RAAS INHIBITORS USE AND FACTORS ASSOCIATED WITH ADHERENCE IN CHILDHOOD CKD

Chien-Ning Hsu[1], Shiou-Huei Huang[1], You-Lin Tain[2]

[1]Departments of Pharmacy and [2]Pediatrics, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University, College of Medicine, Kaohsiung, Taiwan

INTRODUCTION & OBJECTIVES

■ Renin-angiotensin II-aldosterone system (RAAS) inhibitors are currently the best documented renal protective treatment strategy to prevent kidney disease progression.

■ It's unclear about the use and adherence to RAAS inhibitors in childhood CKD care setting.

■ Objective: to evaluate patient and clinical characteristics associated with medication adherence to chronic use of RAAS inhibitors in Taiwan youths with CKD.

METHODS

■ **Study population**: Children and adolescents aged < 20 years enrolled in the Taiwan national health insurance program (approximately 10 million youth)

■ **Study cohort**
- 51,846 children and adolescents were identified with CKD by ICD9 codes following KDOQI criteria with ≥2 ICD9 codes at different time and apart ≥ 90days for CKD at age < 20 yrs during 1997-2011.
- Patients were followed from the CKD date to receiving renal replacement therapy (RRT), death or censored.

■ **RAAS inhibitors assessment**
- Incident users of RAAS inhibitors were those who initiated with ACEI/ARB/aliskirin after the CKD date
- Only patients with RAAS inhibitors persistent therapy for at least 90 days with a permissible gap less than 30 days were analyzed
- Adherence measured by proportion of days covered (PDC): the number of follow-up days covered with medication divided by the total number of days in follow-up.

■ **Statistical analysis**
- Patients with PDC≥80% and <80% in the study period were compared with respect to baseline characteristics, groups of medication concomitantly used and comorbid conditions.
- A multivariate logistic regression analysis was conducted to assess baseline patient and medication-related factors (ie, age, sex, previous comorbid conditions, and the number of medication group) associated with high adherence (PDC ≥80%). Two-sided p values less than 0.05 were considered statistically significant.

- **Proportion of Days Covered for Concomitant Therapy**
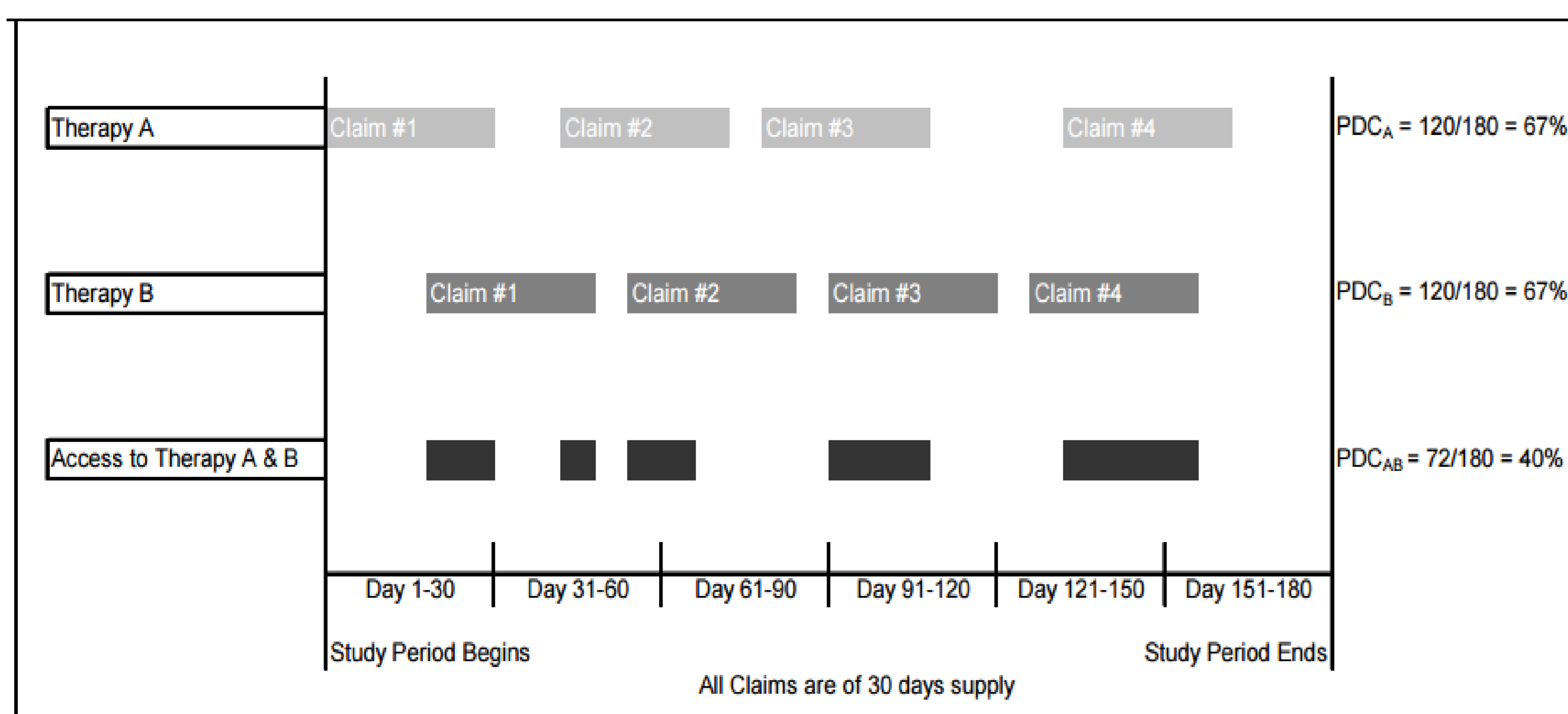
- PDC= proportion of days in the measurement period "covered" by the prescription for the same medication of another
- Strength of PDC measure: Avoid double counting of overlap period for the same drug

RESULTS

■ Of the 51,846 children diagnosed as having CKD, 7,174 (13.84%) children ever prescribed with RASI and 1,271 children met inclusion and exclusion criteria for chronic use.
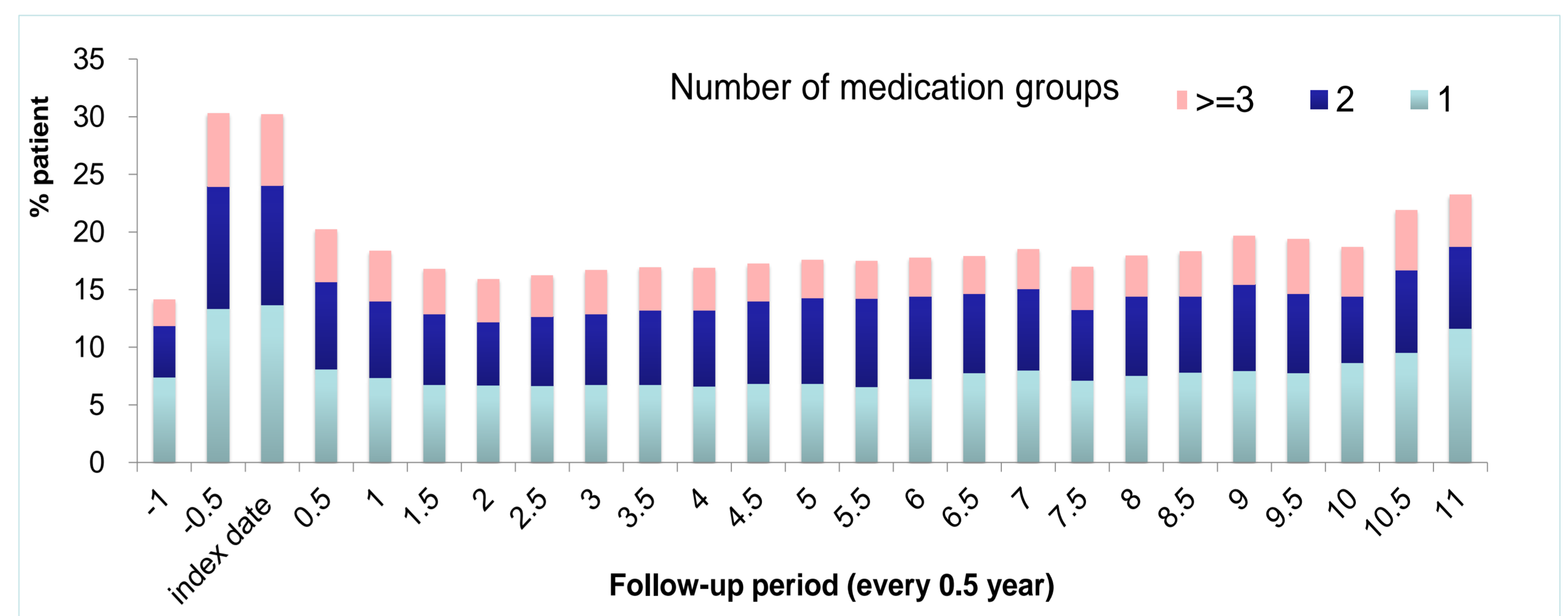
Trends in Pills Burden over time

Year/level	-1	-0.5	index date	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	5.5	6	6.5	7	7.5	8	8.5	9	9.5	10	10.5	11
1	7.39	13.34	13.64	8.10	6.75	6.72	6.65	6.73	6.77	6.60	6.84	6.84	6.58	7.27	7.75	7.91	7.14	7.34	7.79	7.11	7.76	8.63	9.52	11.61
2	4.43	10.59	10.38	7.58	6.62	6.10	5.43	6.01	6.17	6.42	6.60	7.11	7.40	7.62	7.11	6.88	7.08	6.13	6.87	6.60	7.45	6.87	5.76	7.14	7.10
≥3	2.30	6.39	6.21	4.57	4.39	3.94	3.75	3.59	3.81	3.73	3.67	3.29	3.35	3.29	3.39	3.27	3.45	3.75	3.55	3.91	4.26	4.78	4.32	5.24	4.52
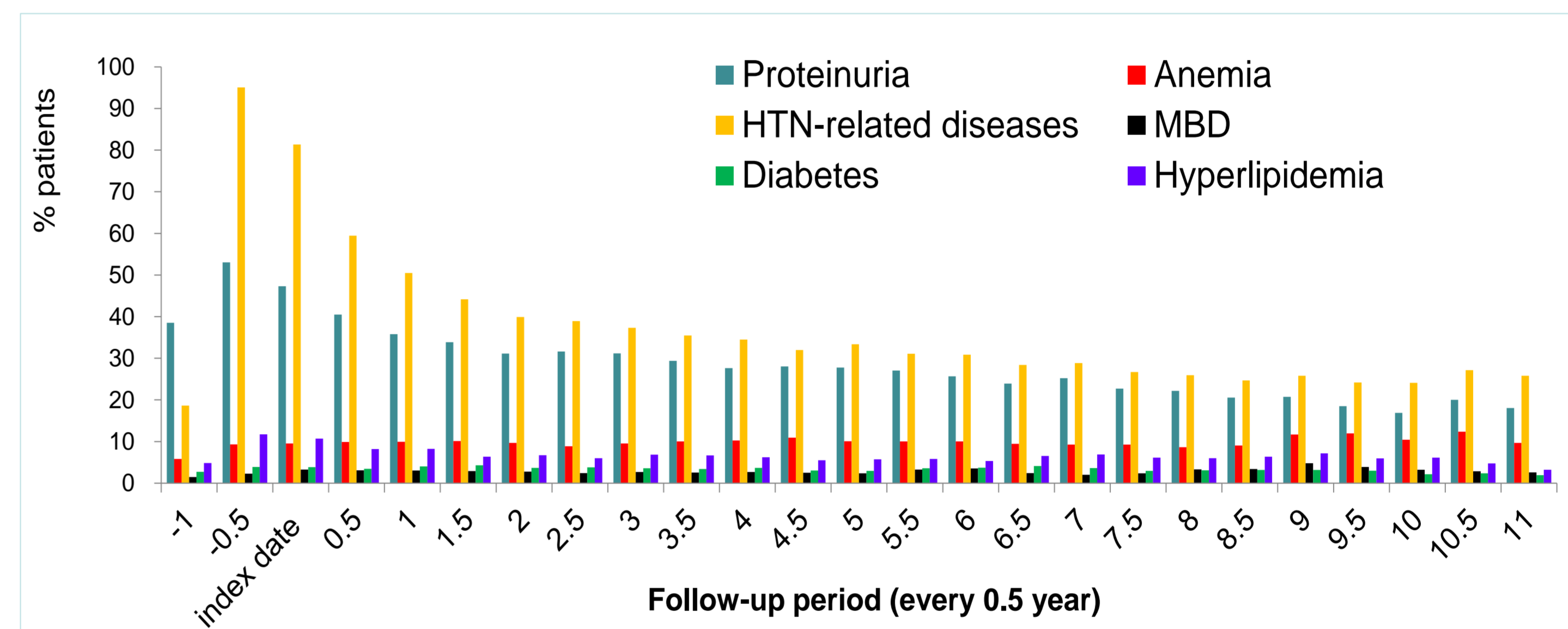
Trends in Comorbidity over time

Year	-1	-0.5	index date	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	5.5	6	6.5	7	7.5	8	8.5	9	9.5	10	10.5	11
n	1218	1237		1224	1161	1117	1066	1012	948	892	857	818	760	716	669	619	581	551	506	451	409	376	335	278	210	155

Tables. (A) Patient characteristics grouped by PDC. (B) Factors associated medication adherence to RAAS inhibitors chronic therapy (PDC≥80%)

A	Overall (n=1271)		PDC < 80% (n=1056)		PDC ≥ 80% (n=215)		P value
Age at start of chronic use, mean (SD), year	14.39 (4.86)		14.40 (4.79)		14.35 (5.19)		0.513
Sex							0.003
Female	621	48.86	496	46.97	125	58.14	
Male	650	51.14	560	53.03	90	41.86	
CKD diagnosis							
CAKUT	114	8.97	71	6.72	19	8.84	1.000
Glomerular diagnosis	859	67.58	699	66.19	160	74.42	0.020
Diabetes/hypertension/Gout-related	17	1.34	14	1.33	3	1.40	1.000
Nephrotic syndrome	310	24.39	275	26.04	35	16.28	0.002
Glomerulonephritis	301	23.68	267	25.28	34	15.81	0.003
Systemic lupus erythematous	308	24.23	206	19.51	102	47.44	<.0001
Others	488	38.39	430	40.72	58	26.98	<.0001
Nephritis	134	10.54	115	10.89	19	8.84	0.464
Bartter syndrome/Fabry disease	4	0.31	3	0.28	1	0.47	0.524
Proteinuria	191	15.03	166	15.72	25	11.63	0.143
Hematuria	148	11.64	131	12.41	17	7.91	0.062
CKD	65	5.11	57	5.40	8	3.72	0.396
miscellaneous	27	2.12	23	2.18	4	1.86	1.000
Time to RAAS chronic therapy, mean (SD), year	2.67 (2.55)		2.55 (2.46)		3.26 (2.89)		<.000

B	Adj.OR	95% CI	P value
Age at index date, years			
<4	1		
5-8	0.65	(0.30 1.43)	0.240
9-12	0.38	(0.17 0.82)	0.086
13-17	0.45	(0.22 0.93)	0.320
≥18	0.34	(0.16 0.72)	0.009
Male gender	0.68	(0.49 0.94)	0.018
Comorbid conditions			
Proteinuria	1.93	(1.18 3.17)	0.009
Anemia	1.76	(1.20 2.58)	0.004
HTN-related	0.32	(0.12 0.86)	0.023
Mineral bone disorders	1.06	(0.60 1.88)	0.837
Diabetes	0.92	(0.48 1.75)	0.791
Hyperlipidemia	1.09	(0.75 1.59)	0.656
Number of ATCs group (initial < 6 months)	1.31	(0.42 4.08)	0.645
Time to RASI chronic therapy	1.12	(1.06 1.19)	<.001
CKD diagnosis			
CAKUT	1		
Glomerular diagnosis	1.19	(0.59 2.39)	0.630
Others	0.70	(0.33 1.48)	0.349
≥ 2 types of diagnosis	0.64	(0.29 1.42)	0.273

adj.OR= adjusted Odds ratio

DISCUSSION/CONCLUSIONS

■ Only 13.8% study cohort ever treated with RASI, and 30% ever users were treated ≥3 months.

■ CKD-related comorbid conditions are only associated with initiating chronic use of RASI, but also medication adherence (PDC≥80%).

■ HTN-related comorbid conditions were prevalent in the study population, yet it discouraged the adherence to RASI chronic use.

■ Further research to understand medication tolerability and non-clinical characteristics associated medication adherence is warranted