

SUPPLEMENTARY DATA

**Supplementary Table 1. The use of oral anti-diabetic drugs stratified by the status of DR**

<b>Oral anti-diabetic drugs</b>	<b>Total (n=3262)</b>	<b>Non-DR (n=2482)</b>	<b>Mild NPDR (n=355)</b>	<b>Moderate NPDR (n=198)</b>	<b>VTDR (n=227)</b>	<b><i>P</i> for trend</b>
Metformin	26.9%	28.1%	25.9%	25.1%	17.0%	<0.001
Sulfonylureas	22.3%	23.6%	24.1%	15.4%	11.2%	<0.001
Thiazolidinediones	7.1%	6.9%	6.9%	8.7%	7.6%	0.471
Glinides	7.2%	8.3%	5.5%	3.1%	1.8%	<0.001
$\alpha$ -glucosidase inhibitors	29.9%	29.5%	35.7%	20.0%	33.9%	0.724

Data are presented as percentages. DR, diabetic retinopathy; NPDR, nonproliferative diabetic retinopathy; VTDR, vision-threatening diabetic retinopathy.

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**Supplementary Table 2. Characteristics of study participants with diabetes duration < 5 years**

Variables	Non-DR	Mild NPDR	Moderate NPDR	VTDR	P for trend
n	1021	72	27	27	
Male (%)	36.5%	37.5%	38.5%	44.4%	0.427
Age (years)	56 ± 12.9	54.5 ± 10.2	55.4 ± 13.7	54.9 ± 9.8	0.279
Duration (years)	1.5 ± 1.4	1.8 ± 1.3	1.6 ± 1.4	2.2 ± 1.6	0.003
SBP (mmHg)	128.6 ± 16	128 ± 16.8	131.9 ± 16.5	136.6 ± 20.1	0.143
DBP (mmHg)	80.3 ± 9.4	78.9 ± 9.1	82.6 ± 9.3	83.5 ± 11.4	0.661
BMI (Kg/m <sup>2</sup> )	25.3 ± 3.3	25.1 ± 3.6	25.0 ± 2.9	23.5 ± 2.7	0.070
Total cholesterol (mmol/L)	4.8 ± 1.1	4.8 ± 0.9	4.7 ± 1.4	4.7 ± 1.2	0.761
Triglycerides (mmol/L)	2.1 ± 2.1	2.0 ± 2.2	2.0 ± 1.9	1.7 ± 0.9	0.149
HDL-C (mmol/L)	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.2	1.1 ± 0.2	0.045
LDL-C (mmol/L)	3.2 ± 0.9	3.2 ± 0.9	3.1 ± 1.2	3.2 ± 1	0.971
HbA <sub>1c</sub> (%)	9.2 ± 2.5	9.0 ± 1.9	9.5 ± 2.3	9.2 ± 2.7	0.868
HbA <sub>1c</sub> (mmol/mol)	77.0 ± 27.3	75.0 ± 20.8	80.0 ± 25.1	77.0 ± 29.5	
Fasting C-peptide (ng/ml)	2.1 ± 1.2	1.9 ± 1.0	1.9 ± 1.1	1.8 ± 1.2	0.031
SD (mmol/L)	2.2 ± 0.9	2.2 ± 0.8	2.3 ± 1.2	2.3 ± 1.0	0.309
CV (%)	24.9 ± 8.4	25.2 ± 8.2	24.2 ± 11.3	26.4 ± 9.2	0.466
MAGE (mmol/L)	5.6 ± 2.5	5.6 ± 2.3	6.2 ± 3.6	6.1 ± 2.9	0.802
TIR (%)	71.1 ± 23.4	69.5 ± 21.4	58.8 ± 24.5	65.8 ± 26.4	0.015
Current smoker (%)	29.6	29.6	19.2	37.0	0.932
Anti-diabetic agents (%)					
Oral anti-diabetic drugs	67.3	68.6	64.0	74.1	0.630
Insulin	58.8	70.0	60.0	74.1	0.050
Anti-hypertensive agents (%)					
RAAS inhibitors	37.3	25.4	34.6	51.9	0.757
Calcium-channel blockers	14.1	12.7	3.8	11.1	0.234
Beta-blockers	6.3	4.2	3.8	0.0	0.121
Diuretics	1.2	1.4	0.0	0.0	0.514
Lipid-lowering agents (%)					
Statins	20.5	28.2	19.2	7.4	0.434
Fibrates	10.4	9.9	11.5	3.7	0.407

Data are mean ± SD or percentage unless otherwise indicated. DR, diabetic retinopathy; NPDR, nonproliferative diabetic retinopathy; VTDR, vision-threatening diabetic retinopathy; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TIR, time in range; SD, standard deviation; CV, coefficient of variation; MAGE, mean amplitude of glycemic excursions; RAAS, renin-angiotensin-aldosterone system.

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**Supplementary Table 3. Characteristics of study participants with diabetes duration 5-10 years**

Variables	Non-DR	Mild NPDR	Moderate NPDR	VTDR	<i>P</i> for trend
n	587	92	43	34	
Male (%)	41.8	40.7	58.5	31.3	0.879
Age (years)	58.8 ± 10.7	56.2 ± 10.7	62.4 ± 10.9	60.0 ± 9.4	0.878
Duration (years)	6.6 ± 1.4	6.8 ± 1.4	6.6 ± 1.4	6.9 ± 1.1	0.209
SBP (mmHg)	130.7 ± 16.4	133.2 ± 16.2	136.1 ± 20.4	137.4 ± 24.4	0.023
DBP (mmHg)	80.3 ± 9.6	82.4 ± 9.4	80.3 ± 9.8	82.8 ± 14.3	0.107
BMI (Kg/m <sup>2</sup> )	25.3 ± 3.3	25.7 ± 3.6	24.8 ± 2.9	24.3 ± 3.5	0.336
Total cholesterol (mmol/L)	4.7 ± 1.1	4.7 ± 1.1	5.3 ± 1.5	4.6 ± 1.2	0.253
Triglycerides (mmol/L)	2.0 ± 1.6	2.0 ± 1.4	1.9 ± 1.2	1.3 ± 0.6	0.088
HDL-C (mmol/L)	1.1 ± 0.3	1.0 ± 0.2	1.2 ± 0.4	1.2 ± 0.4	0.741
LDL-C (mmol/L)	3.2 ± 1.0	3.2 ± 0.9	3.7 ± 1.4	3.1 ± 1.0	0.252
HbA <sub>1c</sub> (%)	8.5 ± 2.0	9.0 ± 1.9	9.6 ± 2.2	9.6 ± 2.2	<0.001
HbA <sub>1c</sub> (mmol/mol)	69.0 ± 21.9	75.0 ± 20.8	81.0 ± 24.0	81.0 ± 24.0	
Fasting C-peptide (ng/ml)	2.2 ± 1.8	2.1 ± 1.1	1.9 ± 1.1	1.4 ± 1.0	0.002
SD (mmol/L)	2.1 ± 0.8	2.2 ± 0.9	2.4 ± 0.9	2.6 ± 1.0	0.008
CV (%)	24.4 ± 7.8	24.2 ± 8.3	25.6 ± 8.3	27.8 ± 10.3	0.223
MAGE (mmol/L)	5.5 ± 2.3	5.7 ± 2.4	5.6 ± 2.2	6.1 ± 2.4	0.256
TIR (%)	69.7 ± 23.0	64.4 ± 25.8	59.4 ± 24.7	59.7 ± 21.0	<0.001
Current smoker (%)	28.9	28.1	20.0	29.0	0.513
Anti-diabetic agents (%)					
Oral anti-diabetic drugs	69.8	65.5	47.5	43.8	<0.001
Insulin	60.3	74.7	80.0	87.5	<0.001
Anti-hypertensive agents (%)					
RAAS inhibitors	42.6	41.6	50.0	51.6	0.260
Calcium-channel blockers	18.1	20.2	30.0	22.6	0.125
Beta-blockers	10.2	7.9	7.5	3.2	0.148
Diuretics	3.7	2.2	2.5	3.2	0.599
Lipid-lowering agents (%)					
Statins	23.8	36.0	27.5	22.6	0.353
Fibrates	12.0	7.9	12.5	3.2	0.163

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**Supplementary Table 4. Characteristics of study participants with diabetes duration  $\geq 10$  years**

Variables	Non-DR	Mild NPDR	Moderate NPDR	VTDR	P for trend
n	874	191	128	166	
Male (%)	53.7	49.7	57.1	50.6	0.678
Age (years)	66.1 $\pm$ 10.3	63.1 $\pm$ 10.2	62.4 $\pm$ 10.1	64.8 $\pm$ 9.0	<0.001
Duration (years)	14.2 $\pm$ 5.0	14.4 $\pm$ 6.0	15.4 $\pm$ 5.8	16.1 $\pm$ 5.6	<0.001
SBP (mmHg)	133 $\pm$ 17.1	136.3 $\pm$ 19.0	137.2 $\pm$ 18.6	141.4 $\pm$ 21.4	<0.001
DBP (mmHg)	78.7 $\pm$ 9.3	80.2 $\pm$ 9.1	79.5 $\pm$ 9.3	80.4 $\pm$ 10.2	0.029
BMI (Kg/m <sup>2</sup> )	24.7 $\pm$ 3.4	24.8 $\pm$ 3.3	25.1 $\pm$ 4.1	25.0 $\pm$ 3.6	0.389
Total cholesterol (mmol/L)	4.7 $\pm$ 1.1	4.6 $\pm$ 1.1	4.7 $\pm$ 1.1	4.9 $\pm$ 1.4	0.382
Triglycerides (mmol/L)	1.8 $\pm$ 1.6	1.6 $\pm$ 1.2	1.6 $\pm$ 1.4	1.9 $\pm$ 2.1	0.149
HDL-C (mmol/L)	1.2 $\pm$ 0.3	1.1 $\pm$ 0.3	1.2 $\pm$ 0.3	1.2 $\pm$ 0.3	0.592
LDL-C (mmol/L)	3.1 $\pm$ 1	3.0 $\pm$ 0.9	3.1 $\pm$ 0.9	3.2 $\pm$ 1.2	0.679
HbA1c (%)	8.7 $\pm$ 1.9	9.0 $\pm$ 1.8	9.2 $\pm$ 1.8	9.4 $\pm$ 2.0	<0.001
HbA1c (mmol/mol)	72.0 $\pm$ 20.8	75.0 $\pm$ 19.7	77.0 $\pm$ 19.7	79.0 $\pm$ 21.9	
Fasting C-peptide (ng/ml)	1.9 $\pm$ 1.1	1.6 $\pm$ 0.9	1.5 $\pm$ 1.0	1.4 $\pm$ 0.9	<0.001
SD (mmol/L)	2.4 $\pm$ 0.9	2.4 $\pm$ 0.8	2.6 $\pm$ 0.9	2.7 $\pm$ 0.9	<0.001
CV (%)	26.4 $\pm$ 8.7	26.2 $\pm$ 8.8	27.5 $\pm$ 9.1	28.3 $\pm$ 8.8	0.010
MAGE (mmol/L)	6.1 $\pm$ 2.6	6.3 $\pm$ 2.5	6.2 $\pm$ 2.3	6.6 $\pm$ 2.7	0.007
TIR (%)	64.4 $\pm$ 23.6	60.6 $\pm$ 24.1	57.9 $\pm$ 23.0	58.3 $\pm$ 22.2	<0.001
Current smoker (%)	17.3	30.5	18.3	18.1	0.424
Anti-diabetic agents (%)					
Oral anti-diabetic drugs	61.5	63.5	51.2	53.8	0.019
Insulin	72.2	78.8	88.8	96.3	<0.001
Anti-hypertensive agents (%)					
RAAS inhibitors	45.5	47.6	46.8	60.0	0.003
Calcium-channel blockers	23.4	19.8	23.8	25.6	0.677
Beta-blockers	11.7	8.6	10.3	7.5	0.100
Diuretics	4.5	3.7	1.6	10.0	0.067
Lipid-lowering agents (%)					
Statins	26.7	25.7	31.0	27.5	0.589
Fibrates	9.3	8.6	8.7	8.8	0.745

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