

Long-term adherence to renin-angiotensin system inhibitors and beta blockers after heart failure hospitalization in senior patients

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Supplementary File

Supplementary Table 1: Long-term adherence trends for RASI in patients with CKD vs non-CKD.

	Adherence			trend
	1-year	2-year	3-year	p-value
CKD patients with RASI (n=1061)				
Mean adherence % (SD)	79 (25) ¹	76 (26) ¹	74 (27) ¹	<0.0001
Median adherence % (IQR)	89 (71, 96)	87 (67, 95)	85 (62, 94)	<0.0001
PDC category (n, %)				
1-50%	159 (15.0)	183 (17.3)	202 (19.0)	<0.0001
51-79%	188 (17.7)	246 (20.4)	225 (21.2)	0.11
≥80%	714 (67.3)	662 (62.3)	634 (59.8)	<0.0001
Number of deaths	172 (16.2%)	316 (29.8%)	434 (40.9%)	
Non-CKD patients with RASI (n=2415)				
Mean adherence % (SD)	84 (19) ¹	81 (21) ¹	79 (24) ¹	<0.0001
Median adherence % (IQR)	92 (79, 97)	90 (75, 96)	89 (73, 95)	<0.0001
PDC category (n, %)				
1-50%	209 (8.7)	274 (11.4)	304 (12.6)	<0.0001
51-79%	417 (17.3)	452 (18.7)	497 (20.6)	0.17
≥80%	1789 (74.0)	1689 (69.9)	1614 (66.8)	<0.0001
Number of deaths	267 (11.1%)	521 (21.6%)	710 (29.4%)	

Abbreviations: RASI: renin-angiotensin system inhibitors, CKD: chronic kidney disease, SD: standard deviation, IQR: interquartile range, PDC: proportion of days covered.

¹P-value for difference in mean adherence to RASI for CKD patients vs non-CKD patients, 1-year adherence (p<0.0001), 2-year adherence (p<0.0001), 3-year adherence (p=0.0017).

Supplementary Table 2: Long-term adherence trends for β -blockers in patients with COPD vs non-COPD.

	Adherence			trend
	1-year	2-year	3-year	p-value
COPD patients with β-blockers (n=548)				
Mean adherence % (SD)	69 (27) ¹	65 (29) ¹	63 (30) ¹	<0.0001
Median adherence % (IQR)	77 (52, 93)	72 (44, 91)	69 (39, 91)	<0.0001
PDC category (n, %)				
1-50%	129 (23.5)	158 (28.8)	170 (31.0)	<0.0001
51-79%	165 (30.1)	163 (29.7)	165 (30.1)	0.22
≥80%	254 (46.4)	227 (41.5)	213 (38.9)	<0.0001
Number of deaths	64 (11.7%)	151 (27.6%)	217 (39.6%)	
Non-COPD patients with β-blockers (n=1817)				
Mean adherence % (SD)	75 (25) ¹	72 (26) ¹	71 (26) ¹	<0.0001
Median adherence % (IQR)	84 (58, 95)	82 (55, 94)	80 (54, 93)	<0.0001
PDC category (n, %)				
1-50%	318 (17.5)	373 (20.5)	390 (21.5)	<0.0001
51-79%	480 (26.4)	493 (27.1)	516 (28.4)	0.63
≥80%	1019 (56.1)	951 (52.4)	911 (50.1)	0.004
Number of deaths	204 (11.2%)	372 (20.5%)	509 (28.0%)	

Abbreviations: RASI: renin-angiotensin system inhibitors, COPD: chronic obstructive pulmonary disease, SD: standard deviation, IQR: interquartile range, PDC: proportion of days covered.

¹P-value for difference in mean adherence to β -blockers in COPD patients vs non-COPD patients, 1-year adherence (p<0.0001), 2-year adherence (p<0.0001), 3-year adherence (p<0.0001).

Supplementary Table 3: Multivariable Cox regression models for predictors of first discontinuation (stop gap $\geq$ 90 days) for RASI and β -blockers at 3-year post heart failure discharge.

	RASI (n=3476)		β -blockers (n=2365)	
	HR, 95% CI	p-value	HR, 95% CI	p-value
Female	1.03 (0.90, 1.17)	0.71	1.04 (0.90, 1.19)	0.61
Age	1.02 (1.01, 1.03)	0.003	1.02 (1.01, 1.03)	0.004
Indigenous status	1.52 (0.98, 2.35)	0.06	1.30 (0.79, 2.14)	0.30
Private insurance	0.96 (0.83, 1.11)	0.57	0.88 (0.76, 1.02)	0.09
Year of admission	1.02 (0.98, 1.06)	0.41	0.94 (0.91, 0.98)	0.005
Prevalent HF (20 years prior to index admission)	1.09 (0.93, 1.26)	0.28	0.91 (0.77, 1.06)	0.23
Comorbidities				
IHD	0.90 (0.77, 1.04)	0.15	0.97 (0.81, 1.15)	0.69
Hypertension	1.02 (0.86, 1.20)	0.83	1.11 (0.92, 1.33)	0.28
AF	1.01 (0.88, 1.16)	0.87	1.08 (0.94, 1.25)	0.29
Diabetes	0.92 (0.79, 1.07)	0.27	1.04 (0.88, 1.21)	0.67
COPD	1.13 (0.98, 1.31)	0.09	1.36 (1.16, 1.59)	0.0001
CKD	1.35 (1.16, 1.56)	<0.0001	1.10 (0.95, 1.29)	0.20
PAD	1.05 (0.89, 1.25)	0.53	1.04 (0.88, 1.24)	0.64
Stroke	0.82 (0.66, 1.02)	0.07	1.05 (0.86, 1.29)	0.61
Charlson comorbidity score	1.04 (1.01, 1.08)	0.009	1.03 (1.01, 1.06)	0.04
Prior medications				
RASI	0.74 (0.63, 0.86)	<0.0001	0.70 (0.60, 0.81)	<0.0001
β -blockers	1.03 (0.89, 1.20)	0.65	0.67 (0.58, 0.77)	<0.0001
MRA	0.68 (0.48, 0.98)	0.04	0.90 (0.62, 1.29)	0.55
Digoxin	0.92 (0.69, 1.21)	0.54	1.04 (0.78, 1.39)	0.78
Statins	0.80 (0.69, 0.93)	0.004	0.98 (0.84, 1.15)	0.83
Diuretics	1.06 (0.91, 1.25)	0.45	1.10 (0.85, 1.21)	0.89
Warfarin	0.91 (0.75, 1.09)	0.32	0.83 (0.68, 1.01)	0.06
Antiarrhythmic agents	1.06 (0.82, 1.37)	0.67	1.51 (1.15, 1.96)	0.003
CCB	0.90 (0.77, 1.04)	0.16	1.22 (1.05, 1.42)	0.01
Antipsychotic/and psychoanaleptic agents	1.21 (1.04, 1.42)	0.02	1.14 (0.96, 1.35)	0.13
Number of drugs in previous 6 months prior to index admission	0.99 (0.96, 1.02)	0.35	0.98 (0.95, 1.01)	0.21
Interaction test^a				
Age*sex		0.61		0.33
Age*COPD		0.14		0.04
Age*CKD		0.08		0.32

^aUsed a univariate Cox model to test the interaction term.

Abbreviations: RASI: renin-angiotensin system inhibitors, HF: heart failure, IHD: ischaemic heart disease, AF: atrial fibrillation, COPD: chronic obstructive pulmonary disease, CKD: chronic kidney disease, PAD: peripheral artery disease, MRA: mineralocorticoid receptor antagonists, CCB: calcium channel blockers.

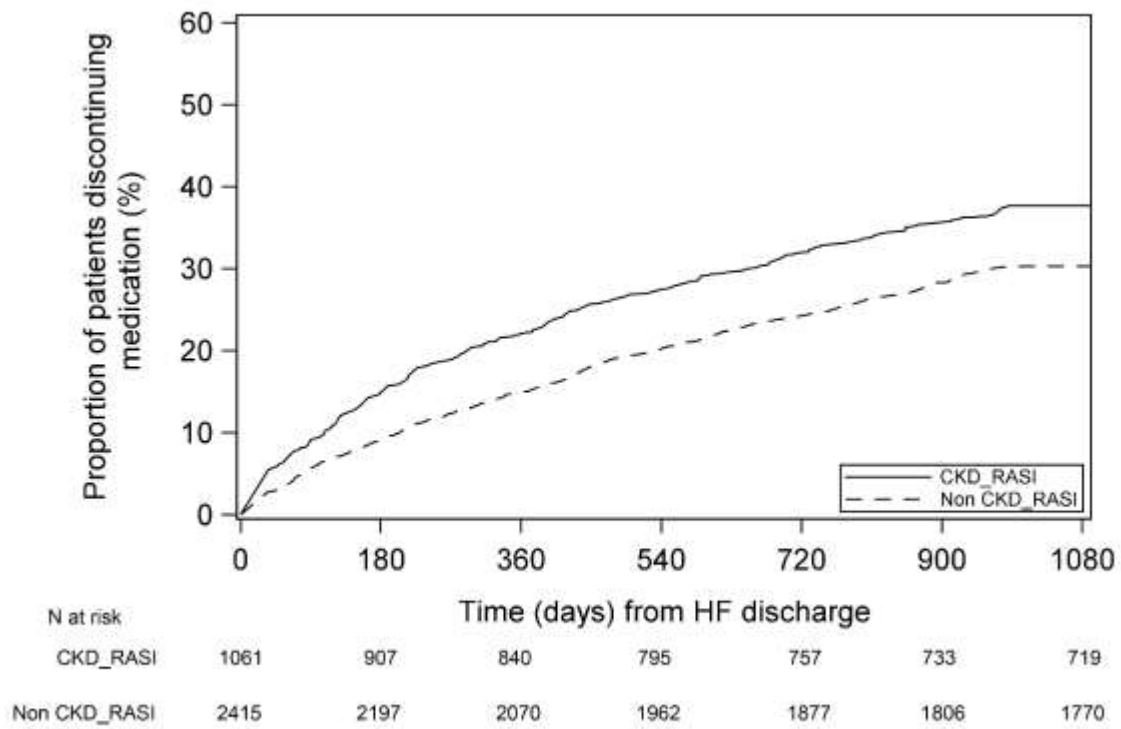
Supplementary Table 4: Multivariable logistic regression models for predictors of subsequent lower adherence (PDC<80%) to RASI and β -blockers after 1-year post heart failure hospital discharge.*

	RASI (n=2598)		β -blockers (n=1398)	
	OR, 95% CI	p-value	OR, 95% CI	p-value
Female	1.01 (0.91, 1.12)	0.86	1.15 (1.01, 1.32)	0.03
Age	1.03 (1.01, 1.04)	0.01	1.03 (1.01, 1.05)	0.02
Indigenous status	1.28 (0.91, 1.80)	0.16	0.77 (0.42, 1.39)	0.38
Private insurance	0.97 (0.92, 1.14)	0.72	0.99 (0.86, 1.14)	0.99
Year of admission	1.03 (0.96, 1.09)	0.49	0.94 (0.87, 1.01)	0.09
Prevalent HF (20 years prior to index admission)	0.99 (0.89, 1.10)	0.81	0.95 (0.82, 1.10)	0.47
HF readmission (identified post HF discharge)	1.00 (0.90, 1.12)	0.95	0.84 (0.72, 0.97)	0.02
Comorbidities				
IHD	0.93 (0.82, 1.05)	0.22	1.01 (0.83, 1.11)	0.55
Hypertension	1.05 (0.92, 1.20)	0.48	1.19 (0.98, 1.42)	0.08
AF	1.04 (0.93, 1.16)	0.55	0.96 (0.83, 1.11)	0.55
Diabetes	1.01 (0.90, 1.14)	0.82	1.14 (0.98, 1.32)	0.11
COPD	1.03 (0.92, 1.15)	0.59	1.06 (0.90, 1.24)	0.50
CKD	1.02 (0.91, 1.14)	0.74	0.87 (0.75, 1.01)	0.07
PAD	0.97 (0.86, 1.10)	0.64	0.98 (0.84, 1.16)	0.83
Stroke	1.04 (0.90, 1.21)	0.63	0.93 (0.76, 1.13)	0.45
Charlson comorbidity score	1.03 (0.98, 1.08)	0.30	1.04 (0.97, 1.11)	0.26
Prior medications				
RASI	1.04 (0.90, 1.20)	0.63	0.92 (0.78, 1.08)	0.31
β -blockers	1.09 (0.98, 1.22)	0.13	0.95 (0.83, 1.09)	0.44
MRA	1.08 (0.96, 1.21)	0.20	1.11 (0.96, 1.27)	0.17
Digoxin	0.91 (0.80, 1.04)	0.18	0.87 (0.73, 1.04)	0.12
Statins	0.92 (0.82, 1.03)	0.13	0.99 (0.84, 1.16)	0.88
Diuretics	1.02 (0.90, 1.15)	0.78	0.84 (0.72, 0.97)	0.02
Warfarin	0.88 (0.78, 1.00)	0.05	1.11 (0.95, 1.29)	0.19
Antiarrhythmic agents	0.99 (0.84, 1.16)	0.90	1.10 (0.88, 1.37)	0.39
CCB	0.99 (0.84, 1.16)	0.84	1.13 (0.93, 1.38)	0.22
Antipsychotics and psychoanaleptic agents	0.97 (0.87, 1.09)	0.63	0.99 (0.85, 1.16)	0.93
Number of drugs in previous 6 months prior to index admission	1.02 (0.99, 1.06)	0.17	0.96 (0.92, 1.00)	0.11
Prior 1-year medication adherence (high adherence as reference group)				
Low adherence to RASI	2.08 (1.83, 2.25)	<0.0001	1.12 (1.00, 1.30)	0.05
Low adherence to β -blockers	1.34 (1.11, 1.48)	<0.0001	2.73 (2.39, 3.10)	<0.0001

Abbreviations: RASI: renin-angiotensin system inhibitors, HF: heart failure, IHD: ischaemic heart disease, AF: atrial fibrillation, COPD: chronic obstructive pulmonary disease, CKD: chronic kidney disease, PAD: peripheral artery disease, MRA: mineralocorticoid receptor antagonists, CCB: calcium channel blockers.

*subsequent adherence is measured to death or at 2 years post hospital discharge whichever event occurred first.

Supplementary Figure 1: Discontinuation of RASI (gaps of 90 days or more) in patients with CKD vs no CKD.



Supplementary Figure 2: Discontinuation of β -blockers (gaps of 90 days or more) in patients with COPD vs no COPD.

