

Optimal medical therapy in the International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA)-Chronic Kidney Disease (CKD): A comparison of patients on and not on dialysis at baseline



Roy O. Mathew, David J. Maron, Rebecca Anthopolos, Jerome Fleg, Sean M. O'Brien, Frank Rockhold, Carlo Briguori, Marek Roik, Tomasz Mazurek, Robert Malecki, Upendra Kaul, Marius Miglinas, Ron Wald, David Charytan, Mandeep S. Sidhu, Judith S. Hochman, Sripal Bangalore

Background

Cardiovascular disease remains a leading cause of morbidity and mortality among patients with CKD. Single risk factor modification has demonstrated limited if any benefit in improving outcomes in advanced CKD. The efficacy of an aggressive multiple risk factor intervention approach (optimal medical therapy – OMT) to reduce major adverse cardiovascular events in patients with CKD G4-5 and CKD on dialysis (CKD G5D) has not been tested.

Objectives

The objective of the current analysis was to compare the ability to attain OMT goals over 2 years of follow-up between patients who, at baseline, had CKD G4-5 (not on dialysis) and CKD G5D. Additional objectives include evaluation of trends of individual goal attainment and cumulative OMT goal attainment at 2 years.

Methods

All randomized participants in ISCHEMIA-CKD were offered aggressive OMT. We modeled longitudinal trajectories of individual OMT components, including smoking cessation, systolic blood pressure (SBP) <140 mmHg (measurement method at site's discretion), low density lipoprotein cholesterol (LDL-C) <70 mg/dL, use of statins, and use of aspirin over study follow-up. We estimated the percentage point difference of risk factor goal attainment between patients in the CKD G4-5 and CKD G5D groups. We computed descriptive statistics of baseline variables in CKD G4-5 and CKD G5D patients separately.

Table 1: Baseline Characteristics of CKD G4-5 and CKD G5D

	CKD G4-5 (n=362)	CKD G5D (n=415)	P-value
Treatment			0.2091
CON	172/362 (48%)	217/415 (52%)	
INV	190/362 (52%)	198/415 (48%)	
DEMOGRAPHIC FEATURES			
Sex			0.7854
Male	247/362 (68%)	288/415 (69%)	
Female	115/362 (32%)	127/415 (31%)	
Age at randomization, years			0.0000
Median (Q1, Q3)	67 (59, 73)	61 (54, 67)	
Race (N (%))			0.0304
American Indian or Alaska Native	1/354 (0%)	4/393 (1%)	
Asian	85/354 (24%)	106/393 (27%)	
Native Hawaiian / Other Pacific Islander	2/354 (1%)	4/393 (1%)	
Black or African American	20/354 (6%)	43/393 (11%)	
White	245/354 (69%)	236/393 (60%)	
Multiple races	1/354 (0%)	0/393 (0%)	
CLINICAL CHARACTERISTICS (N (%))			
Diabetes	223/362 (62%)	221/415 (53%)	0.0230
Hypertension	330/361 (91%)	381/412 (92%)	0.6817
Current smoker	39/362 (11%)	45/415 (11%)	0.8232
Prior MI	69/362 (19%)	64/414 (15%)	0.2177
Prior heart failure	57/362 (16%)	78/415 (19%)	0.3058
Prior stroke	30/362 (8%)	38/415 (9%)	0.7638
Prior PVD	23/362 (6%)	25/415 (6%)	0.9673
Dialysis type			
Hemodialysis	N/A	344/409 (84%)	
Peritoneal dialysis	N/A	60/409 (15%)	
Other	N/A	5/409 (1%)	
Duration of dialysis, years (N=369 with information) (Median (Q1, Q3))	N/A	2 (1, 5)	
Prior renal transplant	7/362 (2%)	17/415 (4%)	0.1259
Renal transplant waitlist	10/342 (3%)	84/382 (22%)	0.0000
eGFR			0.0000
Median (Q1, Q3)	23 (17, 27)	7 (6, 9)	
Ejection fraction			0.4582
N	297	322	
Median (Q1, Q3)	58 (50, 64)	58 (50, 64)	
Prior PCI	68/362 (19%)	78/415 (19%)	1.0000
Prior CABG	15/362 (4%)	13/415 (3%)	0.5745

Results

Figure 1: Probability of individual OMT goal attainment over follow-up by dialysis status.

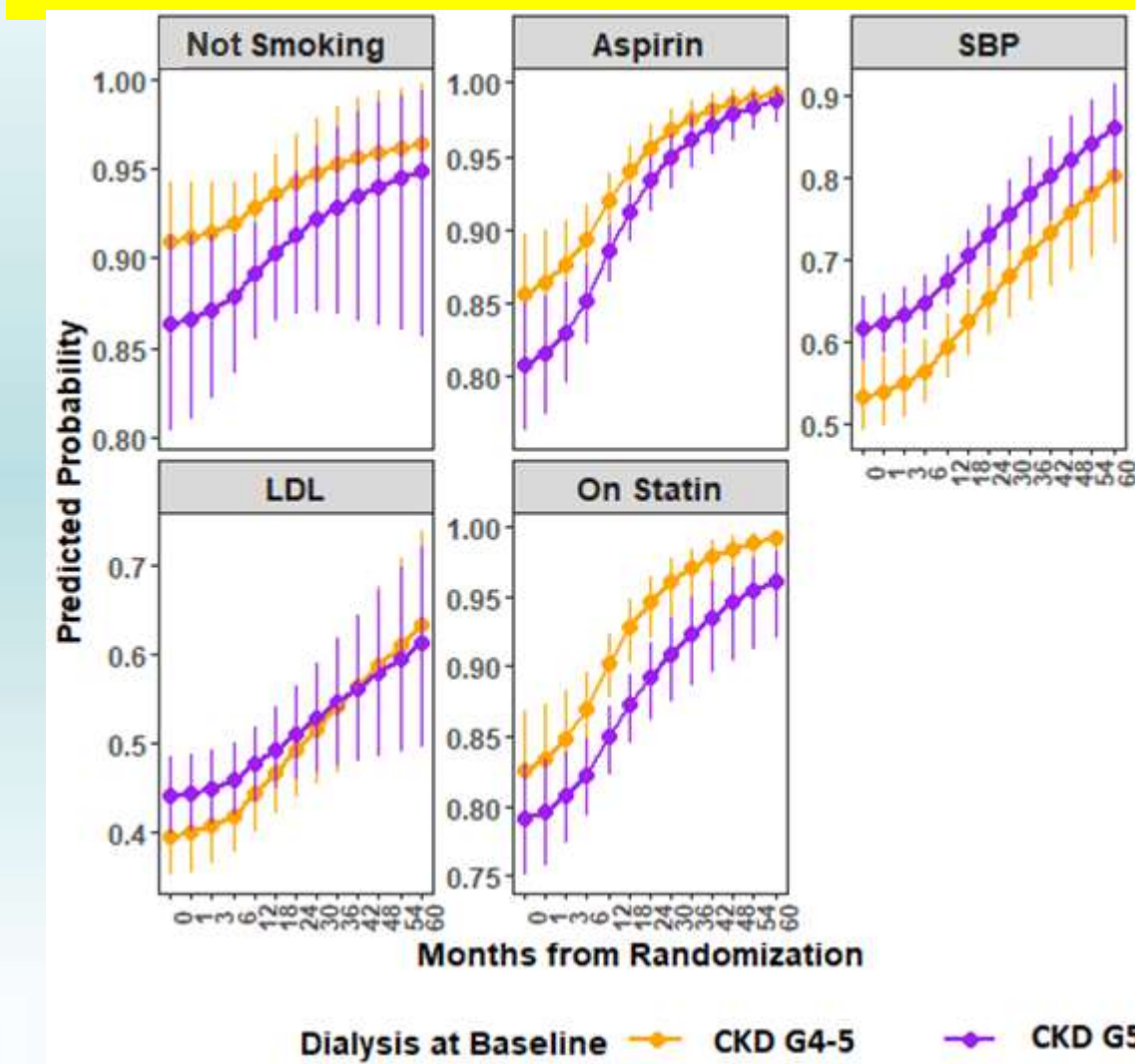


Figure 2: Difference in risk factor goal attainment and 95% credible intervals between CKD G4-5 and 5D, estimated in separate models by individual OMT goal. For example, compared to CKD G4-5 at 24 months, CKD G5D were approximately 5% less likely to be prescribed statins.

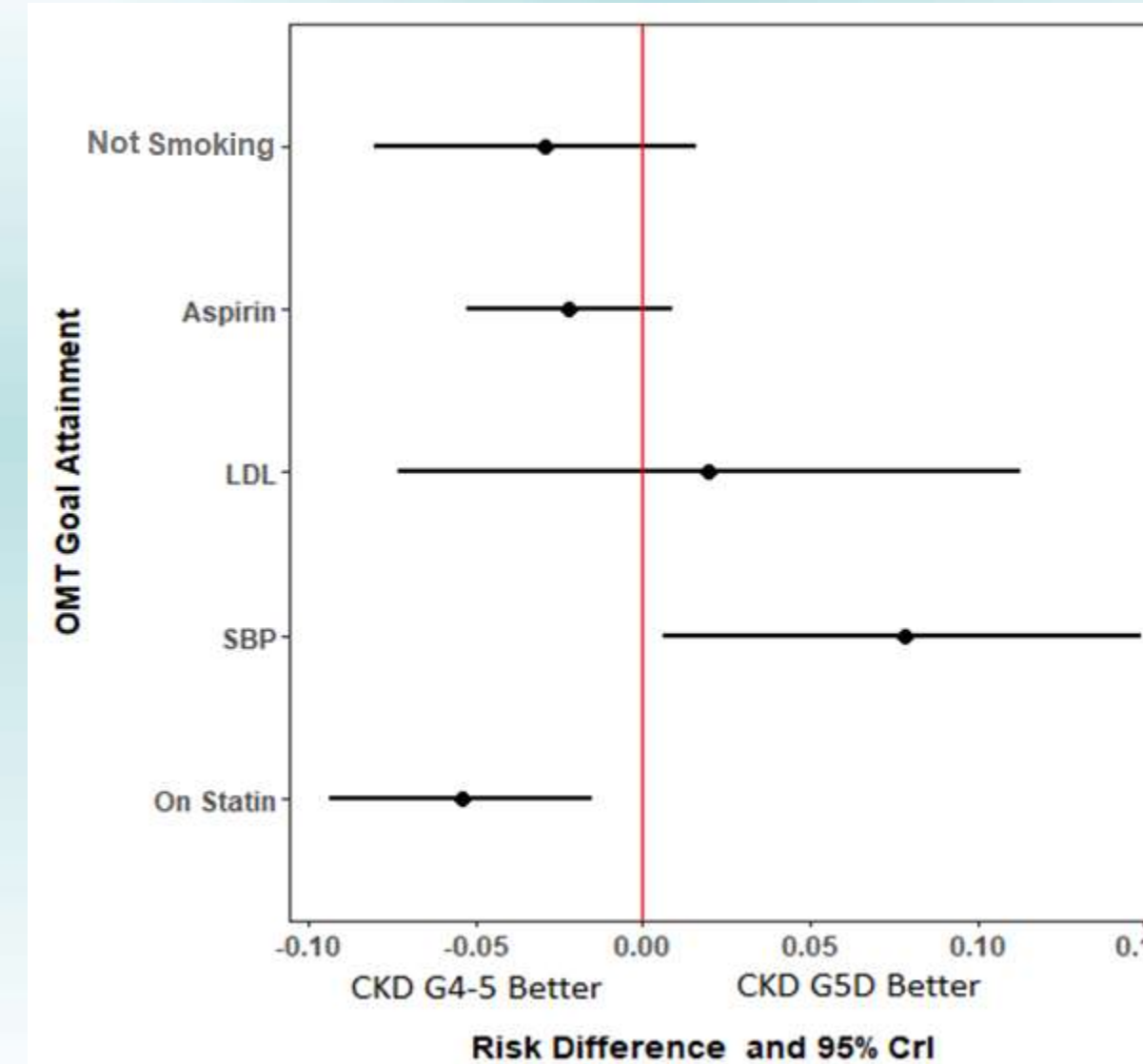
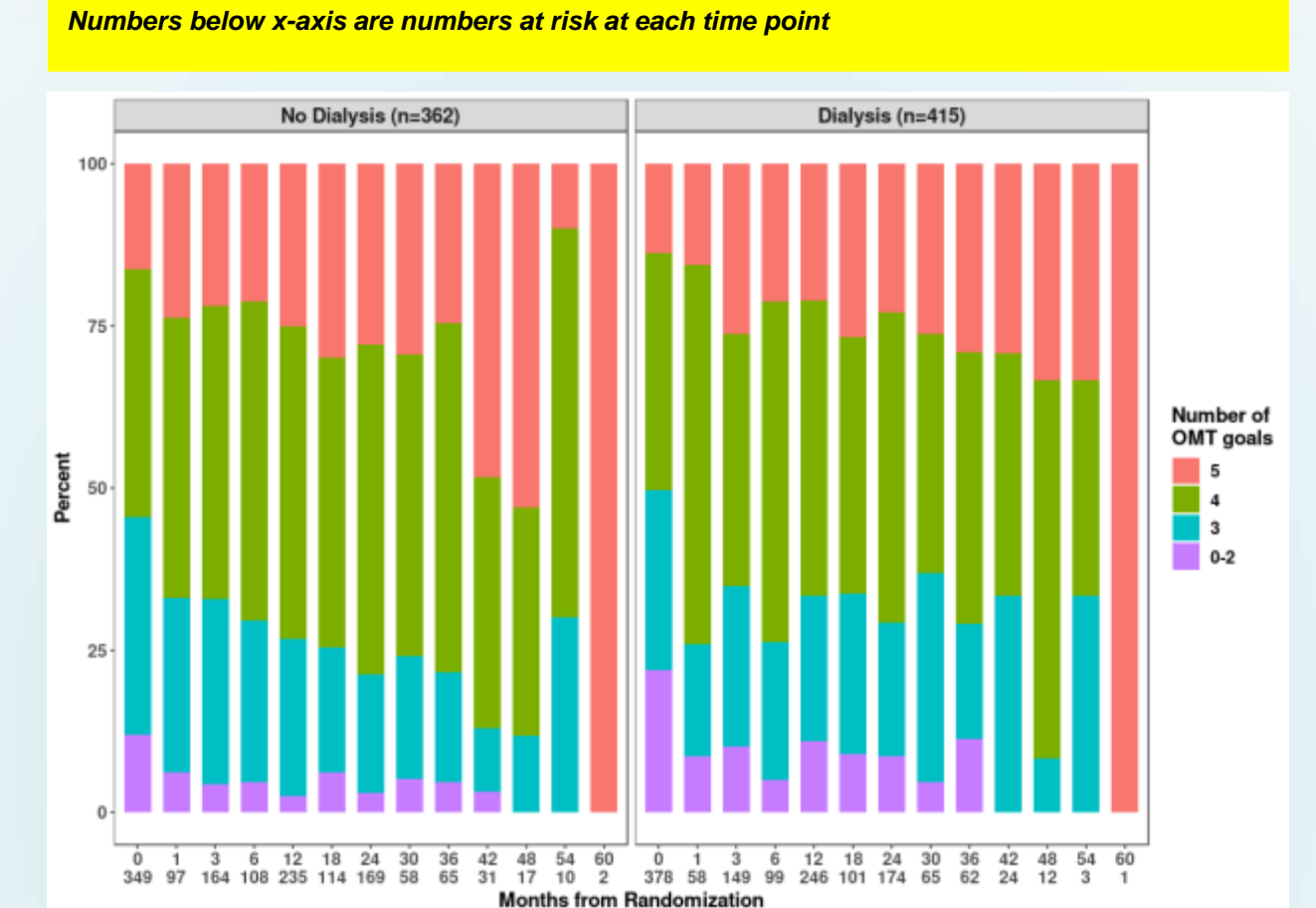


Figure 3. Percent OMT goal attainment by dialysis status at baseline. The count of non-missing values at each follow-up visit is appended below the visit month.



Limitations

- Observational analysis may lead to residual confounding of OMT goal attainment.
- OMT goals (statins and BP in CKD G5D) may have been strongly influenced by prevailing guidelines.
- Dialysis treatments themselves may have altered some parameters such as BP – which may have led to differences between CKD G4-5 and CKD G5D. -65 patients in CKD G4-5 started dialysis during follow-up

Conclusions

- Aggressive multifocal risk factor modification resulted in marked increase in the achievement of pre-specified targets for cardiovascular risk modification in patients with advanced CKD.
 - At baseline, 87.1% of patients with CKD G4-5 and 88.1% of CKD G5D had >2 risk factors at goal. By 24m, it had increased to 92.6% in CKD G4-5 and 93.2% for CKD G5D (difference 0.59%, 95% CrI -1.8 – 3.0%).
- Patients with CKD G5D were more likely to achieve SBP goal than CKD G4-5.
- CKD G4-5 were treated with statins more often than CKD G5D.
- Future studies should explore systemic and patient related barriers to attainment of OMT in this high-risk cohort.