

Supplementary Online Contents

Supplementary Table 1. Drug names used to identify laxative types

Supplementary Table 2. Adjusted odds ratios and 95% confidence intervals of dyskalemia associated with time-varying laxative use (vs. non-use of laxatives) during the last 1-year pre-ESRD period (n=36,116)

Supplementary Table 3. Adjusted odds ratios and 95% confidence intervals of dyskalemia associated with time-varying laxative use (vs. non-use of laxatives) during the last 1-year pre-ESRD period after including patients with missing covariates and imputing missing data (n=44,642)

Supplementary Table 4. Adjusted hazard ratios and 95% confidence intervals of dyskalemia associated with time-varying laxative use (vs. non-use of laxatives) during the last 1-year pre-ESRD period using repeated events survival analysis (n=36,116)

Supplementary Table 5. Adjusted odds ratios and 95% confidence intervals of dyskalemia associated with laxative use (vs. non-use of laxatives) based on data at the first K⁺ measurement during the last 1-year pre-ESRD period (n=42,420)

Supplementary Table 6. Adjusted odds ratios and 95% confidence intervals of dyskalemia associated with time-varying laxative use (vs. non-use of laxatives) during the last 1-year pre-ESRD period using more granular K⁺ categories (n=36,116)

Supplementary Figure 1. Algorithm used to define the analytical cohort

Supplementary Figure 2. The number of K⁺ measurements per patient during the last 1-year pre-ESRD period

Supplementary Figure 3. The time interval between each K⁺ measurement and dialysis initiation during the last 1-year pre-ESRD period

Supplementary Table 1. Drug names used to identify laxative types

Laxative types	Generic names
Stool softener laxative	Docusate sodium
	Docusate calcium
Stimulant laxatives	Bisacodyl
	Castor oil
	Senna
	Sennosides
Hyperosmotics laxatives	Lactulose
	Magnesium citrate
	Magnesium sulphate
	Sodium Biphosphate
	Polyethylene glycol 3350
	Sorbitol
	Glycerin
Bulk laxatives	Calcium polycarbophil
	Cellulose powder
	Methylcellulose
	Psyllium
	Wheat dextrin
Chloride channel blockers	Lubiprostone
Lubricant laxatives	Mineral oil (heavy)

Supplementary Table 2. Adjusted odds ratios and 95% confidence intervals of dyskalemia associated with time-varying laxative use (vs. non-use of laxatives) during the last 1-year pre-ESRD period (n=36,116)

	K ⁺ concentration (mEq/L)		
	<3.5 (hypokalemia)	3.5 to 5.5 (normokalemia)	>5.5 (hyperkalemia)
% of all repeated K ⁺ values	4.0%	91.0%	5.0%
Model 1	0.99 (0.95-1.06)	1 [reference]	0.68 (0.65-0.72)
Model 2	0.99 (0.94-1.05)	1 [reference]	0.68 (0.65-0.72)
Model 3	1.03 (0.98-1.09)	1 [reference]	0.82 (0.78-0.86)
Model 4	1.01 (0.96-1.07)	1 [reference]	0.79 (0.76-0.84)
Model 5	1.01 (0.95-1.07)	1 [reference]	0.79 (0.76-0.84)

Note: Model 1 is unadjusted; model 2 is adjusted for age, sex, race, and marital status; model 3 is adjusted for the variables in model 2 plus smoking status, body mass index averaged over the 1-year pre-ESRD period, comorbidities (diabetes mellitus, congestive heart failure, cardiovascular disease, cerebrovascular disease, peripheral vascular disease, lung disease, liver disease, peptic ulcer disease, atrial fibrillation, malignancies, bowel disorders*, and constipation), Charlson Comorbidity Index, and cumulative length of hospital stay, in-hospital acute kidney injury, number of medical visits, and number of K⁺ measurements during the 1-year pre-ESRD period; model 4 is adjusted for the variables in model 3 plus time-varying medications (renin-angiotensin system inhibitors, sodium polystyrene sulfonate, loop diuretics, thiazide diuretics, potassium sparing diuretics, calcium channel blockers, beta blockers, phosphate binders, digoxin, insulin, oral hypoglycemics, calcineurin inhibitors, azole antifungals, opioid analgesics, and beta-2 agonists); and model 5 is adjusted for the variables in model 4 plus time-varying eGFR. *Bowel disorders include inflammatory bowel disease, irritable bowel syndrome, and diarrhea.

Abbreviations: eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; K⁺ = plasma potassium

Supplementary Table 3. Adjusted odds ratios and 95% confidence intervals of dyskalemia associated with time-varying laxative use (vs. non-use of laxatives) during the last 1-year pre-ESRD period after including patients with missing covariates and imputing missing data (n=44,642)

	K ⁺ concentration (mEq/L)		
	<3.5 (hypokalemia)	3.5 to 5.5 (normokalemia)	>5.5 (hyperkalemia)
% of all repeated K ⁺ values	4.1%	90.8%	5.1%
Model 1	0.99 (0.95-1.05)	1 [reference]	0.67 (0.64-0.70)
Model 2	0.99 (0.95-1.05)	1 [reference]	0.67 (0.65-0.70)
Model 3	1.04 (0.99-1.09)	1 [reference]	0.81 (0.78-0.85)
Model 4	1.02 (0.97-1.07)	1 [reference]	0.79 (0.76-0.84)
Model 5	1.01 (0.96-1.06)	1 [reference]	0.80 (0.77-0.84)

Note: Model 1 is unadjusted; model 2 is adjusted for age, sex, race, and marital status; model 3 is adjusted for the variables in model 2 plus smoking status, body mass index averaged over the 1-year pre-ESRD period, comorbidities (diabetes mellitus, congestive heart failure, cardiovascular disease, cerebrovascular disease, peripheral vascular disease, lung disease, liver disease, peptic ulcer disease, atrial fibrillation, malignancies, bowel disorders*, and constipation), Charlson Comorbidity Index, and cumulative length of hospital stay, in-hospital acute kidney injury, number of medical visits, and number of K⁺ measurements during the 1-year pre-ESRD period; model 4 is adjusted for the variables in model 3 plus time-varying medications (renin-angiotensin system inhibitors, sodium polystyrene sulfonate, loop diuretics, thiazide diuretics, potassium sparing diuretics, calcium channel blockers, beta blockers, phosphate binders, digoxin, insulin, oral hypoglycemics, calcineurin inhibitors, azole antifungals, opioid analgesics, and beta-2 agonists); and model 5 is adjusted for the variables in model 4 plus time-varying eGFR. *Bowel disorders include inflammatory bowel disease, irritable bowel syndrome, and diarrhea.

Abbreviations: eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; K⁺ = plasma potassium

Supplementary Table 4. Adjusted hazard ratios and 95% confidence intervals of dyskalemia associated with time-varying laxative use (vs. non-use of laxatives) during the last 1-year pre-ESRD period using repeated events survival analysis (n=36,116)

	K ⁺ concentration (mEq/L)		
	<3.5 (hypokalemia)	3.5 to 5.5 (normokalemia)	>5.5 (hyperkalemia)
Model 1	0.83 (0.79-0.86)	1 [reference]	0.86 (0.82-0.89)
Model 2	0.83 (0.80-0.87)	1 [reference]	0.86 (0.82-0.89)
Model 3	0.87 (0.83-0.91)	1 [reference]	0.88 (0.85-0.92)
Model 4	0.91 (0.87-0.95)	1 [reference]	0.93 (0.89-0.97)
Model 5	0.88 (0.84-0.93)	1 [reference]	0.92 (0.87-0.96)

Note: Model 1 is unadjusted; model 2 is adjusted for age, sex, race, and marital status; model 3 is adjusted for the variables in model 2 plus smoking status, body mass index averaged over the 1-year pre-ESRD period, comorbidities (diabetes mellitus, congestive heart failure, cardiovascular disease, cerebrovascular disease, peripheral vascular disease, lung disease, liver disease, peptic ulcer disease, atrial fibrillation, malignancies, bowel disorders*, and constipation), Charlson Comorbidity Index, and cumulative length of hospital stay, in-hospital acute kidney injury, number of medical visits, and number of K⁺ measurements during the 1-year pre-ESRD period; model 4 is adjusted for the variables in model 3 plus time-varying medications (renin-angiotensin system inhibitors, sodium polystyrene sulfonate, loop diuretics, thiazide diuretics, potassium sparing diuretics, calcium channel blockers, beta blockers, phosphate binders, digoxin, insulin, oral hypoglycemics, calcineurin inhibitors, azole antifungals, opioid analgesics, and beta-2 agonists); and model 5 is adjusted for the variables in model 4 plus time-varying eGFR. *Bowel disorders include inflammatory bowel disease, irritable bowel syndrome, and diarrhea.

Abbreviations: eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; K⁺ = plasma potassium

Supplementary Table 5. Adjusted odds ratios and 95% confidence intervals of dyskalemia associated with laxative use (vs. non-use of laxatives) based on data at the first K⁺ measurement during the last 1-year pre-ESRD period (n=42,420)

	K ⁺ concentration (mEq/L)		
	<3.5 (hypokalemia)	3.5 to 5.5 (normokalemia)	>5.5 (hyperkalemia)
Model 1	1.17 (0.98-1.41)	1 [reference]	0.83 (0.69-0.98)
Model 2	1.13 (0.94-1.36)	1 [reference]	0.82 (0.69-0.97)
Model 3	1.11 (0.92-1.34)	1 [reference]	0.85 (0.72-1.01)
Model 4	1.05 (0.87-1.28)	1 [reference]	0.80 (0.67-0.96)
Model 5	1.05 (0.87-1.27)	1 [reference]	0.83 (0.69-0.99)

Note: Dyskalemia and laxative use status were assessed at the time of the first K⁺ measurement during the last 1-year pre-ESRD and the risk was estimated using logistic regression models. Model 1 is unadjusted; model 2 is adjusted for age, sex, race, and marital status; model 3 is adjusted for the variables in model 2 plus smoking status, body mass index averaged over the 1-year pre-ESRD period, comorbidities (diabetes mellitus, congestive heart failure, cardiovascular disease, cerebrovascular disease, peripheral vascular disease, lung disease, liver disease, peptic ulcer disease, atrial fibrillation, malignancies, bowel disorders*, and constipation), and Charlson Comorbidity Index; model 4 is adjusted for the variables in model 3 plus medications (renin-angiotensin system inhibitors, sodium polystyrene sulfonate, loop diuretics, thiazide diuretics, potassium sparing diuretics, calcium channel blockers, beta blockers, phosphate binders, digoxin, insulin, oral hypoglycemics, calcineurin inhibitors, azole antifungals, opioid analgesics, and beta-2 agonists) at the first K⁺ measurement during the last 1-year pre-ESRD; and model 5 is adjusted for the variables in model 4 plus eGFR at the first K⁺ measurement during the last 1-year pre-ESRD. The absolute risks for hyperkalemia were 5.9% and 7.1% in patients with and without laxative use, respectively; while, the respective absolute risks for hypokalemia were 5.1% and 4.4%.

*Bowel disorders include inflammatory bowel disease, irritable bowel syndrome, and diarrhea.

Abbreviations: eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; K⁺ = plasma potassium

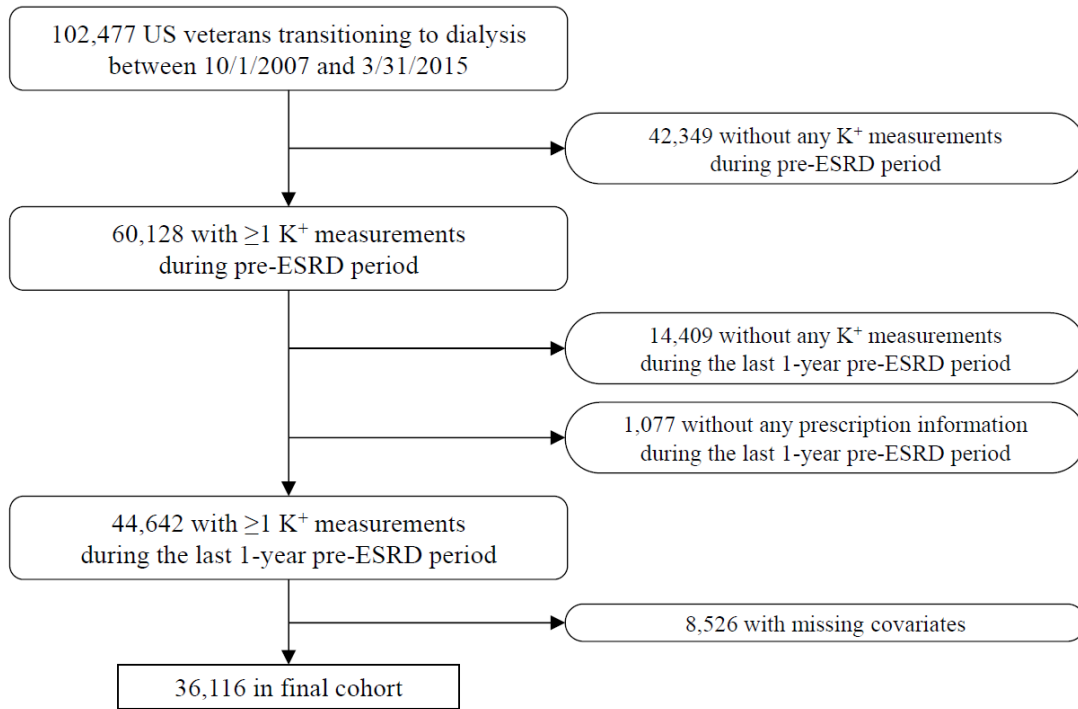
Supplementary Table 6. Adjusted odds ratios and 95% confidence intervals of dyskalemia associated with time-varying laxative use (vs. non-use of laxatives) during the last 1-year pre-ESRD period using more granular K⁺ categories (n=36,116)

	K ⁺ concentration (mEq/L)						
	<3.5	3.5 to <4.0	4.0 to <4.5	4.5 to <5.0	5.0 to <5.5	5.5 to <6.0	≥6.0
% of all repeated K ⁺ values	4.0%	17.0%	30.9%	27.6%	14.1%	4.7%	1.7%
Model 1	1.07 (1.01-1.13)	1.25 (1.19-1.29)	1.16 (1.12-1.19)	1 [reference]	0.86 (0.83-0.88)	0.73 (0.69-0.77)	0.74 (0.68-0.79)
Model 2	1.06 (1.00-1.13)	1.24 (1.19-1.29)	1.16 (1.12-1.19)	1 [reference]	0.86 (0.83-0.88)	0.73 (0.69-0.77)	0.74 (0.68-0.79)
Model 3	1.07 (1.00-1.14)	1.13 (1.08-1.19)	1.08 (1.05-1.11)	1 [reference]	0.90 (0.87-0.93)	0.82 (0.78-0.87)	0.85 (0.79-0.92)
Model 4	1.04 (0.98-1.11)	1.10 (1.06-1.15)	1.07 (1.04-1.10)	1 [reference]	0.91 (0.88-0.94)	0.80 (0.76-0.85)	0.79 (0.73-0.86)
Model 5	1.04 (0.97-1.10)	1.09 (1.05-1.15)	1.07 (1.03-1.09)	1 [reference]	0.91 (0.88-0.94)	0.81 (0.76-0.85)	0.79 (0.73-0.86)

Note: Model 1 is unadjusted; model 2 is adjusted for age, sex, race, and marital status; model 3 is adjusted for the variables in model 2 plus smoking status, body mass index averaged over the 1-year pre-ESRD period, comorbidities (diabetes mellitus, congestive heart failure, cardiovascular disease, cerebrovascular disease, peripheral vascular disease, lung disease, liver disease, peptic ulcer disease, atrial fibrillation, malignancies, bowel disorders*, and constipation), Charlson Comorbidity Index, and cumulative length of hospital stay, in-hospital acute kidney injury, number of medical visits, and number of K⁺ measurements during the 1-year pre-ESRD period; model 4 is adjusted for the variables in model 3 plus time-varying medications (renin-angiotensin system inhibitors, sodium polystyrene sulfonate, loop diuretics, thiazide diuretics, potassium sparing diuretics, calcium channel blockers, beta blockers, phosphate binders, digoxin, insulin, oral hypoglycemics, calcineurin inhibitors, azole antifungals, opioid analgesics, and beta-2 agonists); and model 5 is adjusted for the variables in model 4 plus time-varying eGFR.

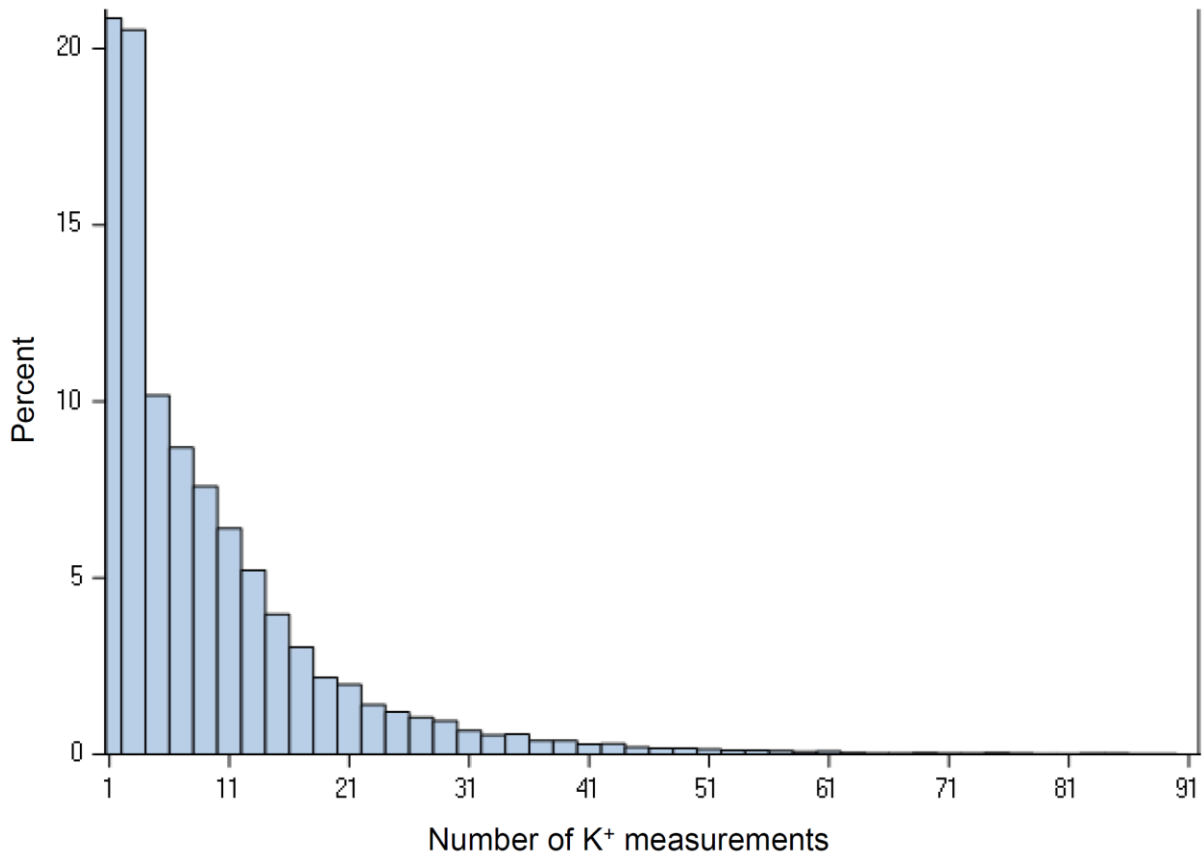
*Bowel disorders include inflammatory bowel disease, irritable bowel syndrome, and diarrhea.

Abbreviations: eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; K⁺ = plasma potassium

Supplementary Figure 1. Algorithm used to define the analytical cohort

Abbreviations: eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; K⁺ = plasma potassium

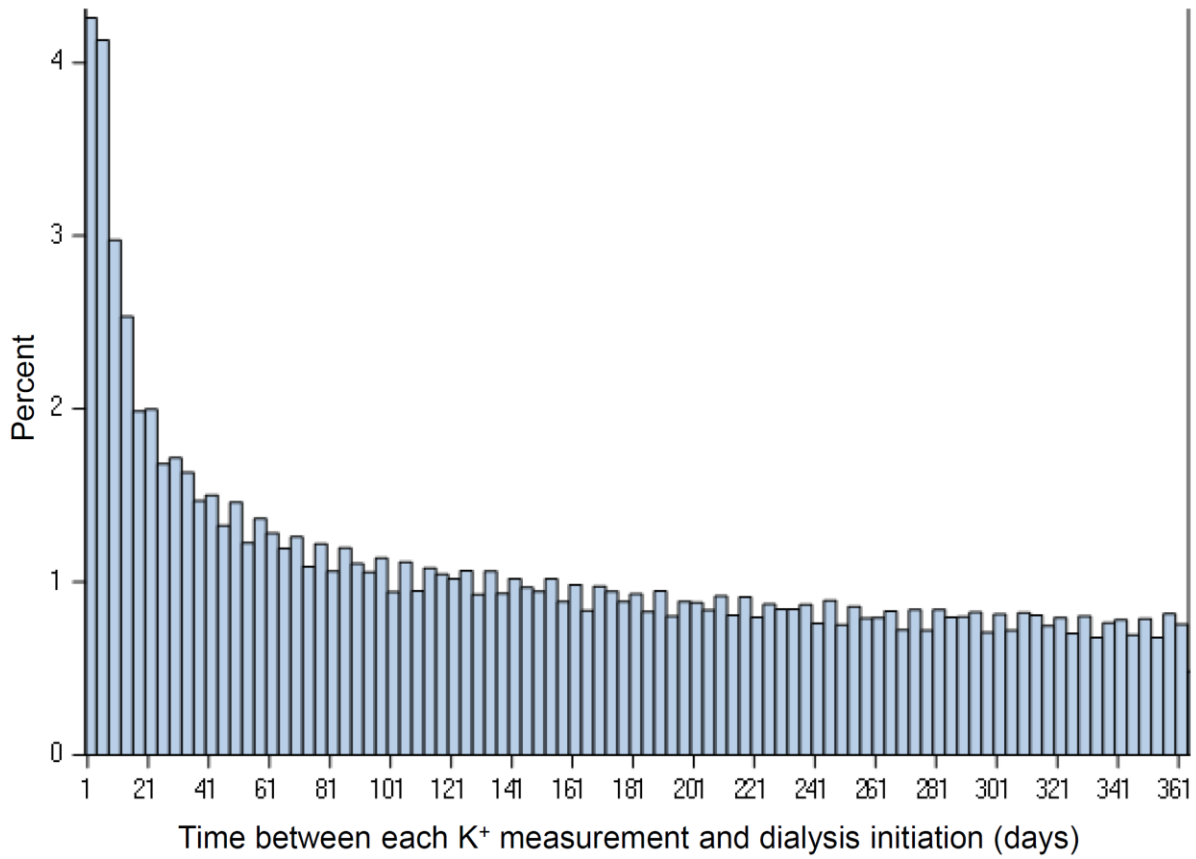
Supplementary Figure 2. The number of K⁺ measurements per patient during the last 1-year pre-ESRD period



Note: The histogram was trimmed at 100 K⁺ measurements (at ~99.9%).

Abbreviations: ESRD = end-stage renal disease; K⁺ = plasma potassium

Supplementary Figure 3. The time interval between each K⁺ measurement and dialysis initiation during the last 1-year pre-ESRD period



Abbreviations: ESRD = end-stage renal disease; K⁺ = plasma potassium