

Table 2. Number of Prevalent and Incident Metformin Users in Geisinger Health System, Frequency of Estimated Glomerular Filtration Rate (eGFR) Measurements, and Mean Daily Metformin Dose by Baseline eGFR Category

Baseline Use of Metformin	Baseline eGFR Category, mL/min/1.73 m ²				
	≥90	60-89	45-59	30-44	<30
Not using at baseline, No.	15 080	15 566	5385	3708	1579
Frequency of eGFR measurements per year, median (IQR)	1.58 (0.77-2.71)	2.19 (1.25-3.46)	2.73 (1.54-4.57)	3.35 (1.81-5.83)	4.72 (2.17-9.70)
Initiated metformin use after baseline, No.	6295	5823	1196	400	67
Using at baseline, No.	17 468	12 637	2759	1045	186
Frequency of eGFR measurements per year, median (IQR)	1.77 (1.02-2.72)	2.24 (1.40-3.33)	2.78 (1.75-4.09)	3.10 (1.69-4.76)	4.29 (2.70-7.16)
Daily dose at baseline, mean (SD), g	1.37 (0.58)	1.34 (0.59)	1.34 (0.60)	1.35 (0.59)	1.38 (0.59)

Abbreviation: IQR, interquartile range.

登録時にメトグルコを服用していない人が41318人。
 服用していた人が34095人。合計75413人が対象。
 経過中にメトグルコを服用した人が13781人

Table 3. Association of Time-Dependent Metformin Use With Acidosis Hospitalization by Time-Dependent Estimated Glomerular Filtration Rate (eGFR) Category in Geisinger Health System

Parameter	HR ^a (95% CI) for Acidosis Associated With Metformin Use by Time-Dependent eGFR Category, mL/min/1.73 m ²					
	Overall ^b	≥90	60-89	45-59	30-44	<30
Person-time (on metformin/off metformin)	188 578/281 536	80 653/98 905	79 788/102 110	21 232/40 861	6358/29 834	548/9827
Acidosis events (on metformin/off metformin)	737/1598	206/323	288/446	157/286	64/314	22/229
Unadjusted (n = 75 413)	0.89 (0.81-0.97)	0.77 (0.65-0.92)	0.82 (0.71-0.95)	1.05 (0.87-1.28)	0.95 (0.73-1.25)	1.71 (1.10-2.64)
Demographic adjusted ^c (n = 75 413)	0.89 (0.81-0.97)	0.75 (0.63-0.90)	0.82 (0.71-0.96)	1.07 (0.88-1.30)	0.98 (0.75-1.28)	1.76 (1.14-2.73)
Fully adjusted ^d (n = 72 232)	0.98 (0.89-1.08)	0.88 (0.73-1.05)	0.87 (0.75-1.02)	1.16 (0.95-1.41)	1.09 (0.83-1.44)	2.07 (1.33-3.22)
Fully adjusted with time-dependent medication use ^e (n = 72 232)	0.94 (0.83-1.05)	0.80 (0.66-0.97)	0.81 (0.68-0.95)	1.14 (0.93-1.40)	1.13 (0.85-1.49)	2.21 (1.42-3.44)
Sensitivity analyses						
Fully adjusted ^d excluding baseline insulin users (n = 60 112)	1.02 (0.91-1.13)	0.88 (0.71-1.09)	0.89 (0.75-1.06)	1.21 (0.97-1.50)	1.16 (0.87-1.57)	2.22 (1.41-3.51)
Fully adjusted ^d including adjustment for baseline hemoglobin A _{1c} (n = 58 093)	1.01 (0.90-1.14)	0.84 (0.67-1.04)	0.93 (0.78-1.12)	1.23 (0.98-1.55)	1.07 (0.78-1.46)	2.22 (1.37-3.59)
Fully adjusted ^d in incident diabetes mellitus cohort (n = 49 839)	0.91 (0.79-1.04)	0.85 (0.68-1.06)	0.82 (0.66-1.01)	1.15 (0.86-1.53)	0.88 (0.55-1.39)	2.37 (1.20-4.71)
Fully adjusted ^d with early censoring of metformin (n = 72 232)	1.04 (0.95-1.15)	0.93 (0.78-1.12)	0.93 (0.80-1.09)	1.23 (1.01-1.50)	1.17 (0.89-1.54)	2.26 (1.45-3.51)

Abbreviation: HR, hazard ratio.

^a Reference for HR: no metformin use.

^b Overall, adjusted for eGFR category.

^c Adjusted for age, sex, and race.

^d Adjusted for baseline age, sex, race, serum bicarbonate level, smoking status, comorbid cardiovascular disease, heart failure, peripheral vascular disease, hypertension, eGFR, use of statin medications, renin-angiotensin system

inhibitors, diuretics, nonsteroidal anti-inflammatory drugs, insulin, and other antidiabetic medications. eGFR category and metformin use were the only time-dependent variables. Patients with missing data were excluded from the fully adjusted analysis.

^e Adjusted for all variables in fully adjusted model; however, all medications were treated as time dependent along with eGFR category and metformin use. Patients with missing data were excluded from the fully adjusted analysis.

eGFRが30以下では危険率が2.07です。