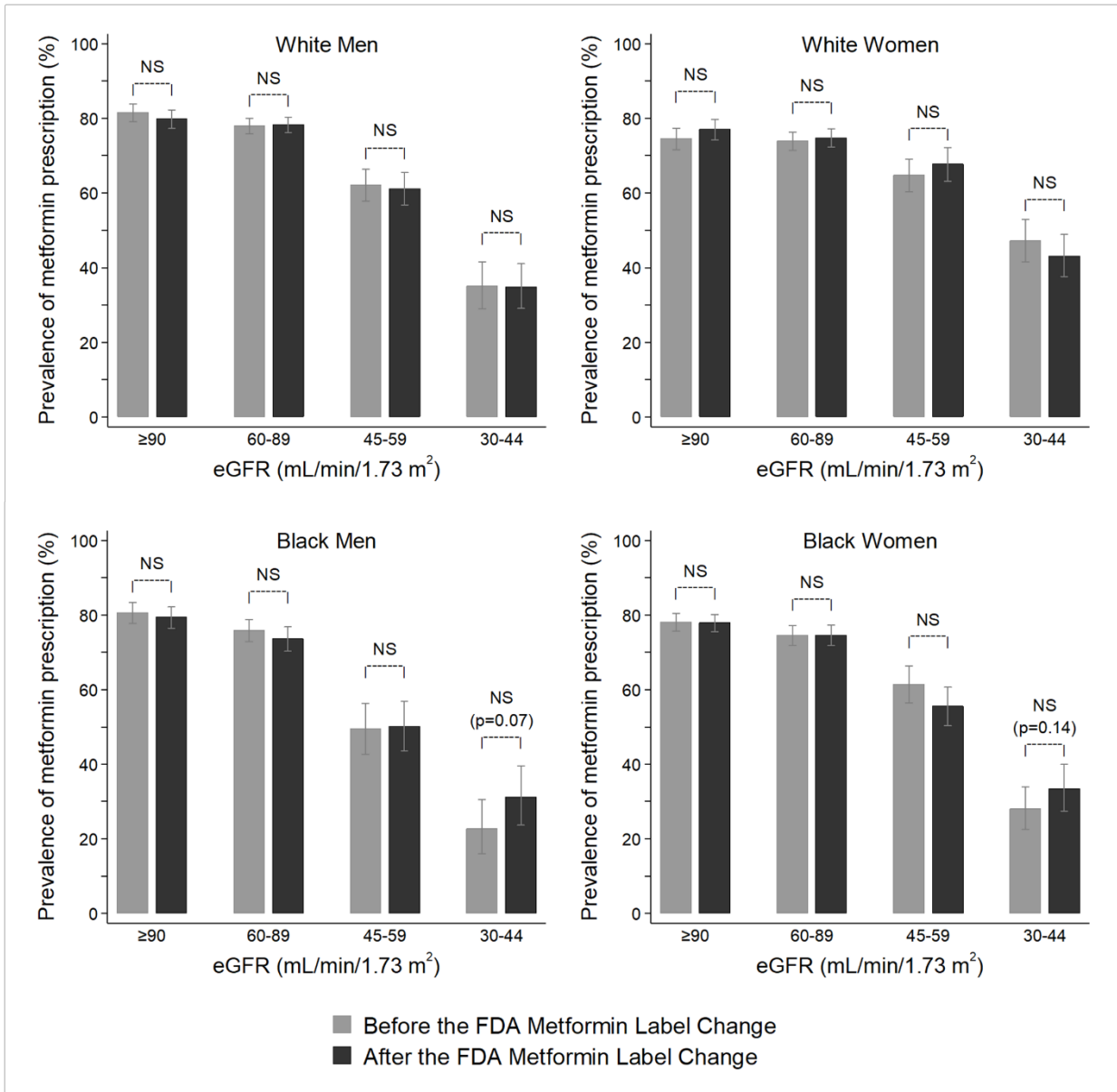**Table of Contents**

Supplemental Figure 1. Prevalence of metformin prescription across eGFR levels among patients with diabetes in Johns Hopkins Medicine, stratified by race and sex

NS, no significant; eGFR, estimated glomerular filtration rate; FDA; US Food and Drug Administration

Supplemental Table 1. Baseline characteristics of the Johns Hopkins Medicine study population, by sex and period (N=15,946)[a]

	Pre-FDA metformin label change		Post-FDA metformin label change	
	Men	Women	Men	Women
N (%)	5,447 (47.8)	5,938 (52.2)	5,360 (48.1)	5,780 (51.9)
Age (years), mean (SD)	61.4 (12.1)	60.9 (13.0)	62.0 (11.9)	61.2 (13.0)
Black	1,989 (36.5)	2,948 (46.7)	1,915 (35.7)	2,869 (49.6)
eGFR (mL/min/1.73 m^2), mean (SD)	79.9 (22.2)	79.9 (25.2)	79.6 (22.3)	80.9 (25.4)
eGFR category				
G1: eGFR ≥90	1,871 (34.4)	2,139 (36.0)	1,861 (34.7)	2,213 (38.3)
G2: eGFR 60-89	2,486 (45.6)	2,373 (40.0)	2,363 (44.1)	2,229 (38.6)
G3a: eGFR 45-59	715 (13.1)	869 (14.6)	737 (13.8)	800 (13.8)
G3b: eGFR 30-44	375 (6.9)	557 (9.4)	399 (7.4)	538 (9.3)
BMI (kg/m^2)[b], mean (SD)	32.9 (6.9)	35.0 (8.3)	33.1 (6.8)	35.1 (8.4)
Missing BMI	253 (4.6)	310 (5.2)	263 (4.9)	282 (4.9)
HbA1c (%)[c], mean (SD)	7.72 (1.71)	7.74 (1.68)	7.77 (1.73)	7.75 (1.73)
Missing HbA1c	1,946 (35.7)	2,193 (36.9)	1,990 (37.1)	2,126 (36.8)
History of comorbidities				
Hypertension	4,250 (78.0)	4,632 (78.0)	4,288 (80.0)	4,649 (80.4)
Congestive heart failure	401 (7.4)	468 (7.9)	438 (8.2)	445 (7.7)
Acidosis	122 (2.2)	167 (2.8)	134 (2.5)	178 (3.1)
Hypoglycemia	251 (4.6)	260 (4.4)	297 (5.5)	299 (5.2)
Myocardial infarction	314 (5.8)	234 (3.9)	330 (6.2)	233 (4.0)
Liver disease	429 (7.9)	479 (8.1)	444 (8.3)	517 (8.9)
Acute kidney injury	287 (5.3)	310 (5.2)	322 (6.0)	344 (6.0)
Median days (IQR) between the first eGFR measurement and the first antidiabetes prescription	0 (-48, 50)	0 (-55, 51)	0 (-51, 48)	0 (-56, 49)

eGFR, estimated glomerular filtration rate; BMI, body mass index; HbA1c, hemoglobin A1c;
SD, standard deviation; IQR, interquartile range
[a]Among 15,946 patients, 6,579 (41.3%) were included in both before and after the label change
[b]only for patients with body mass index values (N=15,286)
[c]only for patients with HbA1c values (N=10,966)
Unless otherwise indicated, data are reported as number (percentage) of patients

Supplemental Table 2. Baseline characteristics of the study population in replicating cohorts from OptumLabs Database Warehouse, by race and period

	Pre-FDA metformin label change		Post-FDA metformin label change	
	Black	White	Black	White
N (%)	85192 (15.4)	467475 (84.6)	98035 (15.6)	529029 (84.5)
Age (years), mean (SD)	58.5 (13.2)	62.2 (13.1)	58.9 (13.2)	62.7 (13.1)
Female	51595 (60.6)	222651 (47.6)	58919 (60.1)	250472 (47.3)
eGFR (mL/min/1.73 m^2), mean (SD)	87.5 (26.8)	78.0 (22.0)	87.1 (26.5)	78.0 (21.8)
eGFR category				
G1: eGFR ≥90	40484 (47.5)	154408 (33.0)	46272 (47.2)	174588 (33.0)
G2: eGFR 60-89	29813 (35.0)	205231 (43.9)	34505 (35.2)	233710 (44.2)
G3a: eGFR 45-59	9465 (11.1)	69339 (14.8)	10811 (11.0)	77155 (14.6)
G3b: eGFR 30-44	5430 (6.4)	38497 (8.2)	6447 (6.6)	43576 (8.2)
BMI (kg/m^2), mean (SD)	34.7 (8.4)	34.1 (7.8)	34.7 (8.4)	34.1 (7.8)
HbA1c (%), mean (SD)	7.91 (1.99)	7.52 (1.62)	7.86 (1.99)	7.49 (1.61)
History of comorbidities				
Hypertension	74006 (86.9)	389157 (83.2)	86311 (88.0)	448914 (84.9)
Congestive heart failure	9452 (11.1)	49425 (10.6)	12620 (12.9)	65178 (12.3)
Acidosis	2375 (2.28)	11774 (2.5)	4272 (4.4)	20559 (3.9)
Hypoglycemia	5701 (6.7)	27031 (5.8)	7659 (7.8)	34692 (6.6)
Myocardial infarction	3432 (4.0)	22030 (4.7)	4999 (5.1)	32068 (6.1)
Liver disease	7584 (8.9)	48134 (10.3)	11426 (11.7)	73899 (14.0)
Acute kidney injury	3732 (4.4)	14547 (3.1)	4825 (4.9)	18033 (3.4)
Median days (IQR) between the first eGFR measurement and the first antidiabetes prescription	0 (-50, 49)	-1 (-67, 45)	0 (-43, 58)	0 (-55, 56)

eGFR, estimated glomerular filtration rate; BMI, body mass index; HbA1c, hemoglobin A1c;

SD, standard deviation; IQR, interquartile range

Unless otherwise indicated, data are reported as number (percentage) of patients

Supplemental Table 3. Baseline characteristics of the study population in replicating cohorts from OptumLabs Database Warehouse, by sex and period

	Pre-FDA metformin label change		Post-FDA metformin label change	
	Men	Women	Men	Women
N (%)	278421 (50.4)	274246 (49.6)	317673 (50.7)	309391 (49.3)
Age (years), mean (SD)	61.5 (12.8)	61.7 (13.5)	62.0 (12.8)	62.2 (13.6)
Black	33579 (12.1)	51595 (18.8)	39116 (12.3)	58919 (19.0)
eGFR (mL/min/1.73 m^2), mean (SD)	80.3 (22.0)	78.7 (24.0)	80.2 (21.9)	78.7 (23.8)
eGFR category				
G1: eGFR ≥90	100632 (36.1)	94260 (34.4)	114472 (36.0)	106388 (34.4)
G2: eGFR 60-89	122449 (44.0)	112595 (41.1)	140321 (44.2)	127894 (41.3)
G3a: eGFR 45-59	36689 (13.2)	42115 (15.4)	41364 (13.0)	46602 (15.1)
G3b: eGFR 30-44	18651 (6.7)	25276 (9.2)	21516 (6.8)	28507 (9.2)
BMI (kg/m^2), mean (SD)	33.3 (7.1)	35.1 (8.5)	33.3 (7.1)	35.1 (8.5)
HbA1c (%), mean (SD)	7.64 (1.70)	7.52 (1.67)	7.61 (1.68)	7.49 (1.68)
History of comorbidities				
Hypertension	233825 (84.0)	229338 (83.6)	272112 (85.7)	263113 (85.0)
Congestive heart failure	31176 (11.2)	27701 (10.1)	41276 (13.0)	36522 (11.8)
Acidosis	6899 (2.5)	7250 (2.6)	12042 (3.8)	12789 (4.1)
Hypoglycemia	14911 (5.4)	17821 (6.5)	19403 (6.1)	22948 (7.4)
Myocardial infarction	15407 (5.5)	10055 (3.7)	22197 (7.0)	14870 (4.8)
Liver disease	25597 (9.2)	30121 (11.0)	39519 (12.4)	45806 (14.8)
Acute kidney injury	8655 (3.1)	9624 (3.5)	11000 (3.5)	11858 (3.8)
Median days (IQR) between the first eGFR measurement and the first antidiabetes prescription	0 (-63, 45)	-1 (-66, 46)	0 (-52, 56)	0 (-55, 56)

eGFR, estimated glomerular filtration rate; BMI, body mass index; HbA1c, hemoglobin A1c;
SD, standard deviation; IQR, interquartile range
Unless otherwise indicated, data are reported as number (percentage) of patients