

SUPPLEMENTARY DATA

Supplementary Table 1

Definitions of chronic conditions used to define the number of serious comorbidities in the study.

<u>Comorbidity</u>	<u>ICD-9 Code</u>	<u>Description</u>
<u>CAD/MI</u>	<u>410.x</u>	<u>Acute myocardial infarction</u>
	<u>411.x</u>	<u>Other acute and subacute forms of ischemic heart disease</u>
	<u>412.x</u>	<u>Old myocardial infarction</u>
	<u>413.x</u>	<u>Angina pectoris</u>
	<u>414.x</u>	<u>Other forms of chronic ischemic heart disease</u>
<u>Chronic Lung Disease</u>	<u>416.8, 416.9</u>	<u>Chronic pulmonary heart diseases</u>
	<u>490.x-505.x</u>	<u>Chronic obstructive pulmonary diseases, asthma, emphysema, bronchiectasis, allergic alveolitis, chronic airway obstruction, pneumoconiosis, asbestosis, pneumonopathy</u>
	<u>506.4</u>	<u>Chronic respiratory conditions due to fumes and vapors</u>
	<u>508.1, 508.2, 508.8</u>	<u>Chronic and other pulmonary manifestations due to radiation, respiratory conditions due to smoke inhalation or to other specified external agents</u>
<u>Chronic Kidney Disease</u>	<u>403.x</u>	<u>Hypertensive chronic kidney disease</u>
	<u>404.x</u>	<u>Hypertensive heart and chronic kidney disease</u>
	<u>582.x</u>	<u>Chronic glomerulonephritis</u>
	<u>583.0-583.7</u>	<u>Glomerulonephritis</u>
	<u>585.x</u>	<u>Chronic kidney disease</u>
	<u>586.x</u>	<u>Renal failure, unspecified</u>
	<u>588.0x</u>	<u>Renal osteodystrophy</u>
	<u>V42.0x, V45.1x, V56.x</u>	<u>Kidney transplant, postsurgical renal dialysis status, dialysis and dialysis catheter care</u>
<u>Heart Failure</u>	<u>398.91</u>	
	<u>402.01, 402.11, 402.91</u>	<u>Hypertensive heart disease</u>
	<u>404.01, 404.03, 404.11, 404.13, 404.91, 404.93</u>	<u>Hypertensive heart and chronic kidney disease, malignant, with heart failure</u>

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	<u>425.4-425.9</u>	<u>Other primary cardiomyopathy, alcoholic cardiomyopathy, nutrition and metabolic cardiomyopathy, cardiomyopathy in other diseases, secondary cardiomyopathy</u>
	<u>428.x</u>	<u>Congestive heart failure</u>
<u>Dementia</u>	<u>290.x</u>	<u>Dementias</u>
	<u>294.1x</u>	<u>Dementia in conditions classified elsewhere</u>
	<u>294.2x</u>	<u>Dementia, unspecified</u>
	<u>331.x</u>	<u>Alzheimer's disease</u>
<u>Depression</u>	<u>296.2x</u>	<u>Major depressive disorder</u>
	<u>296.3x</u>	<u>Major depressive disorder recurrent episode</u>
	<u>311.x</u>	<u>Depressive disorder, not elsewhere classified</u>
<u>Atrial fibrillation</u>	<u>427.31</u>	<u>Atrial fibrillation</u>
<u>Stroke</u>	<u>433.x1</u>	<u>Occlusion and stenosis with cerebral infarction</u>
	<u>434.x1</u>	<u>Occlusion with cerebral infarction</u>
	<u>436.x</u>	<u>Acute, but ill defined, cerebrovascular disease</u>

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Supplementary Table 2

Standardized proportion of privately insured patients with type 2 diabetes who filled each class of glucose-lowering agents, 2006-2013. All trend p-values are <0.001.

	2006	2007	2008	2009	2010	2011	2012	2013
Biguanides	47.6%	47.7%	49.9%	50.6%	51.5%	52.4%	52.0%	53.5%
Sulfonylureas	38.8%	36.0%	35.0%	33.7%	32.6%	32.0%	30.3%	30.8%
TZDs	28.5%	25.4%	19.6%	17.6%	15.5%	12.1%	7.1%	5.6%
Any insulin	17.1%	16.9%	18.2%	19.4%	20.0%	20.9%	21.4%	23.0%
DPP-4 inhibitors	0.5%	5.3%	8.2%	9.2%	10.4%	13.0%	14.5%	14.9%
GLP-1 agonists	3.3%	3.7%	3.8%	3.2%	3.4%	4.0%	4.6%	5.0%
Other	2.9%	2.5%	2.3%	2.1%	1.9%	1.6%	1.6%	2.2%
None	25.7%	27.9%	26.4%	26.3%	25.9%	24.6%	25.9%	24.1%

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Supplementary Table 3

The mean number of days covered per patient per year for each class of oral glucose-lowering medications.

	2006	2007	2008	2009	2010	2011	2012	2013	Trend p value
Biguanides	241.97	236.27	238.25	238.58	240.42	245.19	251.50	250.86	p<0.001
Sulfonylureas	243.46	237.90	241.89	239.06	244.91	248.23	253.34	253.56	p<0.001
TZDs	229.77	218.81	231.03	233.21	227.51	230.16	231.50	244.10	p<0.001
Meglitinides	179.71	178.60	186.10	188.96	188.83	194.61	202.84	196.91	p<0.001
Alpha-glucosidase inhibitors	177.38	177.08	179.57	177.82	173.20	178.61	188.62	190.53	p=0.73
DPP-4 inhibitors	48.61	146.10	198.23	217.38	211.16	211.82	223.79	220.87	p<0.001
Bromocriptine					45.40	117.65	145.18	180.59	p<0.001
SGLT-2 inhibitors								105.08	
GLP-1 agonists	142.72	158.69	172.74	177.17	165.88	176.93	184.17	185.39	p<0.001
Amylin analogs	107.28	122.57	119.82	128.41	130.24	129.96	138.97	149.51	p<0.001

Note: The mean number of days covered for a drug class was calculated among patients who had at least 1 fill of drugs in this class in a particular year. The sum of number of days supplied for a patient for a drug class is capped at 365 days (in rare cases, patients' total days of supplied for a drug class is more than 365 days).

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Supplementary Table 4

Proportion of privately insured patients with type 2 diabetes who filled each class of glucose-lowering agents, 2006-2013, by age group. All trend p-values are <0.001.

A. Youngest adults (18-44 years)

	2006	2007	2008	2009	2010	2011	2012	2013
N	57559	63209	62865	63014	60165	59618	58116	56097
Biguanides	55.5%	53.3%	54.9%	55.4%	55.8%	55.3%	55.1%	55.4%
Sulfonylureas	32.7%	28.9%	28.3%	27.1%	25.9%	25.2%	25.0%	24.5%
TZDs	30.9%	24.9%	18.9%	16.8%	14.4%	10.3%	5.6%	4.2%
Any insulin	21.1%	20.5%	21.9%	23.2%	23.2%	23.6%	24.1%	24.5%
DPP-4 inhibitors	0.5%	5.9%	9.2%	10.4%	11.4%	13.8%	15.1%	14.5%
GLP-1 agonists	6.0%	6.5%	6.6%	5.6%	6.3%	7.5%	8.3%	8.7%
Other	3.0%	2.4%	2.0%	1.8%	1.6%	1.5%	1.3%	2.6%
None	18.7%	23.6%	22.5%	22.0%	22.1%	22.4%	22.7%	22.8%

B. Middle age adults (45-64 years)

	2006	2007	2008	2009	2010	2011	2012	2013
N	225937	251833	257767	270877	271899	283093	283764	287884
Biguanides	59.0%	57.0%	60.1%	59.7%	59.7%	59.7%	59.6%	60.3%
Sulfonylureas	40.2%	35.7%	35.1%	33.2%	31.4%	30.2%	29.1%	28.8%
TZDs	36.8%	31.3%	24.7%	22.4%	19.4%	15.2%	8.9%	6.8%
Any insulin	16.7%	16.5%	18.4%	19.8%	20.5%	21.4%	22.5%	23.7%
DPP-4 inhibitors	0.7%	7.1%	11.2%	12.7%	13.8%	16.4%	18.3%	17.8%
GLP-1 agonists	5.3%	6.1%	6.1%	5.1%	5.5%	6.3%	7.1%	7.5%
Other	3.6%	2.9%	2.6%	2.3%	2.0%	1.7%	1.8%	3.0%
None	18.3%	23.1%	20.3%	20.6%	21.0%	21.1%	21.6%	21.0%

C. Older adults (65-74 years)

	2006	2007	2008	2009	2010	2011	2012	2013
N	57133	73930	83146	114587	148554	171560	195576	204045
Biguanides	43.9%	46.0%	47.8%	49.4%	50.9%	52.8%	52.1%	54.4%
Sulfonylureas	39.4%	37.7%	36.4%	35.4%	34.7%	34.5%	32.2%	33.9%
TZDs	25.7%	24.3%	18.4%	16.2%	14.3%	11.3%	6.6%	5.5%
Any insulin	16.4%	16.4%	17.7%	19.2%	19.9%	20.9%	21.2%	23.6%
DPP-4 inhibitors	0.4%	4.7%	6.8%	7.3%	8.6%	11.3%	12.7%	14.1%
GLP-1 agonists	2.0%	2.1%	2.2%	1.9%	1.9%	2.3%	2.8%	3.4%
Other	2.6%	2.5%	2.3%	1.9%	1.6%	1.4%	1.3%	1.8%
None	29.2%	29.1%	28.3%	27.7%	26.8%	24.5%	26.3%	22.9%

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D. Oldest adults (75 years and older)

	2006	2007	2008	2009	2010	2011	2012	2013
N	44335	58662	65750	89761	112804	128546	144854	152091
Biguanides	27.9%	30.1%	31.3%	33.0%	35.0%	37.2%	36.5%	38.4%
Sulfonylureas	37.9%	36.8%	35.6%	34.6%	34.4%	34.6%	32.0%	32.9%
TZDs	15.8%	16.0%	11.9%	10.6%	9.7%	8.0%	4.8%	4.1%
Any insulin	17.2%	17.2%	17.4%	17.8%	18.1%	18.9%	18.7%	20.4%
DPP-4 inhibitors	0.1%	2.6%	4.1%	4.8%	5.9%	8.3%	9.3%	10.8%
GLP-1 agonists	0.4%	0.4%	0.4%	0.4%	0.4%	0.6%	0.7%	1.0%
Other	2.0%	2.1%	2.1%	1.8%	1.8%	1.7%	1.4%	1.7%
None	37.3%	36.7%	36.8%	36.7%	35.3%	32.4%	35.0%	32.1%

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Supplementary Table 5

Proportion of privately insured patients with type 2 diabetes who filled each class of glucose-lowering agents, 2006-2013, by subgroup based on the number of other serious comorbidities. All trend p-values are <0.001.

A. No other serious comorbidities

	2006	2007	2008	2009	2010	2011	2012	2013
N	238317	271478	276820	300478	320297	341623	355550	358899
Biguanides	57.1%	55.6%	58.3%	58.0%	58.0%	58.4%	58.1%	59.4%
Sulfonylureas	39.3%	35.5%	34.4%	32.8%	31.5%	30.9%	29.7%	30.2%
TZDs	33.9%	29.1%	22.9%	20.4%	17.5%	13.6%	8.0%	6.2%
Any insulin	14.8%	14.4%	15.5%	16.1%	16.1%	16.7%	17.1%	18.3%
DPP-4 inhibitors	0.6%	6.1%	9.6%	10.6%	11.5%	13.9%	15.6%	15.8%
GLP-1 agonists	4.3%	4.9%	5.0%	4.1%	4.2%	4.7%	5.2%	5.6%
Other	3.0%	2.4%	2.2%	1.9%	1.6%	1.5%	1.4%	2.3%
None	20.4%	24.6%	23.0%	23.7%	24.5%	24.0%	25.2%	23.9%

B. One other serious comorbidity

	2006	2007	2008	2009	2010	2011	2012	2013
N	89475	105010	114549	135927	153066	166837	178000	183567
Biguanides	50.4%	49.6%	51.7%	51.5%	51.8%	52.6%	51.7%	53.4%
Sulfonylureas	37.1%	34.3%	34.2%	33.2%	32.6%	32.4%	30.7%	31.7%
TZDs	30.8%	26.6%	20.4%	18.0%	15.7%	12.4%	7.0%	5.8%
Any insulin	17.9%	17.6%	19.2%	20.1%	20.7%	21.4%	21.8%	23.4%
DPP-4 inhibitors	0.6%	6.2%	9.4%	9.9%	10.8%	13.3%	14.4%	15.0%
GLP-1 agonists	4.9%	5.1%	4.9%	3.8%	3.9%	4.4%	4.7%	5.2%
Other	3.3%	2.7%	2.6%	2.2%	1.9%	1.9%	1.7%	2.4%
None	24.2%	27.0%	25.0%	25.5%	25.3%	24.1%	25.8%	23.6%

C. Two or more other serious comorbidities

	2006	2007	2008	2009	2010	2011	2012	2013
N	57172	71146	78159	101834	120059	134357	148760	157651
Biguanides	37.4%	36.3%	37.5%	38.1%	38.4%	39.4%	38.4%	40.0%
Sulfonylureas	38.7%	35.6%	35.0%	34.4%	33.8%	33.1%	31.0%	31.3%
TZDs	24.9%	21.3%	15.3%	13.2%	11.4%	8.7%	5.0%	4.0%
Any insulin	27.4%	27.1%	28.7%	29.8%	30.3%	31.2%	31.6%	33.4%
DPP-4 inhibitors	0.5%	5.1%	7.6%	8.2%	8.9%	11.2%	12.2%	13.1%
GLP-1 agonists	3.8%	3.4%	3.1%	2.4%	2.3%	2.6%	3.0%	3.4%
Other	3.7%	3.3%	3.1%	2.5%	2.2%	2.0%	1.9%	2.2%
None	26.5%	29.6%	28.3%	28.1%	27.5%	25.8%	27.5%	25.2%

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Supplementary Table 6

Characteristics of patients with type 2 diabetes in the study with and without hemoglobin A1c level available in the dataset.

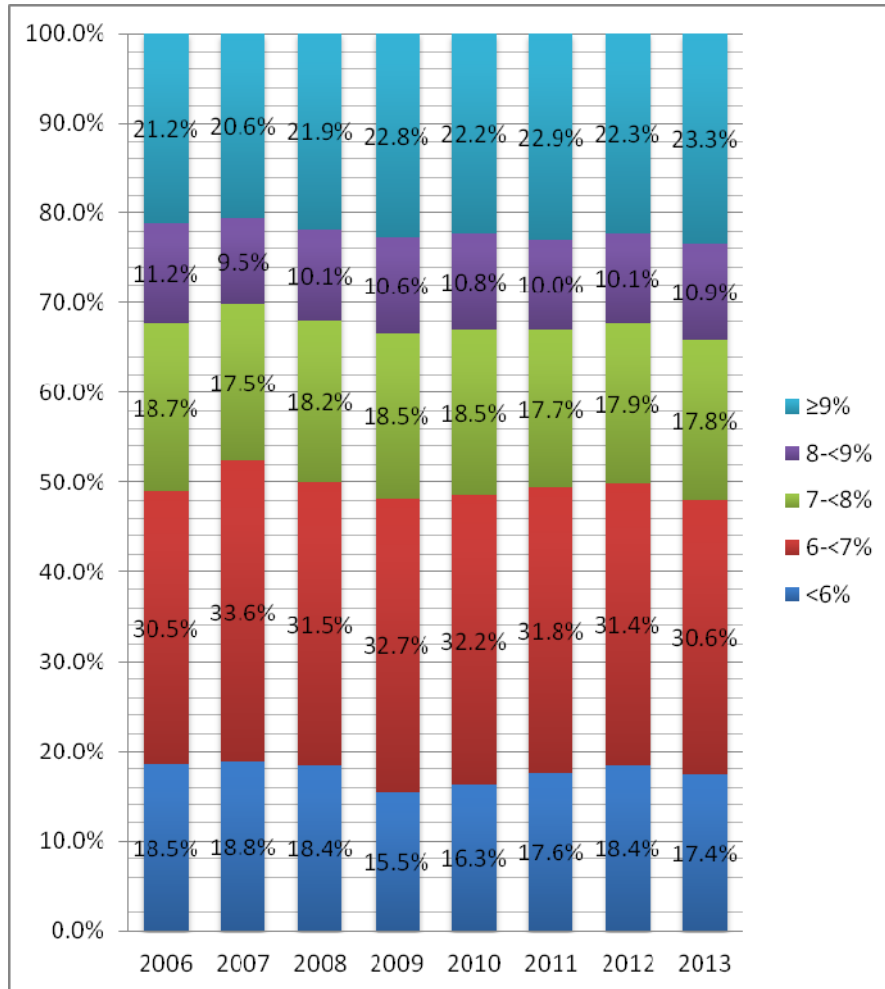
	Without A1C	With A1C	P-value
N	292614	92749	
Age, years, median (IQR)	57.0 (17.0)	57.0 (16.0)	0.433
Age, years, N (%)			<0.0001
18-44	44334 (15.2%)	13225 (14.3%)	
45-54	74389 (25.4%)	23905 (25.8%)	
55-64	95633 (32.7%)	32010 (34.5%)	
65-74	42828 (14.6%)	14305 (15.4%)	
≥ 75	35430 (12.1%)	9304 (10.0%)	
Gender, N (%)			<0.0001
Female	139137 (47.5%)	43201 (46.6%)	
Male	153477 (52.5%)	49548 (53.4%)	
Race, N(%)			<0.0001
Asian	10528 (3.6%)	5462 (5.9%)	
Black	27684 (9.5%)	9333 (10.1%)	
Hispanic	29765 (10.2%)	10489 (11.3%)	
Unknown	35962 (12.3%)	12188 (13.1%)	
White	188675 (64.5%)	55277 (59.6%)	
Household Income, N(%)			<0.0001
<40k	43521 (14.9%)	12418 (13.4%)	
40k-49k	15487 (5.3%)	4664 (5.0%)	
50k-59k	14468 (4.9%)	4607 (5.0%)	
60k-74k	19395 (6.6%)	6444 (6.9%)	
75k-99k	25283 (8.6%)	9158 (9.9%)	
100k+	46732 (16.0%)	19582 (21.1%)	
Unknown	127728 (43.7%)	35876 (38.7%)	
Region, N(%)			<0.0001
Midwest	80858 (27.6%)	15369 (16.6%)	
Northeast	41542 (14.2%)	32011 (34.5%)	
South	112692 (38.5%)	41947 (45.2%)	
Unknown	2874 (1.0%)	558 (0.6%)	
West	54648 (18.7%)	2864 (3.1%)	
Comorbidities, N(%)			
CAD/MI	52169 (17.8%)	19983 (21.5%)	<0.0001
CHF	24401 (8.3%)	7376 (8.0%)	0.0002
Chronic Lung Disease	40062 (13.7%)	13081 (14.1%)	0.0015
Chronic Kidney Disease	18114 (6.2%)	5438 (5.9%)	0.0003
Cancer	18481 (6.3%)	6539 (7.1%)	<0.0001
Depression	18772 (6.4%)	4888 (5.3%)	<0.0001
Dementia	7838 (2.7%)	1226 (1.3%)	<0.0001
Stroke	8750 (3.0%)	2442 (2.6%)	<0.0001
Atrial fibrillation	13504 (4.6%)	3851 (4.2%)	<0.0001
Arthritis	47659 (16.3%)	15908 (17.2%)	<0.0001

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Supplementary Figure 1

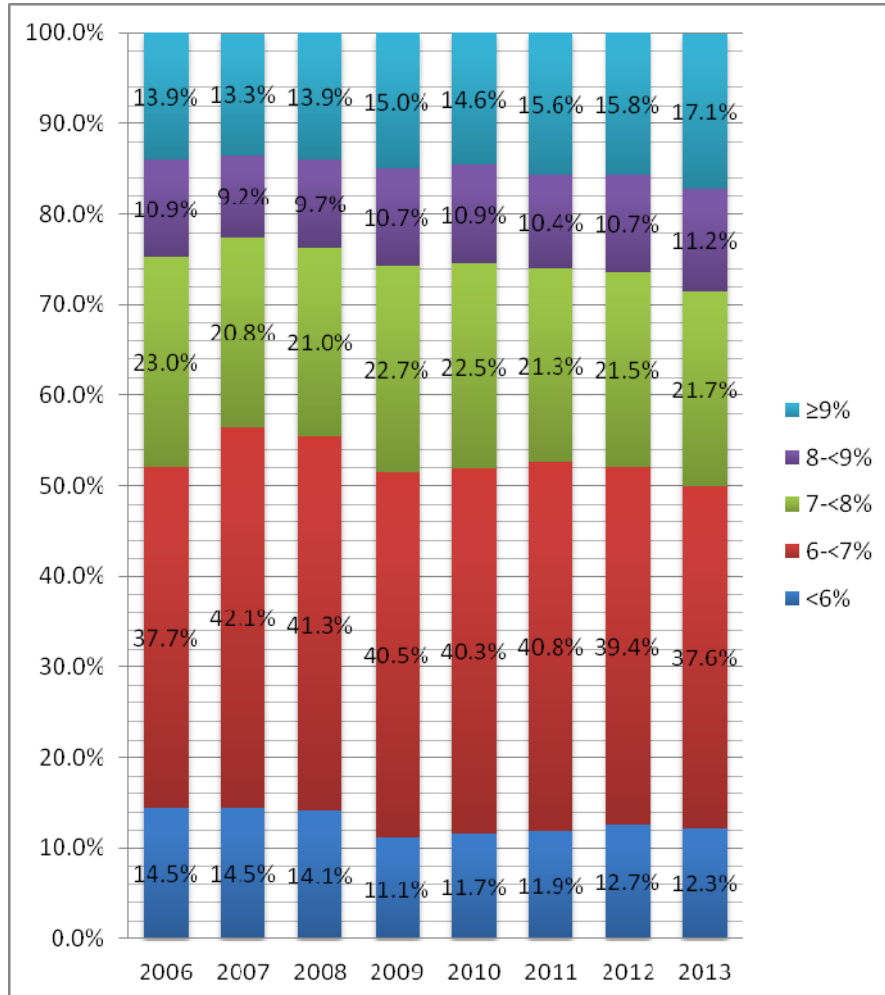
Glycemic control among patients with type 2 diabetes by age subgroup.

A. Youngest adults (18-44 years)



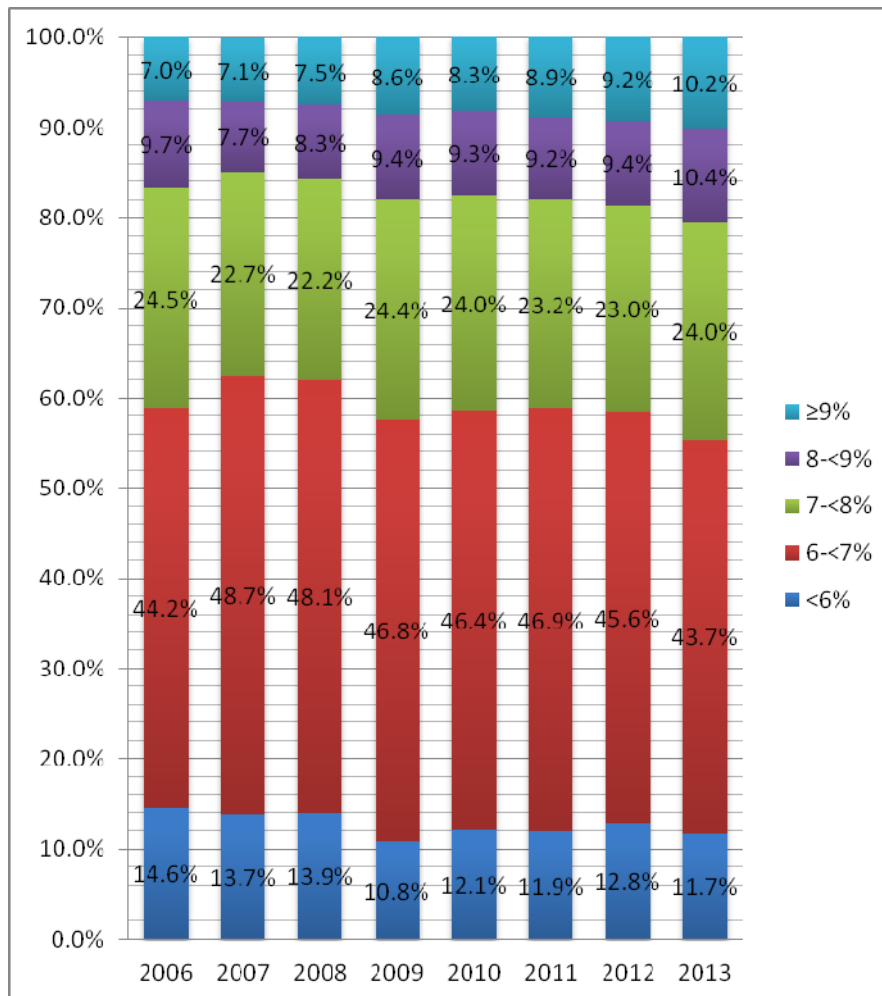
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B. Middle age adults (45-64 years)



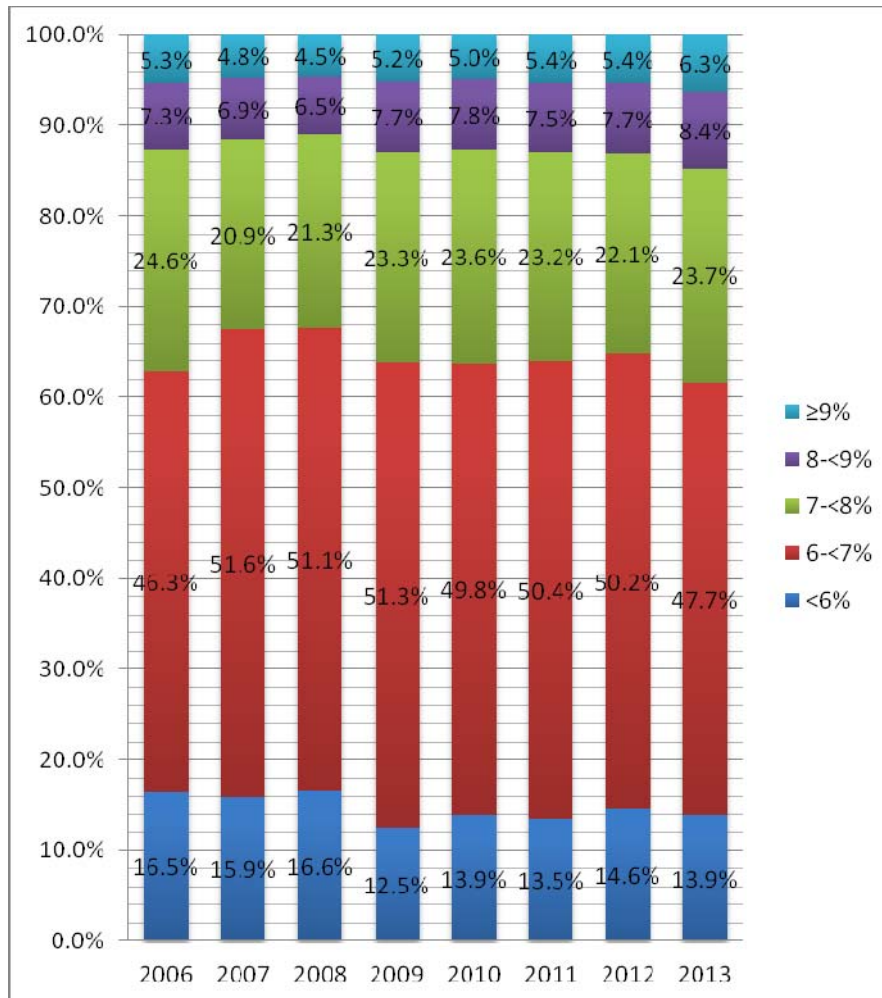
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C. Older adults (65-74 years)



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D. Oldest adults (75 years and older)

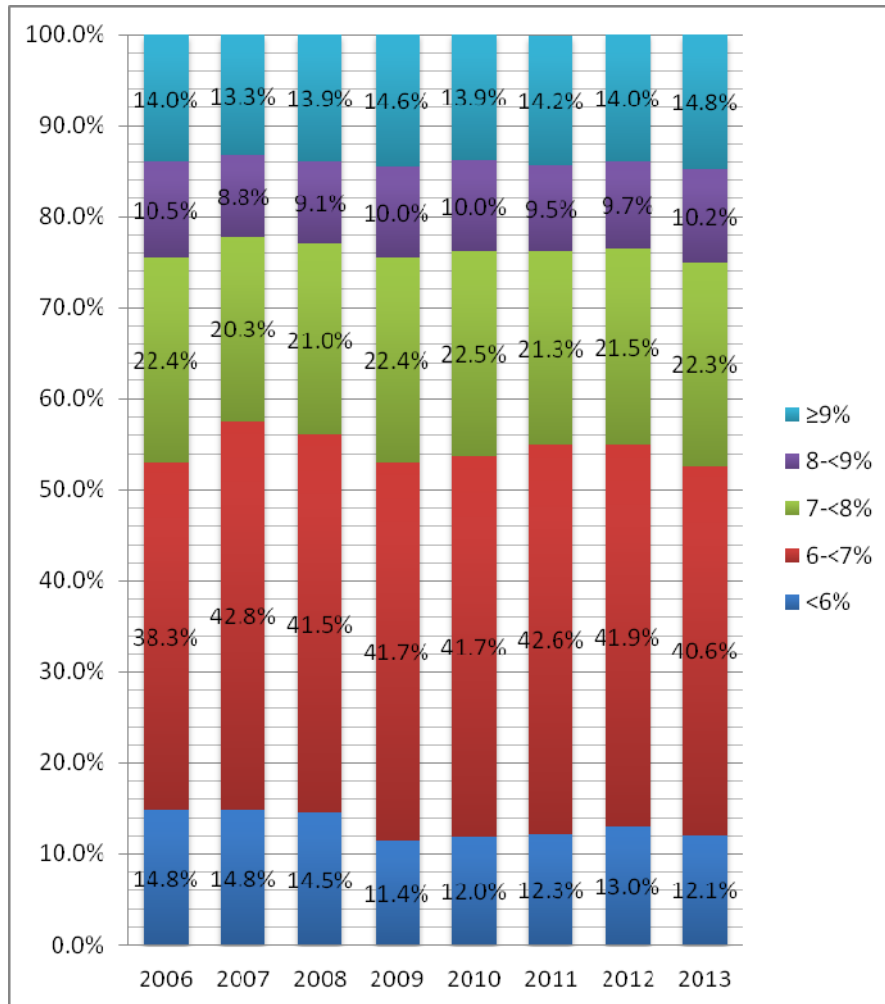


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Supplementary Figure 2

Glycemic control among patients with type 2 diabetes by comorbidity subgroup.

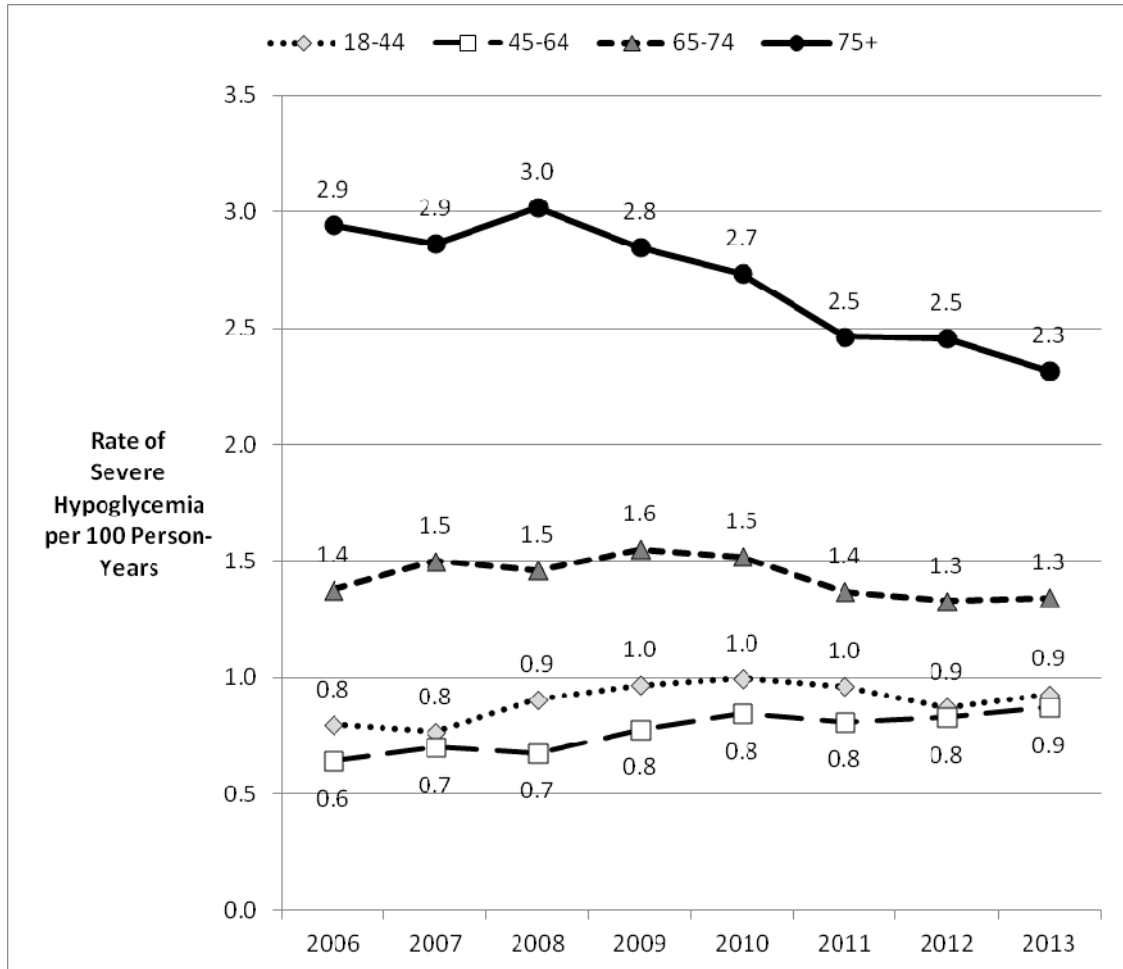
A. No other serious comorbidities



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Supplementary Figure 3

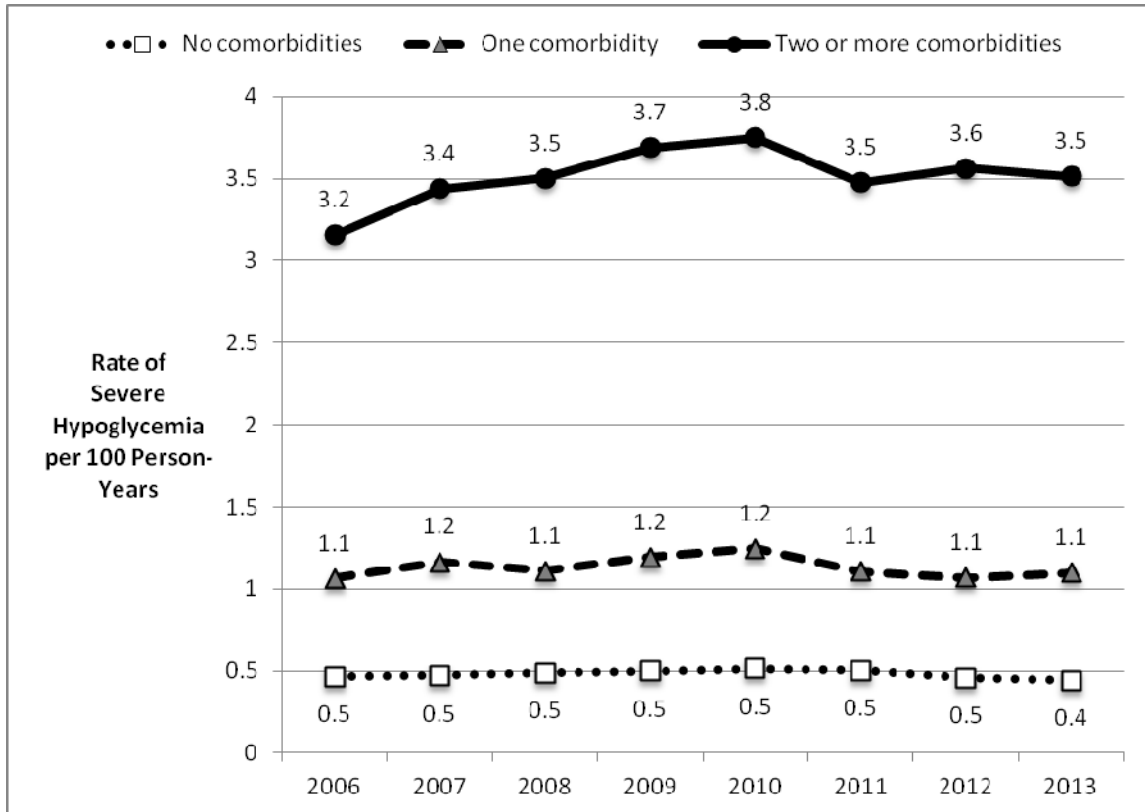
Rates of severe hypoglycemia among patients with type 2 diabetes who filled at least one glucose-lowering agent, by age subgroup.



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Supplementary Figure 4

Rates of severe hypoglycemia among patients with type 2 diabetes who filled at least one glucose-lowering agent, by comorbidity subgroup.



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Supplementary Table 7

Sensitivity analysis: Proportion of patients with type 2 diabetes in each glycemic control category, with only one year of data per patient (the year for each patient was selected at random).

	2006	2007	2008	2009	2010	2011	2012	2013	Trend p-value
N	60130	38545	55958	66238	68841	72235	79194	136368	
Percent of original cohort	64.9%	49.1%	46.9%	45.4%	44.6%	44.4%	46.8%	62.7%	
HbA1c									
<6%	16.5%	16.0%	16.5%	12.8%	13.9%	14.1%	15.0%	13.9%	<0.0001
6-<7%	40.5%	44.9%	44.1%	43.7%	43.4%	44.4%	43.2%	41.1%	0.0154
7-<8%	23.1%	20.5%	20.4%	22.5%	22.4%	21.1%	21.3%	22.3%	0.2476
8-<9%	9.7%	8.3%	8.6%	9.5%	9.8%	9.1%	9.3%	10.4%	<0.0001
≥9%	10.2%	10.2%	10.3%	11.5%	10.5%	11.3%	11.3%	12.4%	<0.0001

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Supplementary Figure 5

Sensitivity analysis: Adjusted rate of severe hypoglycemia among patients with type 2 diabetes who filled at least one glucose-lowering drug, with only one year of data per patient (the year for each patient was selected at random).

