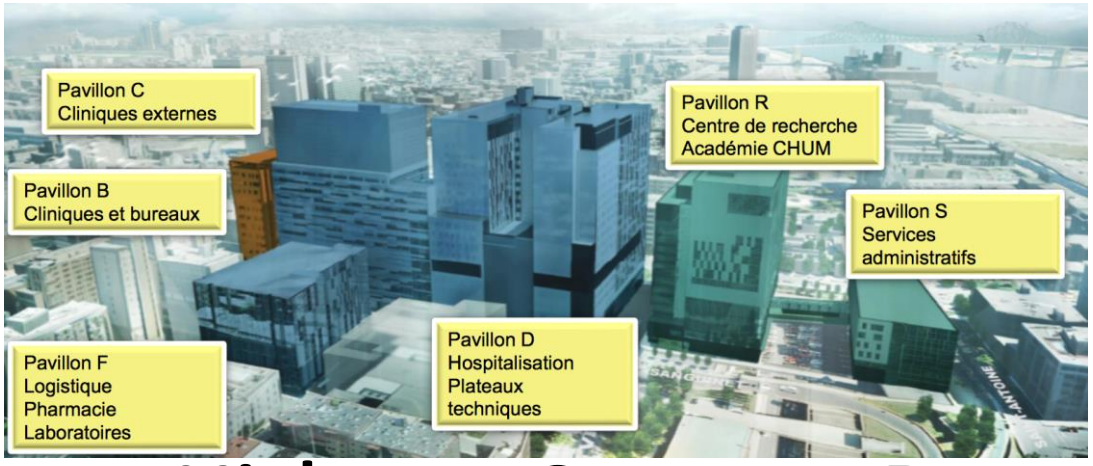
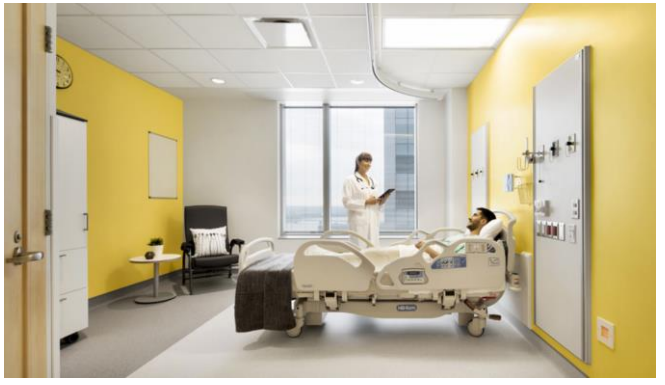


Kidney Cancer Population-Based Research: real life examples.

Pierre I. Karakiewicz, MD
Professor of Surgery, Université de Montréal,
Urologic Oncologist, CHUM
Director, Cancer Prognostics
and Health Outcomes Unit,
Centre de Recherche CHUM



Disclosures

- No financial COI

- All data are:
  - non-randomized
  - retrospective

- Despite best efforts
  - risk of bias persists

ORIGINAL ARTICLE

Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma

B.I. Rini, E.R. Plimack, V. Stus, R. Gafanov, R. Hawkins, D. Nosov, F. Pouliot, B. Alekseev, D. Soulières, B. Melichar, I. Vynnychenko, A. Kryzhanivska, I. Bondarenko, S.J. Azevedo, D. Borchiellini, C. Szczylik, M. Markus, R.S. McDermott, J. Bedke, S. Tartas, Y.-H. Chang, S. Tamada, Q. Shou, R.F. Perini, M. Chen, M.B. Atkins, and T. Powles, for the KEYNOTE-426 Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 21, 2019 VOL. 380 NO. 12

Avelumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma

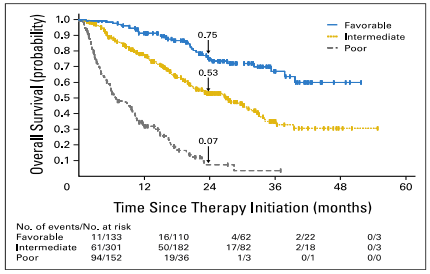
Robert J. Motzer, M.D., Konstantin Penkov, M.D., Ph.D., John Haanen, Ph.D., Brian Rini, M.D., Laurence Albiges, M.D., Ph.D., Matthew T. Campbell, M.D., Balaji Venugopal, M.D., Christian Kollmannsberger, M.D., Sylvie Negrier, M.D., Ph.D., Motohide Uemura, M.D., Ph.D., Jae L. Lee, M.D., Ph.D., Aleksandr Vasiliev, M.D., Wilson H. Miller, Jr., M.D., Ph.D., Howard Gurney, M.D., Manuela Schmidinger, M.D., James Larkin, M.D., Ph.D., Michael B. Atkins, M.D., Jens Bedke, M.D., Boris Alekseev, M.D., Jing Wang, Ph.D., Mariangela Mariani, Ph.D., Paul B. Robbins, Ph.D., Aleksander Chudnovsky, M.D., Camilla Fowst, M.D., Subramanian Hariharan, M.D., Bo Huang, Ph.D., Alessandra di Pietro, M.D., Ph.D., and Toni K. Choueiri, M.D.

Sources of population-based data

High-quality multi-institutional, international databases: IMDC

Prognostic Factors for Overall Survival in Patients With Metastatic Renal Cell Carcinoma Treated With Vascular Endothelial Growth Factor–Targeted Agents: Results From a Large, Multicenter Study

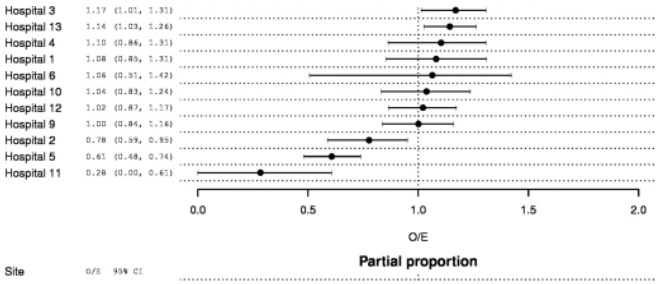
Daniel Y.C. Heng, Wanling Xie, Meredith M. Regan, Mark A. Warren, Ali Reza Golshayan, Chakshu Sahi, Bernhard J. Eigl, J. Dean Ruether, Tina Cheng, Scott North, Peter Venner, Jennifer J. Knox, Kim N. Chi, Christian Kollmannsberger, David F. McDermott, William K. Oh, Michael B. Atkins, Ronald M. Bukowski, Brian I. Rini, and Toni K. Choueiri



High quality national databases: CKCIS

Benchmarking quality for renal cancer surgery: Canadian Kidney Cancer information system (CKCis) perspective

Keith A. Lawson, MD, MSc[1]; Olli Saarela, PhD[2]; Zhihui Liu, PhD[2]; Luke T. Lavallée, MD, MSc[3]; Rodney H. Breau, MD, MSc[3]; Lori Wood, MD[4]; Michael A.S. Jewett, MD[1]; Anil Kapoor, MD[5]; Simon Tanguay, MD[6]; Ronald B. Moore, MD, PhD[7]; Ricardo Rendon, MD, MSc[8]; Frederic Pouliot, MD, PhD[9]; Peter C. Black, MD[10]; Jun Kawakami, MD, MSc[11]; Darrel Drachenberg, MD[12]; Antonio Finelli, MD, MSc[1]



Large scale national databases:

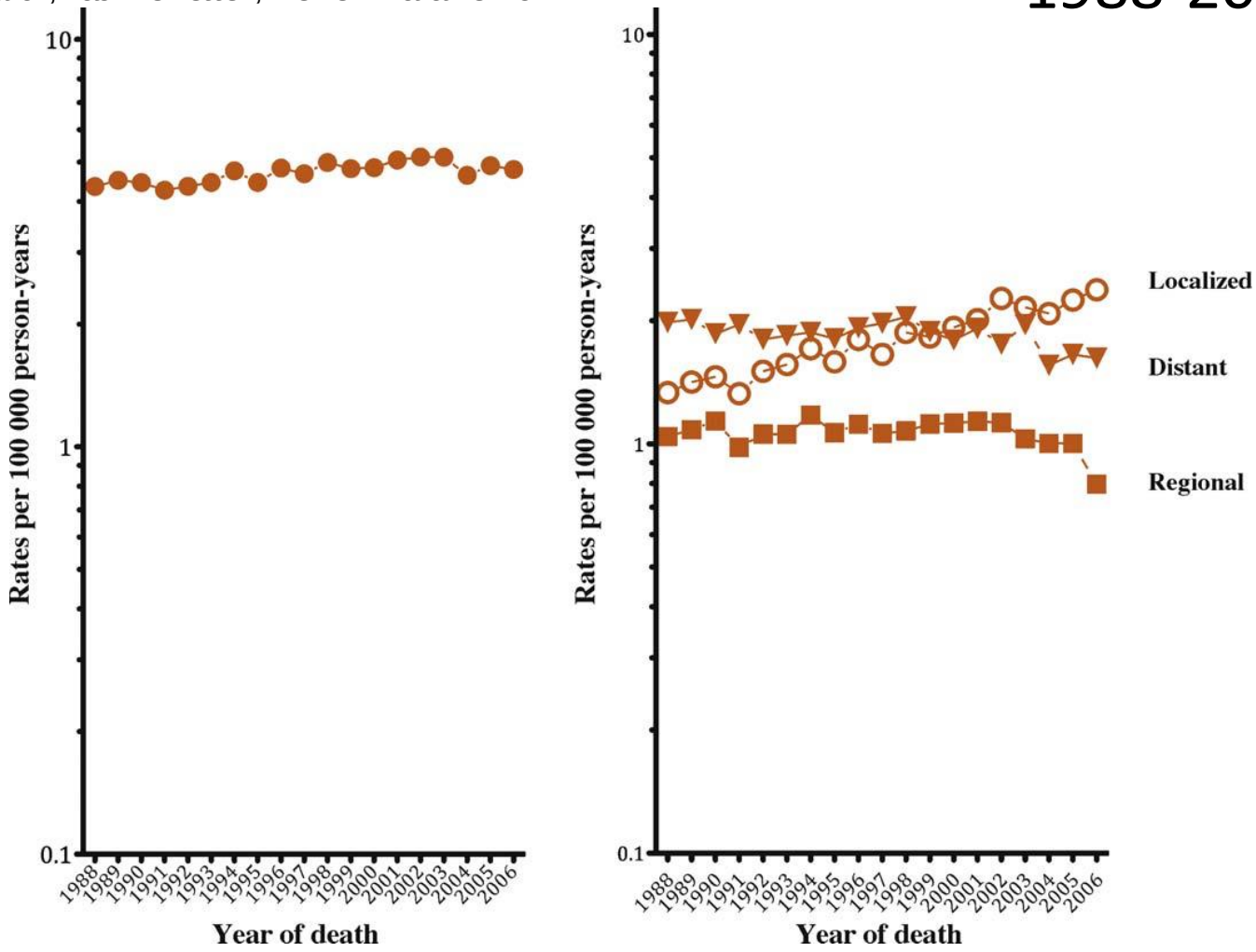
- NCDB: 1,500 Commission on Cancer facilities. 70% US sample, only all cause mortality
- NIS: largest all-payer inpatient care US database, 7M+ observations
- SEER: 28% of the population of the United States. SEER coverage includes 26% of African Americans, 41% of Hispanics, 43% of American Indians and Alaska Natives, 54% of Asians, and 71% of Hawaiian/Pacific Islanders
- SEER Medicare: Data include patient demographics, primary tumor site, tumor morphology and stage at diagnosis, first course of treatment, and follow-up for vital status (CSM+OCM). SEER in 65+ years, baseline comorbidities and more detail than SEER.

Age-Adjusted Incidence, Mortality, and Survival Rates of Stage-Specific Renal Cell Carcinoma in North America: A Trend Analysis

EUROPEAN UROLOGY 59 (2011) 135–141

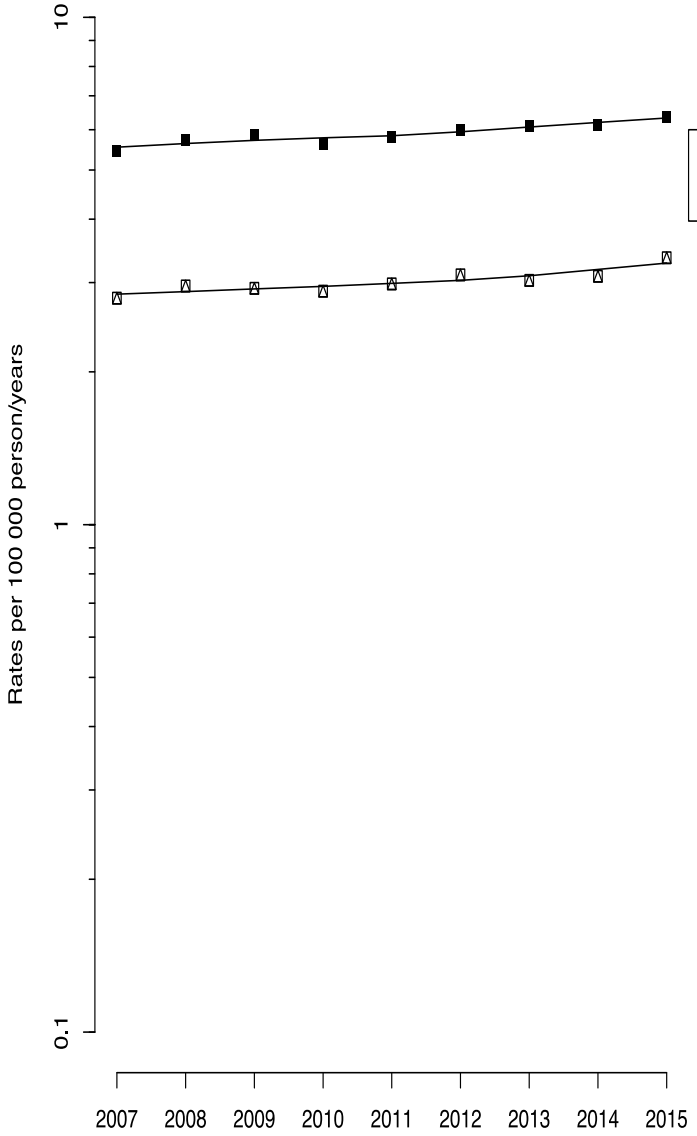
Maxine Sun [a,*,1], Rodolphe Thuret [a,b,1], Firas Abdollah [a,c], Giovanni Lughezzani [a,c], Jan Schmitges [d], Zhe Tian [a], Shahrokh F. Shariat [e], Francesco Montorsi [c], Jean-Jacques Patard [f], Paul Perrotte [g], Pierre I. Karakiewicz [a,g]

1988-2006



Age-Adjusted Incidence, Mortality, and Survival Rates of Stage-Specific Renal Cell Carcinoma in North America: A Trend Analysis

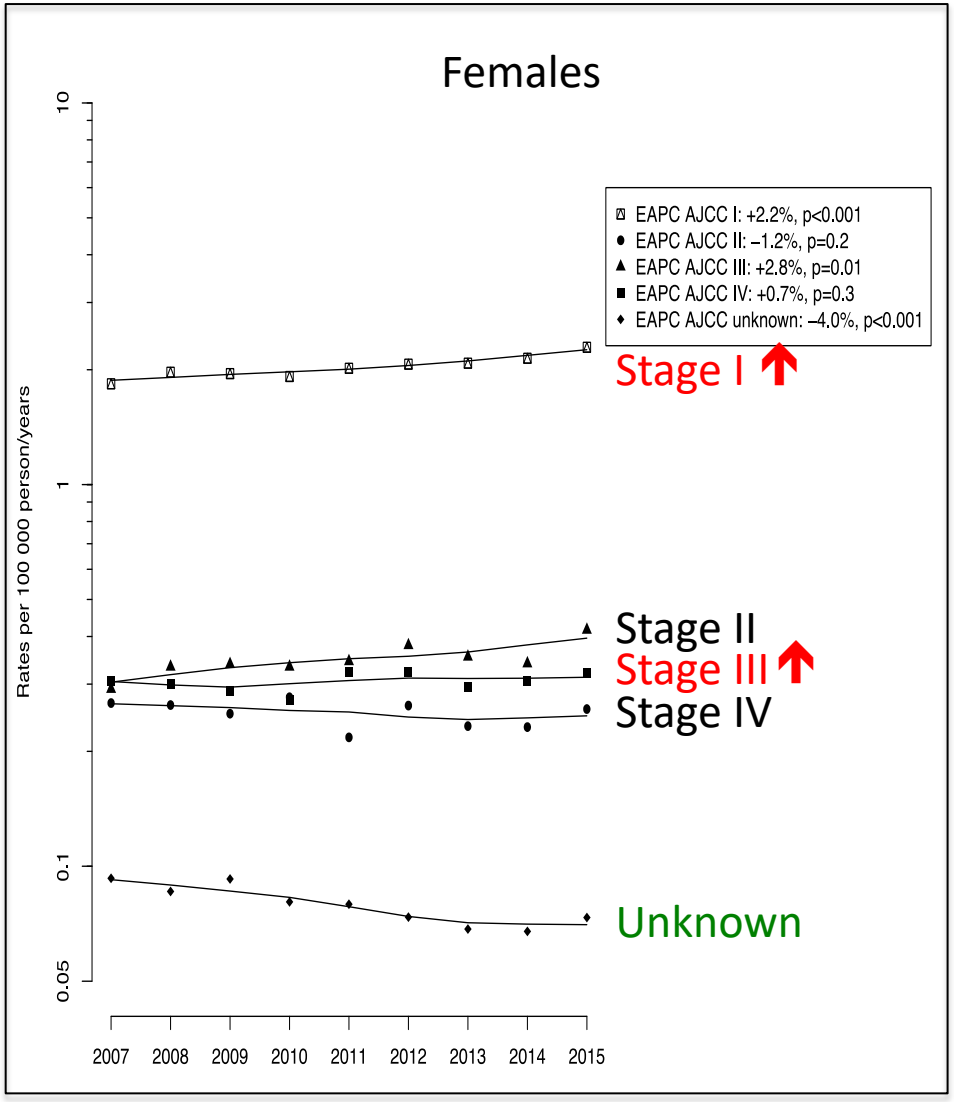
2007-2015

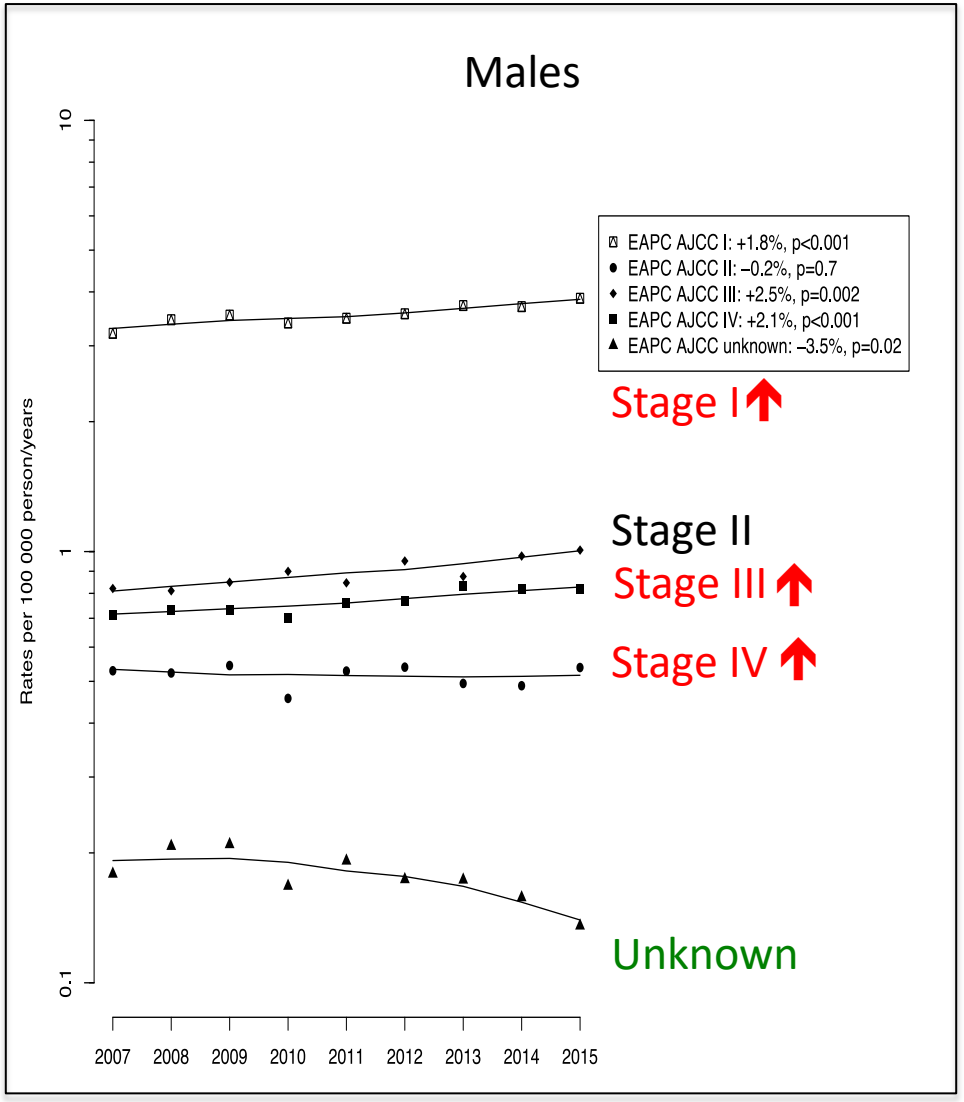


Males: +1.8% per year

Females: +1.7% per year

Age-Adjusted Incidence, Mortality, and Survival Rates of Stage-Specific Renal Cell Carcinoma in North America: A Trend Analysis 2007-2015

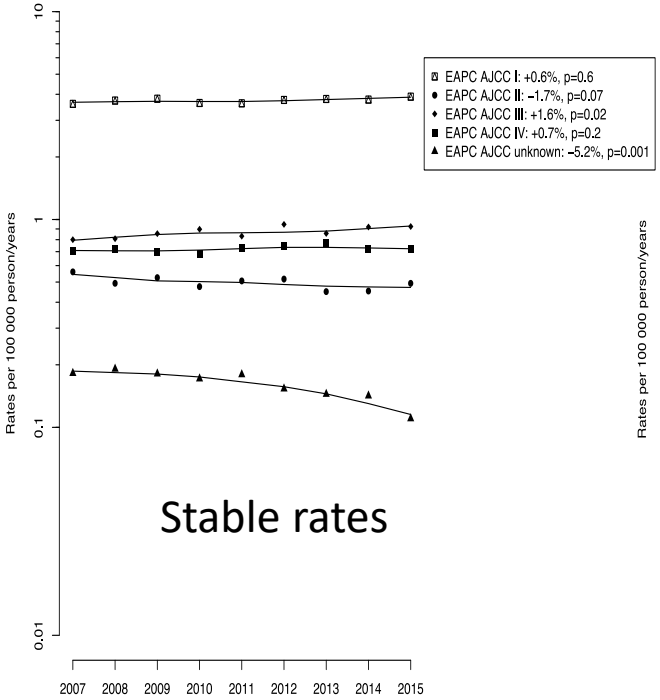




Age-Adjusted Incidence, Mortality, and Survival Rates of Stage-Specific Renal Cell Carcinoma in North America: A Trend Analysis **2007-2015**

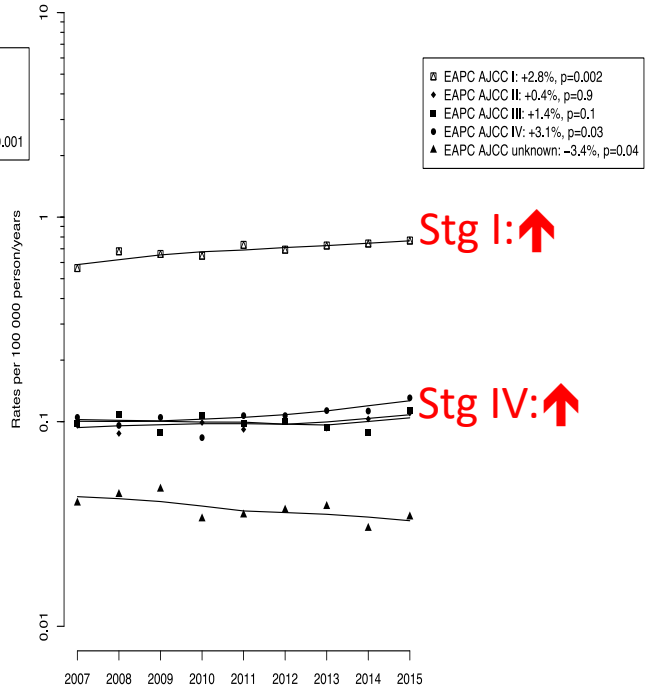
Stratification vs. race

Caucasians



Stable rates

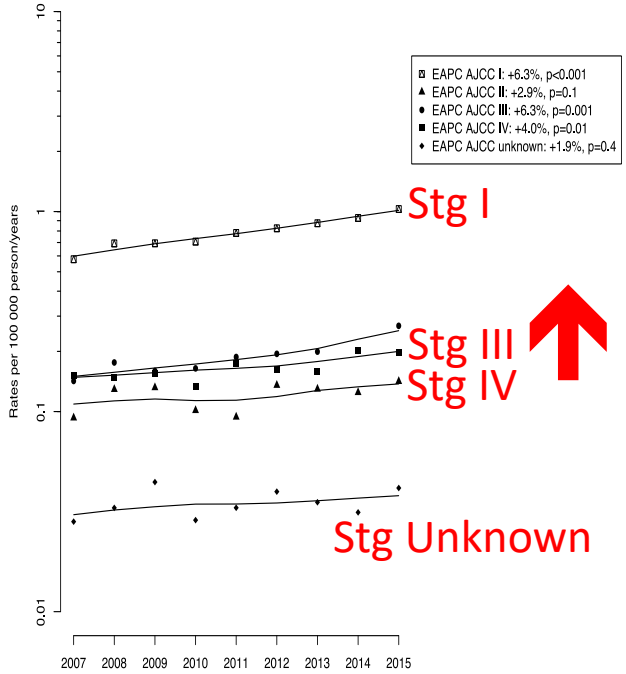
African Americans



Stg I:↑

Stg IV:↑

Hispanics



Stg I

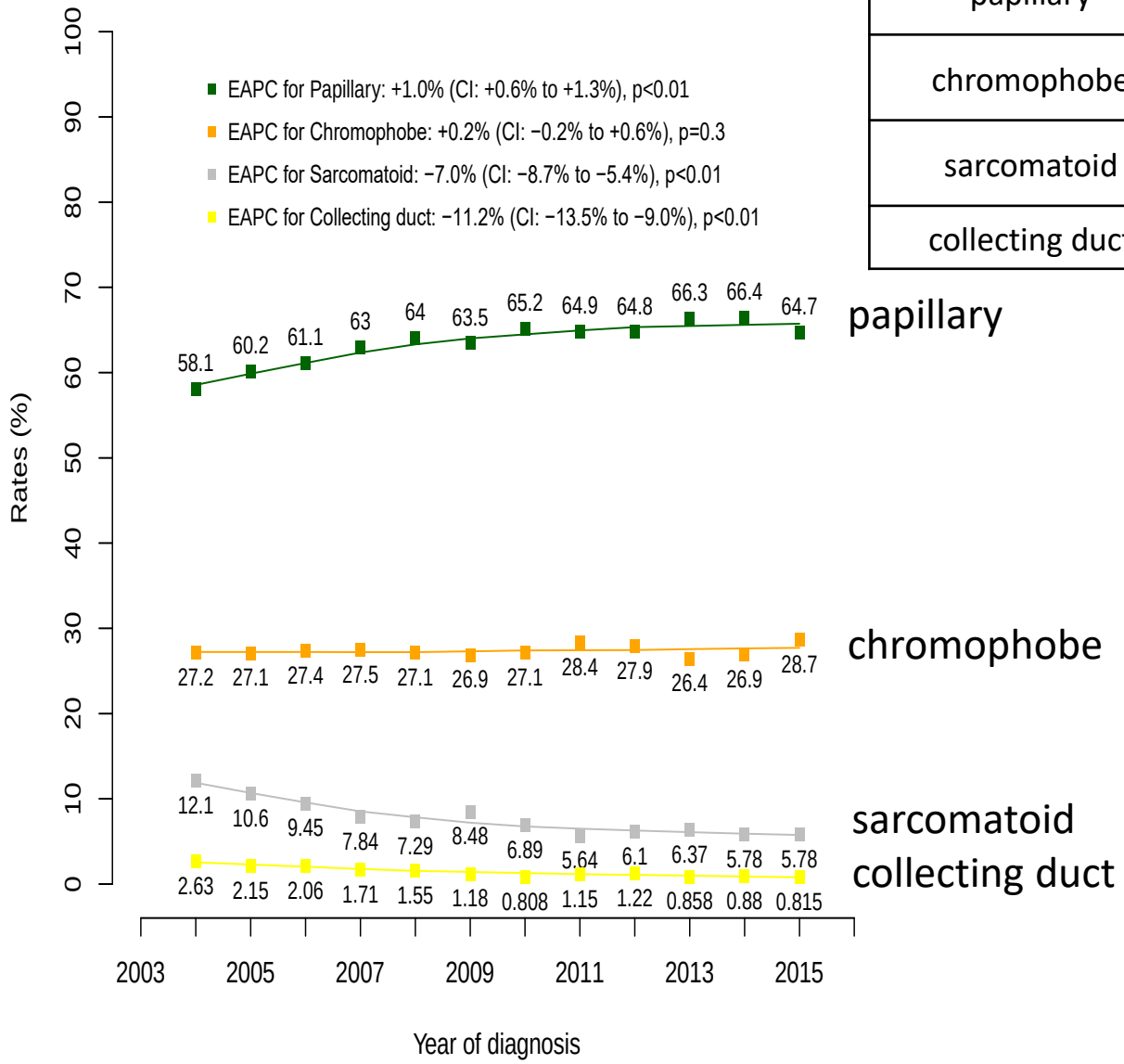
Stg III

Stg IV

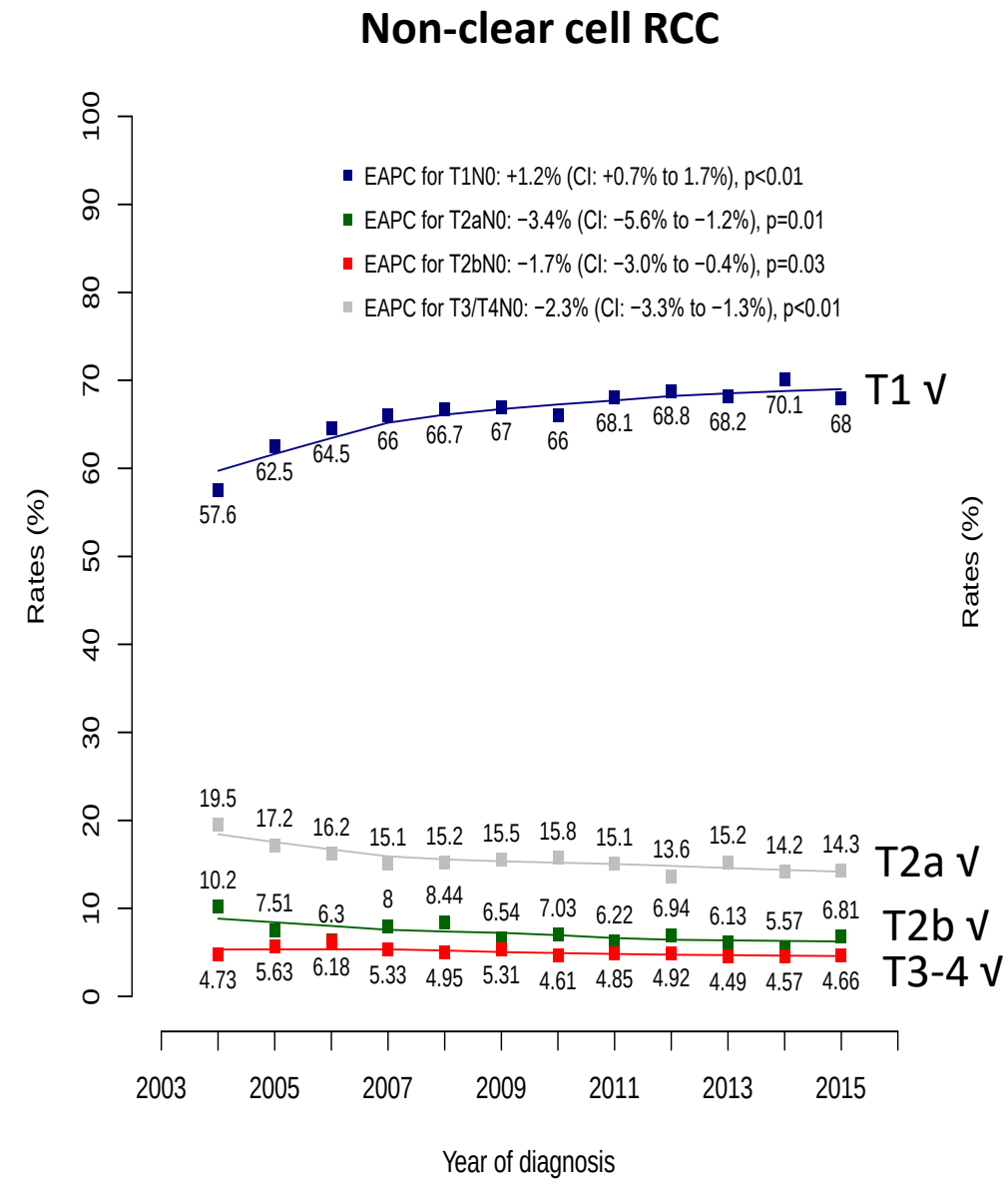
Stg Unknown

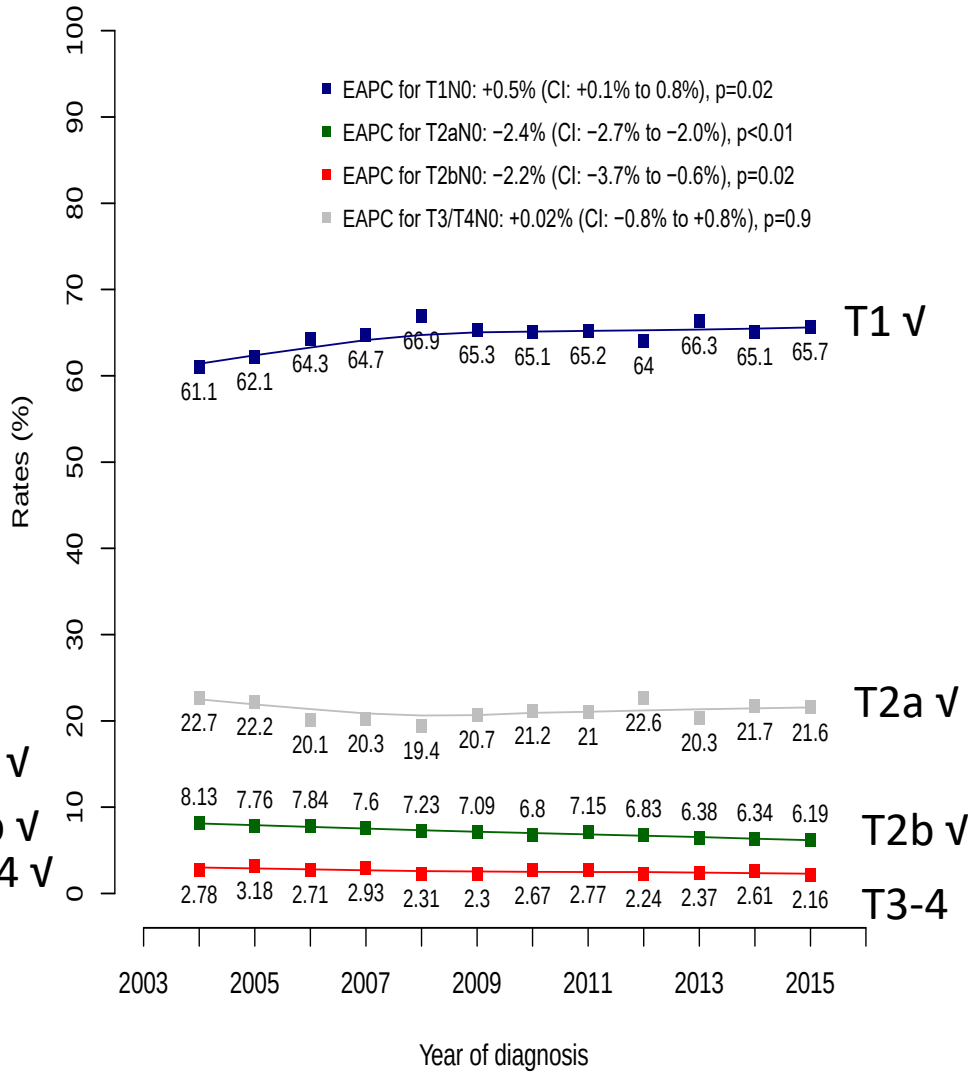
Rates of non-clear cell histological subtypes (all stages) over time

papillary	15822 (63.9)
chromophobe	6784 (27.4)
sarcomatoid	1815 (7.3)
collecting duct	325 (1.3)

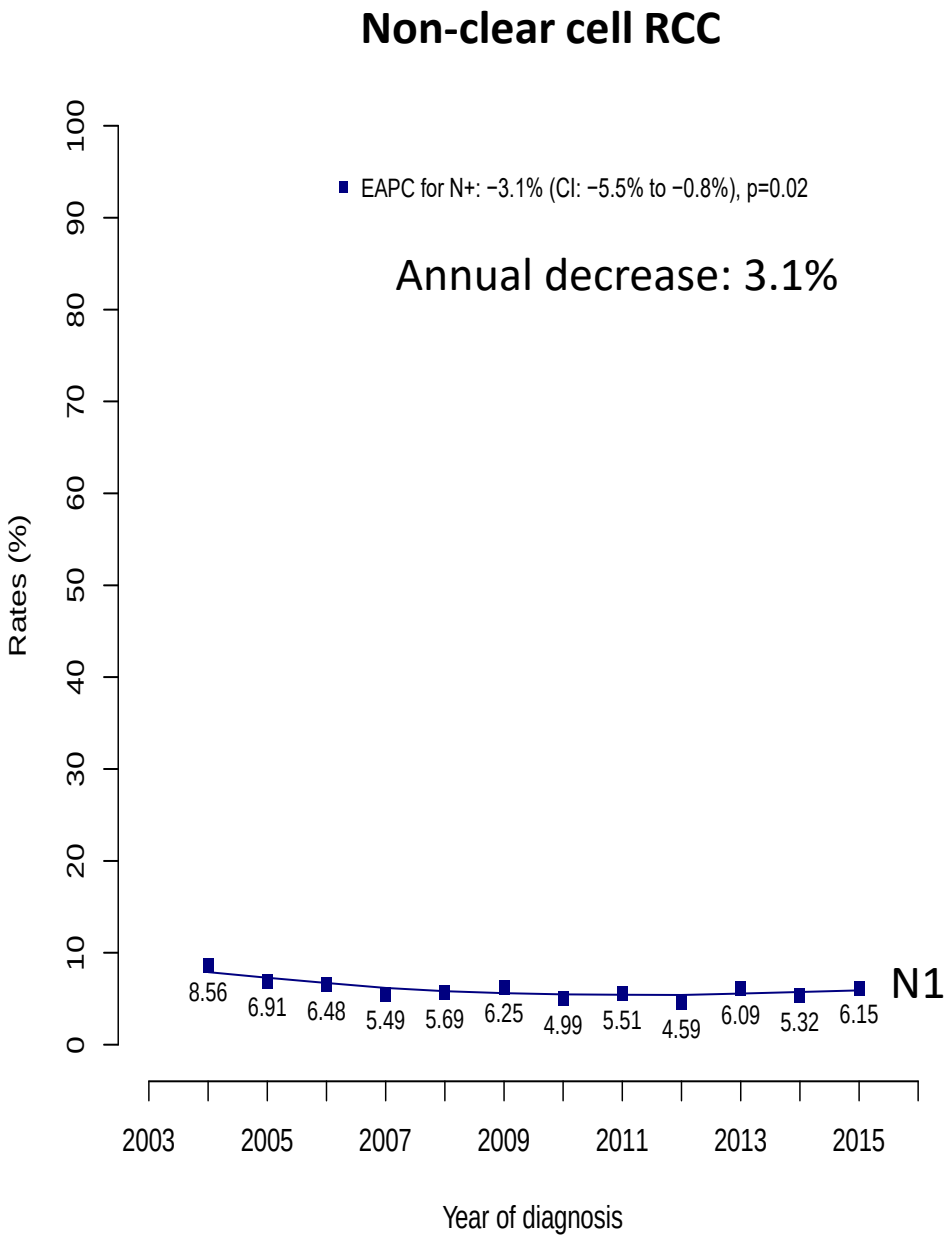


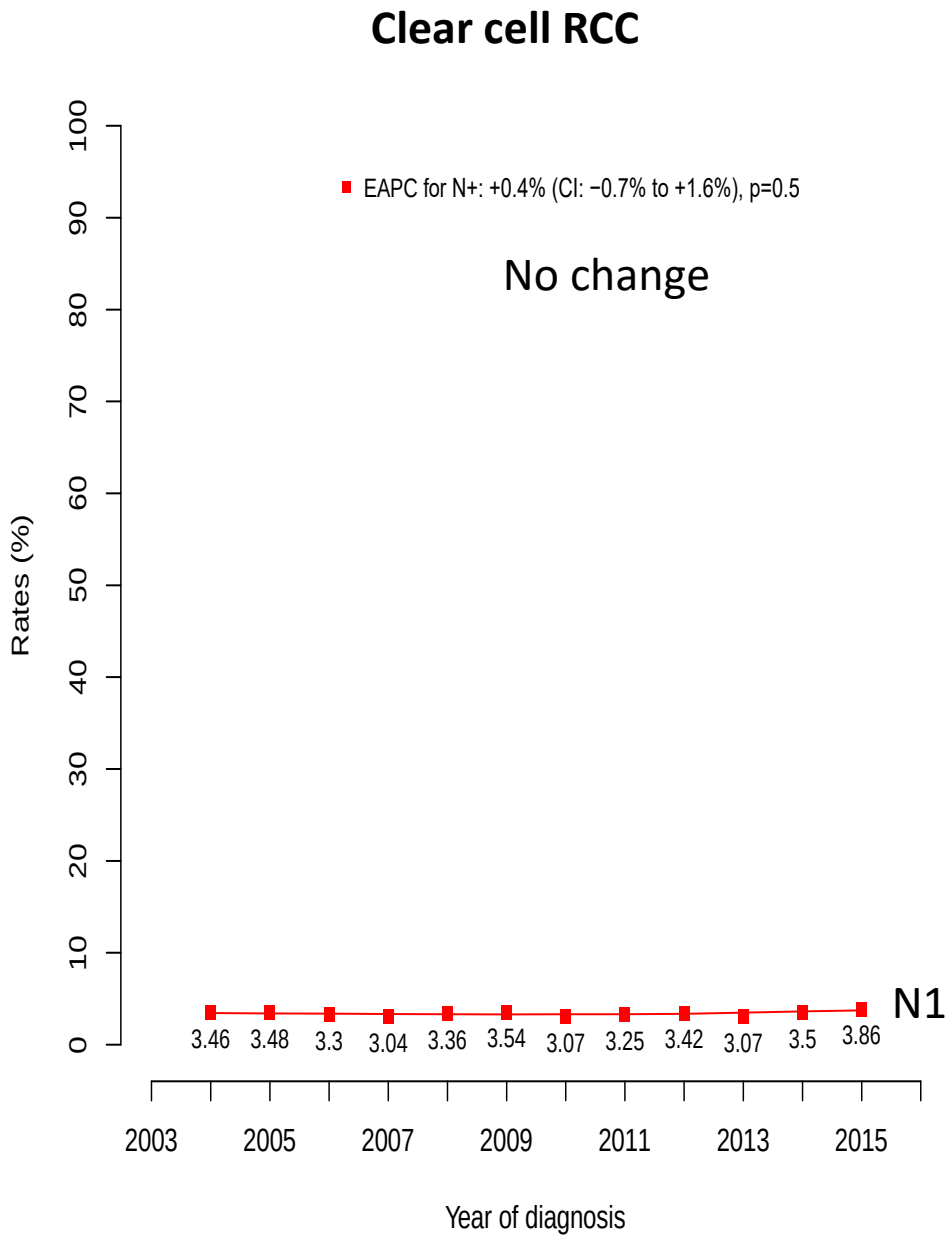
T stage distribution over time



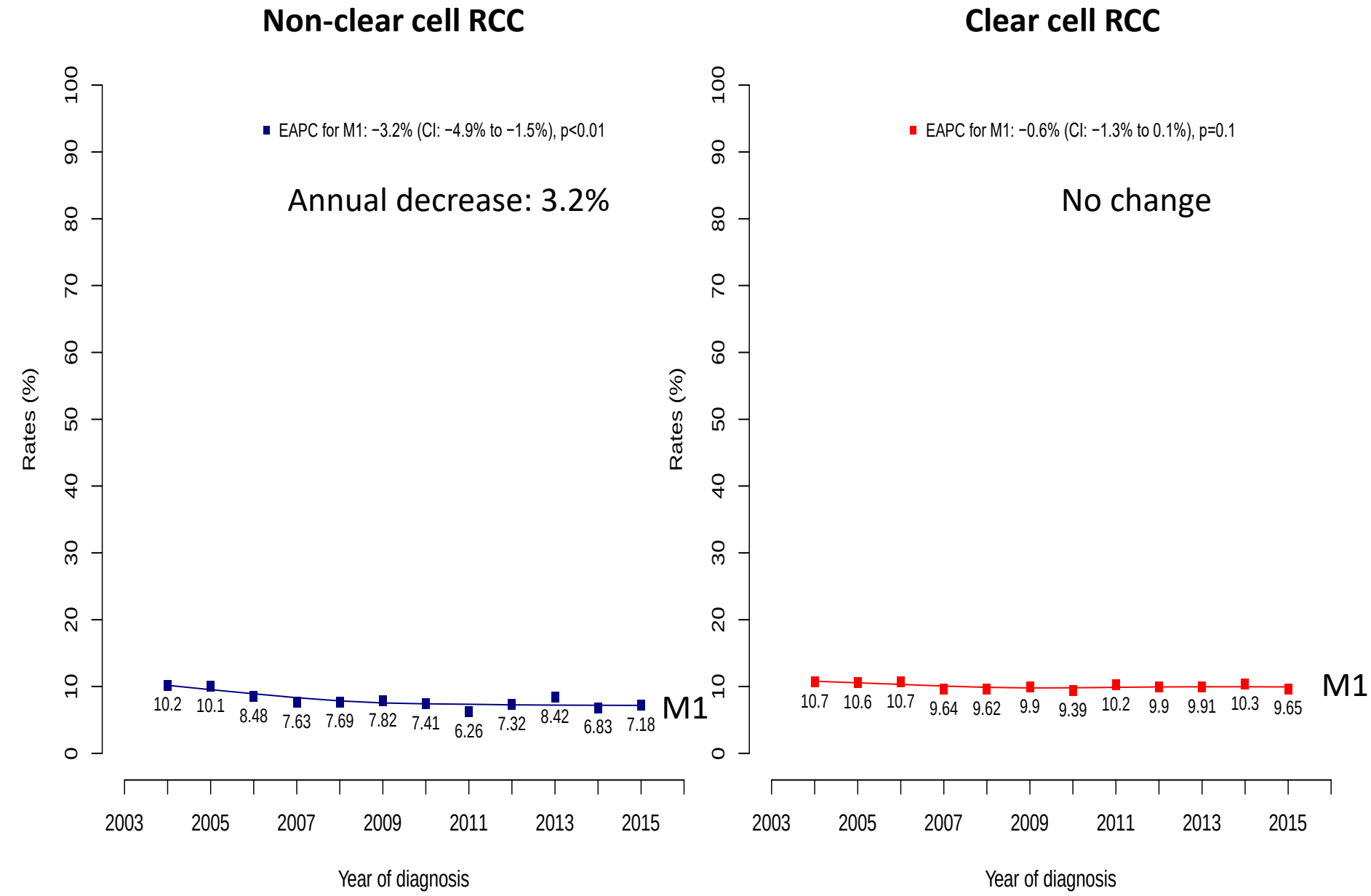


N1 Stage distribution over time



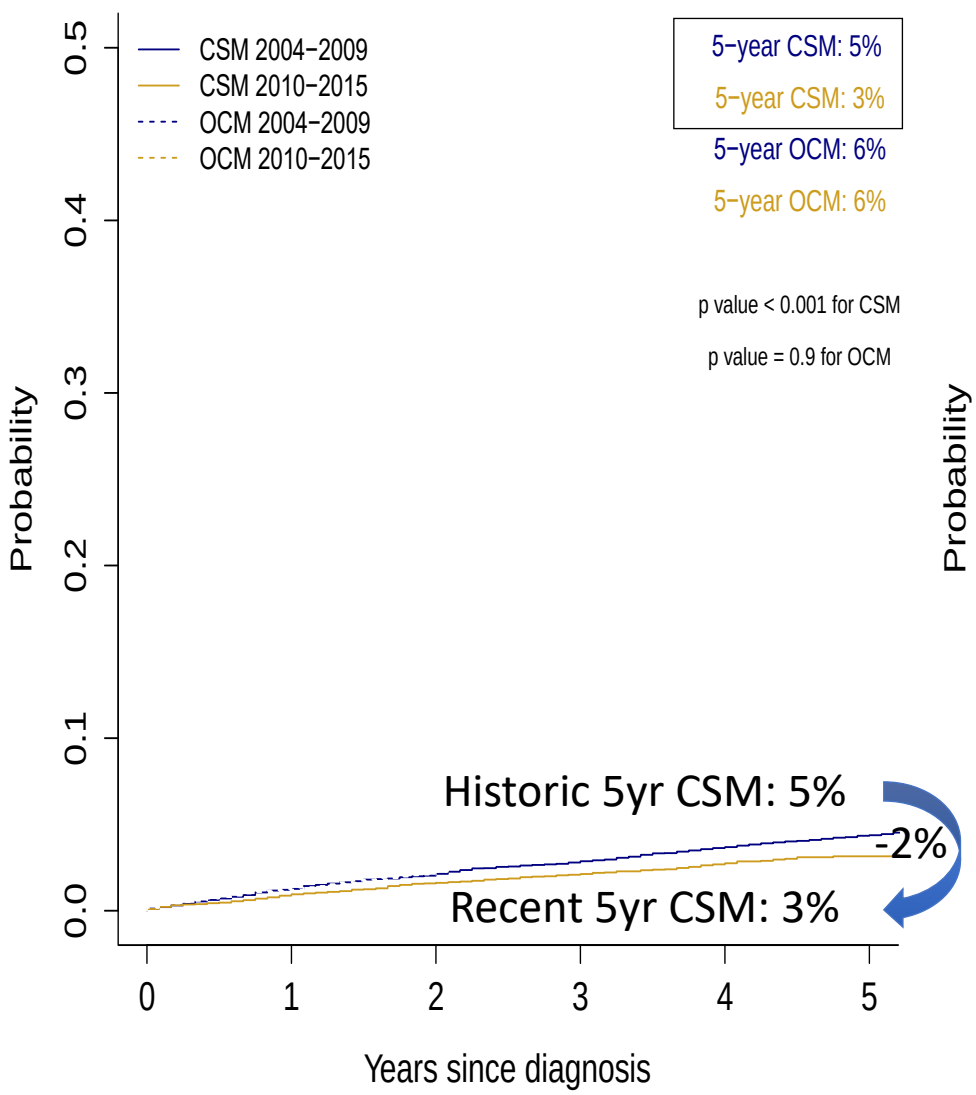


M1 Stage distribution over time

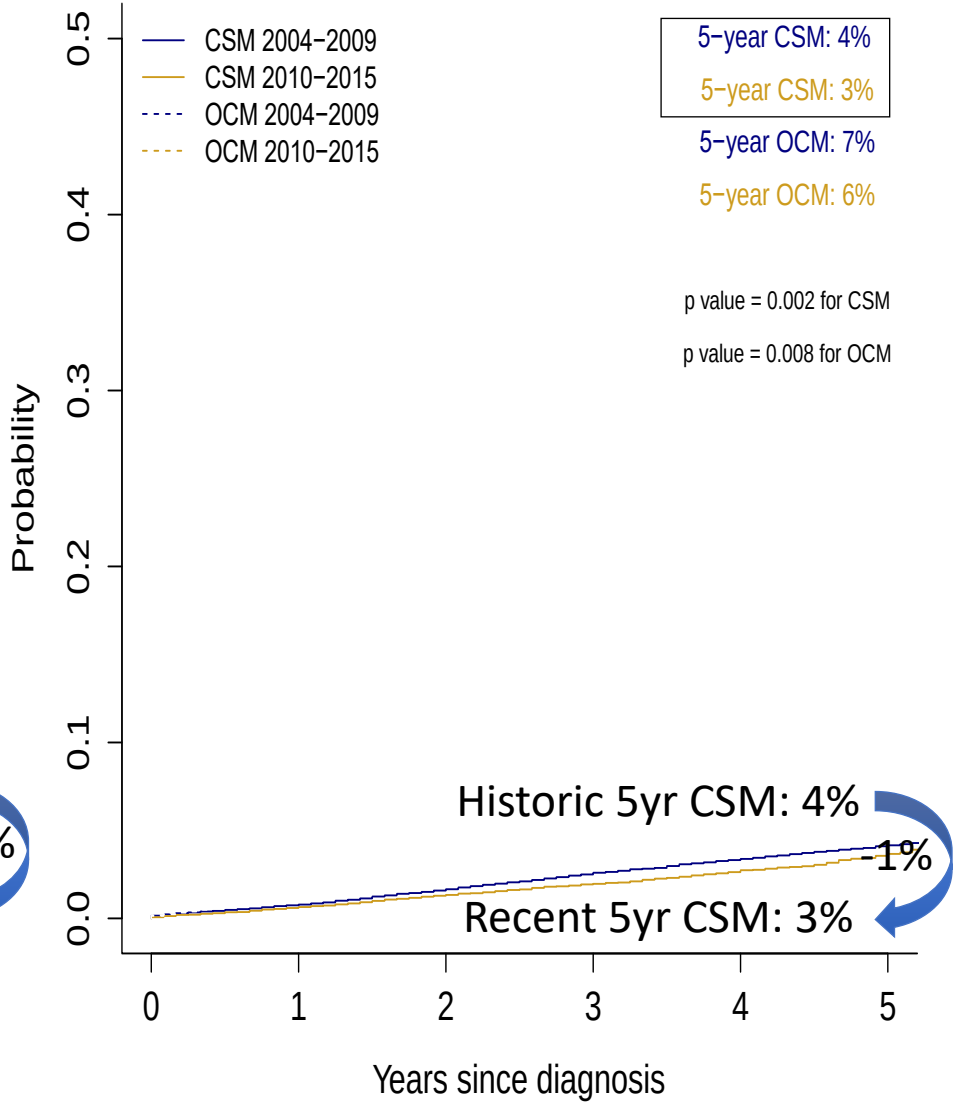


Survival over time: T1-T2

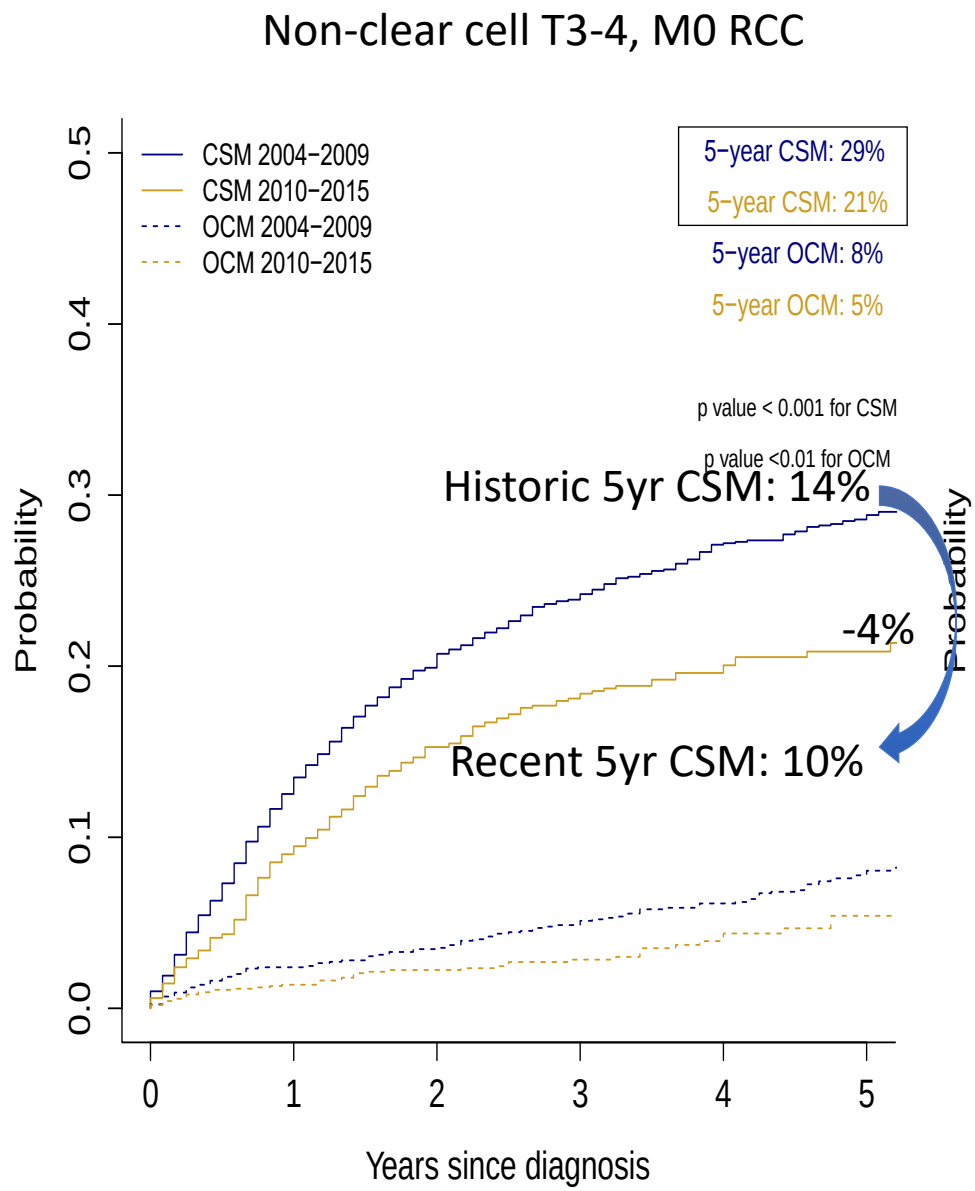
Non-clear cell T1-2, M0 RCC

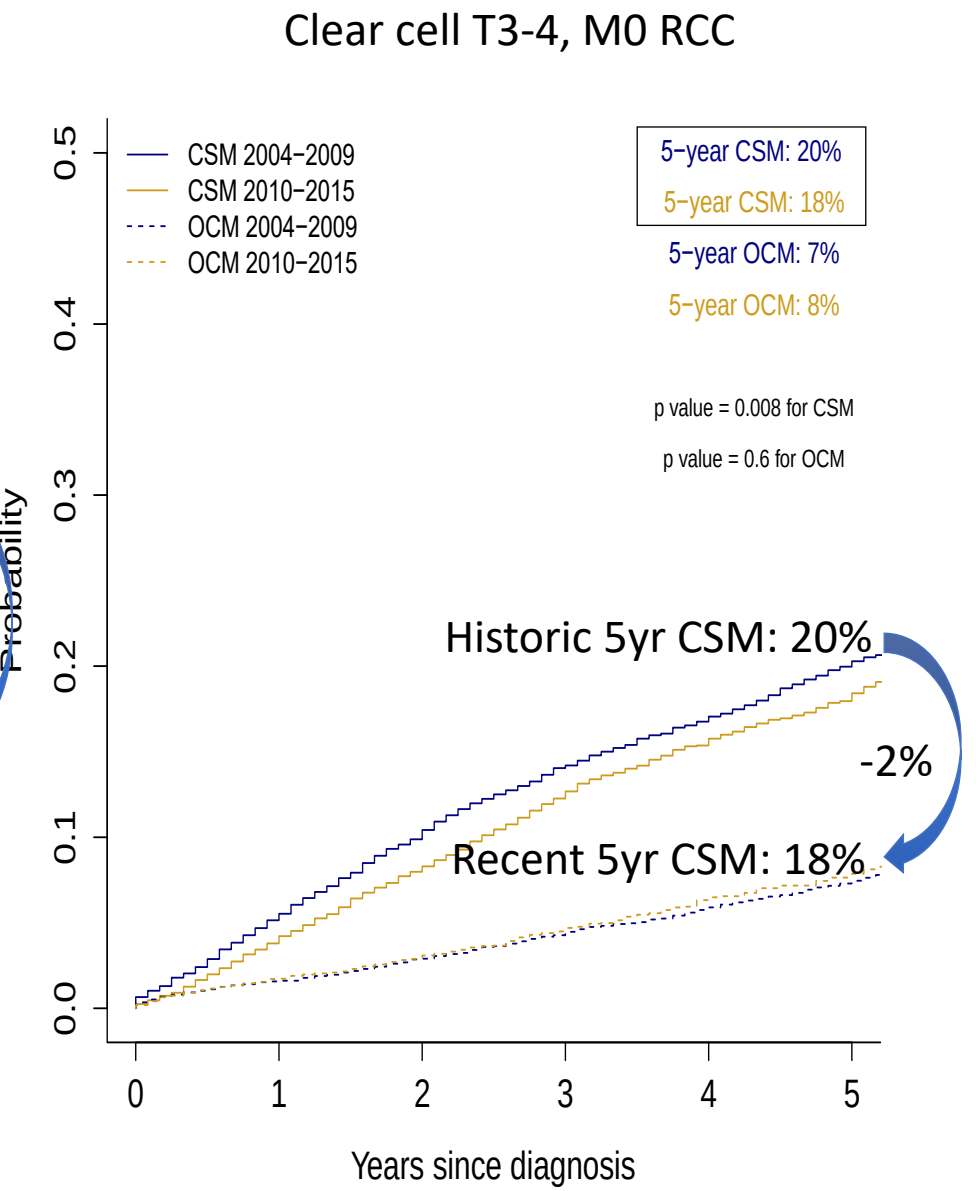


Clear cell T1-2, M0 RCC



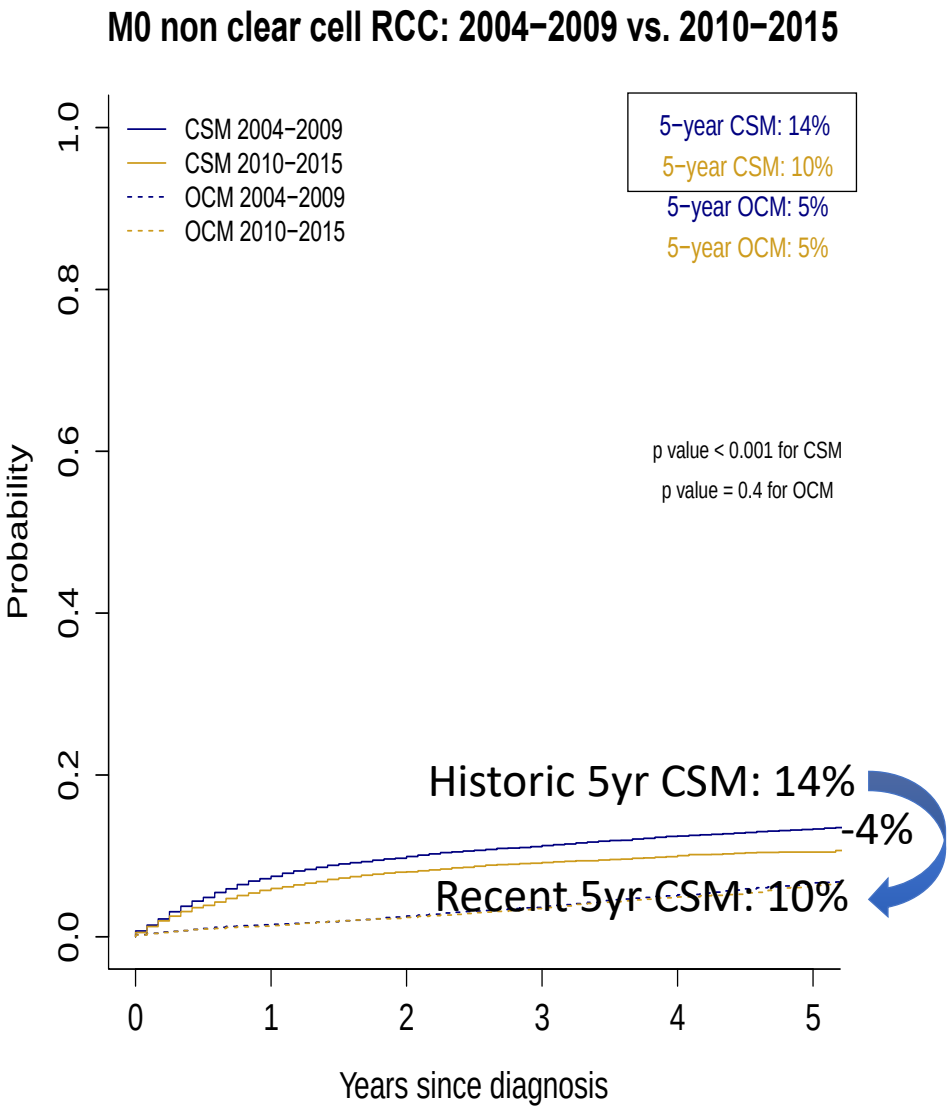
Survival over time: T3-T4



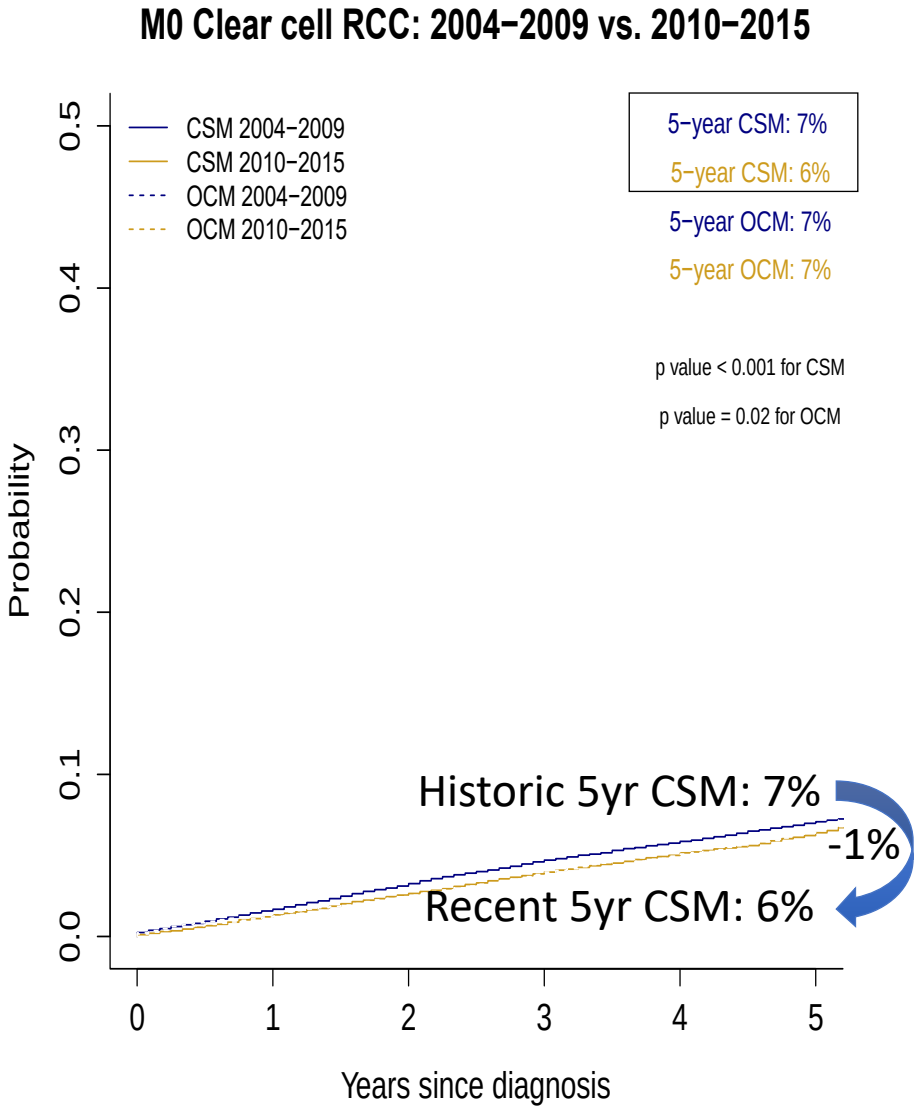


Survival over time

Non-clear cell M0 RCC



Clear cell M0 RCC

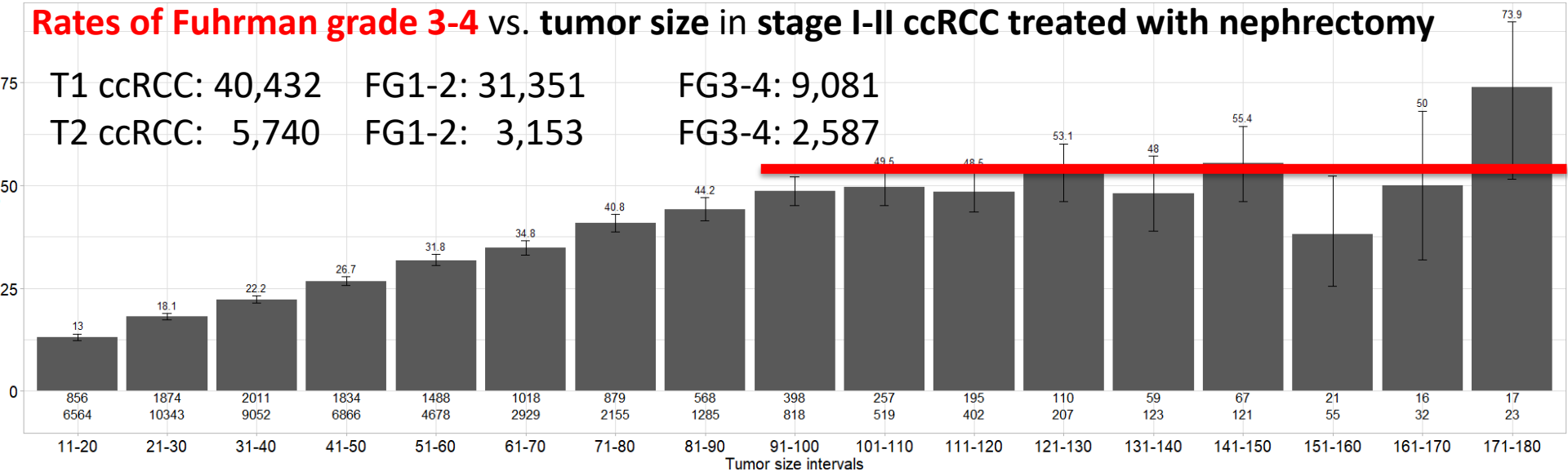


Stage T_{1-2} ccRCC

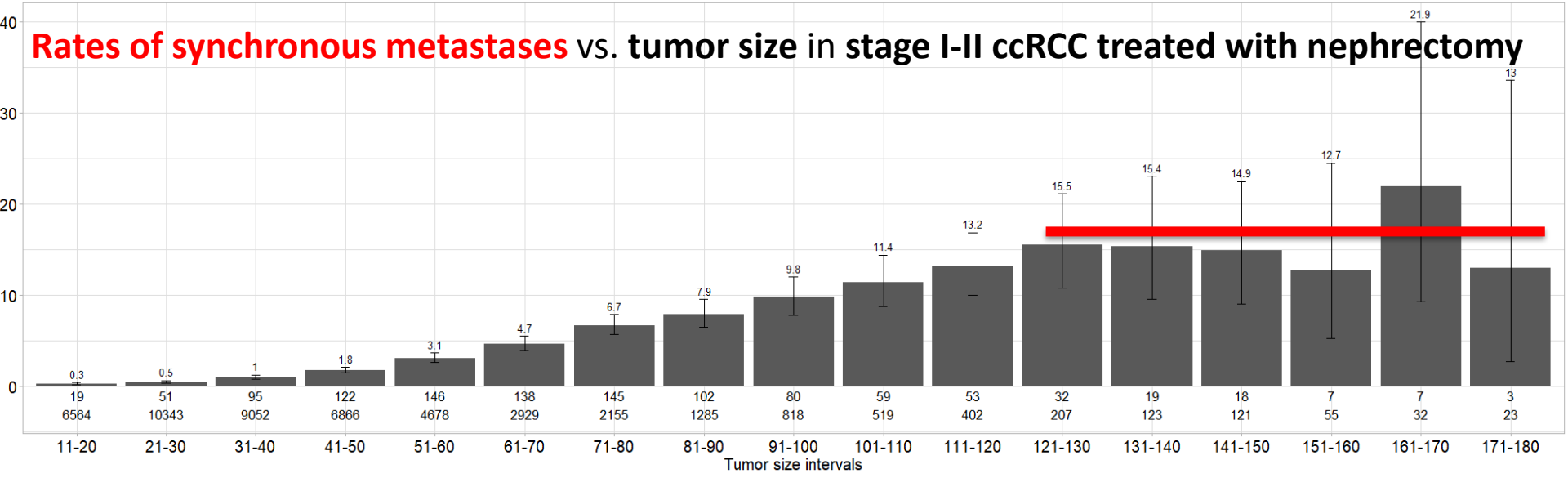
Rates of Fuhrman grade 3-4 vs. **tumor size** in **stage I-II ccRCC treated with nephrectomy**

T1 ccRCC: 40,432 FG1-2: 31,351 FG3-4: 9,081

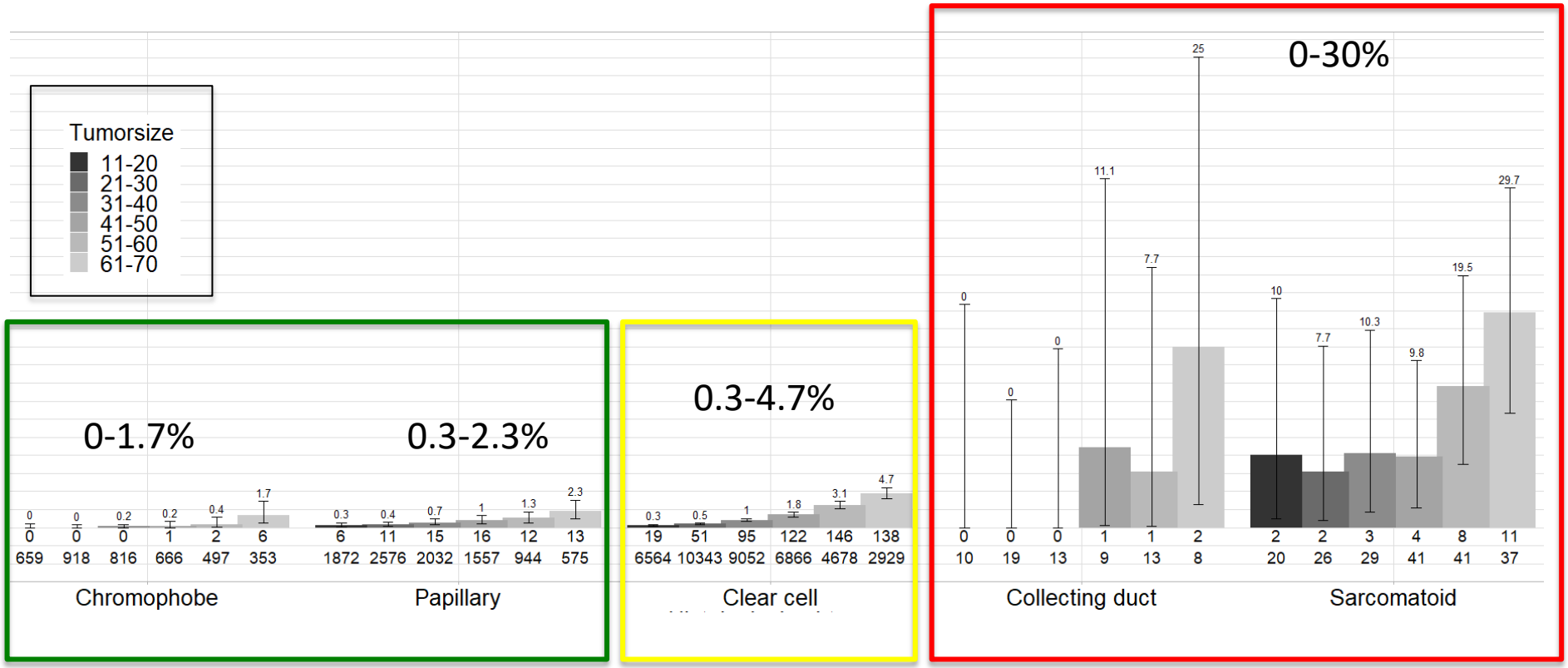
T2 ccRCC: 5,740 FG1-2: 3,153 FG3-4: 2,587



Rates of synchronous metastases vs. **tumor size** in **stage I-II ccRCC treated with nephrectomy**



Stage I RCC treated with nephrectomy: rates of synchronous metastases Vs. tumor size



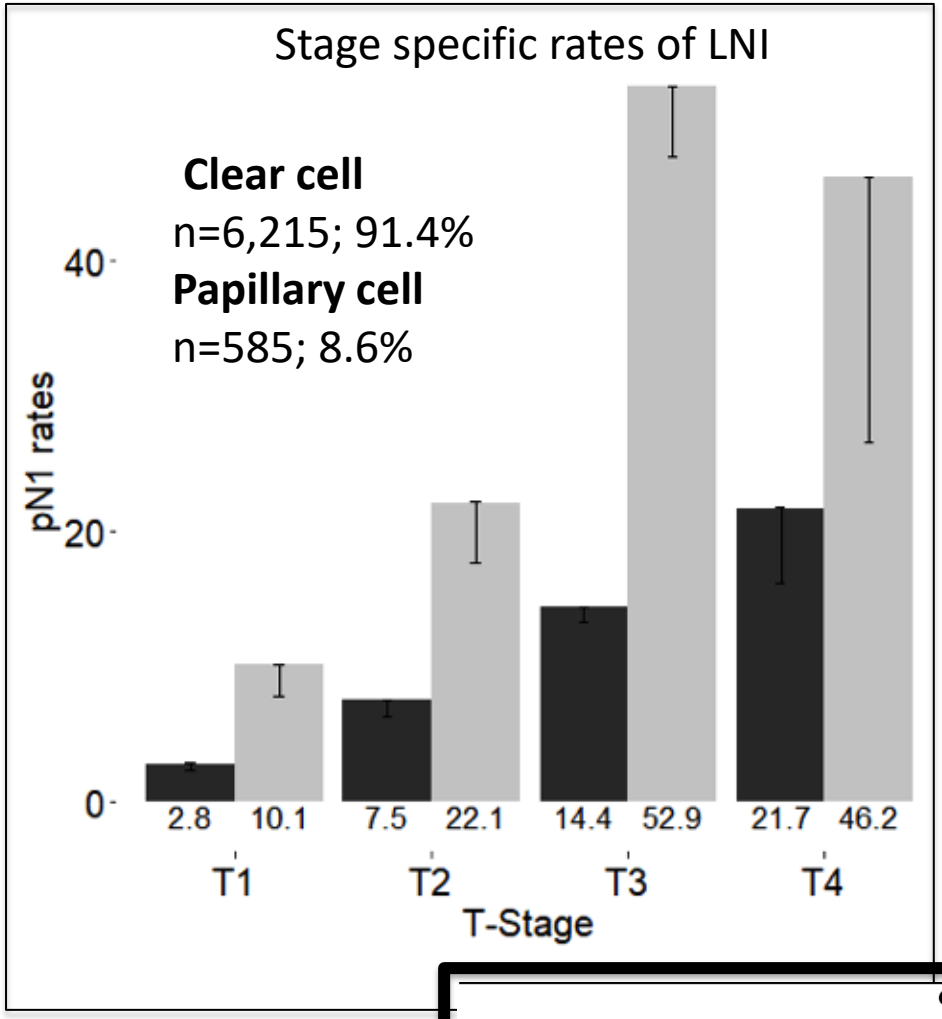
Low risk of synchronous metastases

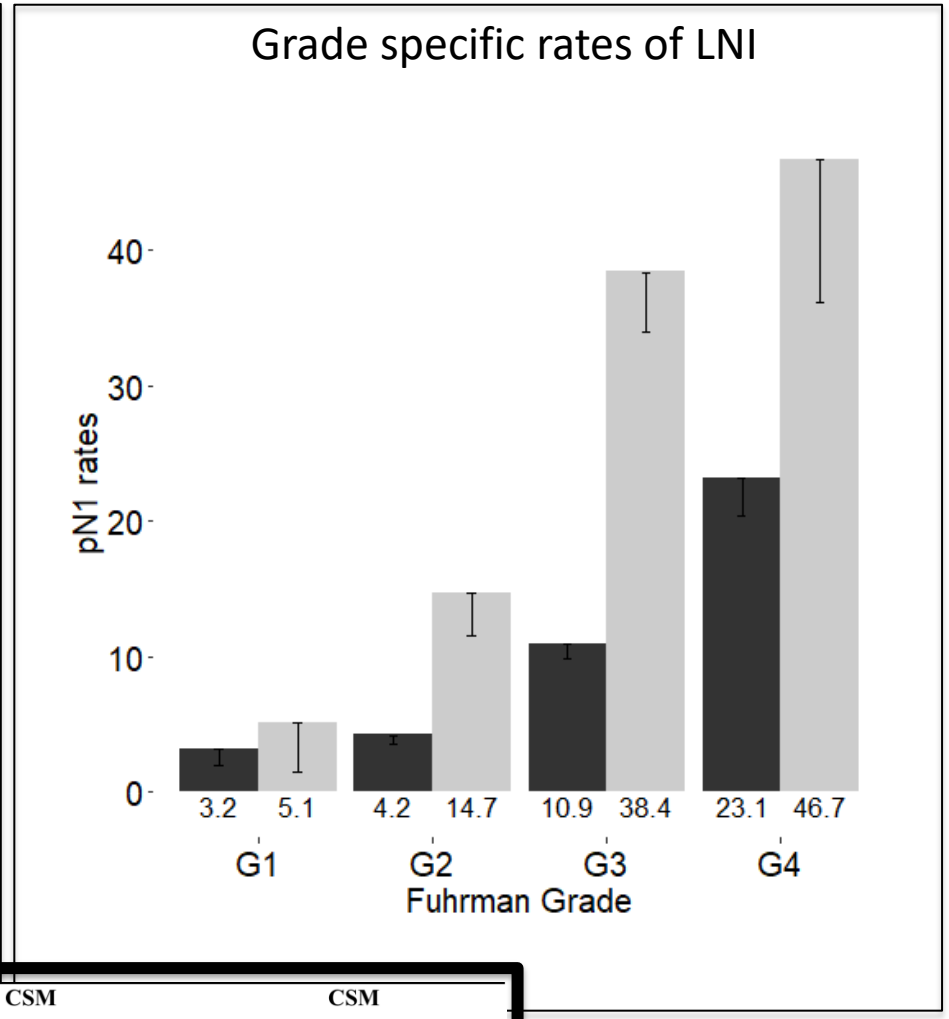
Intermediate risk of synchronous metastases

Elevated risk of synchronous metastases

RMB

Rates of lymph node metastases at LND for clear cell vs. papillary RCC





		CSM Clear-cell			CSM Papillary		
		HR	CI	p-value	HR	CI	p-value
Pathological N-Stage	pN1	3.58	(3.17-4.03)	<0.001	4.31	(3.20-5.81)	<0.001

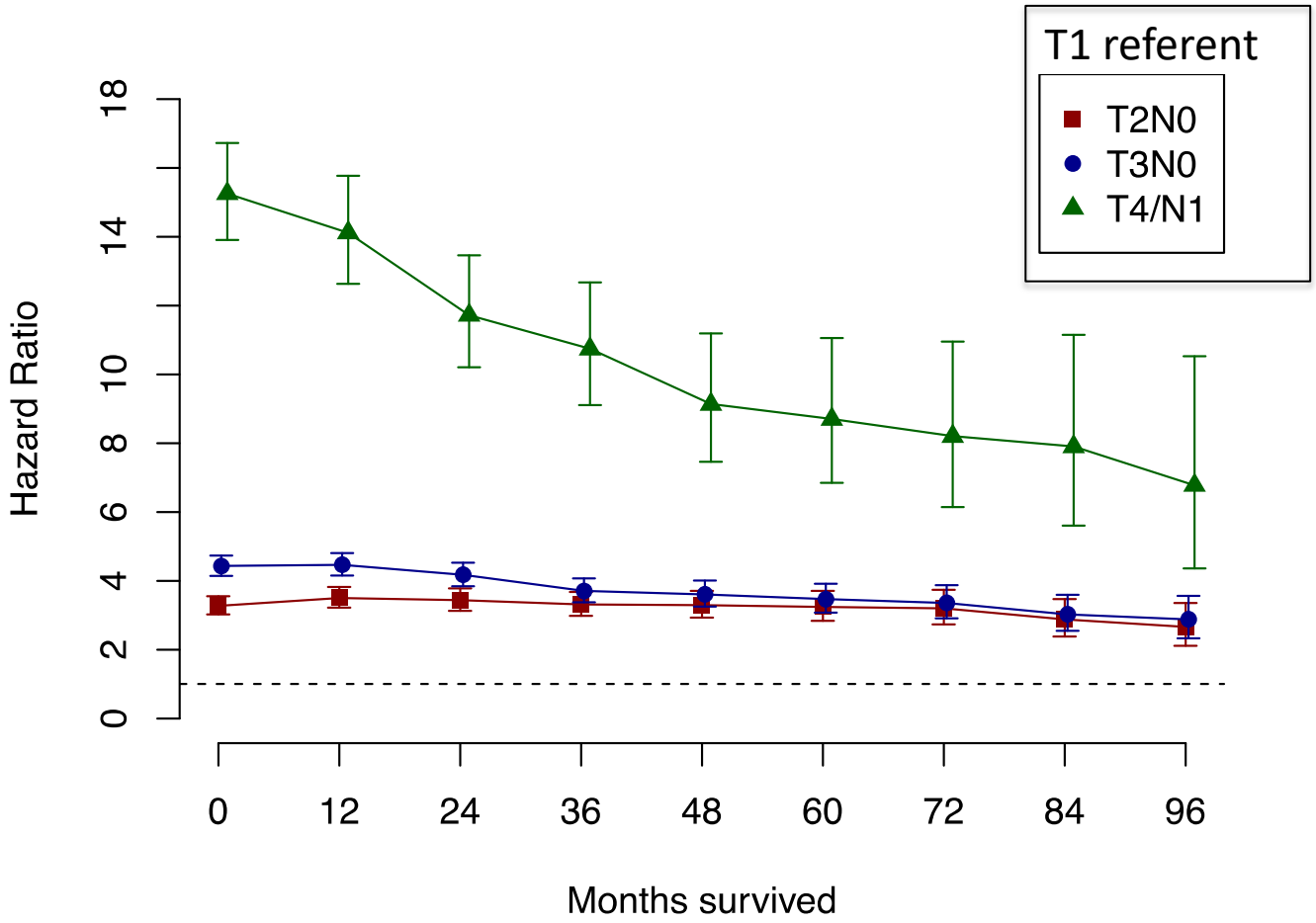
Same effect on CSM when LNI present

RMB

Follow-up considerations:

Hazard of cancer mortality over time after nephrectomy for RCC Vs. pathologic stage

n=77,892
2005-2015



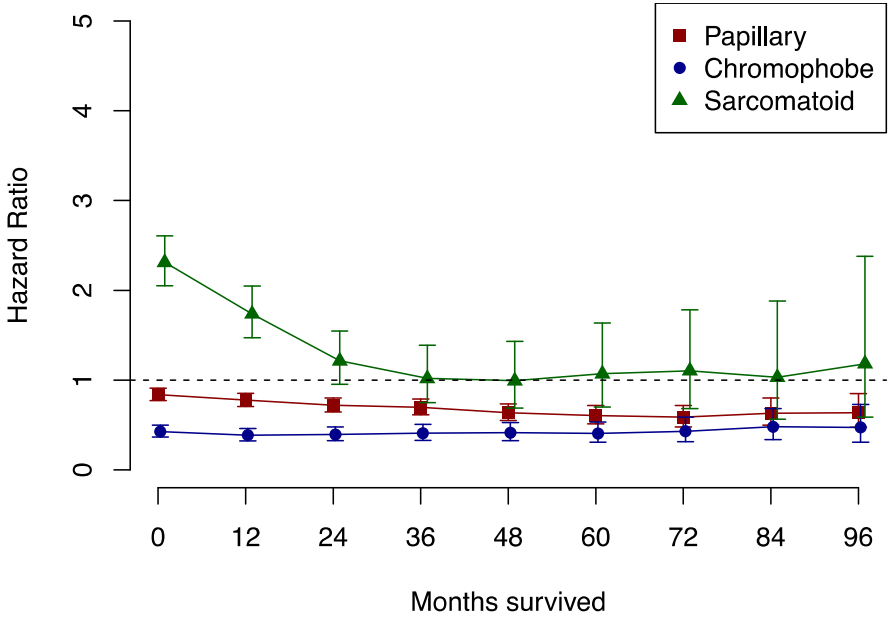
pT1	54824	70.4%
pT2	8488	10.9%
pT3	12876	16.5%
pT4/N1	1704	2.2%
Total	77892	100%

n=77,892
2005-2015

Follow-up considerations:
Hazard of cancer mortality over time after nephrectomy for RCC

Vs. histologic subtype

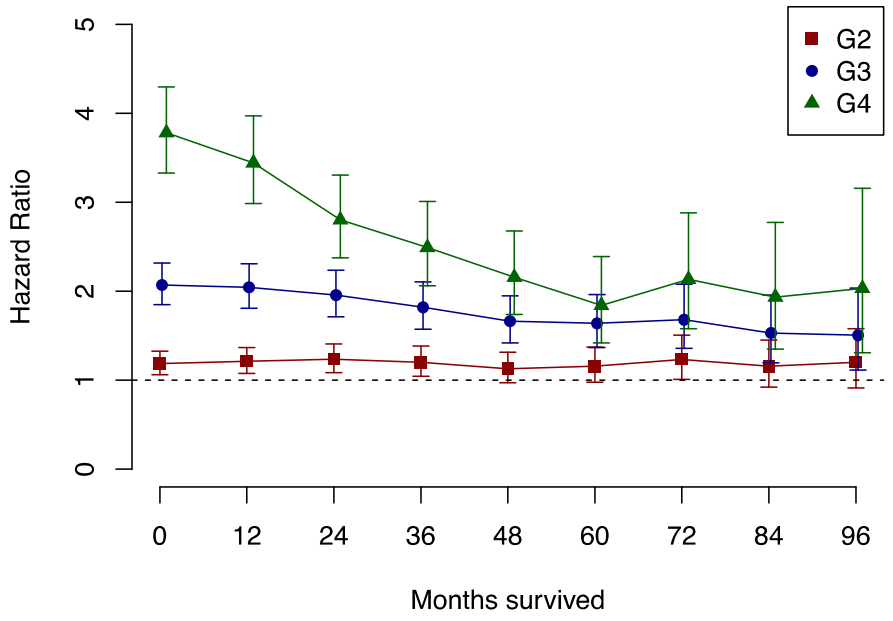
Clear cell: referent



Clear-cell	60,398 (77.5)
Papillary	12,200 (15.7)
Chromophobe	4,551 (5.8)
Sarcomatoid	743 (1.0)

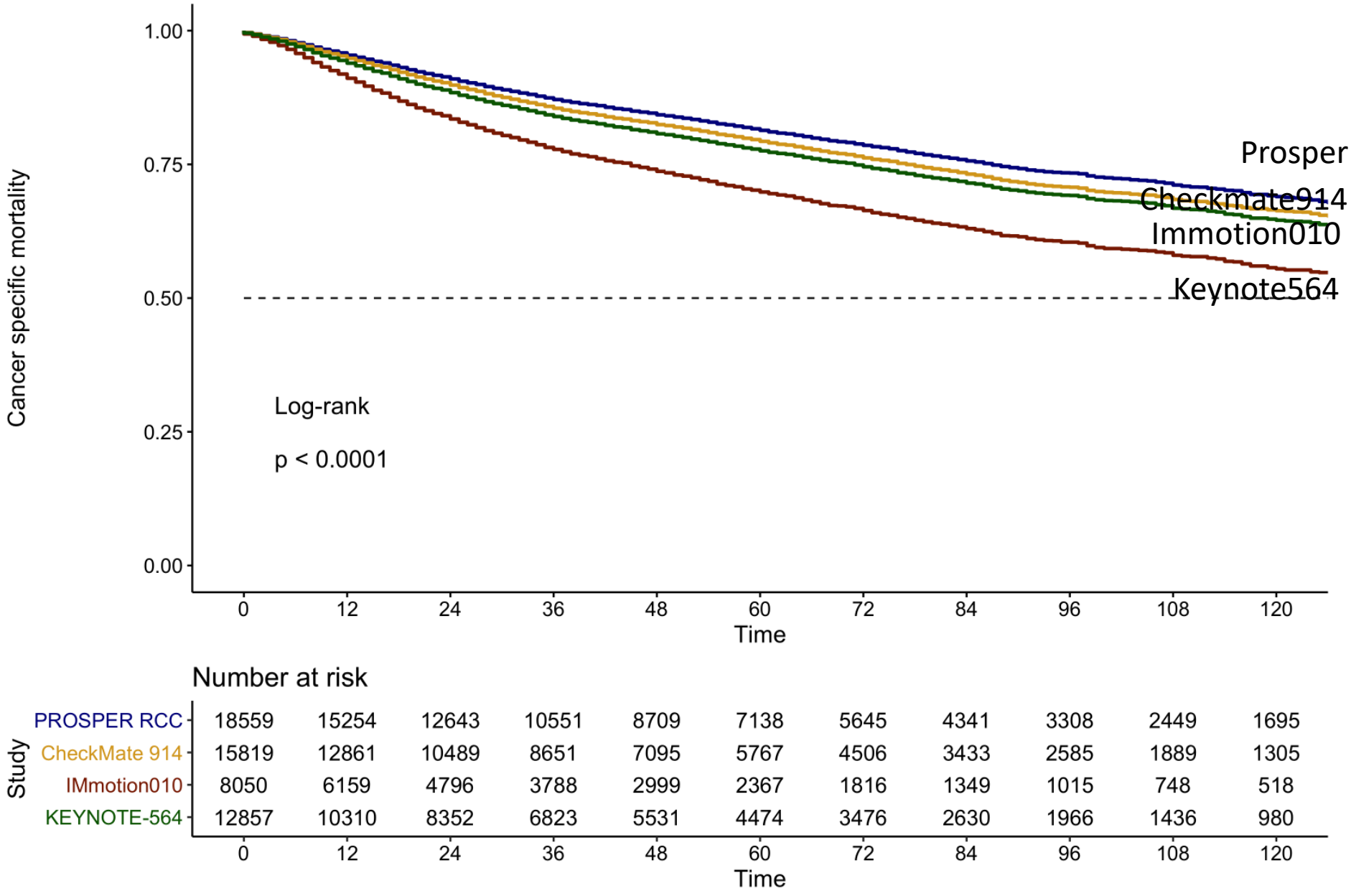
Vs. grade

G1: referent

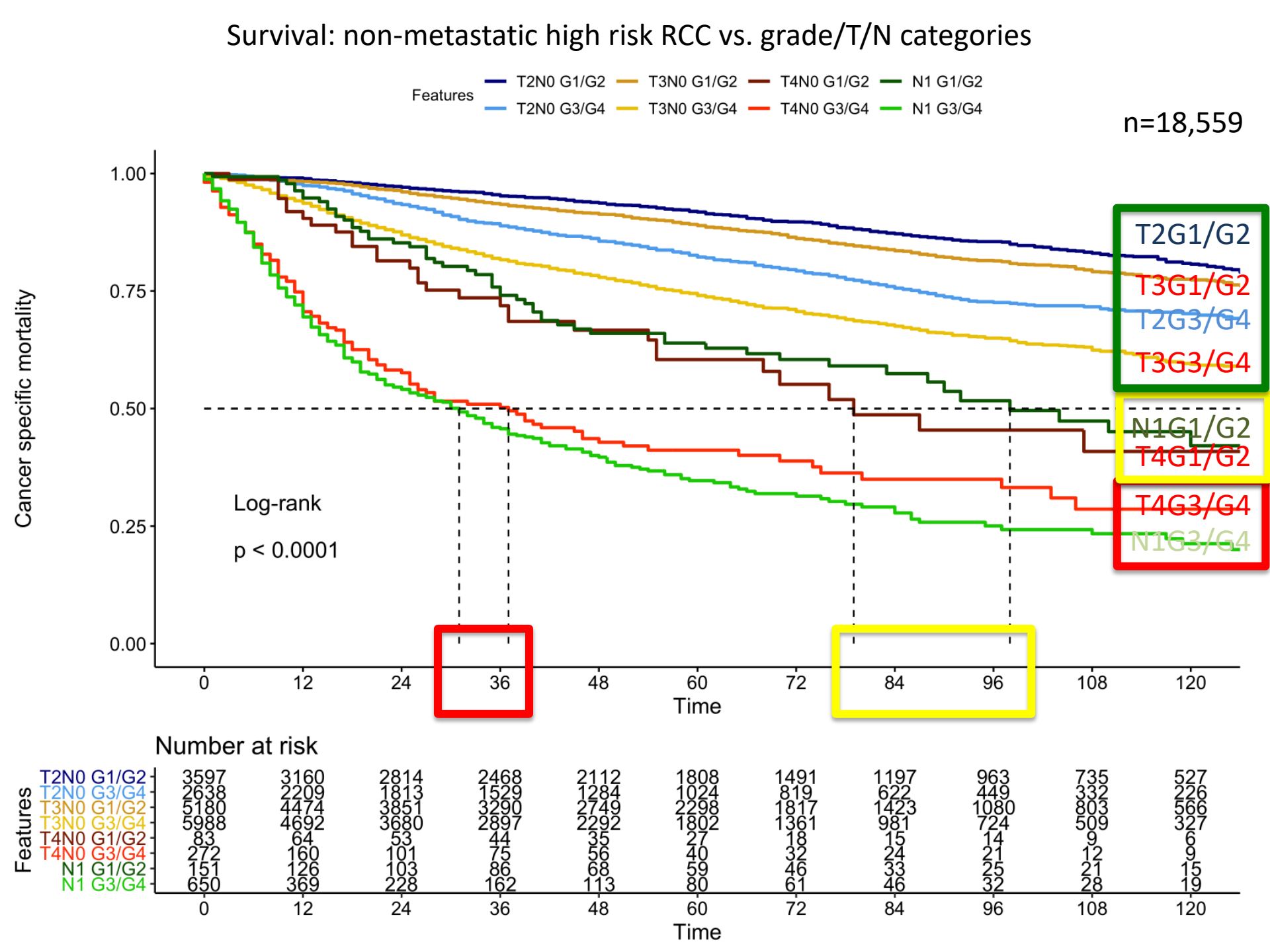


G1	9,824 (12.6)
G2	42,714 (54.8)
G3	21,371 (27.4)
G4	3,983 (5.1)

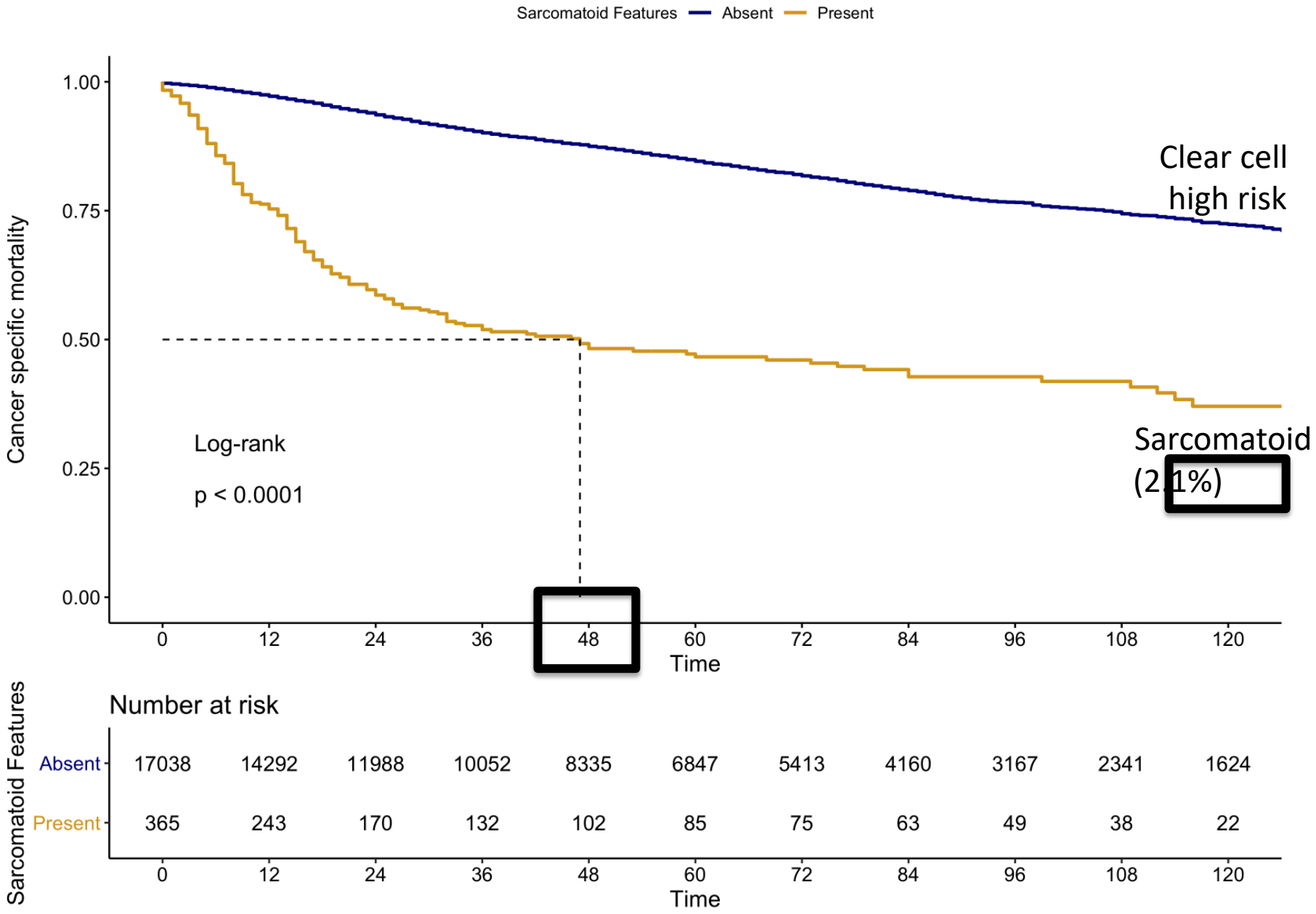
Non-metastatic high risk RCC: simulated placebo arms of adjuvant IO studies



Survival: non-metastatic high risk RCC vs. grade/T/N categories

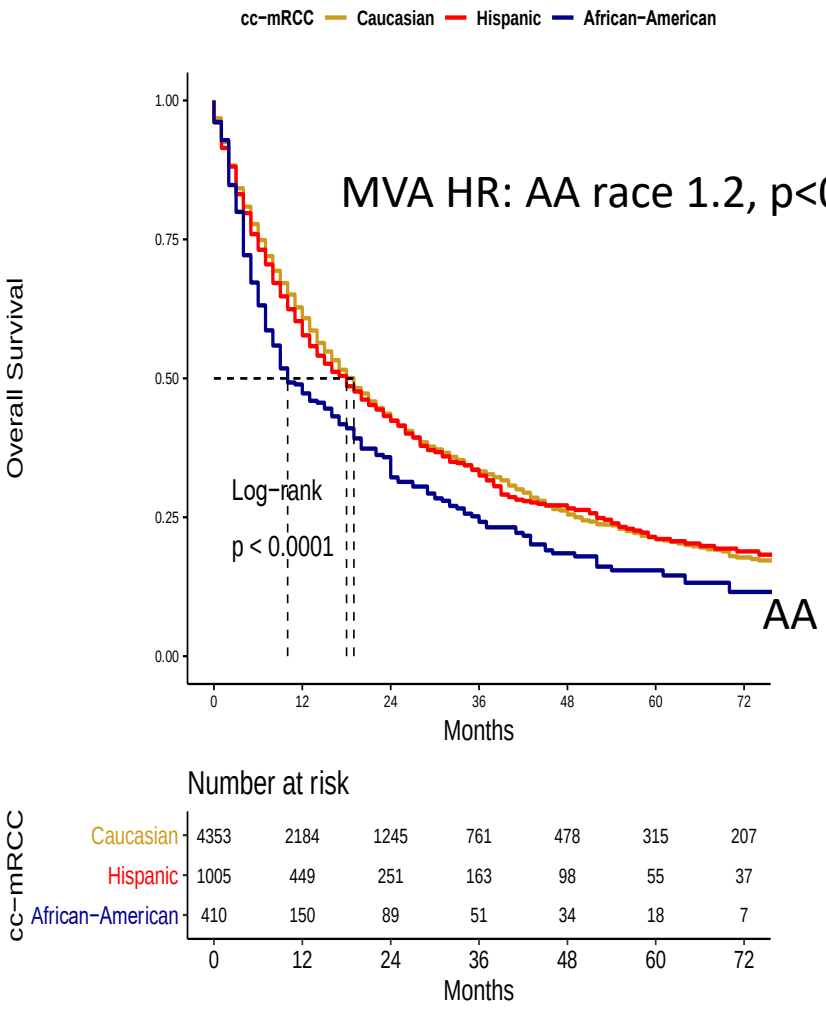


Survival: non-metastatic high risk RCC

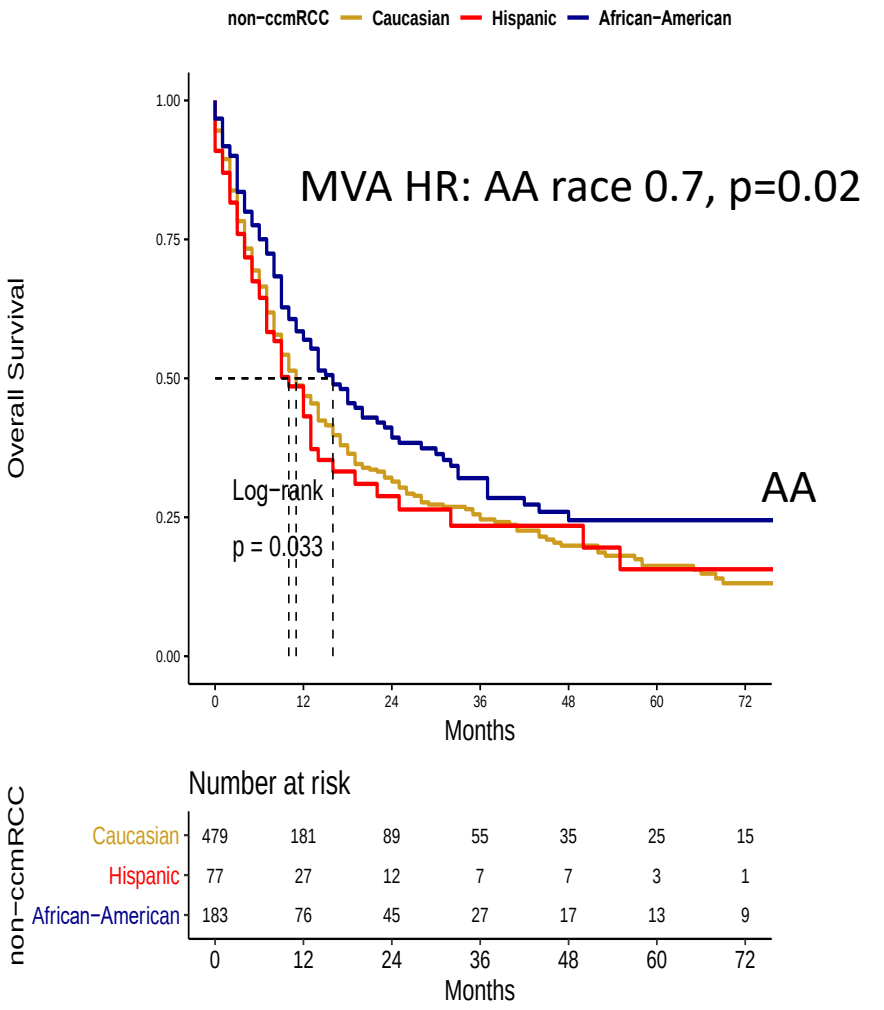


Effect of race on survival in metastatic RCC

Clear cell metastatic RCC

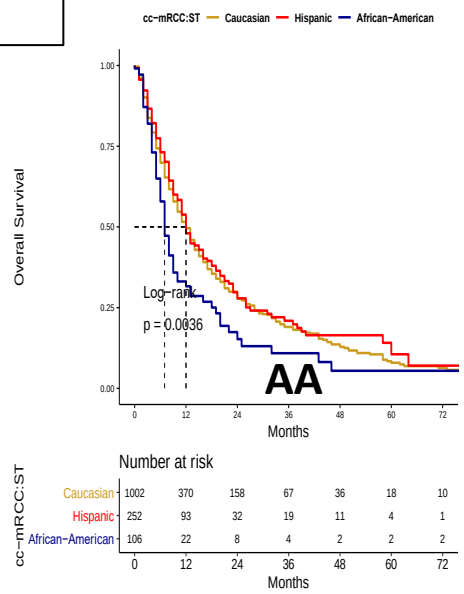


Non-clear cell metastatic RCC

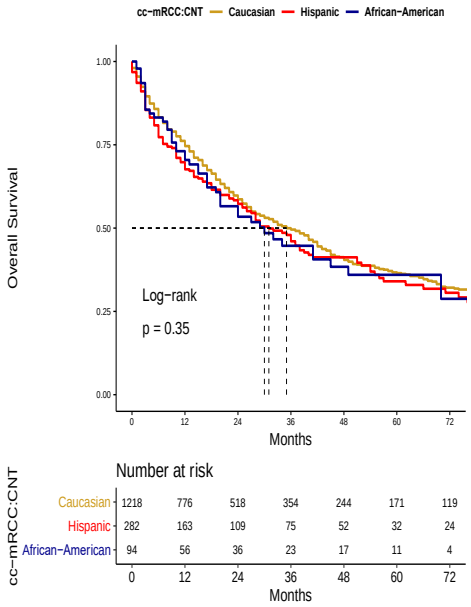


Clear cell mRCC

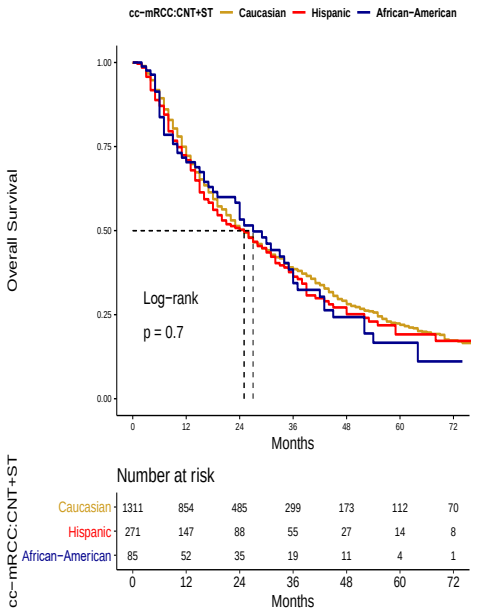
Systemic therapy (ST)



Cytoreductive nephrectomy (CNT)

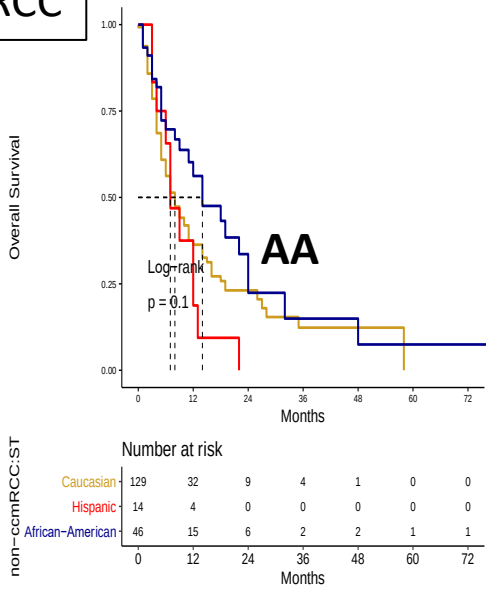


ST + CNT

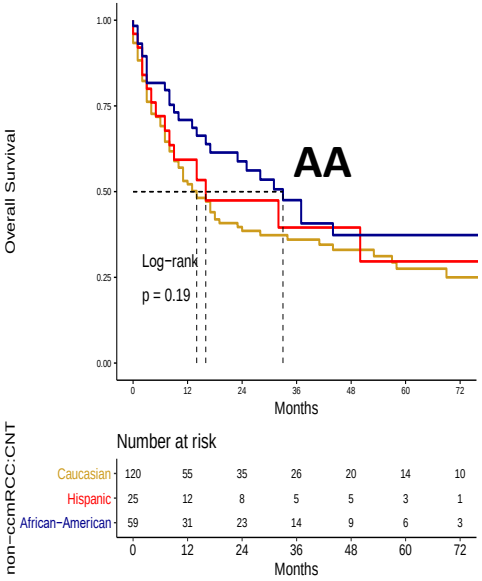


Non-clear Cell mRCC

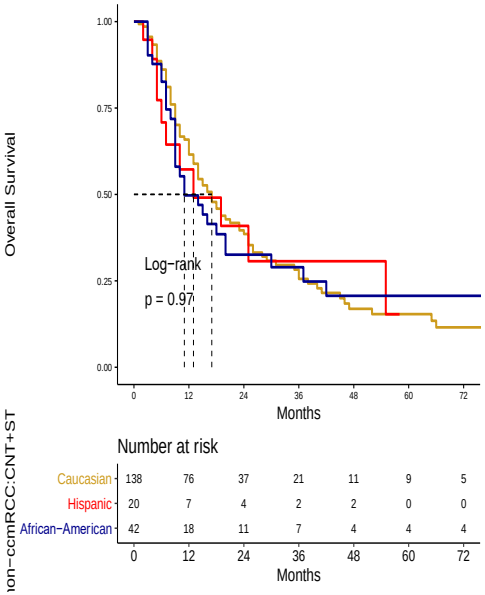
Systemic therapy (ST)



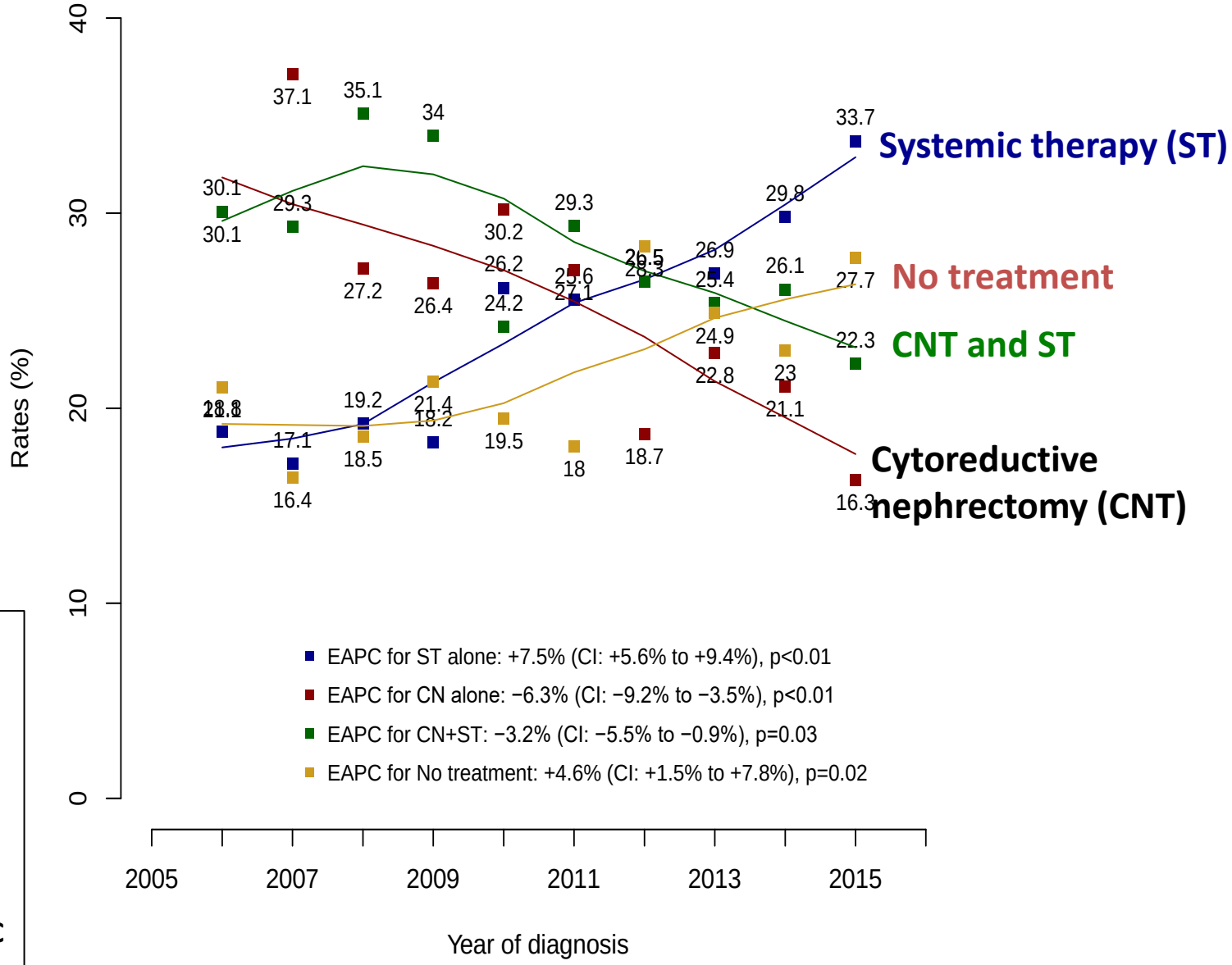
Cytoreductive nephrectomy (CNT)



ST + CNT



Treatment rates over time: non-clear cell mRCC RCC

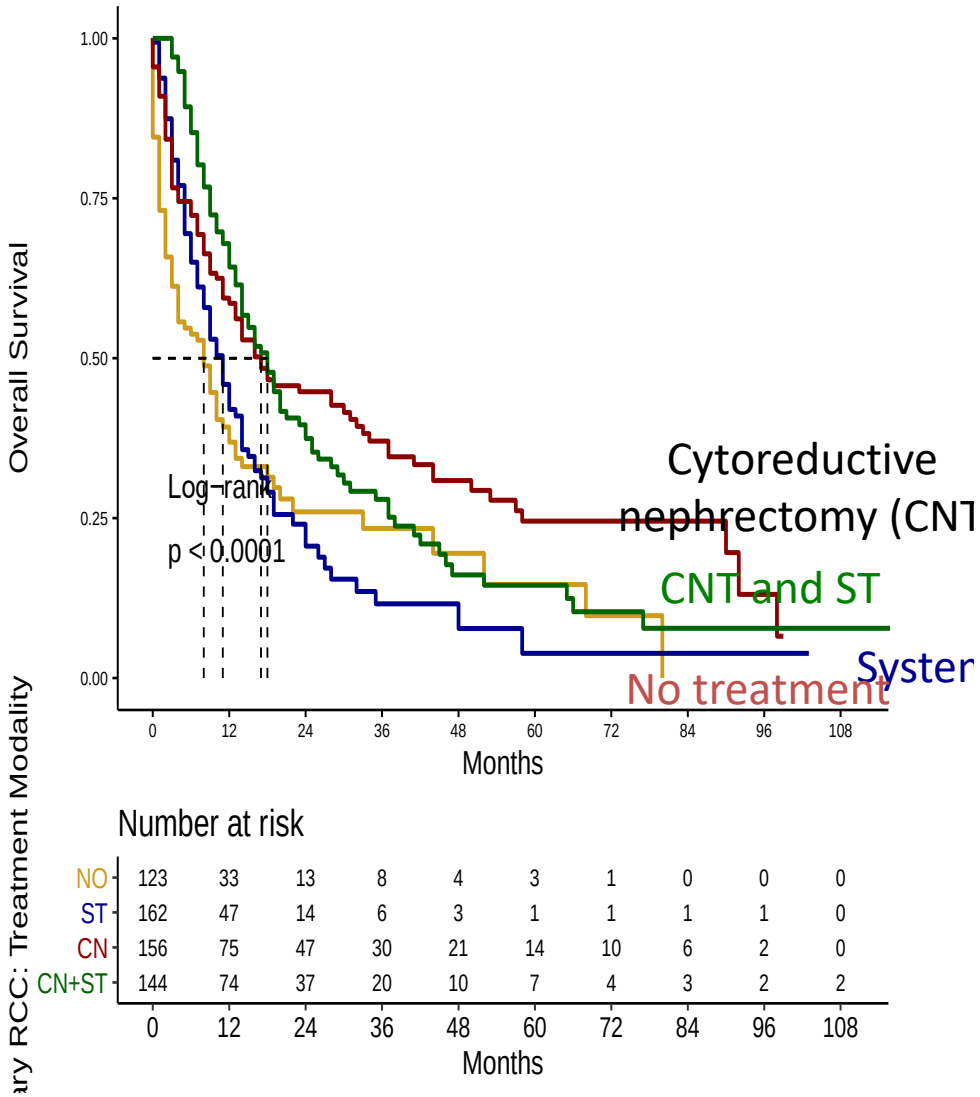


Overall
(n=1573)
Papillary mRCC
(n=585; 37%)
Chromophobe mRCC
(n=101; 6.5%)
Sarcomatoid mRCC
(n=786; 50%)
Collecting duct mRCC
(n=101; 6.5%)

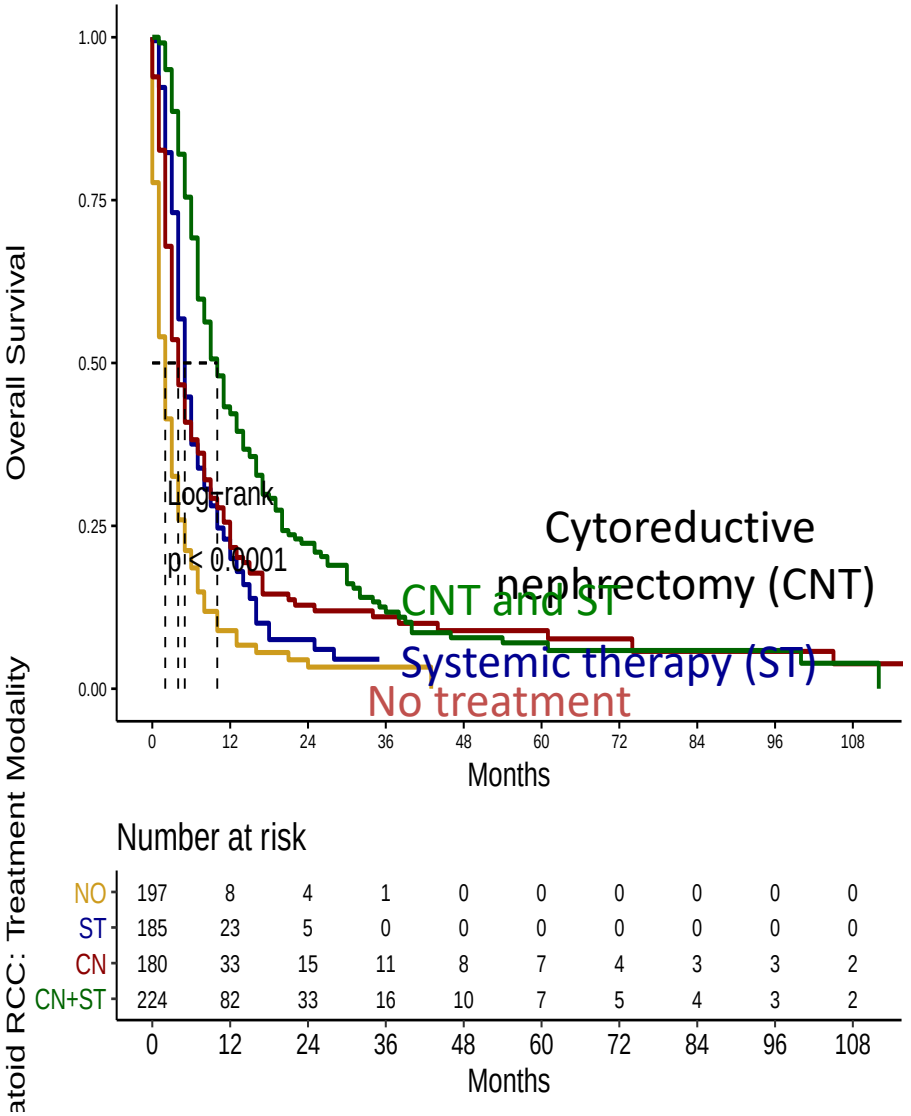
Survival: non-clear cell mRCC Vs. treatment type

Survival Vs. treatment type: mRCC

Papillary mRCC

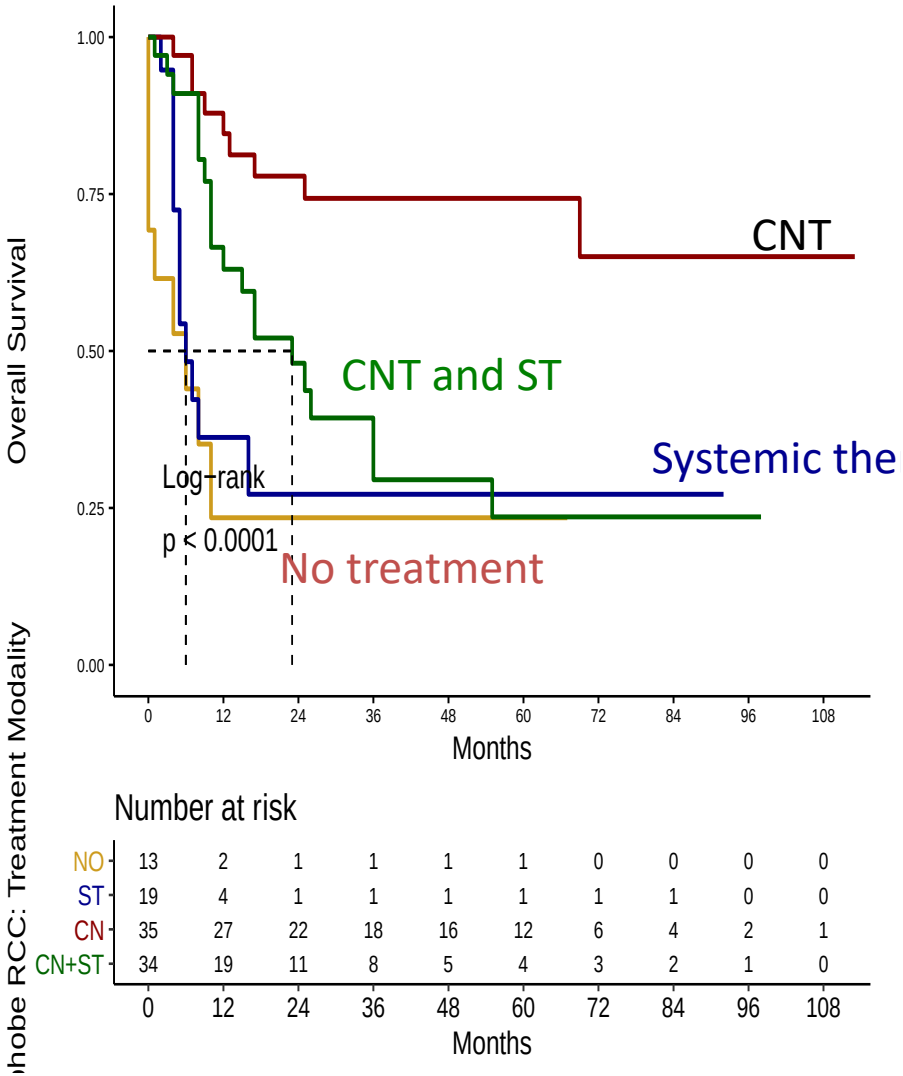


Sarcomatoid mRCC

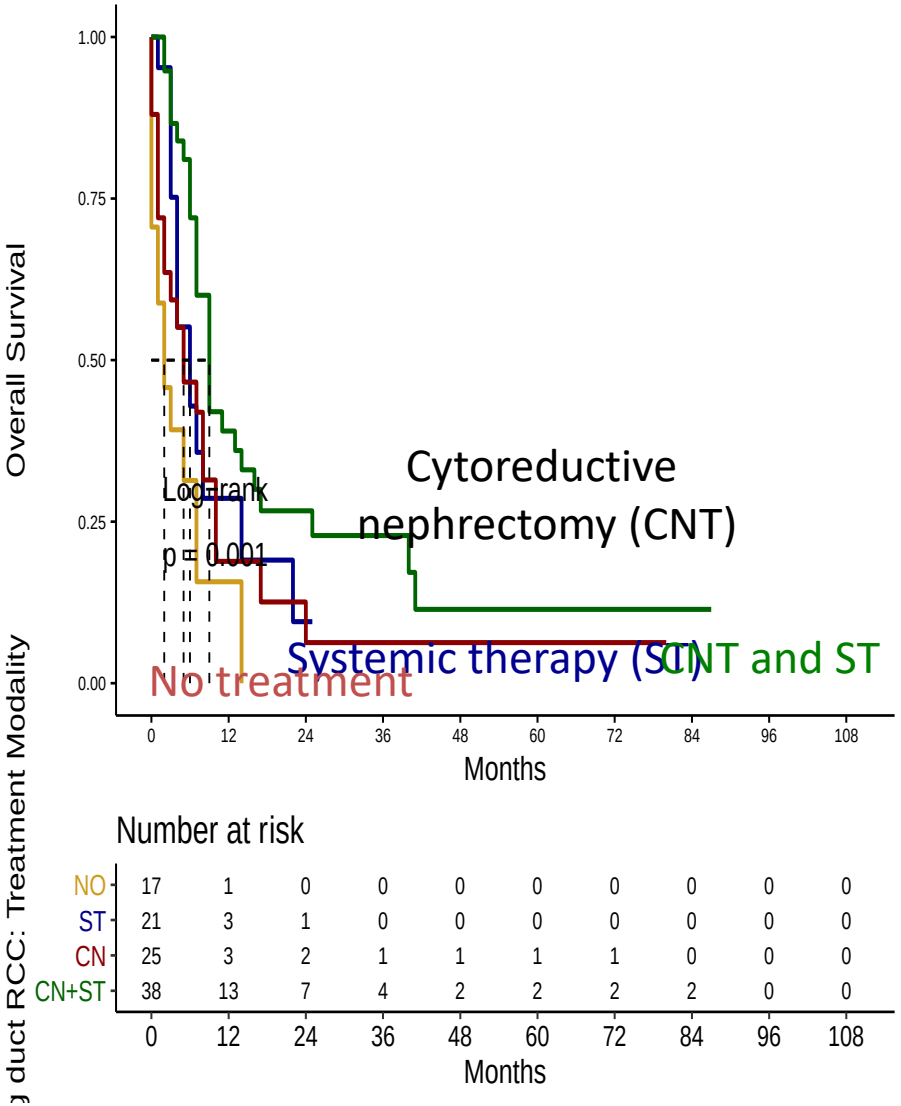


Survival according to treatment type

Chromophobe mRCC



Collecting duct mRCC



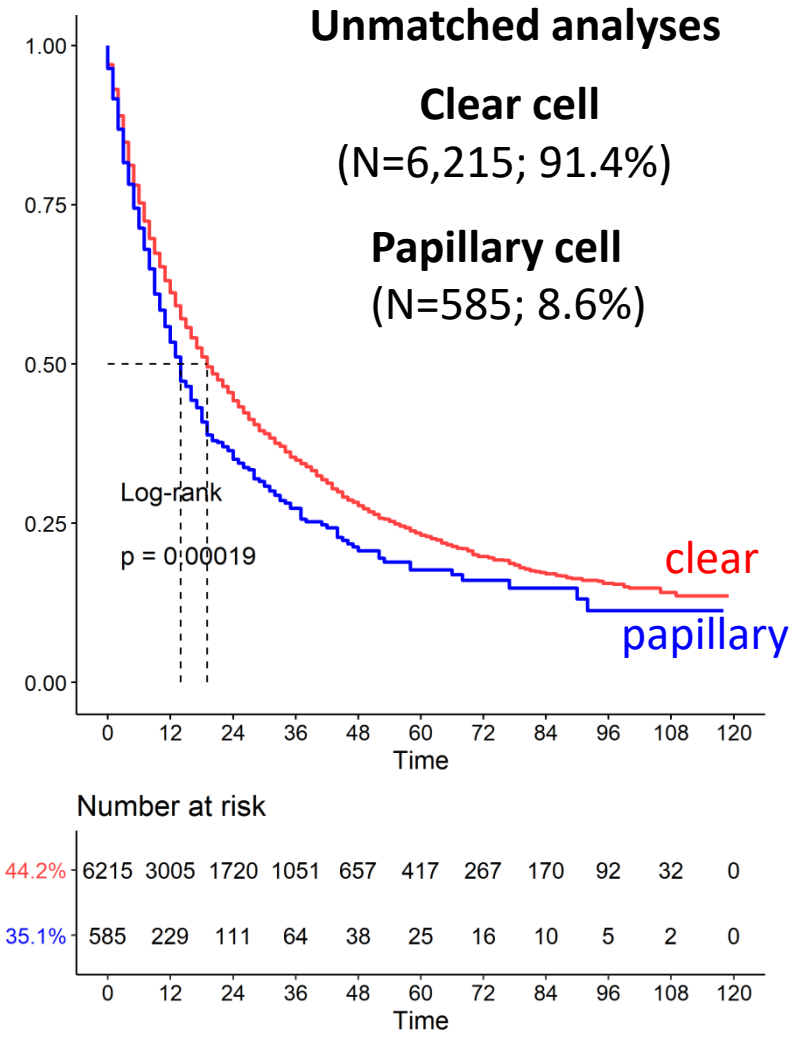
Determinants of mortality in metastatic non-clear cell RCC

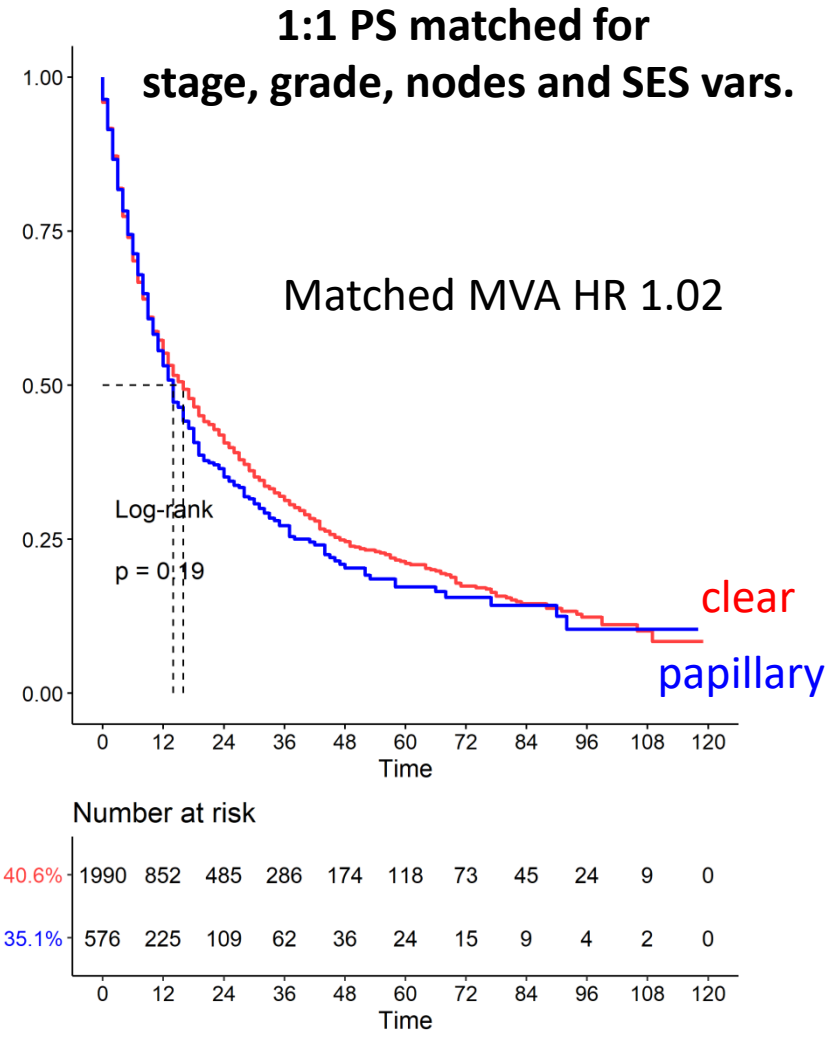
Multivariable Cox regression analyses

		HR (95% CI)	p-value
Treatment modality	No treatment	Ref.	
	ST alone	0.5 (0.4-0.6)	**<0.001**
	CN alone	0.4 (0.3-0.5)	**<0.001**
	CN + ST	0.3 (0.2-0.3)	**<0.001**
Histological subtype	Papillary	Ref.	
	Chromophobe	0.7 (0.5-0.9)	**<0.01**
	Sarcomatoid	2.1 (1.8-2.5)	**<0.001**
	Collecting duct	1.9 (1.5-2.5)	**<0.001**
T stage	T3/T4 vs. T1/T2	1.3 (1.2-1.6)	**<0.001**
N stage	N1	1.4 (1.2-1.6)	**<0.001**
Metastasectomy	Performed	0.8 (0.7-0.9)	**0.01**

Adjusted for age, SES variables

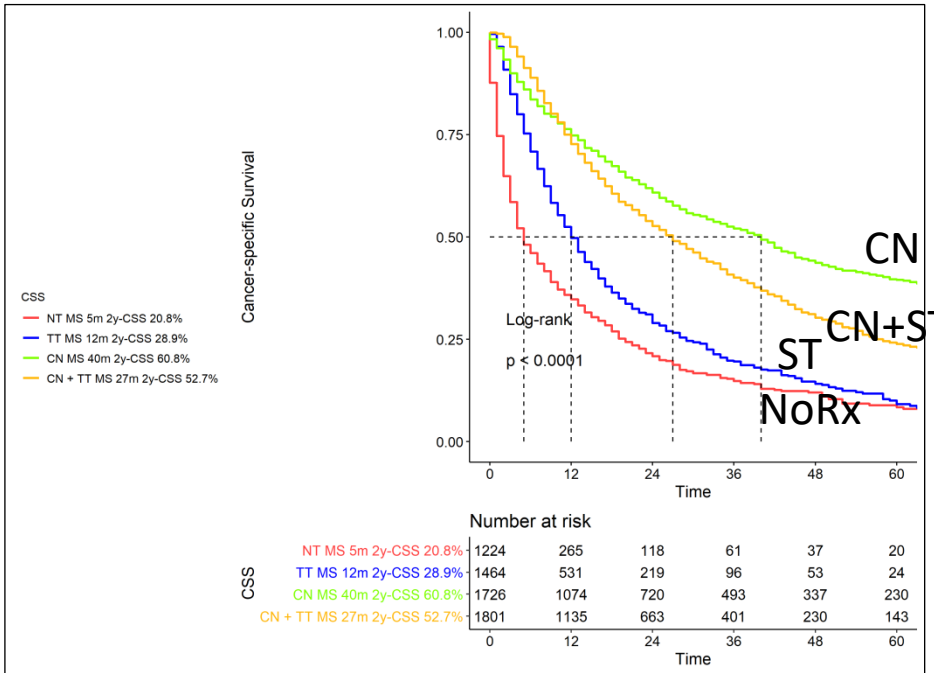
Survival in mRCC: papillary vs. clear cell histology



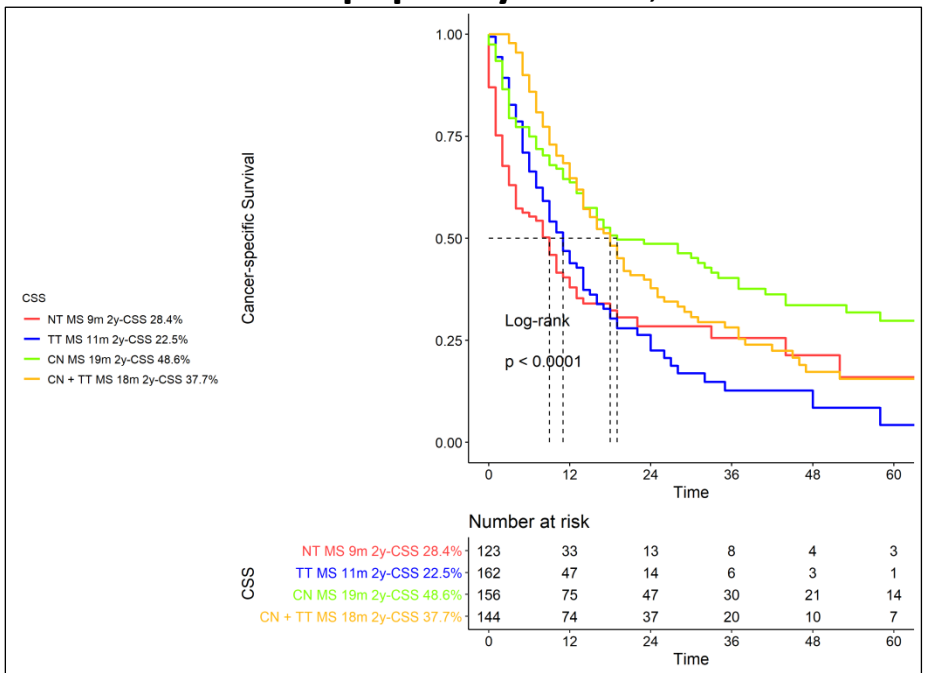


Survival in mRCC Vs. histologic subtype Vs. treatment type

mRCC clear cell n=6215; 91.4%

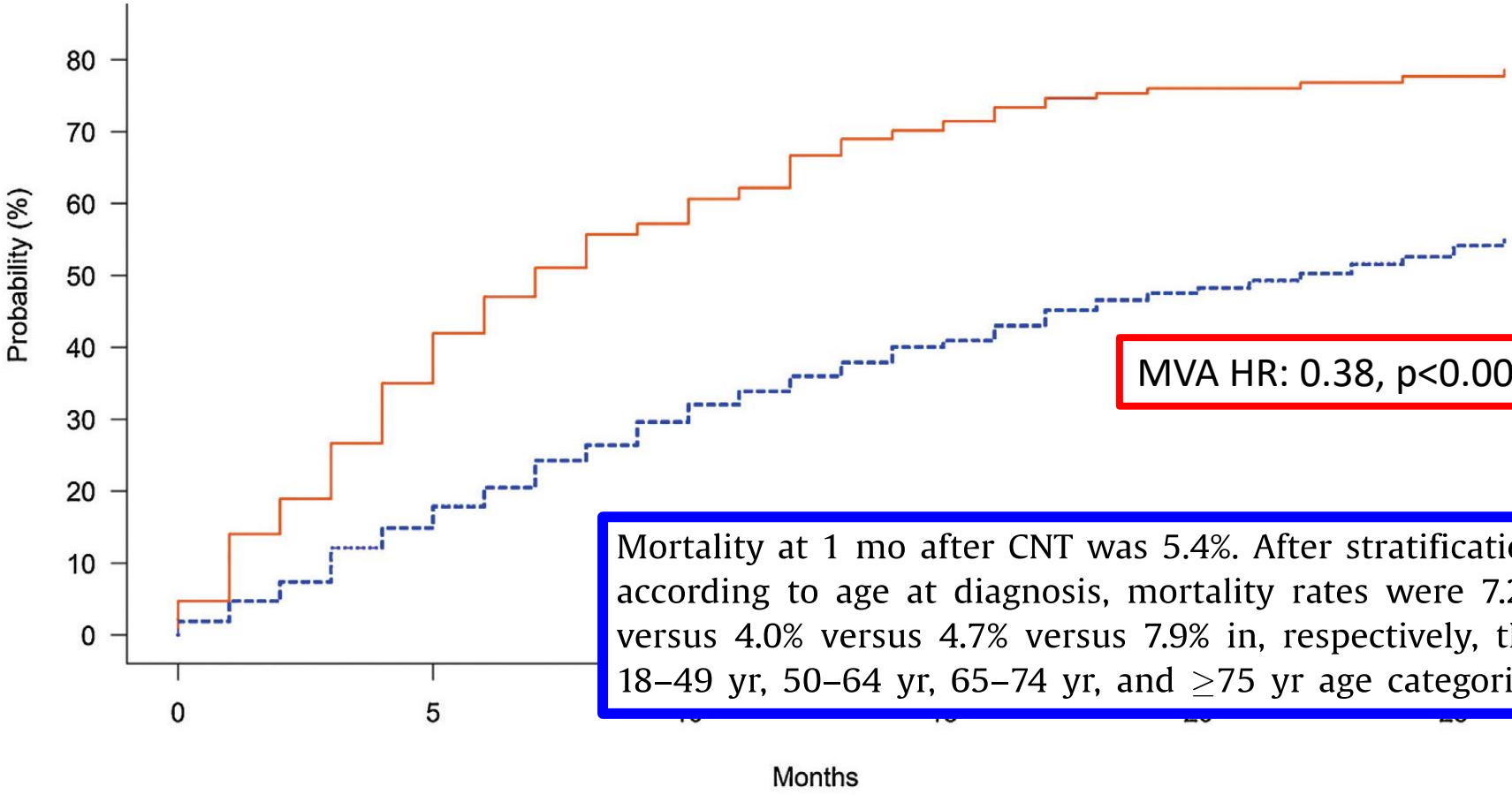


mRCC papillary n=585; 8.6%



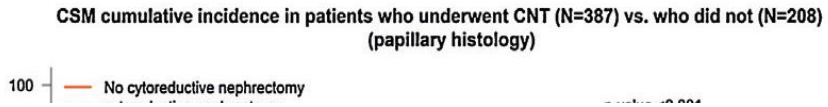
	CSM Clear cell			CSM Papillary		
	HR	CI	p-value	HR	CI	p-value
Targeted therapy	0.6	(0.5-0.6)	<0.001	0.8	(0.6-1.1)	0.1
Cytoreductive nephrectomy	0.2	(0.2-0.3)	<0.001	0.4	(0.3-0.6)	<0.001
C. nephrectomy + T. therapy	0.3	(0.2-0.3)	<0.001	0.4	(0.3-0.5)	<0.001

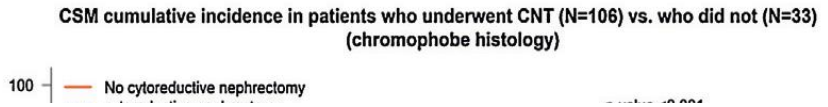
Survival after Cytoreductive Nephrectomy in Metastatic Non-clear Cell Renal Cell Carcinoma Patients: A Population-based Study



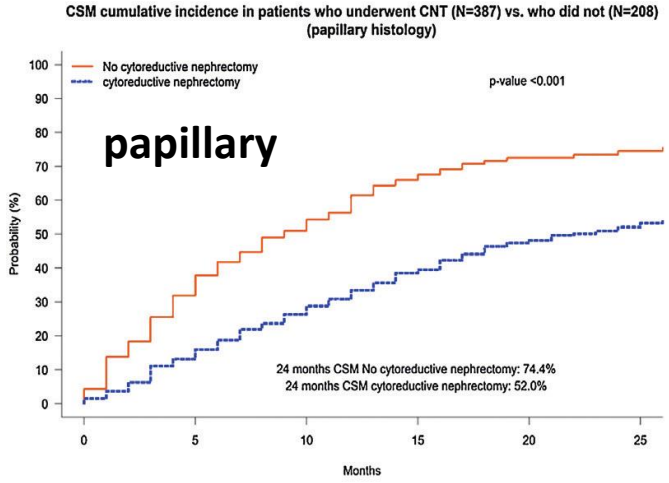
MVA HR: 0.38, p<0.001

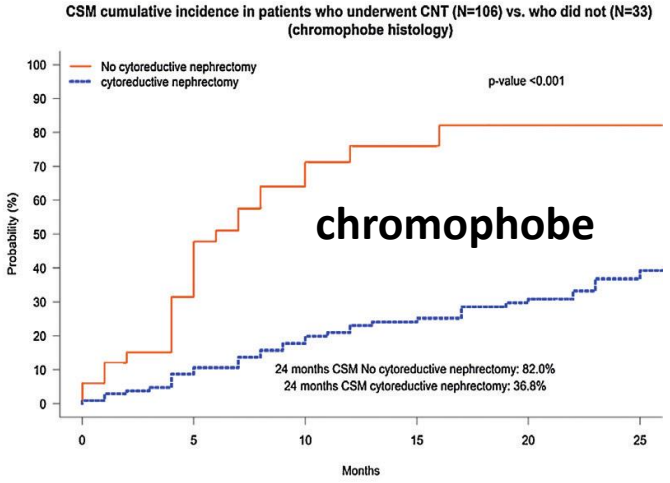
Mortality at 1 mo after CNT was 5.4%. After stratification according to age at diagnosis, mortality rates were 7.2% versus 4.0% versus 4.7% versus 7.9% in, respectively, the 18–49 yr, 50–64 yr, 65–74 yr, and ≥75 yr age categories

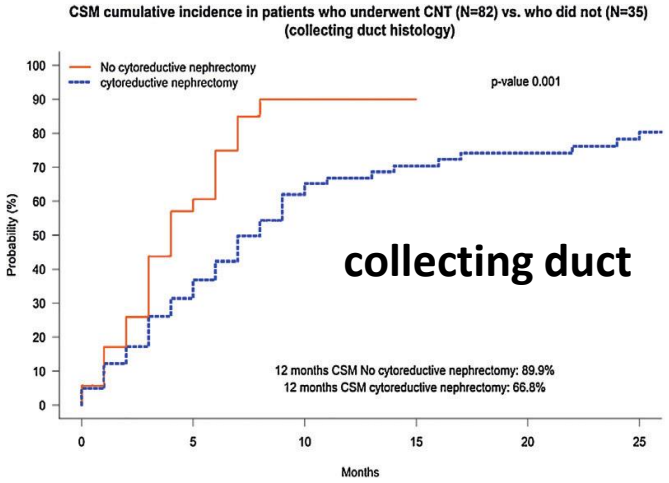


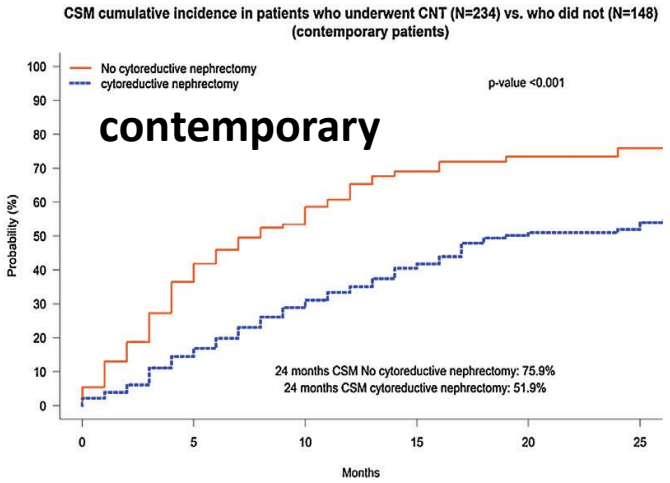


Survival after Cytoreductive Nephrectomy in Metastatic Non-clear Cell Renal Cell Carcinoma Patients: A Population-based Study









Histological subtypes	HR (95% CI) multivariable	*p* value
Papillary + chromophobe + collecting duct (*N* = 851)	0.38 (0.30–0.47)	<0.001
Papillary (*N* = 595)	0.40 (0.30–0.53)	<0.001
Chromophobe (*N* = 139)	0.14 (0.07–0.28)	<0.001
Collecting duct (*N* = 117)	0.43 (0.21–0.84)	0.02
Contemporary (2010–2014) (*N* = 382)	0.32 (0.22–0.48)	<0.001

CI = confidence interval; HR = hazard ratio.

Cancer Epidemiology 56 (2018) 118–125

Contents lists available at ScienceDirect

Cancer Epidemiology

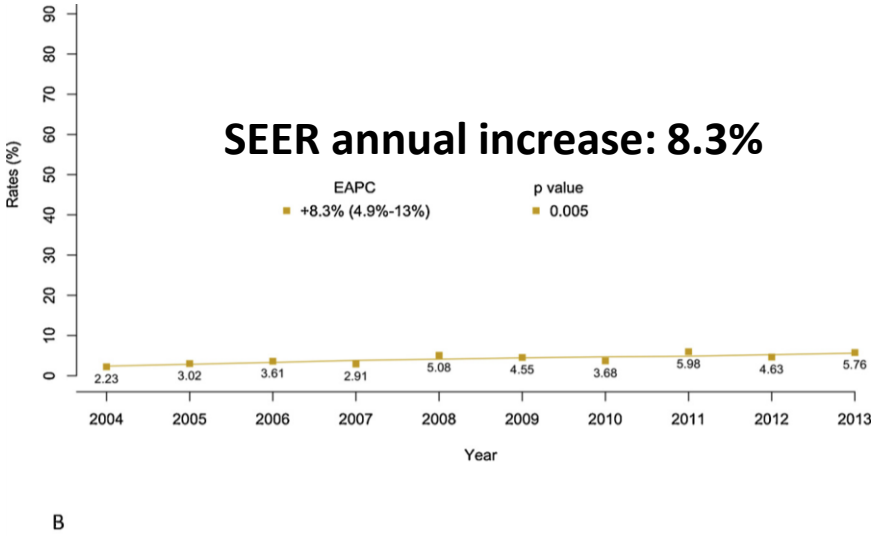
journal homepage: www.elsevier.com/locate/canep

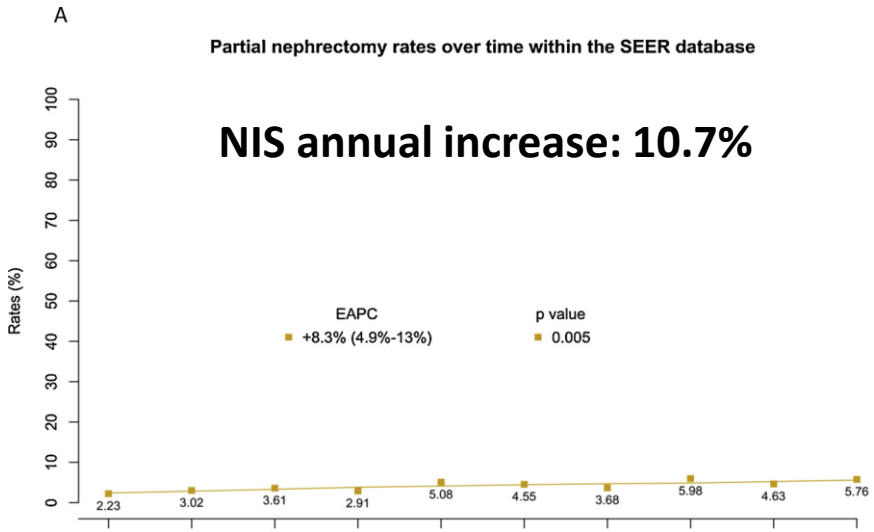
Partial nephrectomy seems to confer a survival benefit relative to radical nephrectomy in metastatic renal cell carcinoma

Elio Mazzone[a,b,c,*], Sebastiano Nazzani[a,d], Felix Preisser[a,e], Zhe Tian[a], Michele Marchioni[a,f], Marco Bandini[a,b,c], Umberto Capitanio[b,c], Anil Kapoor[g], Derya Tilki[e,h], Francesco Montorsi[b,c], Shahrokh F. Shariat[i], Fred Saad[a], Alberto Briganti[b,c], Pierre I. Karakiewicz[a]

Table 2
Baseline characteristics of 5138 patients with metastatic renal cell carcinoma within the Nationwide Inpatient Sample database, stratified according to surgery type with and without propensity score matching.

Variables	Initial Cohort				Propensity Score adjusted (Ratio 4:1)			
	Overall = 5138 (100%)	Radical nephrectomy = 4912 (95.6)	Partial nephrectomy = 226 (4.4)	p value	Overall = 1120 (100%)	Radical nephrectomy = 894 (79.8)	Partial nephrectomy = 226 (20.2)	p value





Survival benefit: partial vs. radical nephrectomy in metastatic RCC

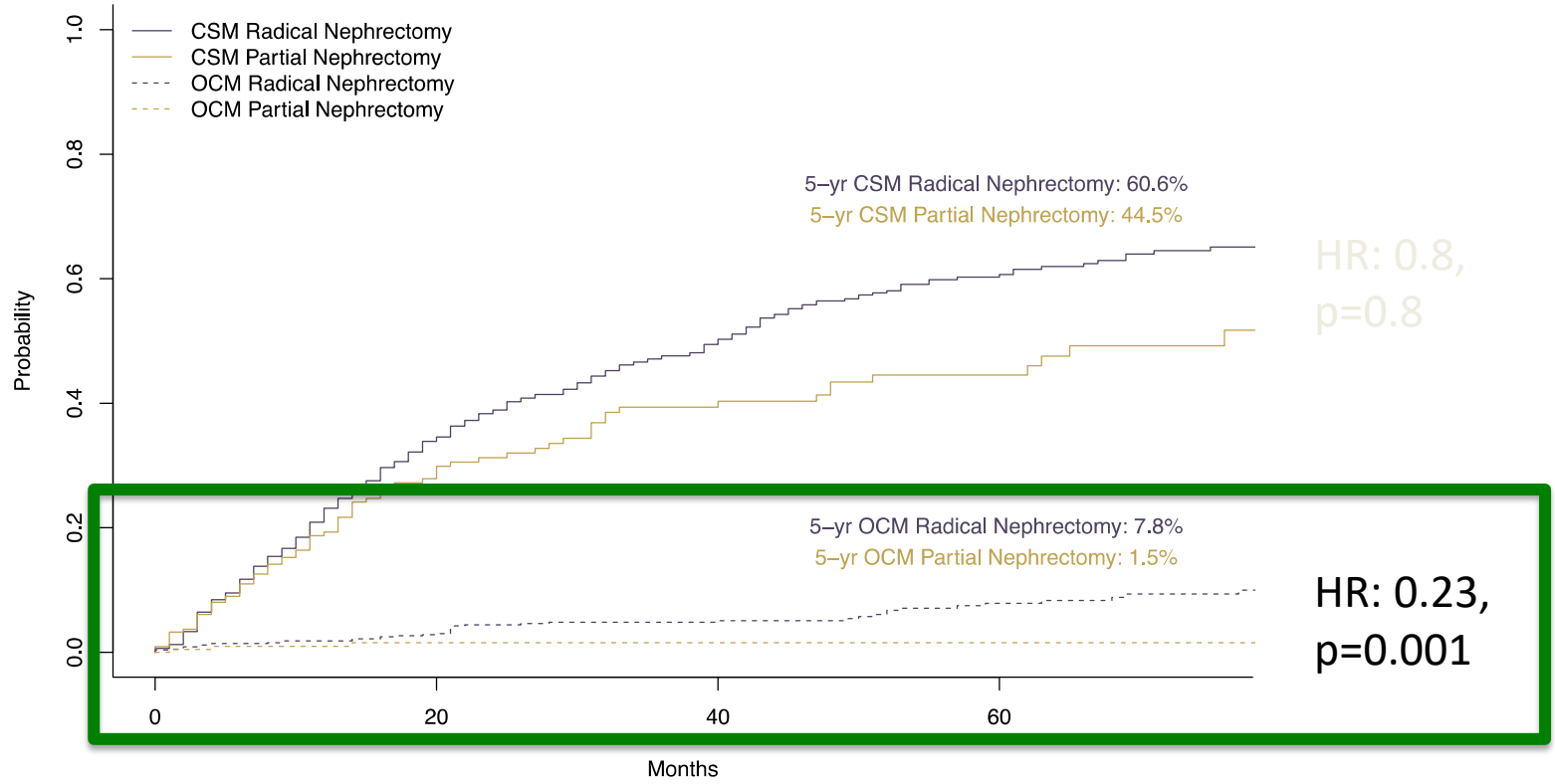
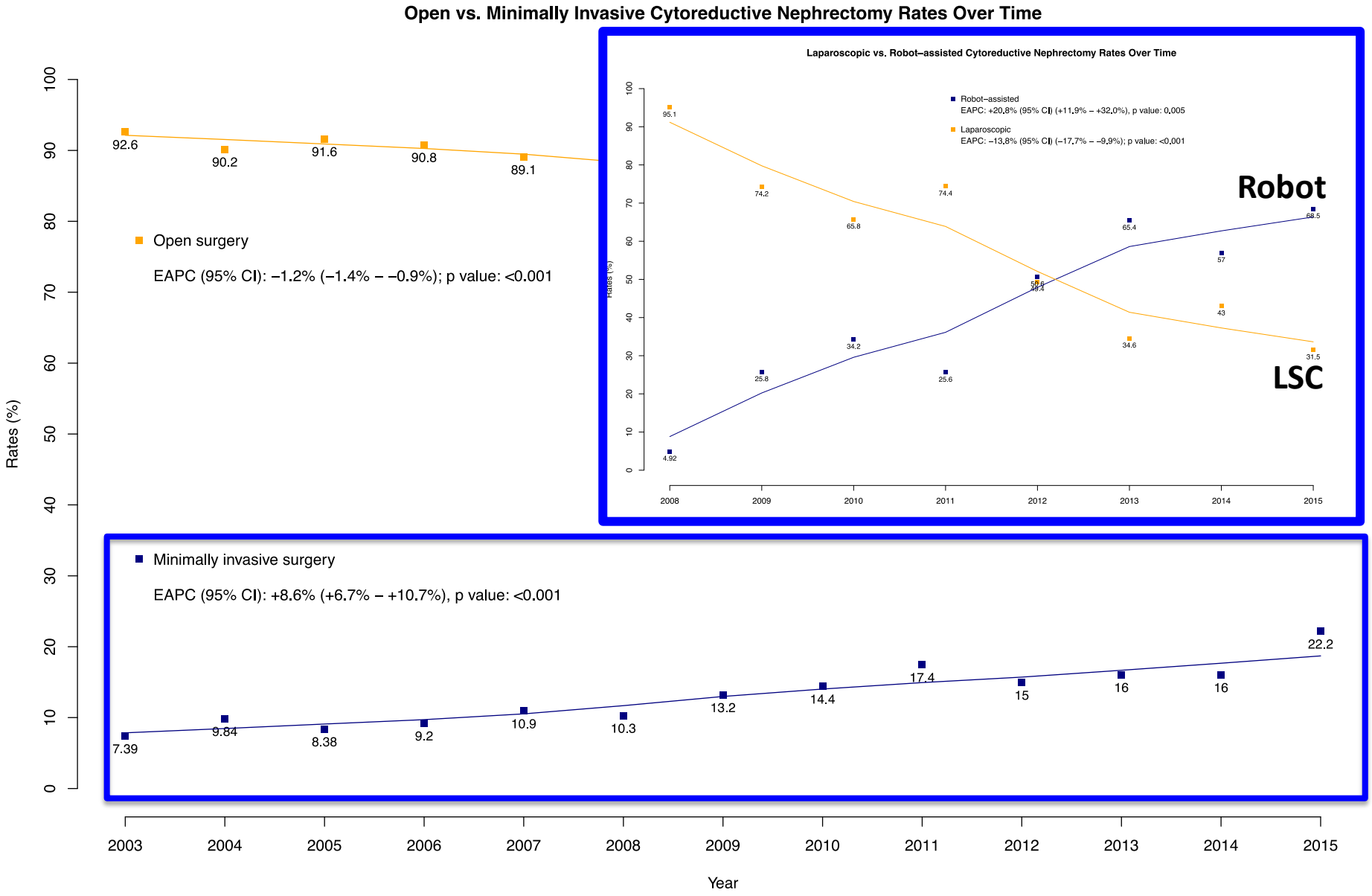


Fig. 2. Propensity score–matched cumulative incidence plots depicting cancer-specific mortality and other-cause mortality rates in patients with metastatic renal cell carcinoma, stratified according to nephrectomy type (Partial vs. Radical nephrectomy).

Multivariable competing-risks regression models[a] predicting cancer-specific mortality and other-cause mortality in patients with newly diagnosed metastatic renal cell carcinoma, after propensity-score matching (Ratio 4:1) adjustment.

Variable		Cancer-specific Mortality		Other-cause Mortality	
		Multivariable Model		Multivariable Model	
		HR (95% CI)	p value	HR (05% CI)	p value
	Partial Nephrectomy	0.8 (0.62-1.03)	0.08	0.23 (0.07-0.76)	0.01

Minimally invasive cytoreductive nephrectomy: NIS analysis



Minimally invasive vs. open cytoreductive nephrectomy: NIS analysis

Table 3. Multivariable analyses predicting early postoperative outcomes of metastatic renal cell carcinoma patients treated with open (N=3,304) vs. minimally invasive cytoreductive nephrectomy (N=839), after propensity score matching and adjustment for clustering. Analyses adjusted for year of diagnosis, age at diagnosis, race, gender, Charlson comorbidity index, insurance status, region, teaching status, hospital volume, bed-size, type of surgery (partial vs. radical nephrectomy) and site of metastases.

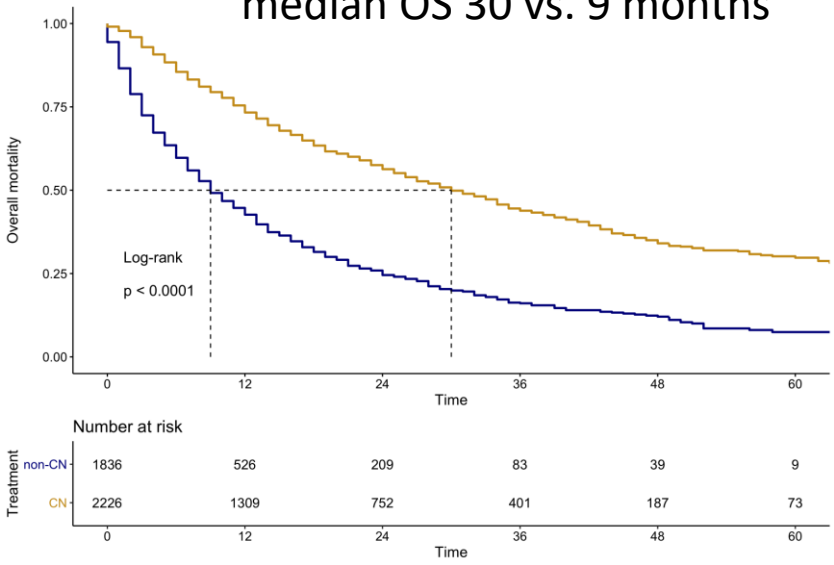
Outcome of interest		Odds ratio (95% Confidence interval)	p-value
Intraoperative complication		0.67 (0.46-1.00)	0.05
Postoperative complication			
	Overall	0.67 (0.57-0.79)	**<0.001**
	Transfusions	0.38 (0.31-0.47)	**<0.001**
	Vascular	0.49 (0.30-0.81)	**0.006**
	Cardiac	0.71 (0.51-0.98)	**0.04**
	Respiratory	0.68 (0.53-0.86)	**0.001**
	Genitourinary	1.18 (0.90-1.56)	0.2
	Infectious	0.77 (0.47-1.28)	0.3
	Wound	0.78 (0.40-1.51)	0.5
	Miscellaneous Medical	0.82 (0.68-0.99)	**0.045**
	Miscellaneous Surgical	0.59 (0.43-0.80)	**<0.001**
In-hospital mortality		0.72 (0.31-1.66)	0.4
Length of stay (Multivariable Poisson Regression model) *		0.82 (0.76-0.87) **	**<0.001**
Total Hospital Charges (Linear Regression Model) *		+ 2,145 $ (+656 $ – +3,634 $) ***	**0.005**

* Model additionally adjusted for all complications.

839 MIS CN → $1.8M cost increase Vs. open CN

Effect of cytoreductive nephrectomy on OS in mccRCC (2010-2015)

Overall cohort
4,062 patients: CN 2,226 (54.8%)
median OS 30 vs. 9 months

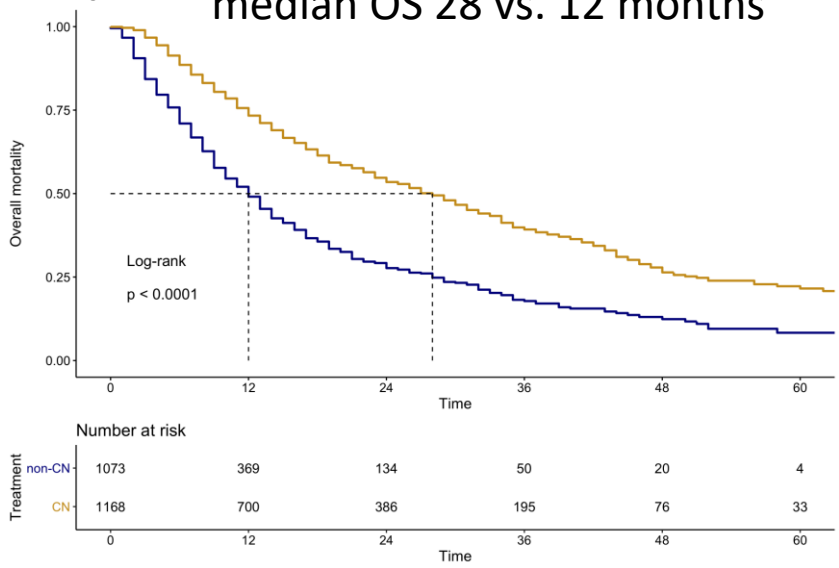


MVA CRR HR 0.43, p<0.001

PS matched MVA CRR: HR 0.45, p<0.001

Landmark analyses:
3 mos HR 0.49, p<0.001
6 mos HR 0.51, p<0.001

Targeted therapy cohort
2,241 patients: CN 1,168 (52.1%)
median OS 28 vs. 12 months

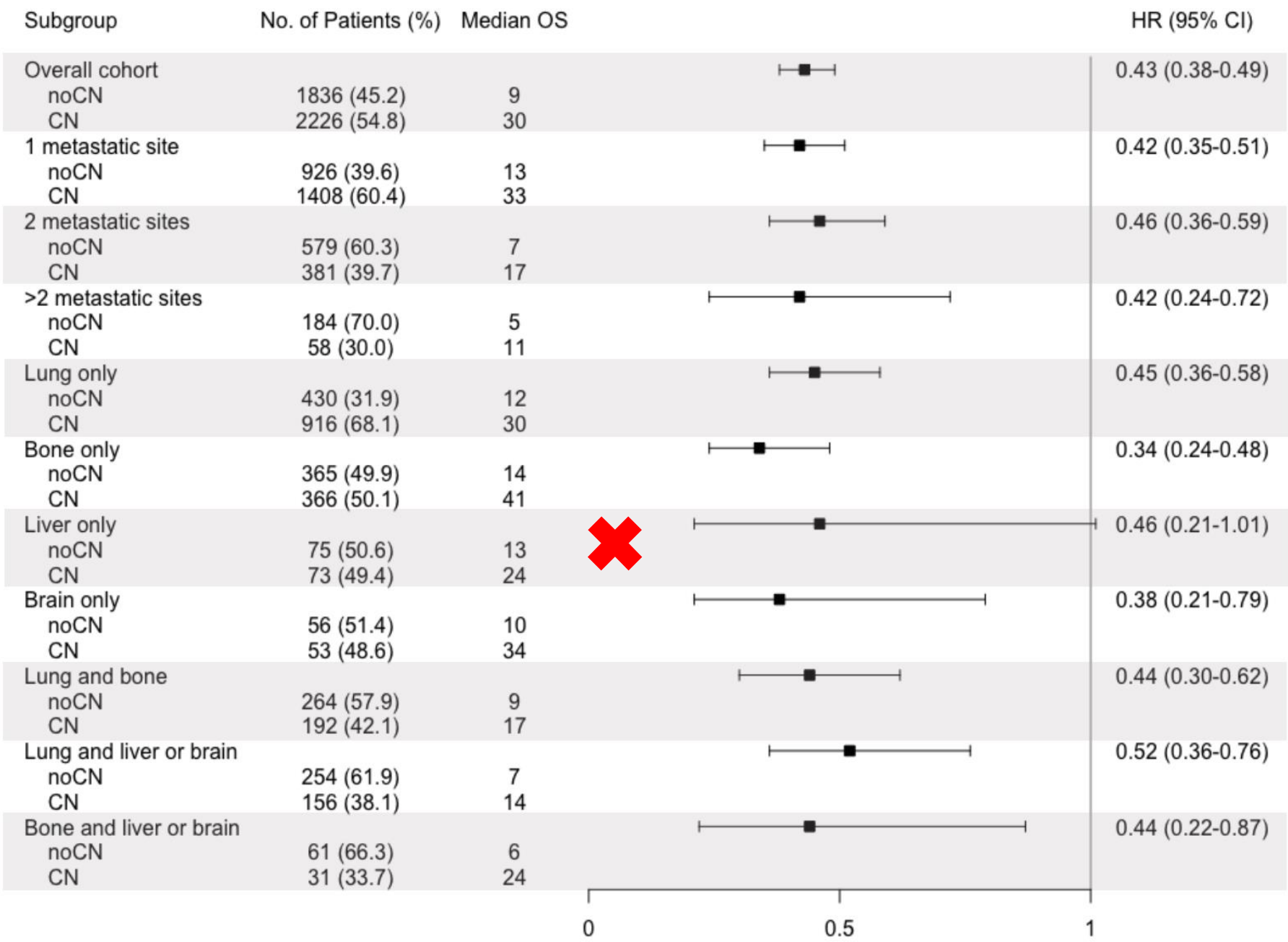


MVA CRR HR 0.49, p<0.001

PS matched MVA CRR: HR 0.50, p<0.001

Landmark analyses:
3 mos HR 0.41, p<0.001
6 mos HR 0.53, p<0.001

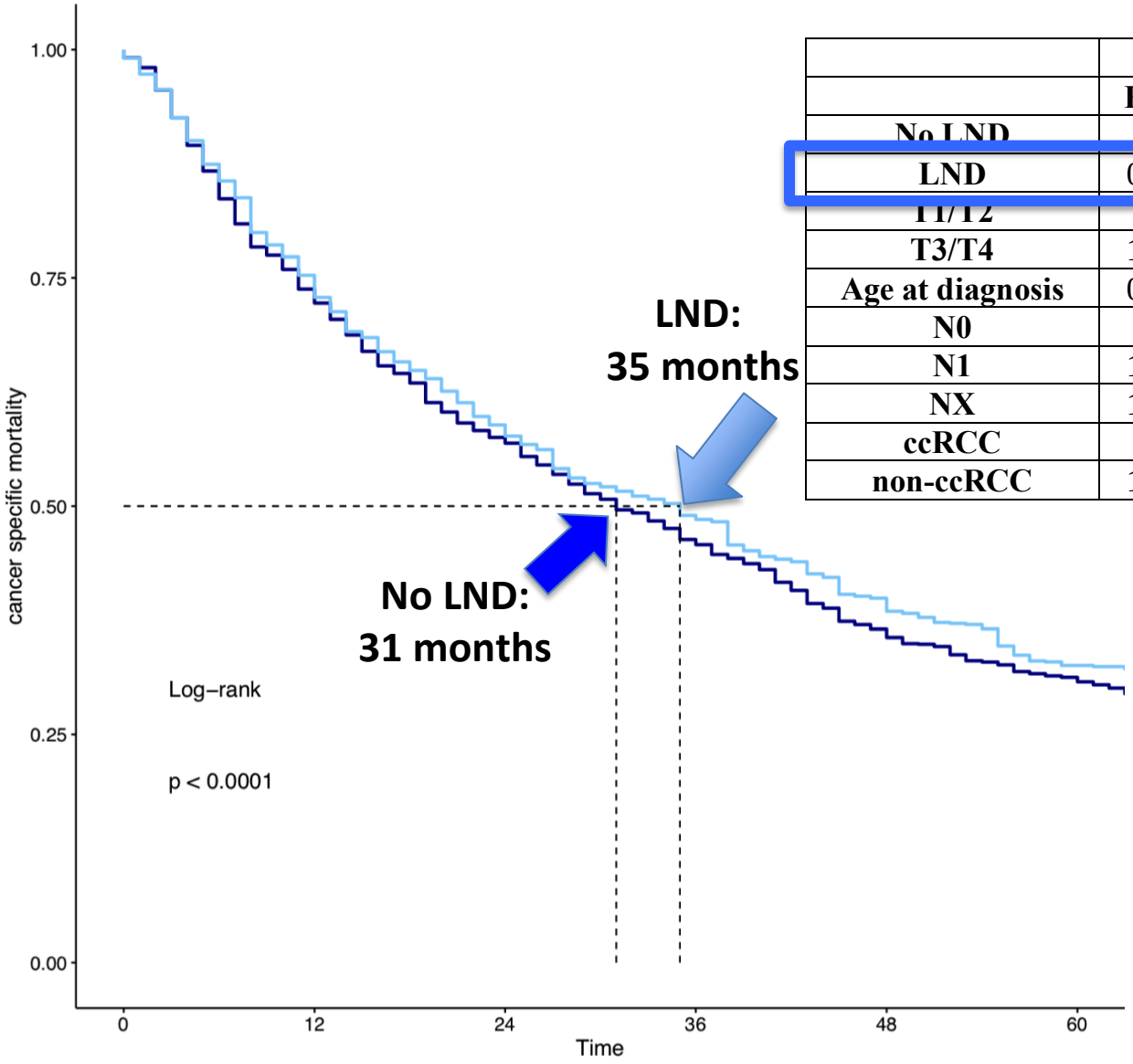
Effect CNT on OS: SEER 2010-2015



Incremental survival analyses of cytoreductive nephrectomy stratified by estimated survival time in patients with clear-cell metastatic renal cell carcinoma, identified within the Surveillance, Epidemiology, and End Results database from 2010 to 2015.

Overall cohort	**Median OS (months) non-CN**	**Median OS (months) CN**	**Incremental benefit (months)**	**p (log-rank)**	**HR (95% CI)*, p**
OS months	1	2	+1	<0.001	0.62 (0.47-0.82)
	no = 465	no =152			p=0.001
< 6	2	3	+1	<0.001	0.56 (0.46-0.69)
	no = 653	no = 300			p<0.001
< 12	3	6	+3	<0.001	0.62 (0.52-0.74)
	no = 868	no = 522			p<0.001
< 18	4	7	+3	<0.001	0.53 (0.45-0.62)
	no = 987	no = 682			p<0.001
< 24	4	9	+5	<0.001	0.61 (0.53-0.71)
	no = 1048	no = 780			p<0.001
< 36	5	11	+6	<0.001	0.53 (0.46-0.61)
	no = 1103	no = 916			p<0.001
TT cohort					
OS months	**Median OS (months) non-CN**	**Median OS (months) CN**	**Incremental benefit (months)**	**p (log-rank)**	**HR (95% CI)#, p**
< 3	2	3	+1	0.002	0.62 (0.35-1.13)
	no = 154	no =37			p=0.12
< 6	3	4.5	+1.5	<0.001	0.73 (0.54-1.00)
	no = 272	no = 124			p=0.054
< 12	5	7	+2	<0.001	0.83 (0.65-1.05)
	no = 439	no = 272			p=0.12
< 18	6	9	+3	<0.001	0.59 (0.48-0.72)
	no = 525	no = 375			p<0.001
< 24	7	10	+3	<0.001	0.72 (0.60-0.88)
	no = 566	no = 343			p=0.001
< 36	7	12	+5	<0.001	0.64 (0.53-0.76)
	no = 601	no = 517			p<0.001

Lymph node dissection at cytoreductive nephrectomy - SEER



	Multivariable Models			
	HR	2.5 %	97.5 %	p
No LND	Ref			
LND	0.85	0.79	0.92	<0.001
T1/T2	Ref			
T3/T4	1.43	1.31	1.55	<0.001
Age at diagnosis	0.99	0.99	1.00	0.1
N0	Ref			
N1	1.64	1.45	1.87	<0.001
NX	1.48	1.37	1.59	<0.001
ccRCC	Ref			
non-ccRCC	1.40	1.30	1.50	<0.001

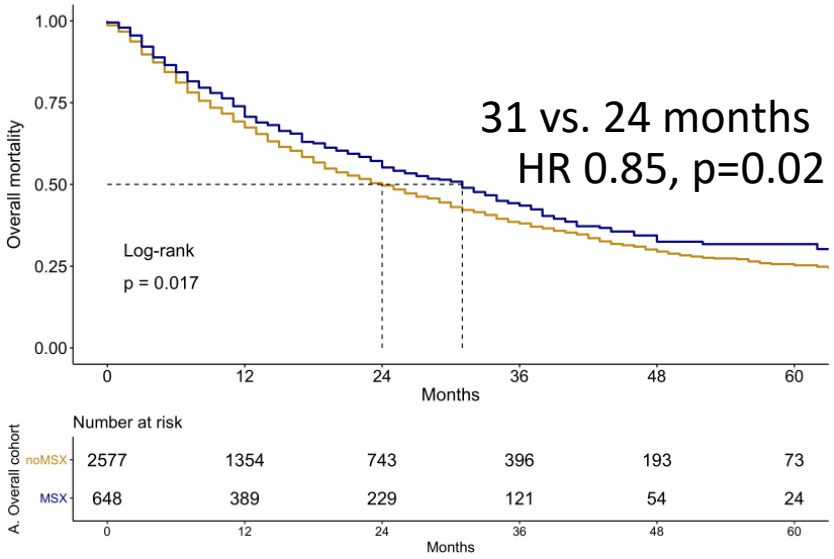
Overall=5,710 (100%)

No LND=3,394 (59.4%)

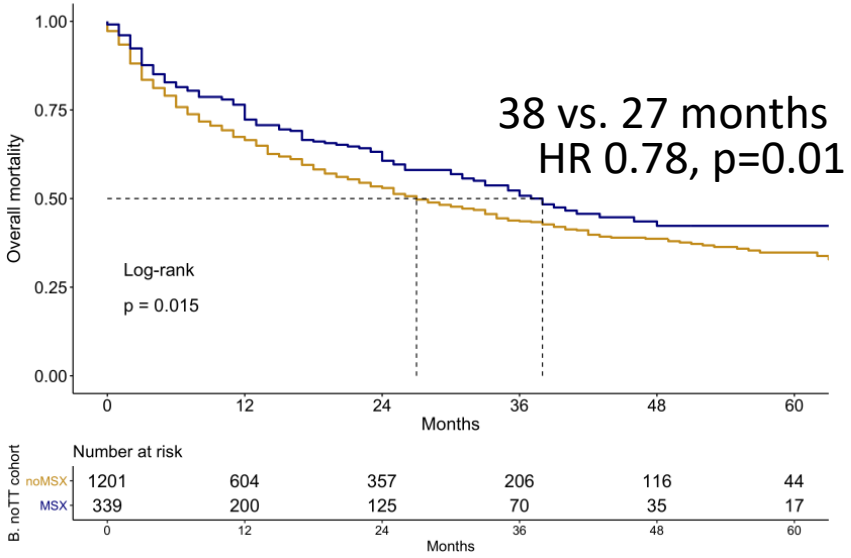
LND=2,316 (40.6%)

Effect of metastasectomy on OS in CNT patients: SEER 2010-2015

n=3,225 mRCC patients treated with CN, 648 (20.1%) received MSX



n=1541 no targeted therapy patients treated with CN, 339 received MSX



Sensitivity analyses:
PS matched n=321 MSX vs. 321 noMSX
MVA CRR models HR 0.76, p=0.03.

Landmark analyses:
- three-months: HR 0.78, p=0.03
- six-months HR 0.76, p=0.04

Metastatic cc renal carcinoma

Time trends of unmarried status according to gender

Descriptive characteristics of 6,975 patients (4,806 men and 2,169 women) with metastatic clear cell renal carcinoma within Surveillance, Epidemiology and End Results database (2004-2015), stratified according to marital status: married vs. unmarried.

		Male (n=4,806; 68.9%)			Female (n=2,169; 31.1%)		
		Unmarried (n=1,450; 30.2%)	**Married** (n=3,356; 69.8%)	**p-value**	**Unmarried** (n=1,018; 47.0%)	**Married** (n=1,151; 53.0%)	**p-value**
Age at diagnosis, n	Mean	60.6	63.1	**<0.001**	67.0	62.7	**<0.001**
	Median	60	63	**<0.001**	67	63	**<0.001**
	Interquartile Range	52-68	56-70		59-76	55-71	
Cytoreductive nephrectomy, n(%)	Performed	744 (51.3)	2,113 (63.0)	**<0.001**	518 (50.9)	735 (63.9)	**<0.001**
Metastasectomy, n(%)	Performed	220 (15.2)	655 (19.5)	**<0.001**	152 (14.9)	215 (18.7)	**0.02**
Systemic therapy, n(%)	Treated	656 (45.2)	1740 (51.8)	**<0.001**	431 (42.3)	571 (49.6)	**<0.001**

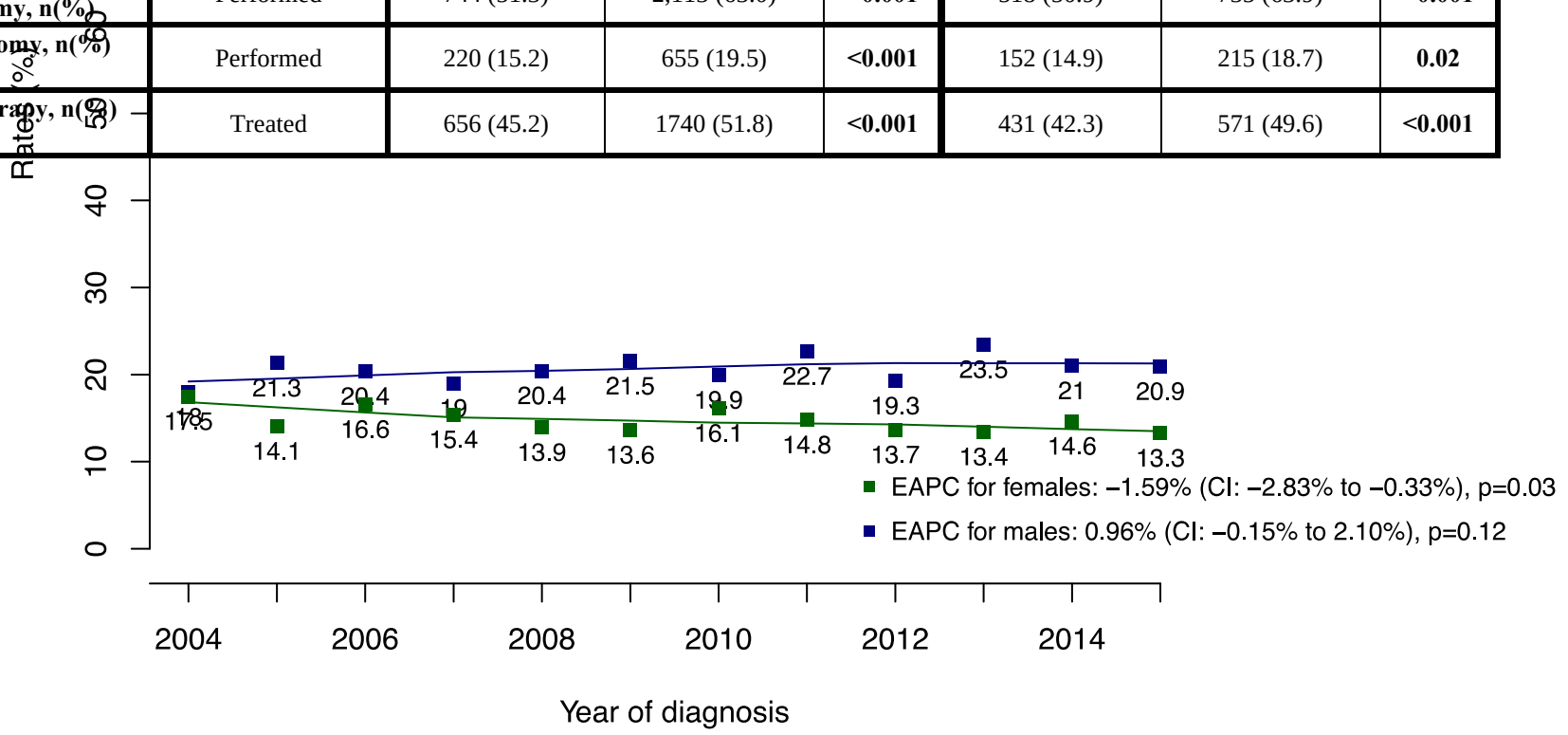


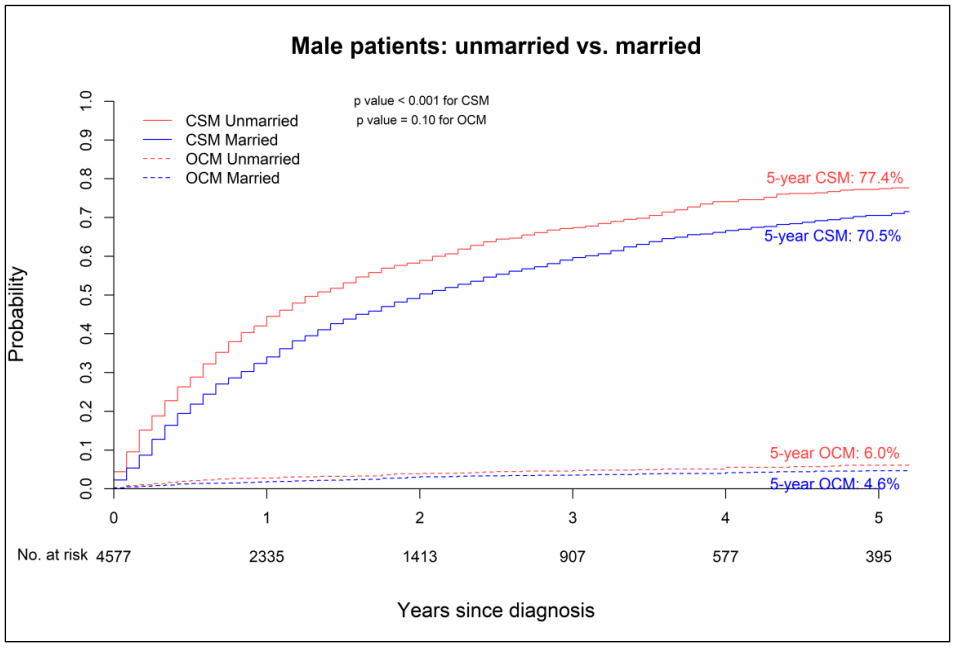
Table 2
Multivariable logistic regression analyses predicting rates of cytoreductive nephrectomy, metastasectomy and systemic therapy according to gender, in 6,975 patients with metastatic clear cell renal carcinoma.
!

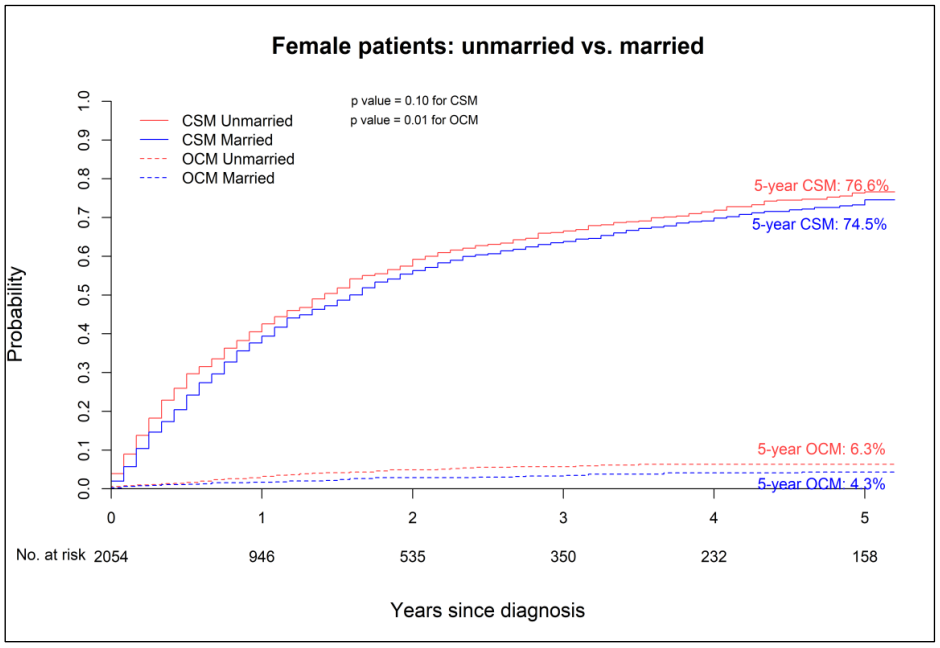
		Male			Female		
		Odds ratio	**Confidence Interval**	**p-value**	**Odds ratio**	**Confidence interval**	**p-value**
Cytoreductive nephrectomy	**Unmarried vs. Married**	0.54	0.45-0.65	**<0.001**	0.63	0.48-0.81	**<0.001**
Metastasectomy	**Unmarried vs. Married**	0.70	0.59-0.83	**<0.001**	0.83	0.65-1.05	0.1
Systemic therapy	**Unmarried vs. Married**	0.70	0.62-0.80	**<0.001**	0.80	0.67-0.96	**0.02**

Multivariable competing risk analyses predicting cancer-specific mortality and other-cause mortality, according to gender, in 6,975 patients (4,806 men and 2,169 women) with metastatic clear cell renal carcinoma.

		Cancer-specific mortality in males			Cancer-specific mortality in females		
		HR	**CI**	**p-value**	**HR**	**CI**	**p-value**
Marital status	**Unmarried vs. Married**	1.15	1.06-1.25	**<0.001**	0.97	0.86-1.09	0.6

		Other-cause mortality in males			Other-cause mortality in females		
		HR	**CI**	**p-value**	**HR**	**CI**	**p-value**
Marital status	**Unmarried vs. Married**	1.28	0.94-1.73	0.1	1.31	0.85-2.02	0.2





Cancer-specific mortality in males **Cancer-specific mortality in females**

		HR	CI	p-value	HR	CI	p-value
Marital status	**Unmarried vs. Married**	1.15	1.06-1.25	**<0.001**	0.97	0.86-1.09	0.6

!

Other-cause mortality in males **Other-cause mortality in females**

		HR	CI	p-value	HR	CI	p-value
Marital status	**Unmarried vs. Married**	1.28	0.94-1.73	0.1	1.31	0.85-2.02	0.2