

SUPPLEMENTARY DATA

Supplementary Table S1. Percentage of individuals with prediabetes by metformin use meeting different criteria for the diagnosis of prediabetes

Definition	Prediabetes on metformin, % (SE)* (n=91)	Prediabetes not on metformin, % (SE)* (n=7561)	p-value†
Prediabetes based on IGT alone	7.5 (7.1)	6.9 (0.5)	0.93
Prediabetes based on IFG alone	0	35.9 (0.9)	<0.001
Prediabetes based on HbA1c 5.7-6.4% alone	20.4 (5.5)	25.4 (0.7)	0.36
Self-reported prediabetes alone	0	0	n/a

Abbreviations: SE, Standard Error; IGT, impaired glucose tolerance; IFG, impaired fasting glucose; HbA1c, hemoglobin A1c; n/a, not applicable

*Represents weighted percentages

†p-value for comparison of proportions using logistic regression accounting for sampling weights

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Supplementary Table S2. Characteristics of U.S. adults with prediabetes on metformin stratified by BMI (n=87).

Characteristic	Prediabetes on Metformin and BMI ≥ 35 kg/m ² (n=34)*†		Prediabetes on Metformin and BMI < 35 kg/m ² (n=53) *‡		p-value§
	mean [SE] or % [SE]	N¶	mean [SE] or % [SE]	N¶	
Mean age	50.7 (2.8)		57.5 (2.5)		0.09
Age < 60 years , %	73.2 (10.3)	19	55.3 (7.9)	19	0.22
Female, %	54.9 (13.4)	18	57.4 (9.1)	28	0.88
Race, %					
White	75.8 (7.8)	15	64.8 (6.9)	22	
Black	10.8 (4.5)	9	9.1 (4.3)	9	
Other/multiracial	0	0	15.0 (6.5)	6	0.04
Mexican American	6.6 (3.6)	5	7.2 (2.6)	10	
Other Hispanic	6.8 (3.7)	5	3.9 (1.9)	6	
Have health insurance coverage	89.7 (6.6)	30	94.9 (2.5)	49	0.37
Education					
Greater than high school	56.2 (12.6)	15	60.6 (8.4)	20	
High school grad/GED or equivalent	23.4 (10.7)	7	23.4 (7.4)	15	0.71
Less than high school	20.4 (8.9)	12	16.1 (4.5)	18	
Income					
Greater than 200% of poverty level	53.1 (12.4)	12	70.1 (6.7)	28	
100-200% of poverty level	27.8 (10.4)	11	15.6 (4.9)	12	0.02
Less than poverty level	19.1 (7.8)	11	9.0 (3.6)	9	
Mean BMI (kg/m²)	42.2 (2.2)		28.9 (0.6)		<0.001
Mean systolic blood pressure (mmHg)	128.3 (3.4)		124.6 (3.4)		0.44
Mean cholesterol (mg/dL)					
Total	197.9 (11.3)		185.8 (6.0)		0.26
HDL	47.2 (3.0)		50.6 (3.1)		0.40
LDL	123.3 (7.8)		112.8 (7.9)		0.35
Triglycerides	190 (47.4)		147.3 (9.5)		0.18
Mean hemoglobin A1c (%)	5.9 (0.1) (41 mmol/mol)		6.1 (0.1) (43 mmol/mol)		0.11
Hemoglobin A1c $\geq 6\%$	33.1 (10.8)	17	63.6 (8.3)	37	0.05
Mean fasting plasma glucose (mg/dL)	107 (5.8)		120.6 (4.0)		0.05
Mean 2-hour post-stimulation plasma glucose (mg/dL)	153		163.3 (36.6)		0.78
Smoking					
Current smoker	15.0 (9.3)	5	14.6 (7.1)	7	
Ever smoker	37.0 (11.4)	14	45.1 (8.9)	21	0.70
Never smoker	0	15	0	25	
History of hypertension	55.2 (13.6)	21	56.2 (9.1)	37	0.95

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History of heart disease and/or heart attack	13.9 (9.4)	3	10.0 (4.7)	6	0.70
Told by doctor that you are overweight	98.6 (1.4)	33	55.3 (8.4)	27	<0.001
Family history of diabetes	36.2 (10.3)	19	43.2 (8.8)	24	0.60

Abbreviations: BMI, Body Mass Index; GED, General Educational Development; SE, Standard Error

*Total n=87 since n=4 were missing BMI data

†N for subjects with BMI ≥ 35 kg/m² by variable: systolic blood pressure, n=33; high density lipoprotein/total cholesterol, n=31; low density lipoprotein cholesterol/triglycerides, n=17; HbA1c, n=32; 2-hr post-stimulation plasma glucose, n=1; fasting glucose, n=17

‡N for subjects with BMI < 35 kg/m² by variable: systolic blood pressure, n=52; high density lipoprotein/total cholesterol, n=51; low density lipoprotein cholesterol/triglycerides, n=27; HbA1c, n=52; 2-hr post-stimulation plasma glucose, n=4; fasting glucose, n=28; history of heart attack/family history diabetes, n=52

§P-value for comparison of means or proportions using linear or logistic regression, respectively, accounting for sampling weights

| |Represents weighted means or percentages

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Supplementary Table S3. Characteristics of U.S. adults with prediabetes on metformin stratified by age (n=91).

Characteristic	Prediabetes on Metformin and age <60 years (n=40)*		Prediabetes on Metformin and age ≥60 years (n=51)†		p-value‡
	mean [SE] or % [SE]§	N	mean [SE] or % [SE]§	N	
Mean age	45.3 (1.9)		70.3 (1.10)		<0.001
Female	64.1 (9.6)	22	41.2 (9.1)	25	0.09
Race					
White	73.6 (6.8)	21	61.0 (9.0)	17	
Black	10.4 (3.5)	9	10.7 (3.2)	11	
Other/multiracial	6.5 (4.5)	2	10.2 (6.3)	4	0.73
Mexican American	5.4 (2.7)	5	11.1 (3.8)	11	
Other Hispanic	4.1 (2.4)	3	6.9 (3.2)	8	
Have health insurance coverage	88.9 (5.1)	33	97.3 (2.0)	49	0.02
Education					
Greater than high school	66.9 (8.3)	22	41.8 (9.9)	14	
High school grad/GED or equivalent	18.3 (7.0)	9	32.5 (10.5)	14	0.07
Less than high school	14.8 (5.5)	9	25.6 (6.9)	23	
Income					
Greater than 200% of poverty level	71.4 (7.8)	20	43.7 (9.2)	21	
100-200% of poverty level	13.9 (5.0)	11	37.5 (9.8)	15	0.31
Less than poverty level	13.5 (5.8)	8	13.1 (4.2)	12	
Mean BMI (kg/m²)	37.1 (2.1)		31.5 (1.3)		<0.001
BMI (kg/m²)					
<35	46.6 (10.5)		65.9 (10.7)		0.20
≥35	53.4 (10.5)		34.1 (10.7)		
Mean systolic blood pressure (mmHg)	122.9 (3.3)		132.3 (3.9)		0.04
Mean cholesterol (mg/dL)					
Total	194.5 (9.9)		184.2 (4.4)		0.26
High Density Lipoprotein	48.0 (2.8)		50.6 (3.1)		0.50
Low Density Lipoprotein	123.8 (7.1)		105.9 (7.0)		0.46
Triglycerides	185.2 (40.0)		150.9 (16.4)		0.28
Mean hemoglobin A1c (%)	5.8 (0.08)		6.3 (0.1)		<0.001
	(40 mmol/mol)		(45 mmol/mol)		
Hemoglobin A1c ≥ 6%	39.4 (9.5)	17	70.8 (11.1)	39	0.05
Mean fasting plasma glucose (mg/dL)	110.5 (5.7)		120.3 (3.1)		0.15
Mean 2-hour post-stimulation plasma glucose (mg/dL)	120.9 (1.1)		145.6 (2.2)		<0.001
Smoking					
Current smoker	10.9 (5.9)	6	20.5 (10.6)	6	
Ever smoker	41.1 (10.1)	15	40.8 (8.8)	21	0.37
Never smoker	0	0	0	0	
History of hypertension	48.3 (10.8)	20	69.4 (10.9)	41	0.16

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History of heart disease and/or heart attack	3.6 (2.1)	3	26.0 (11.2)	6	<0.001
Told by doctor that you are overweight	80.8 (7.0)	28	63.2 (9.1)	33	0.15
Family history of diabetes	47.3 (10.7)	24	30.6 (7.7)	23	0.23

Abbreviations: BMI, Body Mass Index; GED, General Educational Development; SE, Standard Error

*N for subjects with age <60 years by variable: BMI and systolic blood pressure, n=38; high density lipoprotein/total cholesterol, n=37; low density lipoprotein cholesterol/triglycerides, n=20; HbA1c, n=38; fasting glucose, n=21; 2-hr post-stimulation plasma glucose, n=4

†N for subjects with age ≥60 years by variable: BMI and systolic blood pressure, n=49; high density lipoprotein/total cholesterol, n=47; low density lipoprotein cholesterol/triglycerides, n=26; HbA1c, n=48; fasting glucose, n=26; 2-hr post-stimulation plasma glucose, n=1; history of heart attack, n=49; family history of diabetes, n=51

‡P-value for comparison of means or proportions using linear or logistic regression, respectively, accounting for sampling weights

§Represents weighted means or percentages

||Represents unweighted n

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Supplementary Table S4. Number of participants with prediabetes who were on metformin and prevalence of metformin use, stratified by NHANES survey cycle

Survey Cycle	Prediabetes on metformin (total n=91)	Prevalence of metformin, % (SE)*
2005-2006	8	0.4% (0.2)
2007-2008	23	0.7% (0.2)
2009-2010	32	0.9% (0.3)
2011-2012	28	0.7% (0.2)

Abbreviations: SE, Standard Error

*Represents weighted percentages