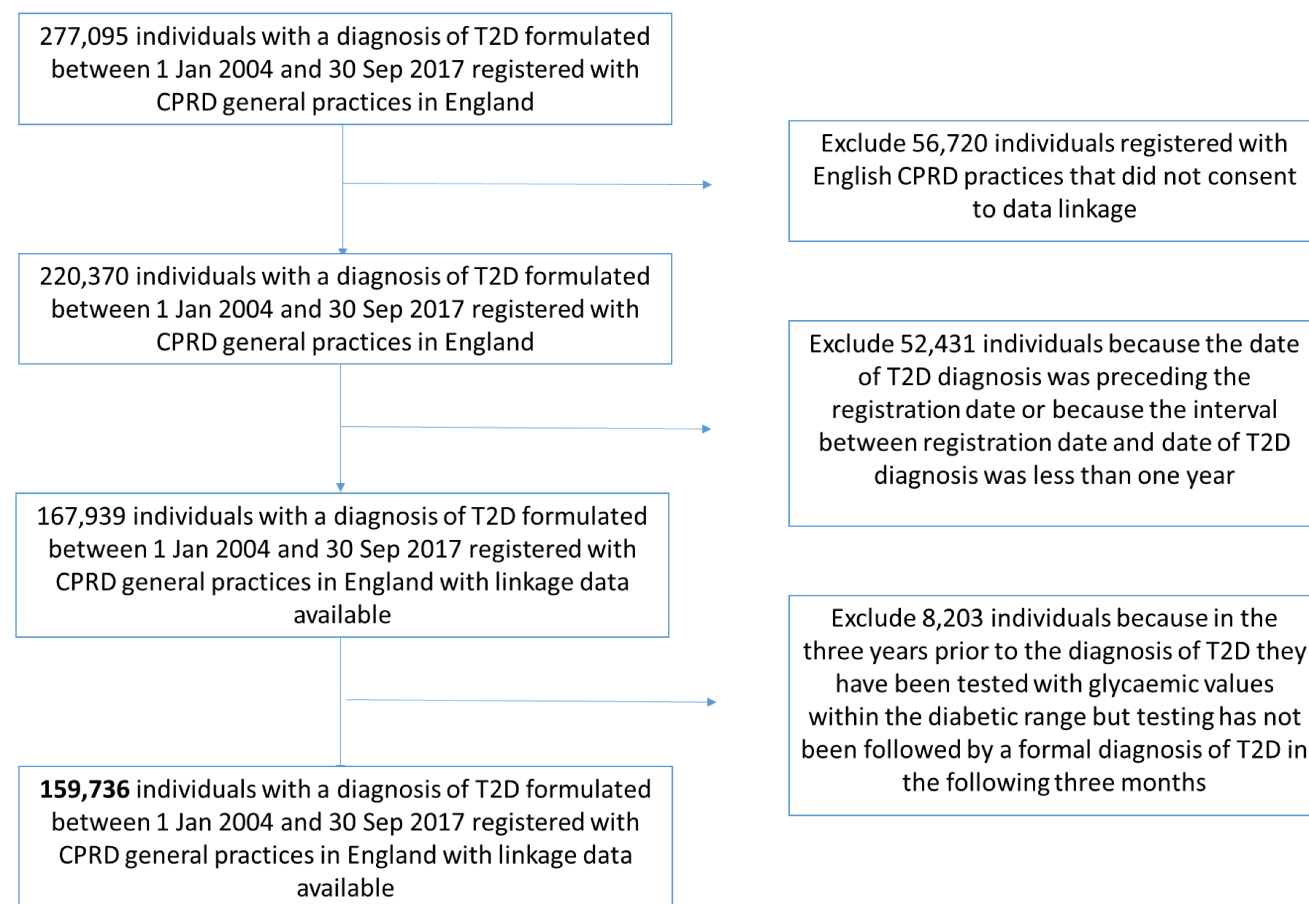


Supplementary Material

Association between pre-diabetes and microvascular and macrovascular disease in newly diagnosed type 2 diabetes

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Supplementary Figure S1. Study diagram

Abbreviations: T2D: Type 2 diabetes.

Supplementary Table S2. Definition of pre-diabetes and study outcomes

Detection of Pre-diabetes	<p>Laboratory diagnostic criteria:</p> <ul style="list-style-type: none"> - World Health Organization/International Expert Committee: FPG 6.1-6.9 mmol/L; OGTT 7.8-11.1 mmol/L; HbA1c 42 to 47 mmol/mol (6.0-6.4%) - NICE: FPG 5.5-6.9 mmol/L; OGTT 7.8-11.1 mmol/L; HbA1c 42 to 47 mmol/mol (6.0-6.4%) - American Diabetes Association: FPG 5.6-6.9 mmol/L; OGTT 7.8-11.1 mmol/L; HbA1c 39 to 47 mmol/mol or 5.7-6.4% <p>Diagnostic codes for pre-diabetes, Impaired Glucose Tolerance, Impaired Glucose Metabolism, Intermediate Hyperglycaemia, and Non-diabetic Hyperglycaemia</p>
Microvascular disease present at time of diagnosis of Type 2 diabetes (diagnosed in the five years before and fifteen months after the diagnosis of Type 2 diabetes)	
Diabetic retinopathy	<ul style="list-style-type: none"> - Diagnostic codes for diabetic retinopathy (including codes for photocoagulation/vitrectomy, diabetic cataract, and acquired blindness) - Results from Diabetic retinopathy screening - ICD-X (E11.3; H36.0; H28.0) - OPCS-4 (C81.1; C81.2; C81.8; C81.9; C79.1; C79.2; C74.2)
Nephropathy	<ul style="list-style-type: none"> - Diagnostic codes for Chronic Kidney Disease stage 3A and above (including end-stage renal disease and renal replacement therapy) - If any of the following conditions is present: Microalbuminuria (albumin:creatinine ratio 30-300 mg/g); Macroalbuminuria (albumin:creatinine ratio \geq 300 mg/g); Serum creatinine \geq 3.3 mg/dL; GFR less than 60 mL/min per 1.73 m² - ICD-10 (N18.3; N18.4; N18.5) - OPCS-4 (M01; X40)
Macrovascular disease at time of diagnosis of Type 2 diabetes (diagnosed before or within the year following the diagnosis of Type 2 diabetes)	
Cerebrovascular disease Stroke, Carotid Endarterectomy (CEA), Carotid artery stenting (CAS)	<p>Stroke</p> <ul style="list-style-type: none"> - Diagnostic codes for haemorrhagic and ischaemic strokes - ICD-10 (I60-I64) <p>CEA & CAS</p> <ul style="list-style-type: none"> - OPCS-4.6: L29.4; L29.5 (CEA); L31.4 (CAS)
Acute Coronary Syndrome Acute Myocardial	<p>AMI</p> <ul style="list-style-type: none"> - Diagnostic codes for acute myocardial infarction - ICD-10 (I21; I22) <p>CAD</p>

<p>Infarction (AMI), Coronary Artery Disease (CAD), Coronary Revascularisation Procedures</p>	<ul style="list-style-type: none"> - Diagnostic codes for CAD - ICD-10 (I20; I25) <p>Coronary Revascularisation Procedures</p> <ul style="list-style-type: none"> - OPCS-4.6: K49; K50; K75; K40-K46)
<p>Peripheral Arterial disease</p> <p>Peripheral arterial disease (PAD), non- traumatic amputation</p>	<p>PAD</p> <ul style="list-style-type: none"> - Diagnostic codes for peripheral arterial disease - ICD-10 (E11.5; I70.2/7; I70.92) <p>AMPUTATION</p> <ul style="list-style-type: none"> -Diagnostic codes for non-traumatic amputation -OPCS-4.6: (X09.2-5,8-9; X10.1,4,8-9; X11.1,2,8,9)

Supplementary Table S3. Characteristics of the study population in the year following the diagnosis of Type 2 diabetes stratified by whether individuals were tested and reached detection thresholds for pre-diabetes before the diagnosis of Type 2 diabetes. Results are presented using NICE and ADA criteria for the definition of pre-diabetes.

Notes: Clinical data within three years before the diagnosis of Type 2 diabetes were used to define the detection of pre-diabetes. For both diagnostic criteria (NICE and ADA) p-values from Chi-square and ANOVA tests, as appropriate, are reported in the last columns for comparison between the two groups defined by testing and detection of pre-diabetes.

Abbreviations: FPG: fasting plasma glucose, OGTT: glucose tolerance test (2-hour after 75 g glucose load), ACEi: Angiotensin-converting-enzyme inhibitor, ARBs: Antiotensin II receptor blockers.

NICE criteria to define pre-diabetes: 5.5-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 42 to 47 mmol/mol or 6.0-6.4%

ADA criteria to define pre-diabetes: FPG: 5.6-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 39 to 47 mmol/mol or 5.7-6.4%
¥Chi-square test was performed to assess the unadjusted difference between groups

§ANOVA test was performed to assess the unadjusted difference between groups

ΩKruskal-Wallis test was performed to assess the unadjusted difference between groups

* Medication groups are not mutually exclusive and patients with multiple medications prescribed are counted multiple times.

	Total	No glycaemic measures recorded before the diagnosis of Type 2 diabetes	NICE DIAGNOSTIC CRITERIA ²			ADA DIAGNOSTIC CRITERIA ³		
			Glycaemic values within the normal range before the diagnosis of T2D	Pre-diabetes detected before the diagnosis of T2D	p-values	Glycaemic values within the normal range before the diagnosis of T2D	Pre-diabetes detected before the diagnosis of T2D	p-values
N	159,736	93,949	14,431	51,356		14,317	51,470	
%		58.8	9.0	32.2		9.0	32.2	
Type of glycaemic measures recorded before diagnosis of T2D (%)								
FPG			72.8	78.1		84.3	74.9	
HbA1C			41.9	54.3		30.5	57.5	
OGTT			2.0	20.6		3.0	20.3	
Multiple tests			16.0	50.9		16.9	50.5	
Time from testing to diagnosis of T2D, months; mean (SD)	33.0 (6.1)		32.7 (6.6)	33.1 (6.0)		33.1 (6.0)	33.0 (6.2)	
Female (%)	49.2	48.8	59.0	47.1	<0.001 [¥]	58.1	47.3	<0.001 [¥]
Age, years (SD)	61.5 (14.4)	60.2 (14.8)	60.4 (15.4)	64.1 (12.7)	<0.001 ^{\$}	60.1 (15.3)	64.2 (12.8)	<0.001 ^{\$}
Ethnicity (%)								
White	83	82.7	84.7	83	<0.001 [¥]	84.9	83	<0.001 [¥]
South Asian	3.6	3.1	3.9	4.5		4.1	4.4	
Black	2.4	2.2	3.3	2.7		3.2	2.7	
Other	3.1	2.9	3.3	3.3	<0.001 [¥]	3.2	3.3	<0.001 [¥]
Unknown	7.9	9.2	4.8	6.5		4.6	6.6	
Smoking status (%)								
Non-smoker	35.4	36.8	30.2	36.7	<0.001 [¥]	37	32.5	<0.001 [¥]
Ex-smoker	51.6	43.4	51.2	47		44.9	51.2	
Current smoker	16.1	19.8	18.6	16.3		18.2	16.3	
(continued)								

	Total	No glycaemic measures recorded before the diagnosis of Type 2 diabetes	NICE DIAGNOSTIC CRITERIA ²			ADA DIAGNOSTIC CRITERIA ³		
			Glycaemic values within the normal range before the diagnosis of T2D	Pre-diabetes detected before the diagnosis of T2D	p-values	Glycaemic values within the normal range before the diagnosis of T2D	Pre-diabetes detected before the diagnosis of T2D	p-values
HbA1c at diagnosis, mmol/mol; mean (SD)	55.2 (20.7)	59.4 (20.8)	45.4 (17.5)	50.8 (19.7)	<0.001 [§]	46.0 (19.3)	50.1 (18.8)	<0.001 [§]
BMI, kg/m ² ; mean (SD)	30.30 (6.7)	30.0 (6.7)	28.9 (6.8)	31.3 (6.6)	<0.001 [§]	29.1 (6.9)	31.2 (6.6)	<0.001 [§]
SBP, mm Hg; mean (SD)	136.4 (15.9)	136.4 (16.6)	132.9 (15.9)	137.2 (14.4)	<0.001 [§]	133.0 (15.9)	137.2 (14.4)	<0.001 [§]
DBP, mm Hg; mean (SD)	79.7 (9.4)	80.1 (9.6)	78.3 (9.4)	79.4 (8.8)	<0.001 [§]	78.5 (9.4)	79.4 (8.8)	<0.001 [§]
Total cholesterol, mmol/L; mean (SD)	5.1 (1.1)	5.2 (1.1)	5.1 (1.1)	4.9 (1.1)	<0.001 [§]	5.1 (1.1)	4.9 (1.1)	<0.001 [§]
Number of chronic diseases; mean (SD)	2.7 (2.0)	2.4 (1.9)	3.2 (2.1)	3.1 (2.0)	<0.001 [§]	3.2 (2.1)	3.1 (2.0)	<0.001 [§]
Medications (%)								
Anti-hypertensive	53.8	47.5	47.2	67.1	<0.001 [¥]	48.2	66.8	<0.001 [¥]
ACEi/ARBs	39	34.1	32.6	49.9	<0.001 [¥]	33.7	49.6	<0.001 [¥]
Anti-lipid medications	49.6	44.2	38.5	62.5	<0.001 [¥]	39.6	62.1	<0.001 [¥]
Anti-diabetic*	38.4	44.7	13.8	33.9	<0.001 [¥]	15.2	33.4	<0.001 [¥]
Biguanides	34.6	39.8	11.6	31.6	<0.001 [¥]	12.9	31.2	<0.001 [¥]
Sulphonylureas	8.5	11.4	2.7	4.7	<0.001 [¥]	3.2	4.6	<0.001 [¥]
Insulin	2.7	3.5	1.8	1.4	<0.001 [¥]	2.0	1.4	<0.001 [¥]
Other	0.1	0.1	0.1	0.2	0.025 [¥]	0.1	0.2	0.006 [¥]
Anti-platelet	27.0	24.2	22.9	33.1	<0.001 [¥]	23.9	32.8	<0.001 [¥]
Number of primary care visits in the year before T2D diagnosis; mean (SD)	12.9 (11.7)	11.1 (10.9)	17.2 (13.8)	14.9 (11.8)	<0.001 ^Ω	16.9 (13.6)	15.0 (11.9)	<0.001 ^Ω
Index of Multiple Deprivation quintiles (%)								
1 Q - least deprived	14.1	14.6	12.7	13.5	<0.001 [¥]	12.6	13.5	<0.001 [¥]
2 Q	19.1	19.5	19.4	18.3		19.2	18.3	
3 Q	19.0	19.1	17.2	19.4		17.6	19.3	
4 Q	22.3	21.1	23.4	24.2	<0.001 [¥]	23.1	24.3	<0.001 [¥]
5 Q - most deprived	25.6	25.8	27.3	24.6		27.4	24.6	

Supplementary Table S4. Characteristics of individuals with pre-diabetes stratified by having a diagnostic code for pre-diabetes recorded. Results are presented using WHO/IEC, NICE, and ADA criteria for the definition of pre-diabetes.

Notes: Clinical data within three years before the diagnosis of Type 2 diabetes were used to define the detection of pre-diabetes. For each diagnostic criteria (WHO/IEC, NICE, and ADA), p-values from Chi-square and ANOVA tests, as appropriate, are reported in the last columns for comparisons between two groups: diagnostic code recorded for pre-diabetes and pre-diabetes without a diagnostic label recorded for pre-diabetes.

Abbreviations: T2D: Type 2 diabetes FPG: fasting plasma glucose, OGTT: glucose tolerance test (2-hour after 75 g glucose load), ACE: Angiotensin-converting-enzyme inhibitor, ArB: Antiotensin II receptor blockers.

WHO/IEC criteria to define pre-diabetes: FPG: 6.1-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 42 to 47 mmol/mol or 6.0-6.4%

NICE criteria to define pre-diabetes: 5.5-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 42 to 47 mmol/mol or 6.0-6.4%

ADA criteria to define pre-diabetes: FPG: 5.6-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 39 to 47 mmol/mol or 5.7-6.4%

¥Chi-square test for the comparison of groups with and without a diagnostic label recorded for pre-diabetes

§ANOVA test for the comparison of groups with and without a diagnostic label recorded for pre-diabetes

ΩKruskal-Wallis test was performed to assess the unadjusted difference between groups

* Medication groups are not mutually exclusive and patients with multiple medications prescribed are counted multiple times.

	WHO/IEC DIAGNOSTIC CRITERIA ¹			NICE DIAGNOSTIC CRITERIA ²			ADA DIAGNOSTIC CRITERIA ³		
	Tested before the diagnosis of T2D (pre-diabetes detected without diagnostic code assigned)	Tested before the diagnosis of T2D (pre-diabetes detected and diagnostic code assigned)	p-values	Tested before the diagnosis of T2D (pre-diabetes detected without diagnostic code assigned)	Tested before the diagnosis of T2D (pre-diabetes detected and diagnostic code assigned)	p-values	Tested before the diagnosis of T2D (pre-diabetes detected without diagnostic code assigned)	Tested before the diagnosis of T2D (pre-diabetes detected and diagnostic code assigned)	p-values
N	23,459	20,426		30,930	20,426		31,044	20,426	
%	53.5	46.5		60.2	39.8		60.3	39.7	
Type of glycaemic measures recorded before diagnosis of T2D (%)									
FPG	81.2	66.5		85.8	66.5		80.40	66.50	
HbA1C	60.5	55.5		53.6	55.50		58.80	55.50	
OGTT	21.1	24.3		18.3	24.30		17.80	24.30	
Multiple tests	55.3	50.3		51.2	50.30		50.70	50.30	
Time from testing to diagnosis of T2D, months; mean (SD)	32.8 (6.4)	33.2 (6.8)		33.0 (6.0)	33.2 (5.8)		32.8 (6.4)	33.2 (5.8)	
Female (%)	47.1	46.3	0.086 [¥]	47.6	46.3	0.004 [¥]	48	46.3	<0.001 [¥]
Age, years (SD)	64.4 (12.8)	64.2 (12.4)	0.137 [§]	64.1 (13.0)	64.2 (12.4)	0.189 [§]	64.2 (13)	64.2 (12.4)	0.667 [§]
Ethnicity (%)									
White	82.4	83.5		82.8	83.5		82.7	83.5	
South Asian	4.8	3.8		4.9	3.8		4.8	3.8	
Black	2.7	2.6	<0.001 [¥]	2.8	2.6	<0.001 [¥]	2.8	2.6	<0.001 [¥]
Other	3.4	3.2		3.4	3.2		3.4	3.2	
Unknown	6.7	7.1		6.2	7.0		6.3	7.0	
Smoking status (%)									
Non-smoker	32.6	32		16.7	15.7		32.8	32	
Ex-smoker	50.9	52.3	0.002 [¥]	36.2	37.5	0.002 [¥]	50.4	52.3	<0.001 [¥]
Current smoker	16.5	15.7		47.1	46.8		16.8	15.7	

(continued)

	WHO/IEC DIAGNOSTIC CRITERIA ¹			NICE DIAGNOSTIC CRITERIA ²			ADA DIAGNOSTIC CRITERIA ³		
	Tested before the diagnosis of Type 2 diabetes (pre-diabetes detected without diagnostic code assigned)	Tested before the diagnosis of Type 2 diabetes (pre-diabetes detected and diagnostic code assigned)	p-values	Tested before the diagnosis of Type 2 diabetes (pre-diabetes detected without diagnostic code assigned)	Tested before the diagnosis of Type 2 diabetes (pre-diabetes detected and diagnostic code assigned)	p-values	Tested before the diagnosis of Type 2 diabetes (pre-diabetes detected without diagnostic code assigned)	Tested before the diagnosis of Type 2 diabetes (pre-diabetes detected and diagnostic code assigned)	p-values
HbA1c at diagnosis, mmol/mol; mean (SD)	49.4 (18.3)	51.1 (19.6)	<0.001 [§]	50.8 (19.7)	50.8 (19.7)	0.001 [§]	49.7 (18.2)	51.1 (19.6)	<0.001 [§]
BMI, kg/m ² ; mean (SD)	31.3 (6.5)	31.4 (6.4)	0.016 [§]	31.2 (6.7)	31.4 (6.4)	<0.001 [§]	31.1 (6.6)	31.4 (6.4)	<0.001 [§]
SBP, mm Hg; mean (SD)	137.4 (14.7)	137.4 (13.9)	0.952 [§]	137.1 (14.8)	137.4 (13.9)	0.021 [§]	137.1 (14.8)	137.4 (13.9)	<0.001 [§]
DBP, mm Hg; mean (SD)	79.4 (8.9)	79.5 (4.9)	0.397 [§]	79.4 (8.9)	79.5 (8.6)	0.297 [§]	79.3 (8.9)	79.5 (8.6)	0.049 [§]
Total cholesterol, mmol/L; mean (SD)	4.9 (1.1)	4.9 (1.1)	0.027 [§]	4.9 (1.1)	4.9 (1.1)	0.013 [§]	4.9 (1.1)	4.9 (1.1)	<0.001 [§]
Number of chronic diseases; mean (SD)	3.1 (2.0)	3.1 (2.0)	0.006 ^Ω	3.1 (2.1)	3.1 (2.0)	0.883 ^Ω	3.1 (2.1)	3.1 (2.0)	0.831 ^Ω
Medications (%)									
Anti-hypertensive	67.6	67.5	0.689 [¥]	66.9	67.5	0.203 [¥]	66.4	67.5	0.015 [¥]
ACEi/ARBs	50	50.5	0.306 [¥]	49.5	50.4	0.035 [¥]	49	50.5	0.001 [¥]
Anti-lipid medications	62.7	64	0.007 [¥]	61.6	64	<0.001 [¥]	61	64	<0.001 [¥]
Anti-diabetic*	33.5	35.5	<0.001 [¥]	32.8	35.5	<0.001 [¥]	32.1	35.4	<0.001 [¥]
Biguanides	31.5	33.2	0.001 [¥]	30.6	33.2	<0.001 [¥]	29.9	33.2	<0.001 [¥]
Sulphonylureas	4.3	4.7	0.052 [¥]	4.7	4.7	0.914 [¥]	4.5	4.7	0.237 [¥]
Insulin	1.2	1.3	0.123 [¥]	1.5	1.3	0.050 [¥]	1.4	1.3	0.415 [¥]
Other	0.1	0.2	0.100 [¥]	0.1	0.2	0.055 [¥]	0.15	0.21	0.147 [¥]
Anti-platelet	33.0	33.3	0.524	33.0	33.3	0.491	32.5	33.3	0.064
Number of primary care visits in the year before T2D diagnosis; mean (SD)	14.3 (11.7)	15.2 (11.6)	<0.001 [§]	14.7 (12.0)	15.2 (11.6)	<0.001 [§]	14.8 (12.1)	15.2 (11.6)	0.002 [§]
Index of Multiple Deprivation quintiles (%)									
1 Q - least deprived	13.1	14.4	<0.001 [¥]	13	14.4	<0.001 [¥]	13	14.4	<0.001 [¥]
2 Q	17.5	19	<0.001 [¥]	17.7	19	<0.001 [¥]	17.8	19	<0.001 [¥]

3 Q	19.7	19.2	19.5	19.2	19.4	19.2
4 Q	25.4	22.8	25.2	22.8	25.3	22.8
5 Q - most deprived	24.3	24.7	24.6	24.7	24.6	24.7

Supplementary Table S5. Glycaemic measures recorded in the three years before the diagnosis of Type 2 diabetes between 2004 and 2011 and between 2012 and 2017 in the study population

Notes: WHO/IEC, NICE, and ADA criteria were used for the detection of pre-diabetes. Results are presented for two time periods based on the date of the diagnosis of Type 2 diabetes: 2004 to 2011 and 2012 to 2017 due to changes in the national clinical guidelines in the UK introducing HbA1c as additional blood glucose testing method for the testing and detection of pre-diabetes.

WHO/IEC criteria to define pre-diabetes: FPG: 6.1-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 42 to 47 mmol/mol or 6.0-6.4%

NICE criteria to define pre-diabetes: 5.5-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 42 to 47 mmol/mol or 6.0-6.4%

ADA criteria to define pre-diabetes: FPG: 5.6-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 39 to 47 mmol/mol or 5.7-6.4%

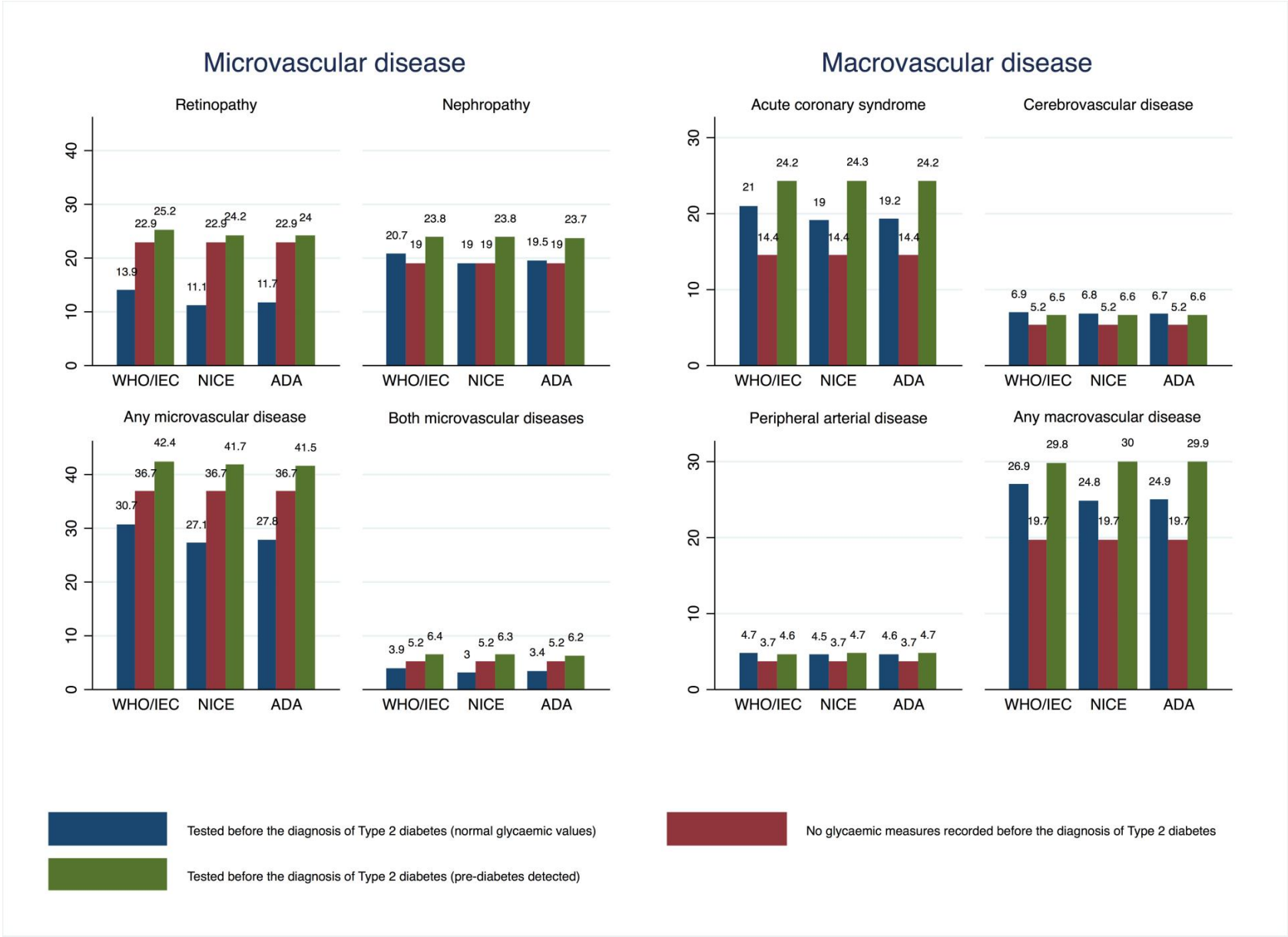
Abbreviations: T2D: Type 2 diabetes FPG: fasting plasma glucose, OGTT: glucose tolerance test (2-hour after 75 g glucose load).

	Glycaemic values within the normal range before the diagnosis of T2D			Pre-diabetes detected before the diagnosis of T2D		
	DIAGNOSTIC CRITERIA			DIAGNOSTIC CRITERIA		
	WHO/IEC ¹	NICE ²	ADA ³	WHO/IEC ¹	NICE ²	ADA ³
Type 2 diabetes diagnosed from 2004 to 2011						
N	11,567	7,086	7,695	27,121	31,602	30,993
TYPE OF GLYCAEMIC MEASURES RECORDED BEFORE THE DIAGNOSIS OF TYPE 2 DIABETES (%)						
FPG	87.8%	80.1%	87.9%	77.7%	80.9%	78.9%
HbA1C	25.7%	29.5%	21.6%	42.5%	39.3%	41.5%
OGTT	6.4%	2.9%	4.2%	26.7%	24.6%	24.7%
Multiple tests	18.6%	11.7%	12.6%	48.7%	46.0%	46.4%
Type 2 diabetes diagnosed from 2012 to 2017						
N	10,335	7,345	6,622	16,764	19,754	20,477
TYPE OF GLYCAEMIC MEASURES RECORDED BEFORE THE DIAGNOSIS OF TYPE 2 DIABETES (%)						
FPG	75.6%	65.7%	80.1%	69.0%	73.7%	68.7%
HbA1C	52.6%	53.8%	40.8%	83.4%	78.3%	81.7%
OGTT	2.4%	1.2%	1.5%	15.9%	14.3%	13.7%
Multiple tests	29.4%	20.2%	21.9%	59.9%	58.7%	56.8%
Type 2 diabetes diagnosed from 2004 to 2017						
N	21,902	14,431	14,317	43,885	51,356	51,470
TYPE OF GLYCAEMIC MEASURES RECORDED BEFORE THE DIAGNOSIS OF TYPE 2 DIABETES (%)						
FPG	82.1%	72.8%	84.3%	74.4%	78.1%	74.9%
HbA1C	38.4%	41.9%	30.5%	58.2%	54.3%	57.5%

OGTT	4.5%	2.0%	3.0%	22.6%	20.6%	20.3%
Multiple tests	23.7%	16.0%	16.9%	53.0%	50.9%	50.5%

Supplementary Figure S6. Prevalence of microvascular (retinopathy and nephropathy) and macrovascular (acute coronary syndrome, cerebrovascular, and peripheral arterial disease) disease present at time of the diagnosis of Type 2 diabetes according to pre-diabetes status in the three years before the diagnosis of Type 2 diabetes.

Notes: A microvascular complication was considered being present at time of Type 2 diabetes diagnosis if the complication was diagnosed between five years before and fifteen months after the diagnosis of Type 2 diabetes. A macrovascular complication was considered being present at time of Type 2 diabetes diagnosis if the complication was diagnosed any time before the diagnosis and during the year following the diagnosis of Type 2 diabetes. 1) WHO/IEC criteria: FPG: 6.1-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 42 to 47 mmol/mol or 6.0-6.4%; 2) NICE criteria: 5.5-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 42 to 47 mmol/mol or 6.0-6.4%; 3) ADA criteria: FPG: 5.6-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 39 to 47 mmol/mol or 5.7-6.4%.

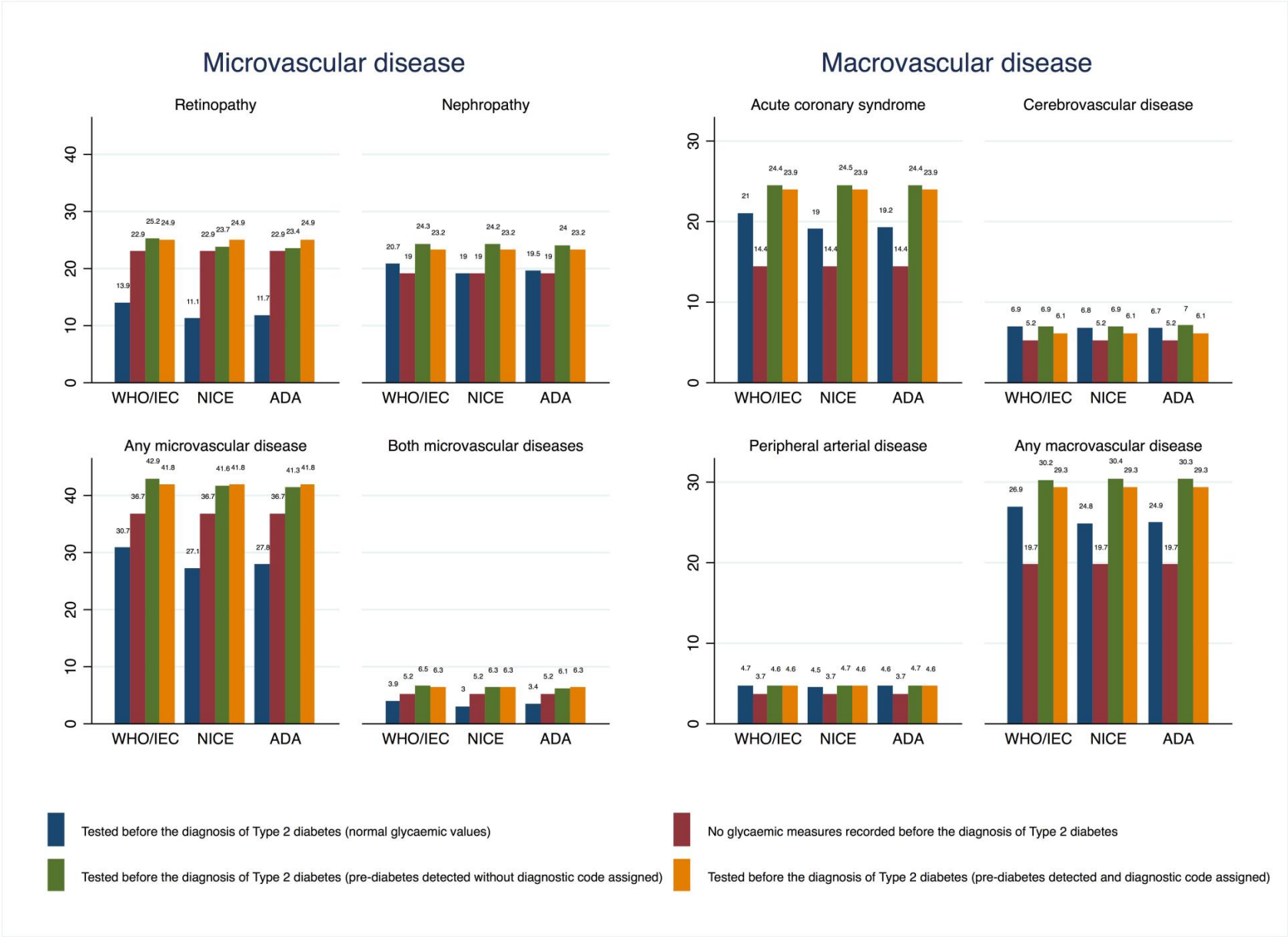


Supplementary Figure S7. Prevalence of microvascular (retinopathy and nephropathy) and macrovascular (acute coronary syndrome, cerebrovascular, and peripheral arterial disease) disease present at time of the diagnosis of Type 2 diabetes according to pre-diabetes status in the three years before the diagnosis of Type 2 diabetes. Individuals with pre-diabetes were further classified into two groups based on whether a diagnostic code for pre-diabetes was recorded in their health records at time of pre-diabetes detection.

Notes: A microvascular complication was defined as being present at time of Type 2 diabetes diagnosis if the complication was diagnosed between five years before and fifteen months after the diagnosis of Type 2 diabetes. A macrovascular complication was defined as being present at time of Type 2 diabetes diagnosis if the complication was diagnosed any time before the diagnosis and during the year of diagnosis of Type 2 diabetes. 1) WHO/IEC criteria: FPG: 6.1-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 42 to 47 mmol/mol or 6.0-6.4%;

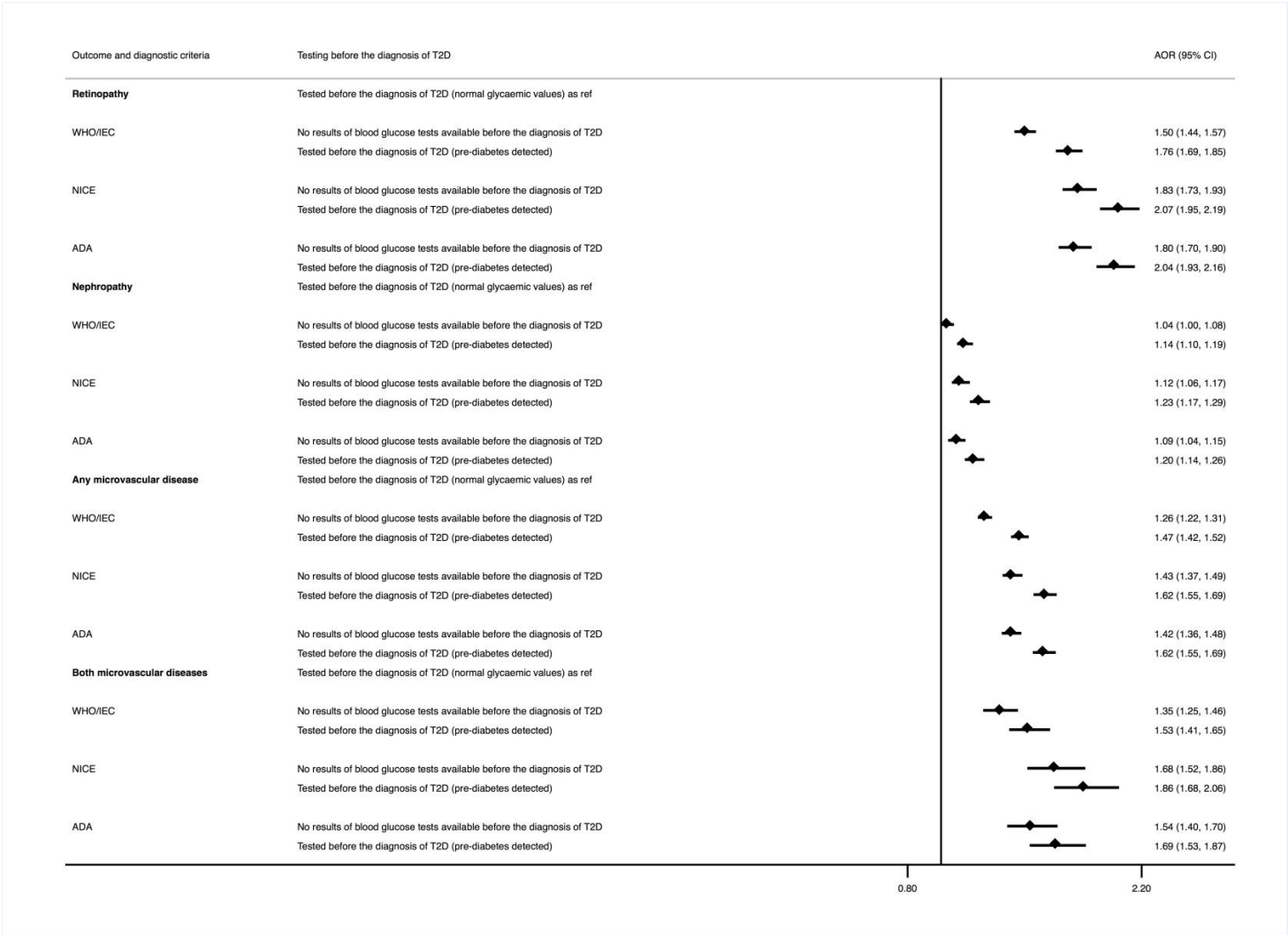
2) NICE criteria: 5.5-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 42 to 47 mmol/mol or 6.0-6.4%;

3) ADA criteria: FPG: 5.6-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 39 to 47 mmol/mol or 5.7-6.4%.



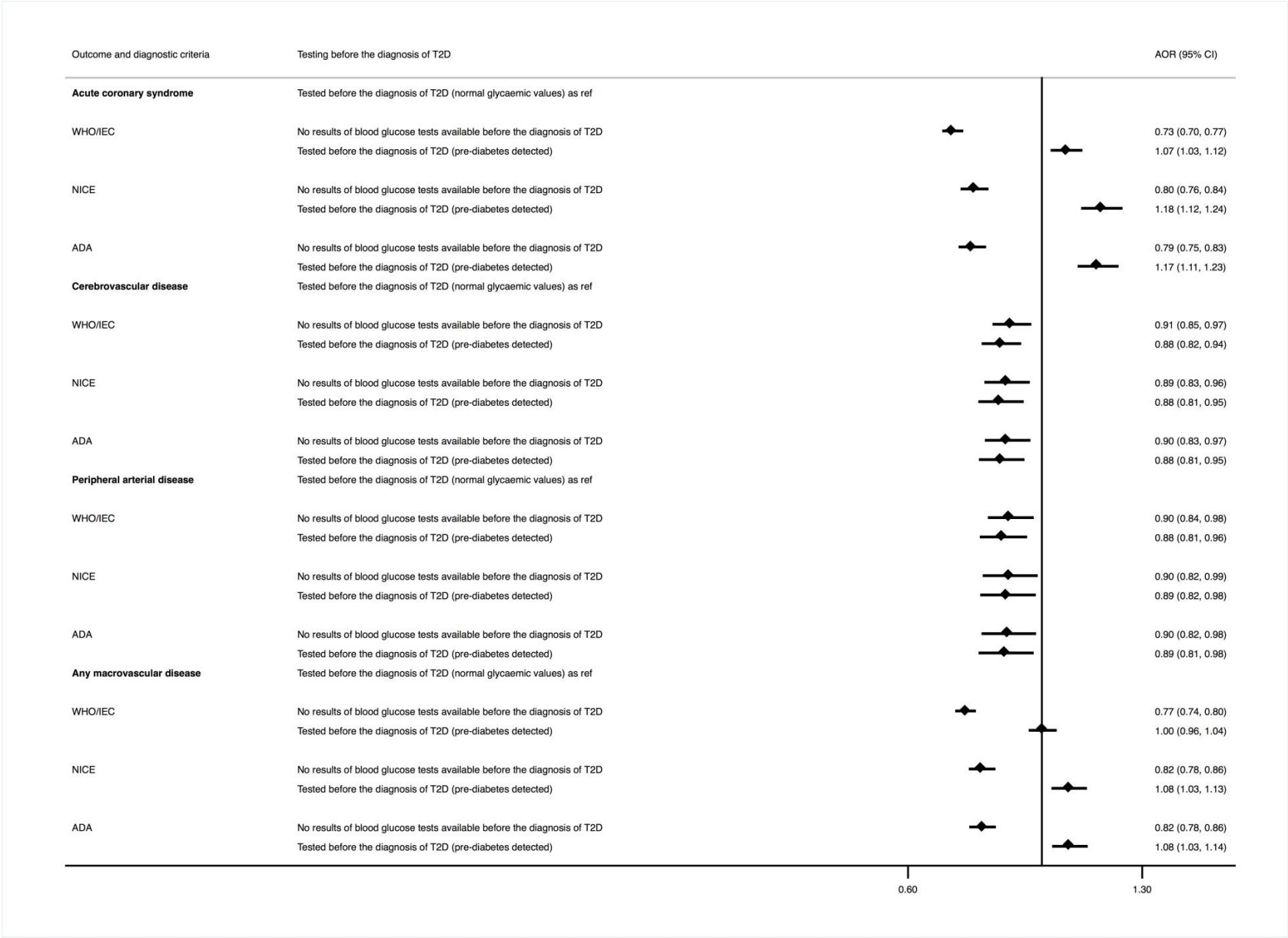
Supplementary Figure S8. Association between glycaemic testing and detection of pre-diabetes and presence of microvascular disease at the time of diagnosis of Type 2 diabetes

Notes: Adjusted Odds Ratios (AOR) and 95% confidence intervals (95% CI) have been estimated employing multivariable logistic regression models adjusted for age, sex, ethnicity (White, South Asian, Black, Other, Unknown), smoking status (non-smoker, ex-smoker, smoker), total cholesterol, systolic and diastolic blood pressure, number of co-existing chronic conditions, number of primary care visits in the previous year, general practice index of multiple deprivation, and year of diagnosis of Type 2 diabetes. Abbreviations: T2D: Type 2 diabetes.



Supplementary Figure S9. Association between glycaemic testing and detection of pre-diabetes and presence of macrovascular disease at the time of diagnosis of Type 2 diabetes

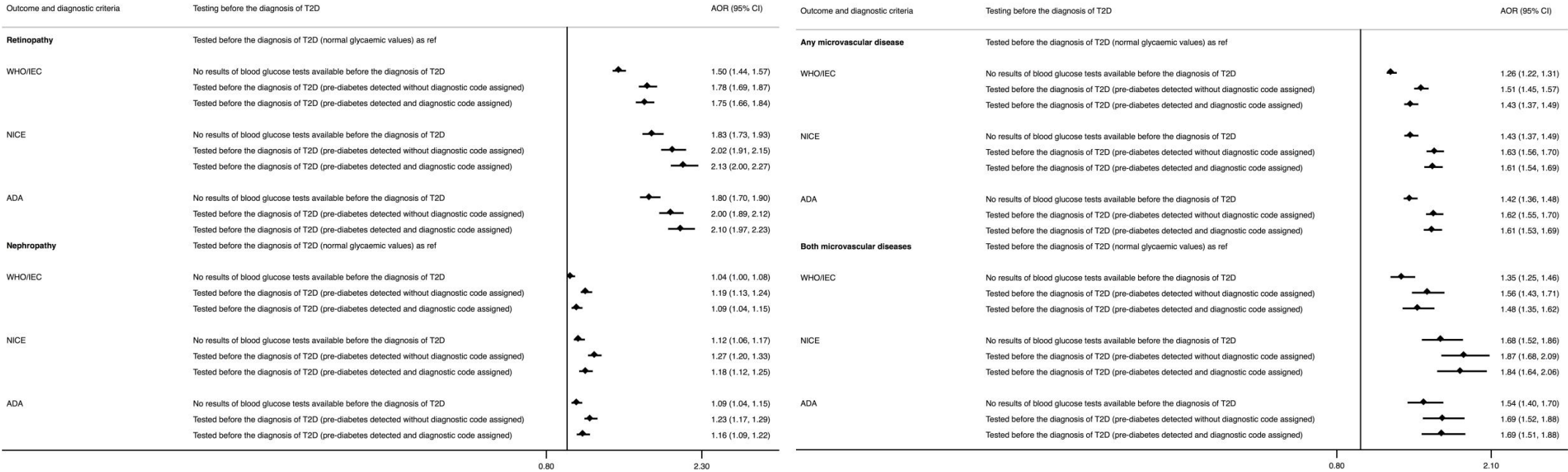
Notes: Adjusted Odds Ratios (AOR) and 95% confidence intervals (95% CI) have been estimated employing multivariable logistic regression models adjusted for age, sex, ethnicity (White, South Asian, Black, Other, Unknown), smoking status (non-smoker, ex-smoker, smoker), total cholesterol, systolic and diastolic blood pressure, number of co-existing chronic conditions, number of primary care visits in the previous year, general practice index of multiple deprivation, and year of diagnosis of Type 2 diabetes. Abbreviations: T2D: Type 2 diabetes.



Supplementary Figure S10. Association between glycaemic testing and detection of pre-diabetes and the presence of microvascular disease at the time of diagnosis of Type 2 diabetes.

Notes: Adjusted Odds Ratios (AOR) and 95% confidence intervals (95% CI) have been estimated employing multivariable logistic regression models adjusted for age, sex, ethnicity (White, South Asian, Black, Other, Unknown), smoking status (non-smoker, ex-smoker, smoker), total cholesterol, systolic and diastolic blood pressure, number of co-existing chronic conditions, number of primary care visits in the previous year, general practice index of multiple deprivation, and year of diagnosis of Type 2 diabetes. Abbreviations: T2D: Type 2 diabetes.

1. WHO/IEC criteria to define pre-diabetes: FPG: 6.1-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 42 to 47 mmol/mol or 6.0-6.4%
2. NICE criteria to define pre-diabetes: 5.5-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 42 to 47 mmol/mol or 6.0-6.4%
3. ADA criteria to define pre-diabetes: FPG: 5.6-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 39 to 47 mmol/mol or 5.7-6.4%



Supplementary Figure S11. Association between testing and detection of pre-diabetes and presence of macrovascular disease at the time of diagnosis of Type 2 diabetes. For individuals with pre-diabetes detected a further stratification has been considered according to whether a corresponding diagnostic code was assigned at time of pre-diabetes detection.

Notes: Adjusted Odds Ratios (AOR) and 95% confidence intervals (95% CI) have been estimated employing multivariable logistic regression models adjusted for age, sex, ethnicity (White, South Asian, Black, Other, Unknown), smoking status (non-smoker, ex-smoker, smoker), total cholesterol, systolic and diastolic blood pressure, number of co-existing chronic conditions, number of primary care visits in the previous year, general practice index of multideprivation, and year of diagnosis of Type 2 diabetes. Abbreviations: T2D: Type 2 diabetes.

WHO/IEC criteria to define pre-diabetes: FPG: 6.1-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 42 to 47 mmol/mol or 6.0-6.4%

NICE criteria to define pre-diabetes: 5.5-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 42 to 47 mmol/mol or 6.0-6.4%

ADA criteria to define pre-diabetes: FPG: 5.6-6.9 mmol/L, OGTT 7.8-11.1 mmol/L, HbA1c 39 to 47 mmol/mol or 5.7-6.4%

