Table S1 Medication regimen and drug contraindications for antihyperglycemic therapy, hypertension control and lipid management in ADA and Chinese guidelines

Treatment strategies	2018 ADA	Chinese guidelines
Antihyperglycemic Therapy		
Medication regimen		
Monotherapy	In patients with newly diagnosed type 2 diabetes who have A1C <9% (75 mmol/mol), metformin is the preferred initial pharmacologic agent. In patients with metformin contraindications or intolerance, consider another drug, including SGLT-2 inhibitors, GLP-1 RAs, DPP-4 inhibitors, thiazolidinediones, sulfonylureas, basal insulin.	If lifestyle management does not achieve the A1C goal (A1C ≥7%), consider metformin as first-line therapy. In patients with metformin contraindications or intolerance, consider alpha-glucosidase inhibitors, sulfonylureas, or glinides.
Dual Therapy	In patients with newly diagnosed type 2 diabetes who have A1C ≥9% (75 mmol/mol) or if the A1C target is not achieved after approximately 3 months of monotherapy, consider a combination of metformin and any one of the preferred six treatment options: sulfonylureas, thiazolidinediones, DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists, or basal insulin.	If monotherapy does not achieve the A1C goal over 3 months, consider to add another drug among the following options: metformin, sulfonylureas, thiazolidinediones, DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists, glinides, alpha-glucosidase inhibitors, or insulin.
Triple Therapy	If A1C target is still not achieved after ~ 3 months of dual therapy, proceed to a three-drug combination.	If dual therapy does not achieve the A1C goal over 3 months, consider a combination of three drugs among the above antihyperglycemic drugs.

Combination Injectable Therapy	In patients with newly diagnosed type 2 diabetes who are symptomatic and/or have A1C ≥10% (86 mmol/mol) and/or blood glucose levels ≥300mg/dL (16.7mmol/L). or if A1C target is not achieved after ~ 3 months of triple therapy, consider a combination use of basal insulin and rapid-acting insulin injection before meal or basal insulin and GLP-1 RA or directly changing to premixed insulin (with or without additional agents).	If triple therapy does not achieve the A1C goal over 3 months, consider a combination use of basal insulin and rapid-acting insulin injection before meal or directly changing to premixed insulin (with or without additional agents). Sulfonylureas and glinides should be avoided if combination injectable therapy was used.
Short-term intensive insulin therapy	-	Consider a combination use of basal insulin and rapid-acting insulin injection before meal or changing to premixed insulin in patients with newly diagnosed type 2 diabetes who are symptomatic and/or have A1C ≥9% (75 mmol/mol) and/or blood glucose levels ≥200mg/dL (11.1 mmol/L).
Drug contraindications	Metformin: discontinue if eGFR <30; Acarbose: Avoid if eGFR <30; Glyburide: Avoid use in patients with renal impairment	Metformin: avoid if eGFR <45; Glyburide: Avoid if eGFR <60; Glimepiride: avoid if eGFR <45; Glipizide: avoid if eGFR <30; Gliquidone: avoid if eGFR <15; Gliclazide: avoid if eGFR <30; Acarbose: Avoid if eGFR <30; Saxagliptin: avoid if eGFR <30
Hypertension Control		
Medication regimen		
Monotherapy	If initial BP between 140/90 mmHg and 160/100 mmHg, start one agent: ACE inhibitors, ARBs, CCBs, diuretics.	If initial BP between 140/90 mmHg and 160/100 mmHg, start one agent: ACE inhibitors, ARBs, diuretics, calcium channel blockers, β-receptor blockers.

Dual Therapy	If initial BP ≥160/100 mm Hg or monotherapy dose not meeting target, start drug from 2 of 3 options: ACE inhibitors or ARBs, CCBs, diuretics.	If BP ≥160/100 mm Hg or monotherapy dose not meeting target, start drug from 2 of 4 options: ACE inhibitors or ARBs, diuretics, calcium channel blockers, β-receptor blockers.
Triple Therapy	If dual Therapy dose not meeting target, add agent from complementary drug class: ACE inhibitors or ARBs, CCBs, diuretics.	If dual Therapy dose not meeting target, start three of the above antihypertensive drugs.
Quadruple therapy	Not meeting target or adverse effects using a drug from each of three classes, consider addition of mineralocorticoid receptor antagonist.	If triple Therapy dose not meeting target, start four of the above antihypertensive drugs.
Drug contraindications	-	Ramipril: avoid if eGFR <15; Lercanidipine: avoid if eGFR <30; Indapamide: avoid if eGFR <30
Lipid Management		
Medication regimen		
Statin	For patients of all ages with diabetes and ASCVD; For patients with diabetes and additional ASCVD risk factors*	If lipid level exceed the treatment target, consider statin as First-line drug.
Statin and additional LDL lowering therapy	For patients with diabetes and atherosclerotic cardiovascular disease, if LDL cholesterol is ≥70 mg/dL on maximally tolerated statin dose, consider adding additional LDL lowering therapy (such as ezetimibe or PCSK9 inhibitor)	If the cholesterol level dose not meeting target using statin, consider adding other lipid-lowing drug, such as ezetimibe.
Fibrate	For patients with fasting triglyceride levels ≥500 mg/dL (5.7 mmol/L)	For patients with fasting triglyceride levels ≥500 mg/dL (5.7 mmol/L)
Drug contraindications	-	Fluvastatin: avoid if eGFR <30; Rosuvastatin: avoid if eGFR <30;

	Fenofibrate: avoid if eGFR <30

Note: treatment target: HbA1C <7%; BP <130/80mmHg; LDL-C <1.8mmol/L for very-high-risk, LDL-C <2.6mmol/L for high-risk. If treatment tolerated and target achieved, consider continuing therapy. For drug contraindication, we only list the drugs that required discontinuation at low eGFR but did not contain the drugs with required dose adjustment or no dosage adjustment necessary at low eGFR.

*ASCVD risk factors include LDL cholesterol ≥100 mg/dL (2.6 mmol/L), high blood pressure, smoking, **chronic kidney disease**, albuminuria, and family history of premature ASCVD.

HbA1c, glycosylated hemoglobin; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; CCB, calcium channel blockers; ASCVD, atherosclerotic cardiovascular disease.

Table S2 Antihypertensive treatment regimen and BP control target for ADA guideline from 2003 to 2018 versions

ADA versions	2003-2007ADA	2008-2012ADA	2013/2014ADA	2015/2016ADA	2017/2018ADA
BP control target for DN patients	130/80mmHg	130/80mmHg	140/80mmHg	140/90mmHg	130/80mmHg
BP level for initial drug treatment	BP ⩾140/90 mmHg		BP ⩾140/80 mmHg	BP >140/90 mmHg	BP >140/90 mmHg start one drug; BP >160/100 mmHg start two drugs
Treatment regiment	1. In the treatment of both micro- and macroalbuminuria, either ACE inhibitors or ARBs should be used except during pregnancy. 2. The use of DCCBs in nephropathy should be restricted to additional therapy to further lower blood pressure in patients already treated with ACE inhibitors or ARBs. 3. In patients unable to tolerate ACE inhibitors	1. In the treatment of the nonpregnant patient with micro- or macroalbuminuria, either ACE inhibitors or ARBs should be used. 2. Other drugs, such as diuretics, calcium channel blockers, and β-blockers, should be used as additional therapy to further lower blood pressure in patients already treated with ACE inhibitors or ARBs, or as alternate therapy in the rare individual unable to tolerate ACE inhibitors or ARBs		1. Either an ACE inhibitor or ARB is suggested for the treatment of the nonpregnant patient with modestly elevated urinary albumin excretion (30-299 mg/day) and is recommended for those with urinary albumin excretion > 300 mg/day. 2. Diuretics, calcium channel blockers, and β-blockers can be used as additional therapy to further lower blood pressure in patients already treated with maximum doses of ACE	1. An ACE inhibitor or ARB is the recommended first-line treatment for hypertension in patients with diabetes and urinary albumin-to-creatinine ratio ≥300 mg/g creatinine or 30-299 mg/g creatinine. If one class is not tolerated, the other should be substituted. 2. Antihypertensive drugs including ACE inhibitors, ARB, thiazide-like diuretics, or dihydropyridine calcium channel blockers. 3. The combination of ACE

	and/or ARBs, consider the use of non-DCCBs, β-blockers, or diuretics.		inhibitors or ARBs or as alternate therapy in the rare individual unable to tolerate ACE inhibitors and ARBs. 3. The combination of ACE inhibitors and ARB should be avoided.	inhibitors and ARB should be avoided.

Note: The 2007, 2012, 2014, 2016 and 2018 versions of ADA were selected as representative of each group to study the association between guideline adherence and BP-goal achieving rate.

Table S3 Guideline adherence rate for five groups of ADA guidelines and associated BP target achievement rate

Group	Representative ADA version	BP control target for DN patients	Guideline adherence rate	Target achievement rate for adherence	Target achievement rate for non-adherence
2017/2018ADA	2018ADA	130/80mmHg	36.00%	34.31%	17.00%
2015/2016ADA	2016ADA	140/90mmHg	55.12%	55.71%	38.43%
2013/2014ADA	2014ADA	140/80mmHg	50.97%	42.63%	26.71%
2008-2012ADA	2012ADA	130/80mmHg	41.80%	31.21%	12.71%
2003-2007ADA	2007ADA	130/80mmHg	44.49%	34.06%	19.46%

Table S4 Hazard ratios (95% confidence intervals) of progression to ESKD by trajectory group of each clinical parameter in the first two years of follow-up.

parameter	longitudinal trajectory	Total number	Number of ESKD	Incidence rate of ESKD	Unadjusted	P value	Model 1	P value	Model 2	P value	Model 3	P value
PRO	Class_1	535	111	20.75%	Reference		Reference		Reference		Reference	
	Class_2	132	82	62.12%	7.16 (5.31-9.66)	<0.001	7.13 (5.29-9.62)	<0.001	4.83 (3.41-6.85)	<0.001	4.41 (3.08-6.30)	<0.001
	Class_3	35	25	71.43%	13.35 (8.50-20.97)	<0.001	13.39 (8.51-21.08)	<0.001	8.86 (5.17-15.19)	<0.001	8.29 (4.81-14.28)	<0.001
	Class_4	20	12	60.00%	10.36 (5.62-19.08)	<0.001	10.52 (5.68-19.48)	<0.001	8.68 (4.06-18.55)	<0.001	7.46 (3.45-16.14)	<0.001
LDL-C	Class_1	386	81	20.98%	Reference		Reference		Reference		Reference	
	Class_2	237	84	35.44%	1.79 (1.32-2.42)	<0.001	1.78 (1.31-2.42)	<0.001	2.11 (1.46-3.06)	<0.001	1.97 (1.37-2.85)	<0.001
	Class_3	75	44	58.67%	4.37 (3.02-6.32)	<0.001	4.37 (3.02-6.33)	<0.001	4.23 (2.56-6.99)	<0.001	3.42 (2.04-5.71)	<0.001
	Class_4	13	9	69.23%	8.83 (4.40-17.70)	<0.001	8.77 (4.37-17.61)	<0.001	7.65 (2.69-21.74)	<0.001	5.84 (2.01-16.96)	0.001
SBP	Class_1	235	61	25.96%	Reference		Reference		Reference		Reference	
	Class_2	318	114	35.85%	1.39 (1.02-1.90)	0.039	1.37 (0.99-1.88)	0.055	1.13 (0.81-1.58)	0.468	1.08 (0.77-1.51)	0.647
	Class_3	24	16	66.67%	3.41 (1.96-5.92)	<0.001	3.36 (1.90-5.94)	<0.001	2.27 (1.21-4.26)	0.010	2.17 (1.16-4.06)	0.016
UA	Class_1	137	17	12.41%	Reference		Reference		Reference		Reference	
	Class_2	306	82	26.80%	2.57 (1.52-4.33)	<0.001	2.69 (1.58-4.56)	<0.001	2.10 (1.12-3.94)	0.021	1.31 (0.76-2.26)	0.277
	Class_3	226	90	39.82%	4.69 (2.79-7.90)	<0.001	5.03 (2.96-8.55)	<0.001	2.69 (1.38-5.25)	0.004	1.35 (0.75-2.42)	0.126
	Class_4	68	42	61.76%	7.32 (4.15-12.9)	<0.001	8.18 (4.56-14.68)	<0.001	3.76 (1.79-7.89)	<0.001	1.94 (1.00-3.74)	0.049

HbA1c	Class_1	290	86	29.66%	Reference		Reference		Reference		Reference	
	Class_2	292	97	33.22%	1.23 (0.92-1.65)	0.167	1.22 (0.91-1.64)	0.191	1.18 (0.85-1.66)	0.325	1.23 (0.88-1.72)	0.220
	Class_3	111	32	28.83%	1.20 (0.80-1.80)	0.384	1.18 (0.78-1.79)	0.433	1.20 (0.75-1.92)	0.438	1.21 (0.76-1.93)	0.427
	Class 4	31	10	32.26%	1.42 (0.74-2.74)	0.295	1.42 (0.74-2.74)	0.296	1.35 (0.66-2.78)	0.409	1.36 (0.66-2.80)	0.407

Note: Model 1 adjusted for age, sex. Model 2 further adjusted for the visit number during follow-up period and the laboratory test results (among HbA1c, SBP, DBP, TC, TG, LDL-C, HDL-C, UA) measured at baseline except selected parameter. Model 3 further adjusted for the baseline eGFR

PRO, Proteinuria; HbA1c, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; UA, uric acid.

Table S5 Hazard ratios (95% confidence intervals) of progression to ESKD by trajectory group of each clinical parameter in the first three years of follow-up

parameter	subgroup	Total number	Number of ESKD	Incidence rate of ESKD	Unadjusted	P value	Model 1	P value	Model 2	P value	Model 3	P value
PRO	Class_1	430	73	16.98%	Reference		Reference		Reference		Reference	
	Class_2	96	48	50.00%	6.08 (4.17-8.86)	<0.001	6.06 (4.15-8.84)	<0.001	4.60 (2.92-7.24)	<0.001	4.04 (2.55-6.40)	<0.001
	Class_3	31	23	74.19%	15.53 (9.44-25.56)	<0.001	15.31 (9.29-25.22)	<0.001	12.01(6.67-21.65)	<0.001	10.09 (5.55-18.34)	<0.001
	Class_4	11	4	36.36%	9.00 (3.24-25.04)	<0.001	9.23 (3.30-25.81)	<0.001	7.10 (2.11-23.82)	0.002	5.31 (1.55-18.13)	0.008
LDL-C	Class_1	157	19	12.10%	Reference		Reference		Reference		Reference	
	Class_2	304	77	25.33%	2.02 (1.22-3.33)	0.006	1.98 (1.20-3.28)	0.008	1.93 (1.09-3.40)	0.023	1.85 (1.05-3.27)	0.033
	Class_3	91	36	39.56%	3.76 (2.15-6.55)	<0.001	3.74 (2.14-6.53)	<0.001	4.45 (2.20-8.98)	<0.001	3.44 (1.69-7.01)	0.001
	Class_4	15	10	66.67%	10.40 (4.81-22.51)	<0.001	9.84 (4.50-21.53)	<0.001	9.09 (3.09-26.73)	<0.001	5.92 (1.97-17.81)	0.002
SBP	Class_1	101	16	15.84%	Reference		Reference		Reference		Reference	
	Class_2	336	94	27.98%	2.25 (1.32-3.84)	0.003	2.17 (1.27-3.73)	0.005	2.02 (1.14-3.57)	0.016	1.89 (1.07-3.33)	0.029
	Class_3	54	22	40.74%	2.85 (1.49-5.44)	0.002	2.65 (1.36-5.15)	0.004	2.53 (1.23-5.21)	0.012	2.26 (1.11-4.62)	0.025
UA	Class_1	113	12	10.62%	Reference		Reference		Reference		Reference	
	Class_2	245	50	20.41%	2.33 (1.24-4.37)	0.009	2.40 (1.27-4.55)	0.007	1.77 (0.88-3.57)	0.109	1.21 (0.59-2.48)	0.604
	Class_3	145	49	33.79%	4.45 (2.36-8.39)	<0.001	4.72 (2.47-8.99)	<0.001	2.72 (1.28-5.76)	0.009	1.84 (0.87-3.86)	0.109
	Class_4	76	37	48.68%	8.10 (4.20-15.61)	<0.001	8.76 (4.47-17.18)	<0.001	5.07 (2.28-11.28)	<0.001	2.92 (1.31-6.48)	0.009

HbA1c	Class_1	208	46	22.12%	Reference		Reference		Reference		Reference	
	Class_2	234	66	28.21%	1.42 (0.98-2.08)	0.067	1.38 (0.94-2.03)	0.096	1.11 (0.72-1.72)	0.624	1.23 (0.79-1.90)	0.356
	Class_3	100	25	25.00%	1.45 (0.89-2.37)	0.139	1.38 (0.84-2.28)	0.207	1.33 (0.78-2.29)	0.298	1.47 (0.85-2.54)	0.170
	Class 4	26	7	26.92%	1.57 (0.71-3.48)	0.269	1.57 (0.71-3.49)	0.268	1.62 (0.70-3.74)	0.257	1.77 (0.76-4.15)	0.187

Note: Model 1 adjusted for age, sex. Model 2 further adjusted for the visit number during follow-up period and the laboratory test results (among HbA1c, SBP, DBP, TC, TG, LDL-C, HDL-C, UA) measured at baseline except selected parameter. Model 3 further adjusted for the baseline eGFR.

PRO, Proteinuria; HbA1c, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; UA, uric acid.

Figure S1 Flowchart of patient enrollment and patient's timeline. (A) Inclusion and exclusion criteria for study population. (B) One outpatient visit of a patient is selected as a sample (dash-line box). Each sample includes diagnosis, laboratory tests and prescription of the patient, so there are multiple samples for one patient. According to the actual clinical situation, the laboratory tests related to current visit are selected from 14 days ago to 3 days later. Short-term control effect is evaluated by the clinical parameter control in 3-6 months of treatment, while long-term outcome is evaluated by ESKD.

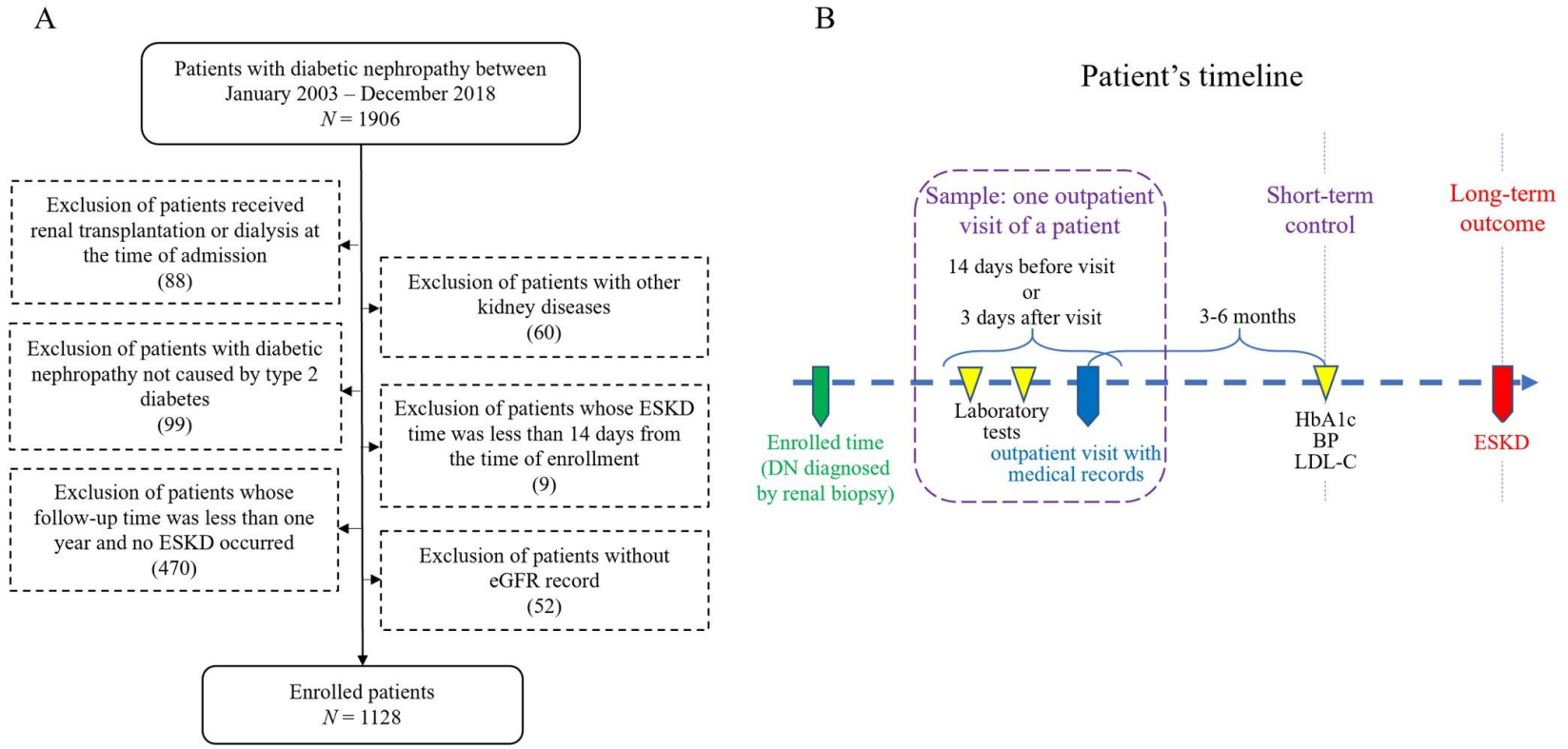

Figure S2 Flowchart of sample inclusion when evaluating the influence of guideline adherence on short-term/long-term outcome. Taking the antihyperglycemic therapy of ADA guideline for example.

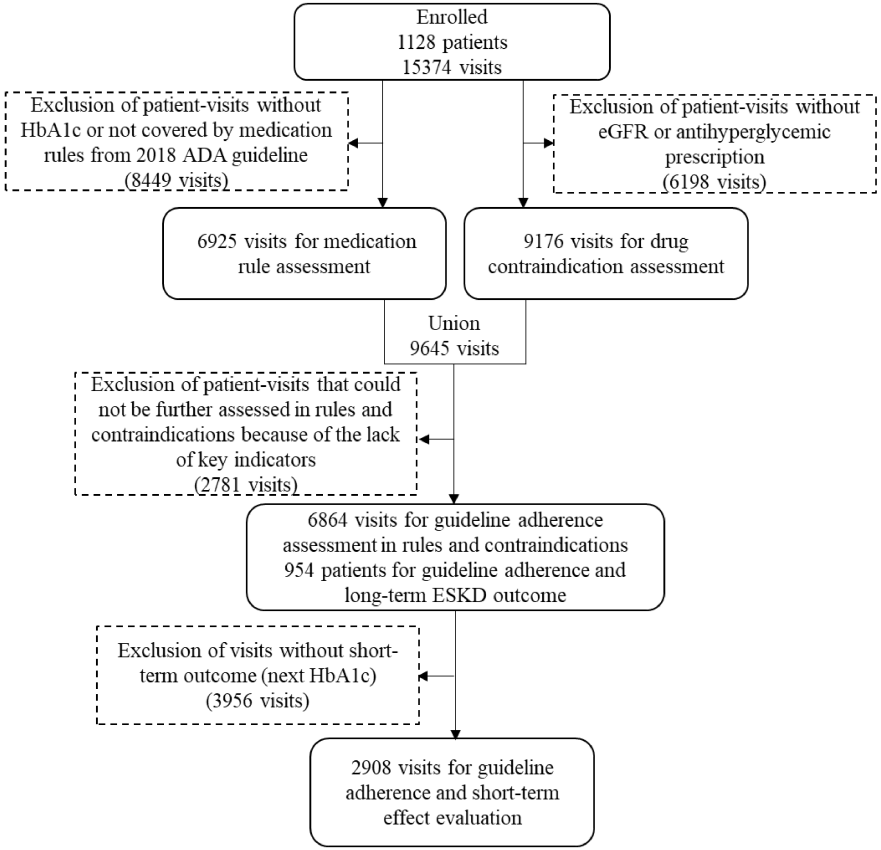

Figure S3 The relationship between the patient's adherence rate and ESKD occurring rate for all patients. Six graphs represent the adherence to ADA (A, B, C) or Chinese guidelines (D, E, F) for antihyperglycemic therapy, hypertension control and lipid management, respectively. Numbers on the broken line represent the

number of patients in the every 10% or 20% adherence rate interval. Abbreviations: ADA, American Diabetes Association guideline; CHN, Chinese guideline.

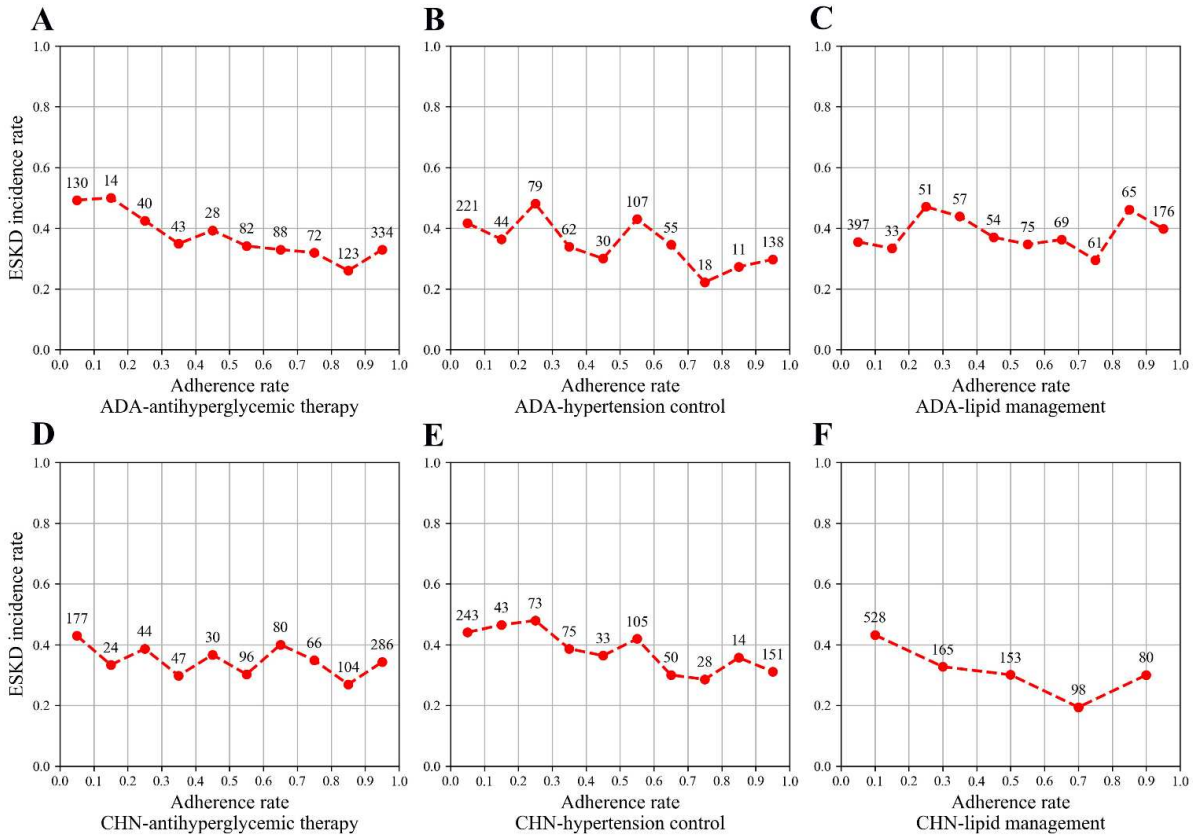

Figure S4 The relationship between the patient's adherence rate and ESKD occurring rate for patients with visit number of 5 or greater. Six graphs represent the adherence to ADA (A, B, C) or Chinese guidelines (D, E, F) for antihyperglycemic therapy, hypertension control and lipid management, respectively. Numbers on

the broken line represent the number of patients in the every 10% or 20% adherence rate interval. Abbreviations: ADA, American Diabetes Association guideline; CHN, Chinese guideline.

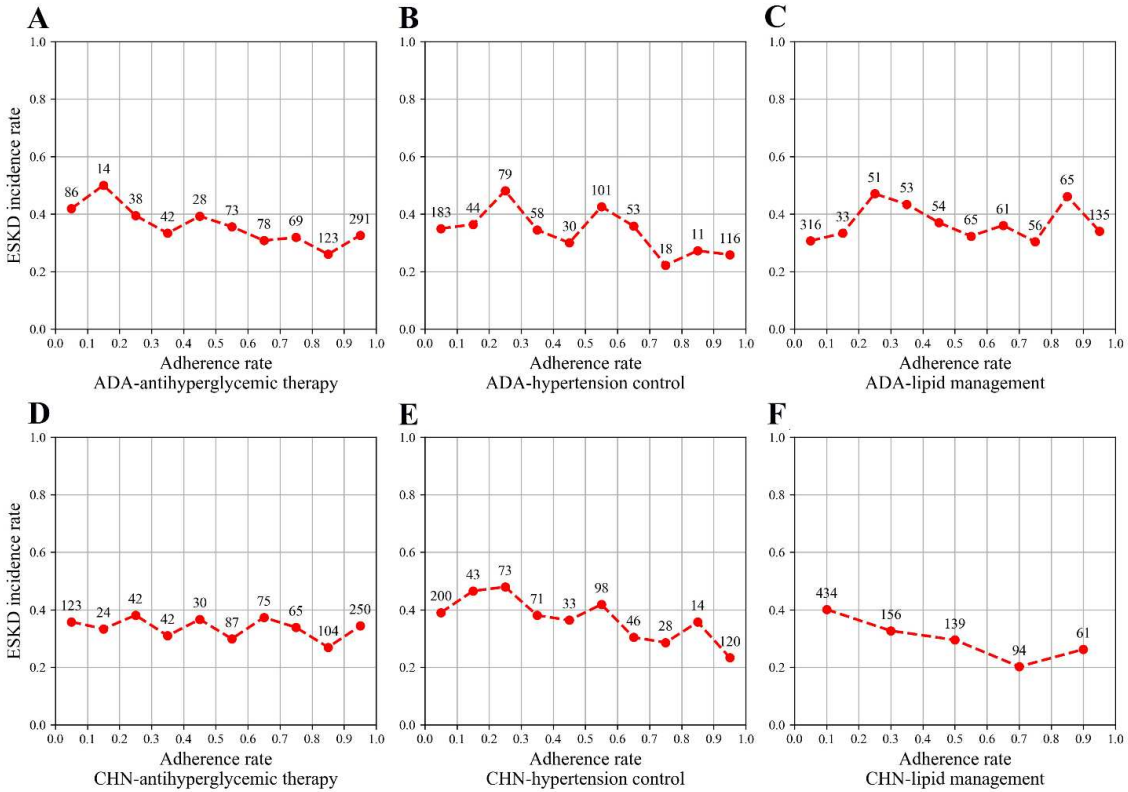

Figure S5 The relationship between the patient's adherence rate and ESKD occurring rate according to hypertension control from different versions of ADA

guideline. The adherence rate to different guideline versions was calculated according to the visit time of each patient, and then analysis the relationship between patient's adherence rate and ESKD occurrence rate.