

Supplementary Online Content

Lazarus B, Wu A, Shin JI, et al. Association of metformin use with risk of lactic acidosis across the range of kidney function: a community-based cohort study. *JAMA Intern Med*. Published online June 4, 2018.
doi:10.1001/jamainternmed.2018.0292

eTable 1. Diagnostic codes (International Classification of Diseases, Ninth Revision, Clinical Modification, ICD-9-CM) used to define comorbid cardiovascular disease, heart failure and hypertension

eTable 2. Baseline characteristics of patients with prevalent diabetes mellitus after excluding baseline insulin users in Geisinger Health System (n = 62,442)

eTable 2. Baseline characteristics of participants in the active comparator cohort using nationwide healthcare claims data (MarketScan, n=82,017)

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Diagnostic codes (International Classification of Diseases, Ninth Revision, Clinical Modification, ICD-9-CM) used to define comorbid cardiovascular disease, heart failure and hypertension

Diagnosis	ICD-9-CM volume 1-2	ICD-9-CM volume 3
Cardiovascular disease		
Coronary artery disease	Starting with 414.0, 410 Or equal to 414.8, 414.9, 412	Starting with 36.1
Stroke	43x, 433.x1, 434.x1, V12.54 Or starting with 43x	
Peripheral arterial disease	443.9, 440.2, 440.3, 443.9, 785.4 Or starting with 440.2, 440.4, 707.1	38.18, 39.50, 39.25, 39.29 Or starting with 84.1
Heart failure	Starting with 428	
Hypertension	Starting with 401-405	

eTable 2. Baseline characteristics of patients with prevalent diabetes mellitus after excluding baseline insulin users in Geisinger Health System (n = 62,442)

Baseline characteristics	Overall	Baseline eGFR, ml/min/1.73m ²					P-for trend
		>90	60-89	45-59	30-44	<30	
Number of participants, n	62,442	26,320	24,529	6,679	3,673	1,241	
Age, mean (SD), years	61.3 (14.9)	51.2 (12.2)	66.0 (11.9)	73.0 (10.5)	75.8 (10.9)	75.9 (11.7)	<0.001
Female sex, %	51.1	49.9	49.6	55.9	59.1	59.5	<0.001
Black race, %	2.4	3.7	1.6	0.9	0.9	1.3	<0.001
eGFR, ml/min/1.73 m ² , mean (SD)	82.4 (24.0)	104.3 (11.2)	76.3 (8.5)	53.1 (4.3)	38.5 (4.2)	24.2 (4.1)	<0.001
Ever Smoking, %	47.6	50.7	46.8	43.7	40.9	37.2	<0.001
BMI, mean (SD), kg/m ²	34.2 (7.9)	35.8 (8.4)	33.2 (7.2)	32.4 (7.1)	32.1 (7.3)	31.8 (7.1)	<0.001
Hypertension, %	70.1	59.1	74.8	83.8	86.5	85.6	<0.001
Cardiovascular disease, %	11.8	5.9	13.6	20.2	24.1	23.1	<0.001
Heart failure, %	9.7	3.8	9.3	18.5	28.2	38.0	<0.001
Serum Bicarbonate, mean (SD), mmol/L	27.3 (3.0)	27.0 (2.8)	27.7 (2.9)	27.5 (3.1)	26.9 (3.6)	25.8 (4.3)	<0.001
HbA1c, mean (SD)	7.2 (1.6)	7.5 (1.9)	7.0 (1.3)	7.0 (1.2)	6.9 (1.3)	7.0 (1.3)	<0.001
Statin, %	42.1	36.1	47.1	47.3	44.5	36.1	<0.001
RASI, %	45.8	40.9	48.7	53.9	50.6	37.2	<0.001
Diuretics, %	32.9	23.9	35.5	47.4	50.0	45.7	<0.001
NSAID, %	21.2	22.6	21.5	19.1	16.1	10.5	<0.001

Abbreviations: eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; RASI, renin-angiotensin-system inhibitor; NSAID, non-steroidal anti-inflammatory drugs; SD, standard deviation

eTable 3. Baseline characteristics of participants in the active comparator cohort using nationwide healthcare claims data (MarketScan, n=82,017)

Baseline characteristics	Metformin	Sulfonylurea
Number of patients at baseline, n	67,578	14,439
Median follow-up time (IQR), months	12.0 (5.5, 22.6)	11.5 (4.6, 22.4)
Age, mean (SD), years	52.3 (9.0)	53.2 (9.0)
Female sex, %	49.5	45.1
eGFR, mean (SD)	89.8 (17.6)	85.4 (23.0)
Hypertension, %	66.1	66.9
Cardiovascular disease, %	14.7	16.9
Heart failure, %	2.4	4.2
Serum Bicarbonate, mean (SD) (n = 4,325)	25.3 (2.9)	25.1 (2.9)
HbA1c, mean (SD) (n = 42,121)	7.7 (1.9)	8.2 (2.0)
Medications		
Statin, %	37.4	36.8
Renin angiotensin system inhibitor, %	45.4	47.5
Diuretics, %	13.9	15.0
Non-steroidal anti-inflammatory drug, %	12.3	10.3
Insulin, %	9.9	11.6

Abbreviations: eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1