Table S1 Association of 27 SNPs with serum uric acid in the discovery cohort of HKDR

No.	SNP	CHR	BP	Nearest Gene	genotyped/ imputed	imputation quality (R-square)	MAF	Risk/ non-Risk Allele	Model 1 (non-adjustment)		Model 2 (adjustment)	
									Beta(SE)	P	Beta(SE)	P
1	rs1471633	1	145723739	PDZK1	Imputed	0.992	0.191	A/C	0.003(0.003)	0.314	-0.003(0.003)	0.308
2	rs1260326	2	27730940	GCKR	Genotyped	1.000	0.458	T/C	0.009(0.002)	8.50×10^{-5}	0.007(0.002)	0.003
3	rs12498742	4	9944052	SLC2A9	Imputed	0.991	0.017	A/G	0.017(0.01)	0.082	0.017(0.009)	0.073
4	rs2231142	4	89052323	ABCG2	Genotyped	1.000	0.314	T/G	0.02(0.003)	5.57×10^{-15}	0.018(0.002)	4.45×10^{-13}
5	rs675209	6	7102084	RREB1	Genotyped	1.000	0.071	T/C	-0.005(0.005)	0.274	-0.003(0.004)	0.545
6	rs1165151	6	25821616	SLC17A1	Imputed	0.997	0.159	G/T	0.001(0.003)	0.667	0.003(0.003)	0.334
7	rs2078267	11	64334114	SLC22A11	Genotyped	1.000	0.019	C/T	0.004(0.009)	0.662	0.006(0.008)	0.488
8	rs478607	11	64478063	NRXN2	Imputed	0.986	0.178	G/A	0.004(0.003)	0.240	0.004(0.003)	0.179
9	rs3741414	12	57844049	INHBC	Genotyped	1.000	0.066	C/T	0.002(0.005)	0.656	0.004(0.005)	0.327
10	rs11264341	1	155151493	TRIM46	Genotyped	1.000	0.311	C/T	0.006(0.003)	0.016	0.007(0.002)	0.003
11	rs17050272	2	121306440	INHBB	Genotyped	1.000	0.458	A/G	-0.001(0.002)	0.777	-0.001(0.002)	0.764
12	rs2307394	2	148716428	ORC4L	Genotyped	1.000	0.474	C/T	-0.003(0.002)	0.235	-0.003(0.002)	0.160
13	rs6770152	3	53100214	SFMBT1	Genotyped	1.000	0.349	G/T	0.005(0.002)	0.028	0.008(0.002)	0.001
14	rs17632159	5	72431482	TMEM171	Imputed	0.972	0.287	G/C	-0.003(0.003)	0.302	-0.001(0.003)	0.628
15	rs729761	6	43804571	VEGFA	Imputed	0.972	0.132	G/T	0.003(0.003)	0.382	-0.001(0.003)	0.875
16	rs1178977	7	72857049	BAZ1B	Genotyped	1.000	0.081	A/G	-0.001(0.004)	0.898	-0.001(0.004)	0.748
17	rs17786744	8	23777006	STC1	Imputed	0.995	0.353	G/A	0.001(0.002)	0.797	0.001(0.002)	0.803
18	rs2941484	8	76478768	HNF4G	Genotyped	1.000	0.336	T/C	0.005(0.003)	0.047	0.004(0.002)	0.113
19	rs10821905	10	52646093	A1CF	Genotyped	1.000	0.037	A/G	-0.014(0.006)	0.034	-0.008(0.006)	0.218
20	rs642803	11	65560620	OVOL1	Genotyped	1.000	0.394	C/T	0.001(0.002)	0.687	-0.002(0.002)	0.426

21	rs1394125	15	76158983	UBE2Q2	Genotyped	1.000	0.078	A/G	-0.005(0.004)	0.230	-0.003(0.004)	0.517
22	rs6598541	15	99271135	IGF1R	Imputed	0.969	0.438	A/G	0.0004(0.002)	0.877	0.002(0.002)	0.310
23	rs7193778	16	69563890	NFAT5	Imputed	0.979	0.042	C/T	-0.007(0.006)	0.222	-0.006(0.006)	0.267
24	rs7188445	16	79734987	MAF	Imputed	0.983	0.289	G/A	0.006(0.003)	0.025	0.005(0.003)	0.076
25	rs7224610	17	53364788	HLF	Genotyped	1.000	0.130	C/A	0.0004(0.004)	0.902	-0.001(0.003)	0.870
26	rs2079742	17	59465697	BCAS3	Imputed	0.864	0.484	T/C	-0.0002(0.002)	0.917	0.002(0.002)	0.374
27	rs164009	17	74283669	QRICH2	Genotyped	1.000	0.346	A/G	0.002(0.002)	0.393	0.001(0.002)	0.640

Model 2 was adjusted for conventional risk factors at baseline, including age, gender, duration of diabetes, smoking, BMI, HbA1c, HDL-C, LDL-C, SBP, DBP, log-transformed ACR, eGFR, retinopathy, use of lipid lowering drugs (yes/no), antihypertensive drugs (yes/no), RAS inhibitors (yes/no), and antihyperglycemic drugs (yes/no), history of stroke, history of CHD, and history of CKD.

Table S2 Clinical characteristics of patients with T2D from the replication cohort of HKDB

	AKI Cases	AKI Controls	P
N	1233	2643	
Age (year)	63.7 ± 11.3	63.2 ± 9.5	0.189
Male sex	60.2% (742)	58.9% (1556)	0.441
Duration of diabetes (year)	12 (5-18)	15 (11-20)	<0.001
Smoking status			0.103
Former	24.6% (303)	21.9% (577)	
Current	10.2% (126)	9.5% (252)	
BMI (kg/m^2)	26.5 ± 4.7	25.9 ± 4.3	0.001
HbA_{1c} (%)	7.8 ± 1.6	7.8 ± 1.3	0.927
HbA_{1c} (mmol/mol)	62 ± 17.5	62 ± 14.2	0.927
HDL cholesterol (mmol/L)	1.2 ± 0.4	1.2 ± 0.3	0.022
LDL cholesterol (mmol/L)	2.4 ± 0.9	2.3 ± 0.7	0.043
Systolic BP (mmHg)	137.9 ± 19.5	135.5 ± 17.2	<0.001
Diastolic BP (mmHg)	74.6 ± 11.6	73.9 ± 10.8	0.097
ACR (mg/mmol)	7.2 (2-44)	2.7 (1-10.7)	<0.001
Retinopathy	36.3% (350)	29.9% (602)	<0.001
Lipid lowering drugs	70.8% (862)	76.4% (1985)	<0.001
SUA (mmol/L)	0.41 ± 0.11	0.37 ± 0.09	<0.001

AKI controls were defined as no AKI at least for 10 years of duration of diabetes.

Table S 3 Association of SUA with clinical outcomes in the discovery cohort of HKDR with or without adjustment for AKI.

	Model 1 (adjustment with exclusion of AKI)		Model 2 (adjustment with inclusion of AKI)	
	HR (95% CI)	P	HR (95% CI)	P
Chronic kidney disease	4.13 (2.9-5.89)	<0.001	3.34 (2.05-5.43)	<0.001
End-stage renal disease	12.96 (8.11-20.7)	<0.001	7.3 (4.49-11.86)	<0.001
All-cause death	2.48 (1.6-3.82)	<0.001	1.36 (0.87-2.1)	0.174

Model 1 was adjusted for conventional risk factors, including age, gender, duration of diabetes, smoking, BMI, HbA1c, HDL-C, LDL-C, SBP, DBP, log-transformed ACR, eGFR, retinopathy, use of lipid lowering drugs (yes/no), antihypertensive drugs (yes/no), RAS inhibitors (yes/no), and antihyperglycemic drugs (yes/no), history of stroke, history of CHD, and/or history of CKD. Model 2 was adjusted for conventional risk factors in addition to AKI, which was used as time-dependent covariates in the Cox models.

Table S4 Association of PRS with clinical outcomes in the replication cohort of HKDB

	Model 1 (non-adjustment)		Model 2 (adjustment)	
	OR	P	OR	P
AKI (1233 cases vs. 2643 controls)				
PRS (per SD; #SNP=27)	1.04 (0.97-1.11)	0.294	**1.14 (1.04-1.25)**	**0.007**
Tertile 1	Ref.	/	Ref.	/
Tertile 2	1.09 (0.91-1.29)	0.36	1.26 (0.99-1.6)	0.065
Tertile 3	1.22 (0.99-1.51)	0.057	**1.57 (1.18-2.1)**	**0.002**
CKD (1975 cases vs. 1996 controls)				
PRS (per SD; #SNP=27)	1.05 (0.99-1.12)	0.12	**1.15 (1.05-1.27)**	**0.004**
Tertile 1	Ref.	/	Ref.	/
Tertile 2	1.15 (0.98-1.35)	0.078	**1.43 (1.12-1.83)**	**0.004**
Tertile 3	1.22 (1.01-1.48)	0.041	**1.58 (1.17-2.14)**	**0.003**
ESRD (219 cases vs. 3286 controls)				
PRS (per SD; #SNP=27)	0.98 (0.85-1.12)	0.728	1.02 (0.83-1.24)	0.886
Tertile 1	Ref.	/	Ref.	/
Tertile 2	0.94 (0.66-1.33)	0.709	1.01 (0.6-1.71)	0.975
Tertile 3	1.06 (0.7-1.6)	0.779	1.15 (0.61-2.16)	0.666
All-cause death (138 cases vs. 5869 controls)				
PRS (per SD; #SNP=27)	0.96 (0.81-1.13)	0.597	0.91 (0.72-1.15)	0.428
Tertile 1	Ref.	/	Ref.	/
Tertile 2	1.03 (0.66-1.6)	0.892	0.79 (0.45-1.41)	0.431
Tertile 3	1.16 (0.69-1.94)	0.583	1.09 (0.56-2.14)	0.791

Model 2 was adjusted for conventional risk factors, including age, gender, duration of diabetes, smoking, BMI, HbA1c, HDL-C, LDL-C, SBP, DBP, log-transformed ACR, retinopathy, use of lipid lowering drugs (yes/no).

Table S5 Associations of AKI (yes/no), the status of AKI severity and recovery with clinical outcomes from the updated definitions.

		Chronic kidney disease		End-stage renal disease		All-cause death	
		HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
AKI (yes/no)		1.9 (1.63-2.21)	<0.001	3.41 (2.96-3.93)	<0.001	5.56 (5.07-6.09)	<0.001
AKI Severity	No AKI	Ref.	/	Ref.	/	Ref.	/
	Stage 1	1.46 (0.92-2.32)	<0.001	1.65 (1.02-2.68)	<0.001	5.09 (4.62-5.6)	<0.001
	Stage 2	1.91 (1.62-2.27)	<0.001	3.42 (2.94-3.97)	<0.001	6.32 (5.19-7.7)	<0.001
	Stage 3	2.16 (1.53-3.06)	<0.001	4.34 (3.35-5.62)	0.041	7.84 (6.81-9.02)	<0.001
AKI Recovery	No AKI	Ref.	/	Ref.	/	Ref.	/
	Complete recovery	1.53 (1.08-2.17)	<0.001	2.42 (1.85-3.17)	<0.001	4.67 (4.16-5.25)	<0.001
	Partial recovery	1.66 (1.30-2.11)	<0.001	2.58 (2.11-3.15)	<0.001	5.61 (4.83-6.51)	<0.001
	Non-recovery	2.71 (1.85-3.98)	<0.001	4.58 (3.38-6.2)	<0.001	8.15 (6.96-9.54)	<0.001

Chronic kidney disease (CKD) and end-stage renal disease (ESRD) were defined by excluding AKI and using eGFR which remained low over 3 months (eGFR <60 mL/min/1.73 m^2 and eGFR <15 mL/min/1.73 m^2 for CKD and ESRD, respectively), in addition to diagnostic codes as described in the primary analysis. The censor date was extended to June 30th, 2019. AKI, AKI severity and AKI recovery were used as time-dependent covariates in the Cox models, HRs and p-values were adjusted for conventional risk factors at baseline, including age, gender, duration of diabetes, smoking, SUA, BMI, HbA1c, HDL-C,

LDL-C, SBP, DBP, log-transformed ACR, eGFR, retinopathy, use of lipid lowering drugs, antihypertensive drugs, RAS inhibitors, and antihyperglycemic drugs, history of stroke, history of CHD, and/or history of CKD.

Table S6 Association of SUA with clinical outcomes in males and females in the discovery cohort of HKDR.

	Male		Female	
	HR (95% CI)	P	HR (95% CI)	P
AKI	2.53 (1.38-4.65)	0.003	4.81 (2.7-8.59)	<0.001
Chronic kidney disease	4.30 (2.50-7.40)	<0.001	4.09 (2.51-6.66)	<0.001
End-stage renal disease	21.91 (10.66-45.02)	<0.001	7.61 (3.96-14.63)	<0.001
All-cause death	2.19 (1.19-4.05)	<0.001	2.77 (1.48-5.17)	0.001

Adjustment for age, duration of diabetes, smoking, BMI, HbA1c, HDL-C, LDL-C, SBP, DBP, log-transformed ACR, eGFR, retinopathy, use of lipid lowering drugs (yes/no), antihypertensive drugs (yes/no), RAS inhibitors (yes/no), antihyperglycemic drugs (yes/no), history of stroke, history of CHD, and/or history of CKD.

Table S7 Association of hyperuricemia with clinical outcomes in male, female and all patients in the discovery cohort of HKDR.

	Male		Female		All	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
AKI	1.18 (1.04-1.35)	0.013	1.34 (1.19-1.52)	<0.001	1.28 (1.17-1.4)	<0.001
Chronic kidney disease	1.37 (1.22-1.54)	<0.001	1.53 (1.37-1.71)	<0.001	1.46 (1.35-1.59)	<0.001
End-stage renal disease	1.86 (1.56-2.21)	<0.001	1.44 (1.21-1.71)	<0.001	1.67 (1.48-1.89)	<0.001
All-cause death	1.19 (1.03-1.37)	0.017	1.04 (0.9-1.21)	0.589	1.12 (1.02-1.24)	0.024

[a]Hyperuricemia was defined as SUA >0.42 mmol/L in male and >0.36 mmol/L in female according to the National Kidney Foundation.

[b]Adjustment for age, duration of diabetes, smoking, BMI, HbA1c, HDL-C, LDL-C, SBP, DBP, log-transformed ACR, eGFR, retinopathy, use of lipid lowering drugs (yes/no), antihypertensive drugs (yes/no), RAS inhibitors (yes/no), antihyperglycemic drugs (yes/no), history of stroke, history of CHD, and/or history of CKD.

Supplementary Table S8. Associations of AKI (yes/no), the status of AKI severity and recovery with CKD and ESRD with all-cause mortality as a competing risk.

		Chronic kidney disease		End-stage renal disease	
		HR (95% CI)	P	HR (95% CI)	P
AKI (yes/no)		11.2 (9.91-12.66)	<0.001	11.65 (10.31-13.16)	<0.001
AKI Severity	No AKI	Ref.	/	Ref.	/
	Stage 1	8.68 (7.54-9.99)	<0.001	9.21 (8.09-10.49)	<0.001
	Stage 2	22.93 (17.87-29.42)	<0.001	18.33 (15.24-22.05)	<0.001
	Stage 3	53.11 (39.01-72.31)	<0.001	51.07 (41.22-63.27)	<0.001
AKI Recovery	No AKI	Ref.	/	Ref.	/
	Complete recovery	13.01 (10.66-15.88)	<0.001	6.26 (5.3-7.39)	<0.001
	Partial recovery	8.69 (6.56-11.51)	<0.001	8.42 (6.9-10.29)	<0.001
	Non-recovery	20.53 (15.54-27.12)	<0.001	20.36 (16.83-24.63)	<0.001

All-cause mortality was considered as a competing risk in Fine-Gray subdistribution hazards model. HRs and p-values were adjusted for conventional risk factors at baseline, including age, gender, duration of diabetes, smoking, SUA, BMI, HbA1c, HDL-C, LDL-C, SBP, DBP, log-transformed ACR, eGFR, retinopathy, use of lipid lowering drugs, antihypertensive drugs, RAS inhibitors, and antihyperglycemic drugs, history of stroke, history of CHD, and/or history of CKD.

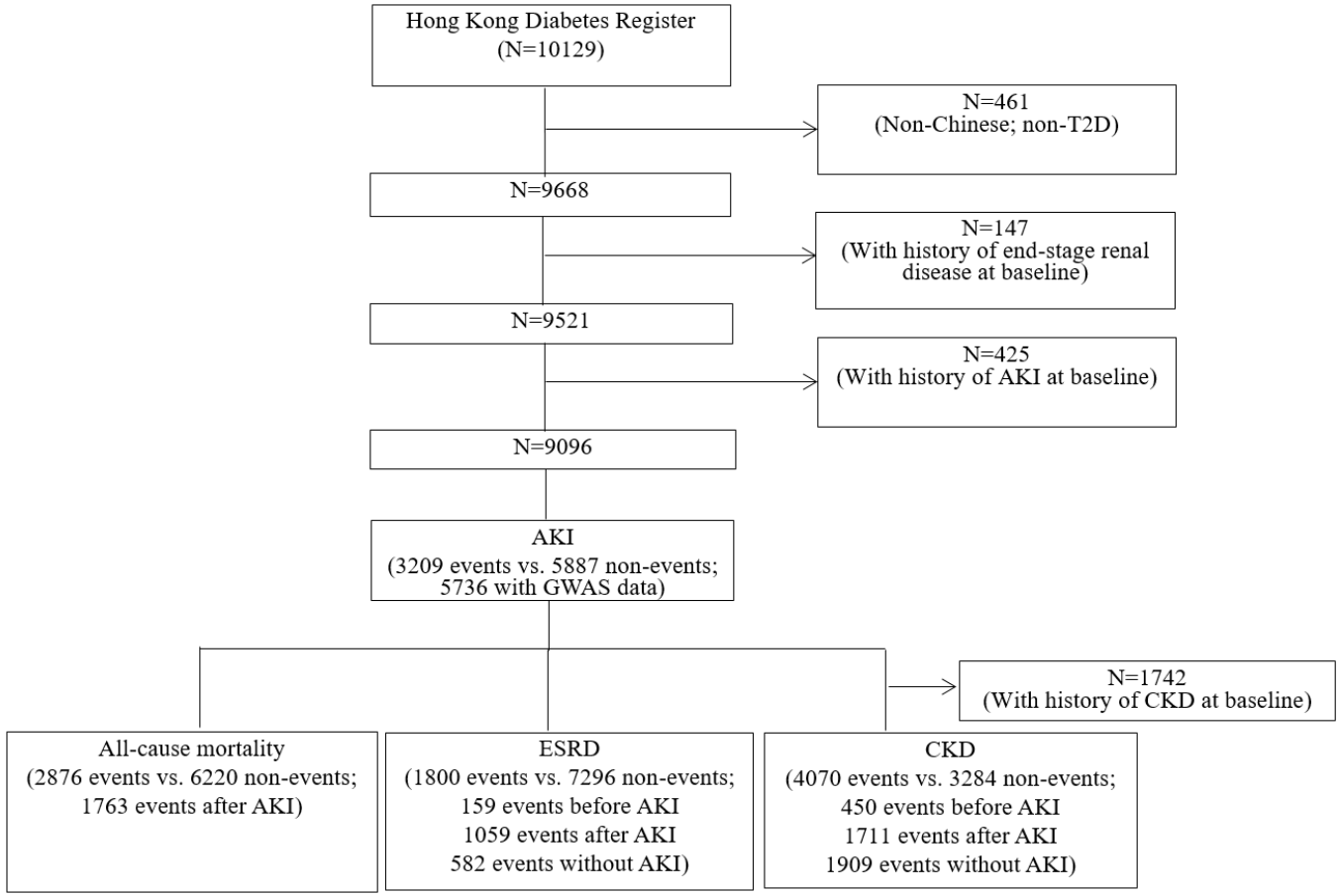

Figure S1 Sample selection from the discovery cohort of Hong Kong Diabetes Register (HKDR).

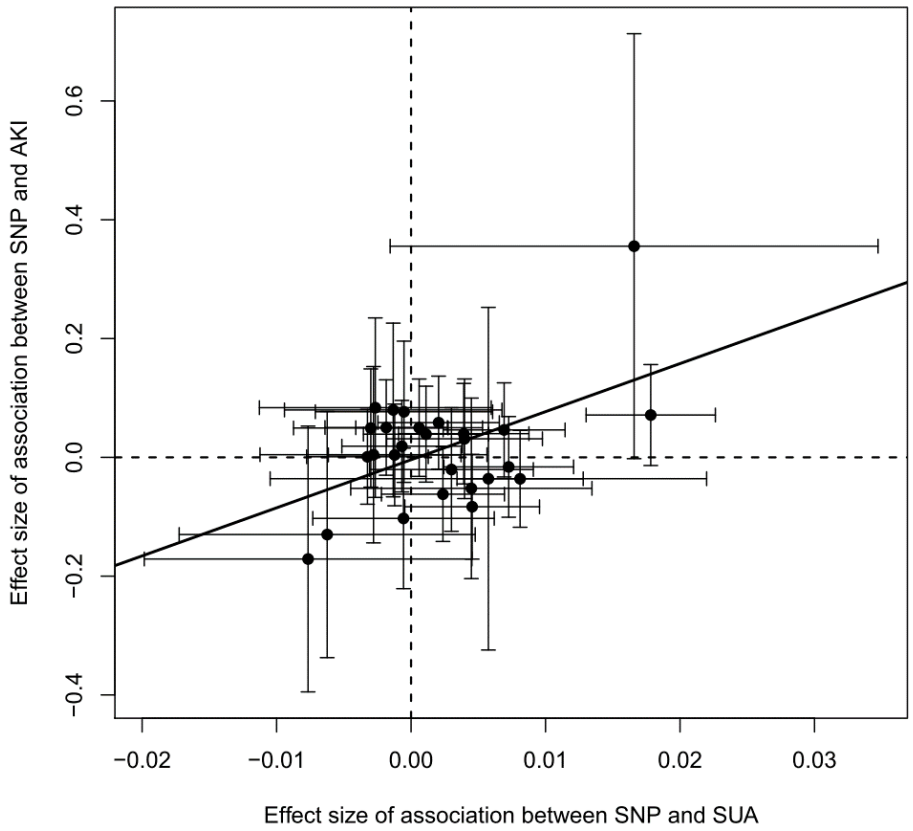

Figure S2 Relationship of association effect sizes of SUA-related SNPs between SUA and AKI in the discovery cohort of HKDR. Linear regression was used to model the relationship between effect sizes for SUA and AKI (solid line). Each point represents the per allele associations of a SNP (lines from each point are 95% confidence intervals for the associations). Effect sizes were obtained from linear model for SUA and Cox model for AKI with adjustment for potential confounders.

Supplementary text

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