Decline in eGFR in HCV-Infected Patients While on Treatment With Sofosbuvir/Ledipasvir or PrOD Regimens Is Not Dependent on Baseline eGFR

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Introduction

- Treatment with newer direct-acting antiviral (DAA) regimens against HCV demonstrates high SVR rates achieved in patients with advanced chronic kidney disease (CKD)
- There have been reports of newer DAA regimens being associated with increased and accelerated progression of kidney disease
- Renal elimination of some of these drugs may be a potential cause of toxicity, particularly among those with preexisting renal impairment
- However, progression of CKD among persons treated with DAA is still poorly understood

Aims

- To determine the proportion of persons who have a decline in renal function while being treated with 2 commonly used DAA regimens, sofosbuvir/ledipasvir (SOF/LDV) and paritaprevir/ritonavir/ombitasvir + dasabuvir (PrOD)

Methods

- We used the Electronically Retrieved Cohort of HCV Infected Veterans (ERCHIVES), a well-established national cohort of HCV-infected persons and age-, sex-, and race-matched controls who received care within any of the Veterans Health Administration (VHA) healthcare facilities
- Demographic, clinical, laboratory, pharmacy, utilization, and vital status data are retrieved from VHA's Corporate Data Warehouse (CDW)
- Patients initiated on SOF/LDV or PrOD were included. We identified those with ≥2 eGFR 3 months apart and prior to baseline and ≥1 eGFR value ≥12 weeks after baseline. eGFR was estimated using the CKD-EPI equation
- HIV- and hepatitis B surface antigen-positive persons were excluded
- CKD stages were classified from stage 1 through 5 using the National Kidney Foundation criteria
- We calculated the proportion of persons who had a decline in eGFR of 10 or 30 mL/min/1.73 m² from baseline
- Mean eGFR was plotted by regimen and use of ribavirin

Results

Table 1. Baseline characteristics

| Characteristic	SOF/LDV no RBV N = 9,837	SOF/LDV+RBV N = 3,826	P-value	PrOD N = 1,017	PrOD+RBV N = 2,944	P-value
Age, median (IQR)	62 (58, 65)	62 (58, 65)	0.18	63 (59, 66)	62 (58, 65)	<0.01
Race/ethnicity, %						
White	45.7	54		37.8	47.1	
Black	37.9	26.7	<0.01	44.1	33.1	<0.01
Hispanic	2.8	4.8		3	3.4	
Other	13.6	14.5		15.1	16.4	
Sex (M), %	96.3	97.5	<0.01	97.6	97.6	0.97
HCV RNA, log₁₀, median (IQR)	6.00 (4.68, 6.51)	5.85 (2.71, 6.45)	<0.01	6.01 (4.75, 6.51)	6.05 (3.41, 6.58)	0.61
Diabetes, %	32.9	41.3	<0.01	31.4	30	0.42
Cardiovascular disease, %	18.9	16.2	<0.01	15	13.2	0.14
FIB-4 score, median (IQR)	2.15 (1.50, 3.33)	3.32 (2.04, 6.00)	<0.01	1.89 (1.44, 2.58)	2.35 (1.61, 3.80)	<0.01
Cirrhosis (by FIB-4 >3.5), %	28.5	10.8	<0.01	47.3	22.9	<0.01
eGFR, mL/min/1.73 m², median (IQR)	82.0 (67.4, 96.0)	84.0 (69.0, 99.0)	<0.01	82.0 (67.0, 96.4)	83.4 (71.0, 97.3)	<0.01

Figure 1. Study flow sheet
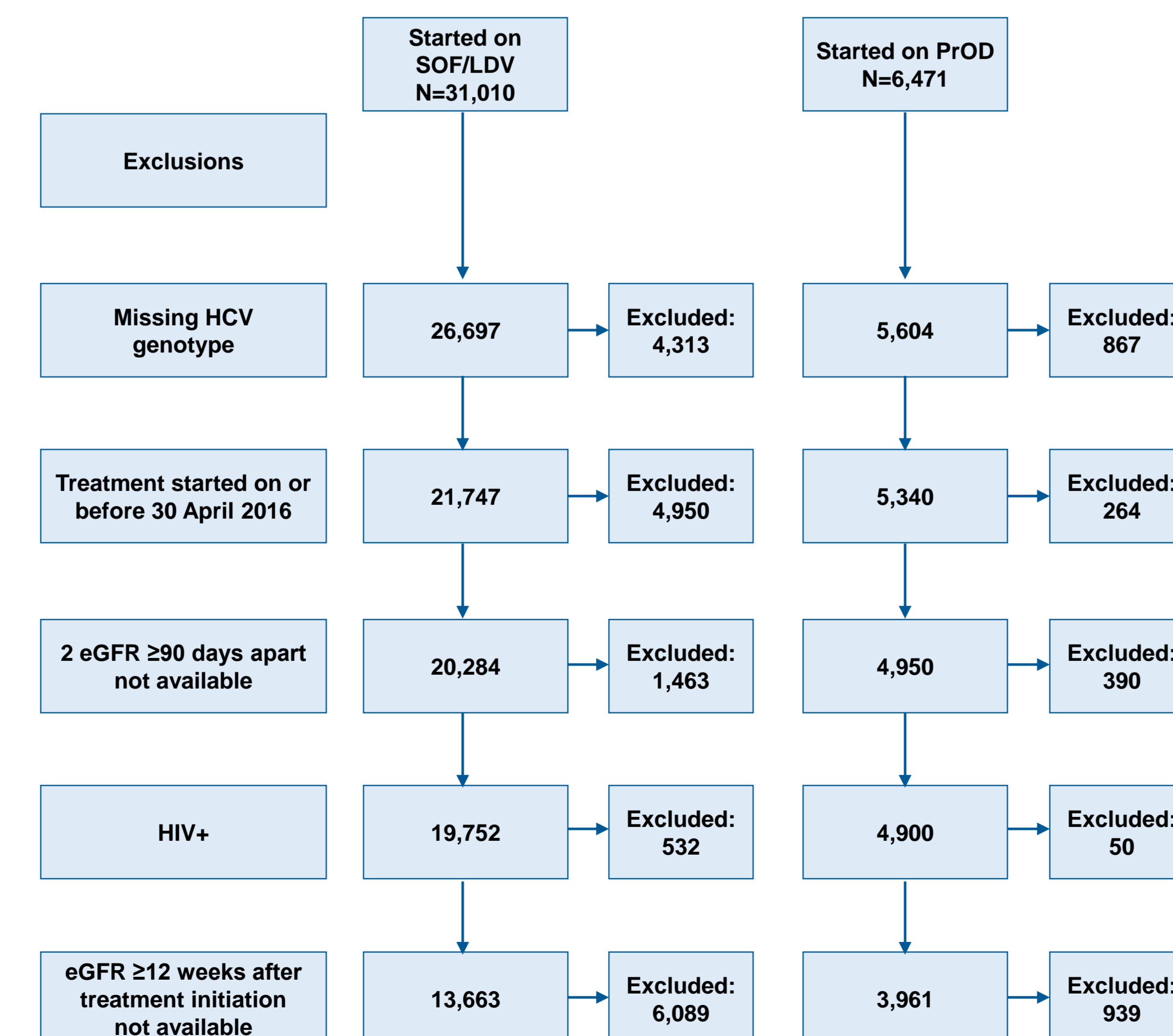
Table 2. eGFR decline of >10 mL/min/1.73 m² by regimen and baseline eGFR

Baseline eGFR/CKD Stage (mL/min/1.73 m²)	N	% With Decline in eGFR >10 ml/min/1.7 3m²				P-value
		SOF/LDV No RBV	SOF/LDV +RBV	PrOD No RBV	PrOD +RBV	
eGFR ≥60	15,086	33.1	37.8	30.1	33.2	0.03
CKD stage 3 (eGFR 30-59)	2,281	16.5	15.9	17.5	14.1	0.58
CKD stages 4-5 (eGFR <30)	257	6.5	3.3	1.8	0	0.03

Results (continued)

Figure 2. eGFR decline by DAA regimen
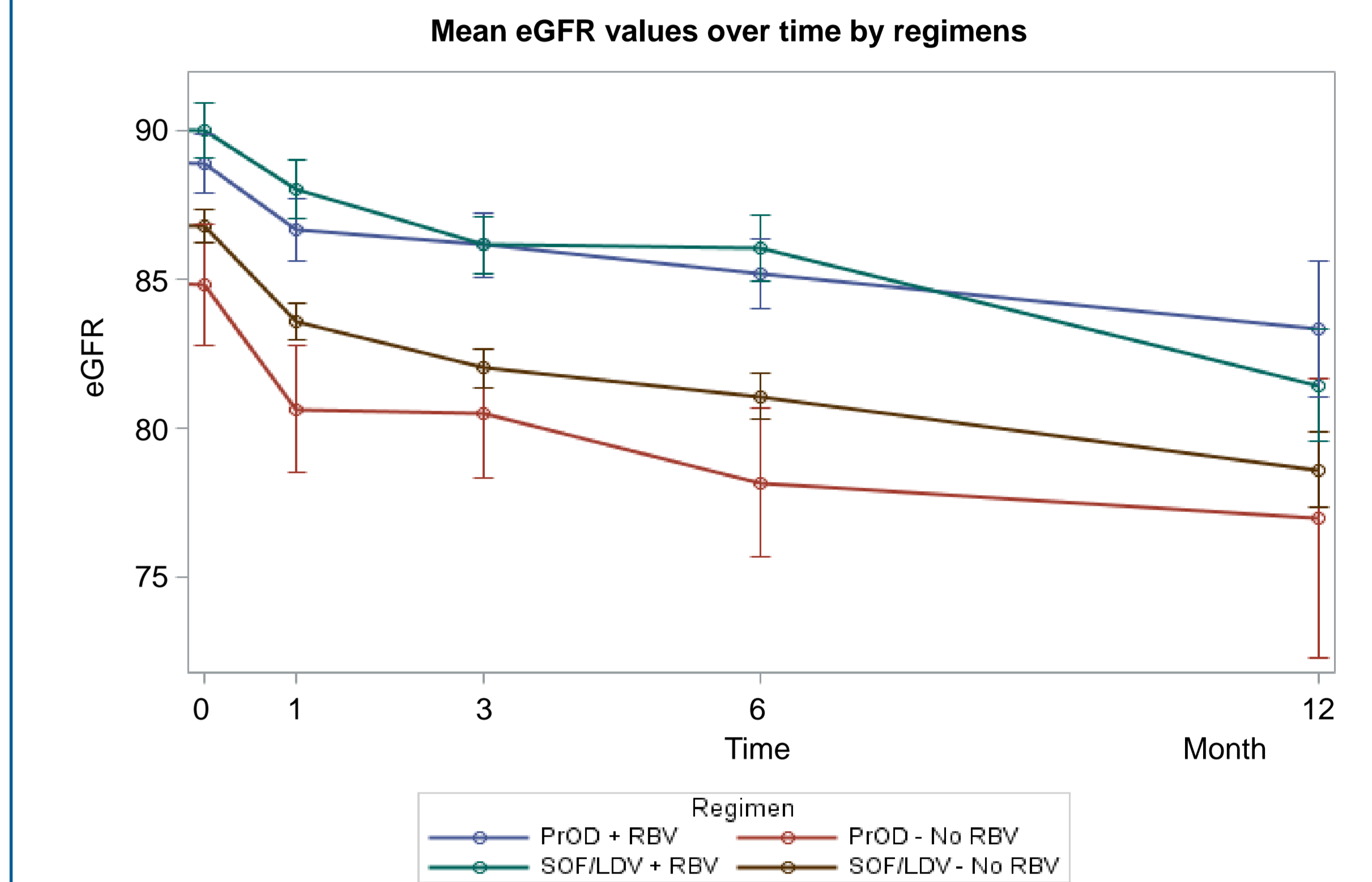
Conclusions

- Over one third of persons treated with SOF/LDV or PrOD regimens experienced a decline in eGFR of >10 mL/min (range from 37.8% (SOF/LDV+RBV) to 30.1% (PrOD, no RBV))
- For stage 4-5 CKD, higher incidence of eGFR decline was observed among patients treated with SOF/LDV (6.5%), followed by SOF/LDV+RBV (3.3%) and PrOD (1.8%)
- Whether these declines are permanent or of any clinical significance is not known
- Number of persons with baseline CKD stage 4-5 was small, and caution should be exerted in interpreting these data for this group

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