Table S1: Baseline characteristics and laboratory measures by smoking groups

	Smoking category			
	Current smoker (n=1243)	**Former smoker (n=3272)**	**Never regular smoker (n=4755)**	**P-value‡**
Total cholesterol (mg/dL)	186 (45)	189 (46)	190 (46)	0.1
LDL cholesterol (mg/dL)	105 (34)	107 (34)	108 (34)	0.004
HDL cholesterol (mg/dL)	44 (13)	43 (13)	43 (13)	0.02
Triglycerides (mg/dL)	207 (154)	212 (156)	201 (156)	0.02
Phosphate (mg/dL)	4.57 (1.48)	4.40 (1.52)	4.36 (1.46)	<0.001
Hemoglobin (g/dL)	12.33 (1.68)	12.14 (1.72)	12.16 (1.65)	0.003
Co-medication				
Antiplatelet therapy	26%	23%	22%	0.008
Oral anticoagulant therapy	2%	4%	3%	0.03
ACE inhibitor or ARB	54%	54%	55%	0.6
Beta blocker	39%	38%	38%	0.8
Calcium channel blocker	42%	42%	41%	0.7
Diuretic	42%	43%	40%	0.06
Erythropoiesis stimulating agent	26%	28%	27%	0.3
Sevelamer	9%	8%	8%	0.3
Renal diagnosis†				0.005
Glomerulonephritis	14%	18%	18%	
Diabetic nephropathy	16%	16%	13%	
Hypertensive/renovascular	20%	15%	17%	
Cystic kidney disease	10%	11%	12%	
Pyelonephritis	7%	7%	7%	
Other known cause	22%	20%	19%	
Unknown cause	12%	14%	13%	
Randomized to simvastatin plus ezetimibe	50%	50%	50%	0.9

Note: Mean (SD) or % shown, adjusted for age, sex, ethnicity, education, prior vascular disease and prior diabetes. Conversion factors for units: cholesterol in mg/dL to mmol/L, x0.02586; triglycerides in mg/dL to mmol/L, x0.01129; phosphate in mg/dL to mmol/L, x0.3229. †Among those not on dialysis at randomization. ‡P value for test of heterogeneity between the three smoking categories.

Table S2: Estimated event rates (per 1000 per year) among current and never smokers with and without a prior diagnosis of CVD and/or diabetes.

	Overall			Prior history of CVD/diabetes			No prior history of CVD/diabetes		
	Rate (SE) among current smokers*	Rate (SE) among never smokers*	Absolute excess risk† (95% CI)	Rate (SE) among current smokers*	Rate (SE) among never smokers*	Absolute excess risk† (95% CI)	Rate (SE) among current smokers*	Rate (SE) among never smokers*	Absolute excess risk† (95% CI)
Vascular events	93 (5)	68 (2)	25 (13 to 36)	134 (8)	98 (4)	36 (19 to 52)	67 (4)	49 (2)	18 (10 to 26)
Cancer incidence	22 (2)	16 (1)	6 (1 to 11)	24 (3)	17 (1)	7 (1 to 12)	21 (2)	15 (1)	6 (1 to 11)
All-cause mortality	86 (5)	59 (2)	28 (17 to 38)	116 (7)	80 (3)	36 (22 to 50)	66 (4)	46 (2)	21 (12 to 29)
Vascular mortality	28 (3)	21 (1)	7 (1 to 13)	42 (4)	32 (2)	10 (1 to 19)	18 (2)	14 (1)	4 (0 to 8)
Non-vascular mortality	50 (4)	32 (1)	19 (10 to 27)	63 (5)	40 (2)	23 (13 to 34)	42 (3)	27 (1)	15 (9 to 22)
Cancer death	12 (2)	5 (1)	7 (3 to 11)	15 (3)	6 (1)	9 (3 to 14)	10 (2)	4 (1)	6 (2 to 9)
Respiratory death	12 (2)	5 (1)	7 (2 to 11)	16 (3)	7 (1)	9 (3 to 15)	9 (2)	4 (1)	5 (2 to 8)

Note: *Poisson regression was used to model the common linear dependence of the log annual event rate on baseline age, sex, ethnicity, country, education, prior vascular disease, prior diabetes and smoking status (current, former, never). Mean (SE) event rates (per 1000 per year) were then estimated by applying the regression coefficients back to the participant characteristics, but forcing the smoking status to be either current or never smokers, as appropriate (estimates by prior disease were constructed similarly).
†Absolute excess risks were calculated by subtracting estimated rates among never regular smokers from estimated rates among current smokers.

Table S3: Summary of literature on relevance of smoking to cardiovascular morbidity and mortality

Author	Year	Design	Population	Mean eGFR	Reported consumption among current smokers	Outcome	N	Events	Average length of follow-up	Results (current vs not current smokers unless stated)	Additional covariates included in model
Grams[1]	2012	Prospective	CKD (39.7 % female)	39	Not stated	Pre-ESRD mortality (from any cause)	1722	243	Median 17.6 yrs	HR 1.5 (1.01-2.23)	Age, sex, ethnicity, SBP, cause of kidney disease, diabetes, presence of CVD, log 24-hour proteinuria, and eGFR.
Ricardo[2]	2015	Prospective	CKD (48% female)	43	Not stated	Atherosclerotic vascular events; all-cause mortality	3006	355; 437	Median 4 years	HR 1.82 (1.33-2.5); 2.22 (1.67-2.94)	Age, sex, ethnicity, education, diabetes, dyslipidemia, hypertension, any CVD, ACEi/ARB, eGFR and log 24-hour urine protein excretion.
Muntner[3]	2005	Prospective	CKD (67% female)		Not collected	CHD	807	108	Average 9 years	HR 1.65 (1.01-2.67)	Age, sex, ethnicity
Shlipak[4]	2005	Prospective	CKD (53% female)	50	Not reported	CV death	1249	342	Average 8.6 years	HR 1.82 (1.27-2.60)	Age, sex, ethnicity, education, diuretic use, prevalent CV disease
Foley[5]	2003	Prospective	Dialysis (47.2% female)	N/A	Not reported	Ischaemic heart disease; Congestive heart failure; cerebrovascular disease; peripheral vascular disease; all-cause mortality	3941	232; 297; 64; 383; 1179	Average 2.2 years	Not associated [HR not given]; HR 1.59 (1.16-2.17); Not associated [HR not given]; HR 1.68 (1.27-2.22); HR 1.37 (1.15-1.64)	Age, sex, ethnicity, primary renal disorder, prior CV disease, diabetic status, dialysis modality
Fishbane[6]	1996	Prospective	Dialysis (41% female)	N/A	Not reported	All-cause and CV mortality	132	28; 16	1 year	Smoking history present vs absent: HR 0.9 (0.5-2.1); HR 1.2 (0.4-2.2)	Age, sex, ethnicity, diabetes, hypertension, cholesterol, kt/V, serum albumin, prior vascular disease, AAI

Abbreviations:
2xCr = doubling of creatinine; 50%↓eGFR = halving of eGFR; AAI = ankle-arm blood pressure index; ACEi = angiotensin coverting enzyme inhibitor; ADPKD = autosomal dominant polycystic kidney disease; ARB = angiotensin receptor blocker; BMI = body-mass index; CCB = calcium channel blocker; CHD = coronary heart disease; CKD = chronic kidney disease; CVD = cardiovascular disease; DBP = diastolic blood pressure; DN = diabetic nephropathy; ESRD = end-stage renal disease; (e)GFR = (estimated) glomerular filtration rate; HR = hazard ratio; HDL-C = high density lipoprotein cholesterol; IgA = IgA nephropathy; IGT = impaired glucose tolerance; NSAID = non-steroidal anti-inflammatory drug; OR = odds ratio; PCR = protein creatinine ratio; SBP = systolic blood pressure

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Table S4: Summary of literature on relevance of smoking to development and progression of CKD

Author	Year	Design	Population	Mean eGFR	Reported consumption among current smokers	Outcome	N	Events	Average length of follow-up	Results (current vs not current smokers unless stated)	Additional covariates included in model
Yoshida[1]	2008	Prospective	CKD		Not stated	Slope of 1/Cr	2012	-		-2.06 ml/min; p=0.014	Age, sex, high BMI, metabolic syndrome, proteinuria, hypertension, high triglyceride, low HDL-C, high fasting plasma glucose, ACEi/ARB therapy, CCB therapy
Grams[2]	2012	Prospective	CKD	39	Not stated	ESRD	1722	1099	Median 17.6 yrs	HR 1.3 (1.09-1.55)	Age, sex, ethnicity, SBP, cause of kidney disease, diabetes, presence of CVD, log 24-hour proteinuria, and eGFR.
Tanaka[3]	2013	Prospective	CKD	55	Not stated	ESRD/2xCr	449	46	Median 3.3 years	HR 1.25 (0.41- 3.84)	Age, sex, diabetes, hypertension, dylipidemia, eGFR, proteinuria, serum albumin, skin autofluorescence
Ricardo[4]	2015	Prospective	CKD	43	Not stated	ESRD or 50%↓eGFR	3006	726	Median 4 years	HR 1.47 (1.19-1.82)	Age, sex, ethnicity, education, diabetes, dyslipidemia, hypertension, any CVD, ACEi/ARB, eGFR and log 24-hour urine protein excretion.
Haroun[5]	2003	Prospective	General		Not stated	CKD	23,534	143	18 years	HR 2.6 (1.8–3.7)	Age, sex, treated diabetes
Shankar[6]	2006	Prospective	General	n/a	Not stated	CKD	3392	114	5 years	HR: 1.93 (1.15-3.25) [current vs never smokers]	Age, sex, education, body mass index, current NSAID use, hypertension status, diabetes status, history of CVD, and heavy drinking.
Ishani[7]	2006	Prospective	General	n/a	Not stated	ESRD	12,866	213	25 years	HR 1.84 (1.35-2.51)	Age, black ethnicity, BMI, family history of diabetes, triglycerides, HDL-C, LDL-C, uric acid, fasting glucose, SBP, eGFR, haematocrit and urine proteinuria

Author	Year	Design	Population	Mean eGFR	Reported consumption among current smokers	Outcome	N	Events	Average length of follow-up	Results (current vs not current smokers unless stated)	Additional covariates included in model
Yamagata[8]	2007	Prospective	General	80	Not stated	CKD3-5	123,764	19,411	10 years	HR 1.13 (1.05-1.22) in men; 1.16 (1.06-1.26) in women	Age, proteinuria, hematuria, concomitant proteinuria and hematuria, IGT, diabetes, hypertension, hypercholesterolemia, low HDL-C, hypertriglyceridemia, obesity, alcohol consumption
Yacoub[9]	2010	Case-control	General	n/a	Not stated	CKD	569	198		OR 1.63 (1.08-2.45) [current vs never smokers]	Age and sex
Hallan[10]	2011	Prospective	General	97	Average 14.5 pack years	CKD5	65,589	124	Median 10.3 yrs	HR 4.01 (1.43-11.25) in <70; 1.09 (0.51-2.33) in ≥70	Age, sex, high education, physical inactivity, diabetes, prevalent CVD, antihypertensive use, SBP, waist circumference, total/HDL-C, eGFR, ACR
Lipworth[11]	2012	Prospective	General	n/a	Not stated	ESRD	79,943	662	4 yrs	HR 1.2 (1.02-1.4)	Age, sex, recruitment source, education, annual household income, history of diabetes, hypertension, stroke, high cholesterol, and MI/CABG.
Carter[12]	2015	Prospective	General		Cigarettes smoked per day: Men 22.6% <10; 39.8% ≥ 20 Women 40.7% <10; 20.9% ≥20	Renal death	954,029	1072	10 years	RR 2.1 (1.6-2.6) in men; 1.9 (1.5-2.5) in women	Age, race, educational level, current alcohol use, and cohort.
Paterson[13]	2005	Prospective	ADPKD	83	Average 18 pack years	Creatinine clearance	406	-		ns	Univariate analyses
Ozkok[14]	2013	Prospective	ADPKD	60	Average 4.2 pack years	>1 ml/min/yr ↓GFR	171	-	8 years	HR 0.78 (0.28-2.16)	Age, gender, baseline serum creatinine, presence of hypertension, abdominal wall hernia, hepatic cyst, familial history of ADPKD, macroscopic hematuria, 24-h proteinuria, urinary stone, palpable kidneys in physical examination and use of ACEIs and/or ARBs

Author	Year	Design	Population	Mean eGFR	Reported consumption among current smokers	Outcome	N	Events	Average length of follow-up	Results (current vs not current smokers unless stated)	Additional covariates included in model
Orth[15]	1998	Case-control	ADPKD/ IgA	n/a		ESRD	204	102		OR for >5 pack years 4.5 (1.9-10.9) in men; 1.0 (0.3-3.4) in women	None
Sawicki[16]	1994	Prospective	DN	n/a	Average 18 pack years	1.36 ml/min ↓GFR	93	25	1 year	OR 2.74 (1.57-4.81) per 10 pack years	Age, sex, diabetes duration, HbA1c, BMI, daily protein intake, 24-h urinary sodium excretion, SBP, DBP
Chuahirun[17]	2002	Prospective	DN	98	Not stated	Slope of eGFR	33	-	5 years	-0.59 to -0.09 ml/min (p=0.009)	Age, gender, ethnicity, initial mean BP, initial PCR
Phisitkul[18]	2008	Prospective	DN	95		Slope of 1/Cr	91	-		Not stated. p=0.041	Age, sex, ethnicity, diabetes, SBP, urine albumin, HbA1c, LDL-C, HDL-C, eGFR

Abbreviations:

2xCr = doubling of creatinine; 50%↓eGFR = halving of eGFR; ACEi = angiotensin coverting enzyme inhibitor; ADPKD = autosomal dominant polycystic kidney disease; ARB = angiotensin receptor blocker; BMI = body-mass index; CCB = calcium channel blocker; CKD = chronic kidney disease; CVD = cardiovascular disease; DBP = diastolic blood pressure; DN = diabetic nephropathy; ESRD = end-stage renal disease; (e)GFR = (estimated) glomerular filtration rate; HR = hazard ratio; HDL-C = high density lipoprotein cholesterol; IgA = IgA nephropathy; IGT = impaired glucose tolerance; NSAID = non-steroidal anti-inflammatory drug; OR = odds ratio; PCR = protein creatinine ratio; SBP = systolic blood pressure

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