

Supplemental Online Content

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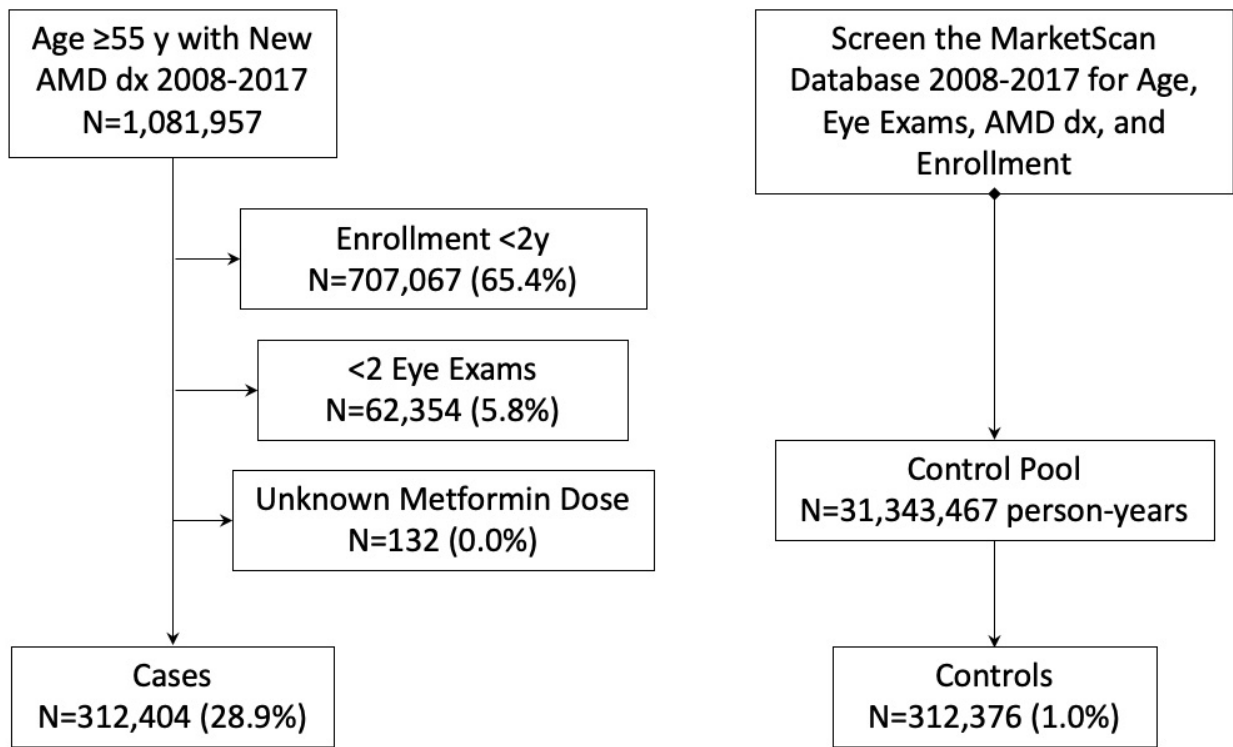
eTable 5. Models for diabetes patients (N=81,262 cases, 79,497 controls), MarketScan Research Databases 2006-2017.*

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

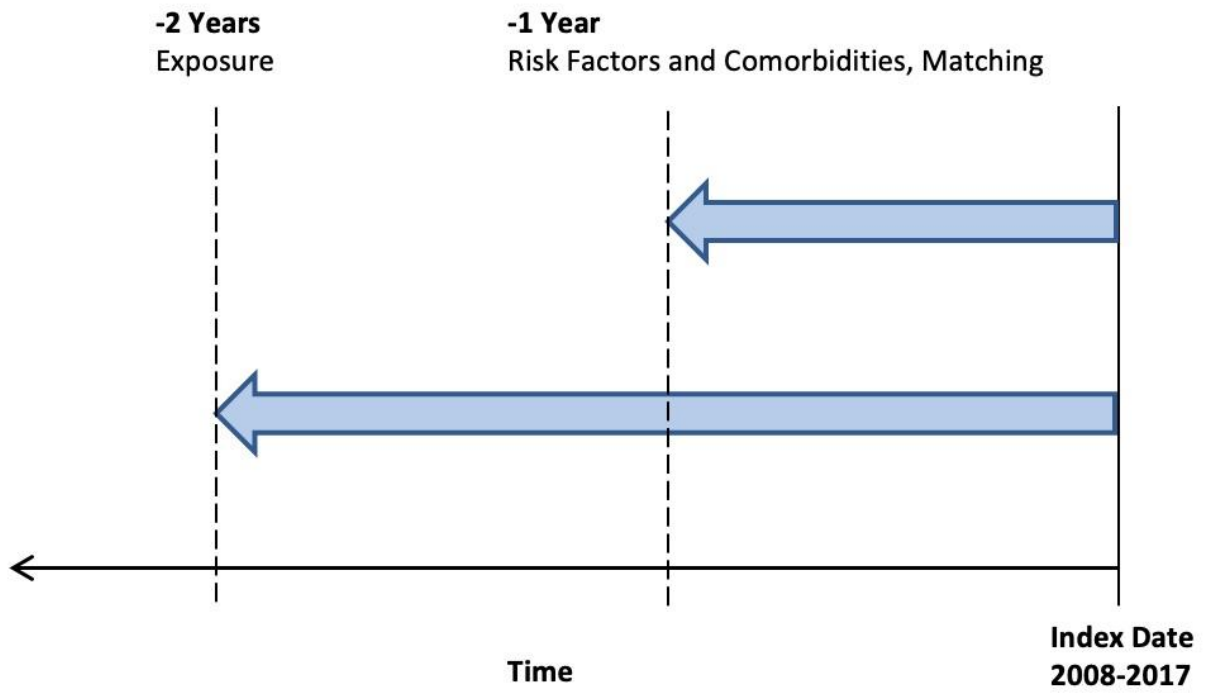
eTable 1. ICD codes, CPT codes, and generic drugs names

Characteristic	ICD-9 Codes	ICD-10 Codes	CPT Codes	Generic drugs names
AMD	362.50, 362.51, 362.52	H35.31, H35.32		
DM	250.xx, 362.0x	E10.x, E11.x		
NPDR	362.01, 362.03-362.07	E10.321, E10.329, E10.331, E10.339, E10.341, E10.349, E11.321, E11.329, E11.331, E11.339, E11.341, E11.349, E11.351, E11.359		
PDR	362.02	E10.351, E10.359, E11.351, E11.359		
Hyperlipidemia	272.xx	E78		
Hypertension	401.xx- 404.xx	I10-I15		
Smoking	305.1x	F17, O99.33, Z71.6, Z72.0, Z87.891		
Eye exam visits			92002, 92004, 92012, 92014, 99201-99205, 99211-99215	
Sulfonylureas				glimepiride, glyburide, glipizide, tolazamide, tolbutamide, chlorpropamide
Glitazones				Rosiglitazone, pioglitazone
Meglitinides				repaglinide, nateglinide
Other antidiabetic drugs				exenatide, sitagliptin, pramlintide
Statin				lovastatin, fluvastatin, pravastatin, rosuvastatin, atorvastatin, pitavastatin, simvastatin, cerivastatin

eFigure 1. Sample selection flowchart.



eFigure 2. Study design.



eTable 2. Balance after matching, MarketScan Research Databases 2008-2017.

	Cases (N=312,404)	Controls (N=312,376)	
Characteristic	Mean (SD)	Mean (SD)	Standardized Difference*
Age			
55-64	0.21 (0.41)	0.21 (0.41)	0.0
65-74	0.27 (0.45)	0.27 (0.45)	0.0
75-84	0.35 (0.48)	0.35 (0.48)	0.0
≥85	0.17 (0.37)	0.17 (0.37)	0.0
Mean (SD)	74.9 (10.3)	74.9 (10.3)	0.0
Hypertension	0.65 (0.48)	0.65 (0.48)	0.0
Anemia	0.06 (0.25)	0.06 (0.25)	0.0
Charlson Index			
0	0.50 (0.50)	0.50 (0.50)	0.0
1	0.20 (0.40)	0.20 (0.40)	0.0
2	0.15 (0.36)	0.15 (0.36)	0.0
≥3	0.15 (0.36)	0.15 (0.36)	0.0
Mean (SD)	1.10 (1.50)	1.11 (1.51)	0.0
Region			
Northeast	0.19 (0.40)	0.19 (0.40)	0.0
North Central	0.31 (0.46)	0.31 (0.46)	0.0
South	0.33 (0.47)	0.33 (0.47)	0.0
West	0.17 (0.38)	0.17 (0.38)	0.0

*Standardized difference = difference / pooled SD. Standardized differences <0.25 are considered acceptable.

eTable 3. Exposures to metformin, other diabetes medications, and statins over 2 years, MarketScan Research Databases 2008-2017.

	Cases	Controls	
	(N=312,404)	(N=312,376)	
Medication	N (%)	N (%)	P-value
Metformin	40,081 (12.8)	40,730 (13.0)	.01
Metformin, g/2 years			<.001
0	272,323 (87.2)	271,646 (87.0)	
1-270	10,141 (3.3)	10,754 (3.4)	
271-600	9,097 (2.9)	9,780 (3.1)	
601-1080	11,010 (3.5)	11,075 (3.6)	
>1080	9,833 (3.2)	9,121 (2.9)	
Metformin, g/2 years, mean (SD)	116 (1403)	116 (1579)	.06
Other medications			
Insulin	18,257 (5.8)	17,383 (5.6)	<.001
Sulfonureas	25,775 (8.3)	26,702 (8.6)	<.001
Glitazones	9,619 (3.1)	9,948 (3.2)	.02
Meglitinides	1,938 (0.6)	1,861 (0.6)	.21
Other diabetes medications	12,089 (3.9)	11,262 (3.6)	<.001
Statins	162,856 (52.1)	165,393 (53.0)	<.001

eTable 4. Exposures to metformin, other diabetes medications, and statins over 2 years among subgroup of diabetes patients (N=81,262 cases, 79,497 controls), MarketScan Research Databases 2008-2017.

	Cases	Controls	
	(N=81,262)	(N=79,497)	
Medication	N (%)	N (%)	P-value
Metformin	38,580 (47.5)	38,388 (48.3)	.001
Metformin, g/2 years			<.001
0	42,681 (52.5)	41,109 (51.7)	
1-270	8,533 (10.5)	8,739 (11.0)	
271-600	8,440 (10.4)	8,881 (11.2)	
601-1080	11,119 (13.7)	11,069 (13.9)	
>1080	10,488 (12.9)	9,699 (12.2)	
Metformin, g/2 years, mean (SD)	433 (2716)	436 (3074)	.14
Other medications			
Insulin	18,277 (22.5)	17,175 (21.6)	<.001
Sulfonureas	25,509 (31.4)	25,919 (32.6)	<.001
Glitazones	9,863 (12.1)	9,958 (12.5)	.02
Meglitinides	1,982 (2.4)	1,858 (2.3)	.18
Other diabetes medications	11,969 (14.7)	10,987 (13.8)	<.001
Statins	57,903 (71.3)	56,673 (71.3)	.88

eTable 5. Models for diabetes patients (N=81,262 cases, 79,497 controls), MarketScan Research Databases 2006-2017.*

Characteristic	Univariable models		Any metformin		Metformin dose	
	OR (CI)	P-value	OR (CI)	P-value	OR (CI)	P-value
Risk Factors						
Women	0.90 (0.89-0.92)	<.001	1.12 (1.09-1.14)	<.001	1.12 (1.10-1.14)	<.001
Smoking	1.58 (1.51-1.65)	<.001	1.61 (1.54-1.69)	<.001	1.61 (1.54-1.69)	<.001
Hyperlipidemia	1.13 (1.11-1.16)	<.001	1.12 (1.10-1.15)	<.001	1.12 (1.10-1.15)	<.001
NPDR	2.26 (2.18-2.34)	<.001	2.28 (2.20-2.37)	<.001	2.28 (2.20-2.36)	<.001
PDR	1.76 (1.64-1.89)	<.001	1.22 (1.13-1.32)	<.001	1.22 (1.13-1.32)	<.001
Medications						
Metformin	0.95 (0.93-0.97)	<.001	0.95 (0.93-0.97)	<.001	---	
Metformin Dose, g/2 y						
1-270	0.93 (0.90-0.96)	<.001	---		0.93 (0.90-0.96)	<.001
271-600	0.90 (0.87-0.93)	<.001	---		0.91 (0.88-0.94)	<.001
601-1080	0.96 (0.93-0.98)	.003	---		0.95 (0.92-0.98)	.002
>1080	1.02 (0.99-1.05)	.28	---		1.01 (0.97-1.04)	.77
Insulin	1.05 (1.03-1.08)	<.0001	0.92 (0.90-0.95)	<.001	0.92 (0.90-0.94)	<.001
Sulfonureas	0.96 (0.94-0.98)	<.0001	0.94 (0.92-0.96)	<.001	0.94 (0.92-0.96)	<.001
Glitazones	0.98 (0.95-1.01)	.19	0.97 (0.94-1.005)	.09	0.97 (0.94-1.000)	.052
Meglitinides	1.06 (1.00-1.14)	.06	1.04 (0.97-1.11)	.30	1.03 (0.97-1.10)	.35
Other diabetes medications	1.07 (1.04-1.10)	<.0001	1.08 (1.05-1.11)	<.001	1.07 (1.04-1.10)	<.001
Statins	1.00 (0.98-1.02)	.83	0.98 (0.96-1.00)	.08	0.98 (0.96-1.001)	.06
AIC			208,593		208,573	

*Stratified by age group, anemia, hypertension, Charlson Index (0, 1, 2, ≥3), region, and year.
 --- Not applicable.