

ESM to ‘Greater daily glucose variability and lower time in range are associated with greater aortic stiffness: The Maastricht Study’

ESM Methods

Ridge regression

The method used in R package glmnet (version 4.0.2) estimates regression coefficients according to the formula: $Ridge = RSS + \frac{1}{n} * \lambda * \sum_{j=1}^p \beta_j^2$, where RSS is the residual sum of squares, n is the sample size, λ is the chosen amount of penalization, and $\sum_{j=1}^p \beta_j^2$ represents the sum of all squared regression coefficients.

ESM Table 1. Participant characteristics of the different study populations and the number of missing values

Characteristic	Complete data on potential confounders (n=825)	Missing data	cf-PWV (n=643)	Missing data	carDC, CWS (n=725)	Missing data	cIMT (n=726)	Missing data	ABI (n=816)	Missing data
Demographics										
Age, y	59.7 ± 8.6	0	60.0 ± 8.5	0	60.1 ± 8.6	0	60.1 ± 8.6	0	59.7 ± 8.6	0
Women	403 (48.8)	0	295 (45.9)	0	350 (48.3)	0	351 (48.3)	0	398 (48.8)	0
Educational level (low/medium/high), n	261/231/333	0	197/184/262	0	226/211/288	0	226/211/289	0	256/227/333	0
Educational level (low/medium/high), %	31.6/28.0/40.4		30.6/28.6/40.7		31.2/29.1/39.7		31.1/29.1/39.8		31.4/27.8/40.8	
Glycaemic parameters										
Glucose metabolism status										
NGM/PreD/T2D/T1D, n	455/179/189/2	0	333/148/160/2	0	384/169/171/1	0	384/169/172/1	0	454/175/185/2	0
NGM/PreD/T2D/T1D, %	55.2/21.7/22.9/0.2		51.8/23.0/24.9/0.3		53.0/23.3/23.6/0.1		52.9/23.3/23.7/0.1		55.6/21.4/22.7/0.2	
Newly diagnosed T2D, n	68 (8.2)	0	57 (8.9)	0	59 (8.1)	0	59 (8.1)	0	68 (8.3)	0
Fasting plasma glucose, mmol/L	5.4 [5.0-6.2]	0	5.5 [5.0-6.4]	0	5.5 [5.0-6.3]	0	5.5 [5.0-6.3]	0	5.4 [5.0-6.2]	0
2-hour post-load glucose, mmol/L	6.6 [5.2-9.1]	39	6.9 [5.3-9.4]	33	6.8 [5.3-9.3]	39	6.9 [5.3-9.3]	39	6.6 [5.2-9.1]	39
MSG _{CGM} , mmol/L	6.1 [5.7-6.7]	0	6.1 [5.7-6.8]	0	6.1 [5.7-6.7]	0	6.1 [5.7-6.7]	0	6.1 [5.7-6.7]	0
SD _{CGM} , mmol/L	0.84 [0.68-1.19]	0	0.86 [0.69-1.22]	0	0.86 [0.69-1.21]	0	0.86 [0.69-1.21]	0	0.84 [0.68-1.17]	0
CV _{CGM} , %	14.0 [11.6-17.6]	0	14.3 [11.6-17.9]	0	14.3 [11.7-17.9]	0	14.3 [11.7-17.9]	0	14.0 [11.6-17.6]	0
TIR _{CGM} , %	99.8 [97.3-100.0]	0	99.7 [96.5-100.0]	0	99.7 [96.8-100.0]	0	99.7 [96.8-100.0]	0	99.8 [97.6-100.0]	0
HbA _{1c} , %	5.5 [5.3-5.9]	0	5.6 [5.4-5.9]	0	5.6 [5.3-5.9]	0	5.6 [5.4-5.9]	0	5.5 [5.3-5.9]	0
HbA _{1c} , mmol/mol	37.0 [34.0-41.0]	0	38.0 [35.0-41.0]	0	38.0 [35.0-41.0]	0	38.0 [35.0-41.0]	0	37.0 [34.0-41.0]	0
Diabetes medication use, n										
Insulin	106 (12.8)	0	90 (14.0)	0	98 (13.5)	0	99 (13.6)	0	102 (12.5)	0
Metformin	21 (2.5)		18 (2.8)		17 (2.3)		17 (2.3)		20 (2.5)	
Sulfonylureas	100 (12.1)		85 (13.2)		94 (13.0)		95 (13.1)		97 (11.9)	
Sulfonylureas	21 (2.5)		19 (3.0)		20 (2.8)		20 (2.8)		21 (2.6)	
GLP-1 analogs	4 (0.5)		4 (0.6)		3 (0.4)		3 (0.4)		4 (0.5)	
DDP-4 inhibitors	1 (0.1)		1 (0.2)		1 (0.1)		1 (0.1)		1 (0.1)	
SGLT-2 inhibitors	1 (0.1)		1 (0.2)		1 (0.1)		1 (0.1)		1 (0.1)	
Lifestyle factors										
BMI, kg/m ²	27.2 ± 4.4	0	27.3 ± 4.4	0	27.2 ± 4.4	0	27.2 ± 4.4	0	27.0 ± 4.2	0
Waist circumference (men), cm	102.4 ± 11.8	0	102.7 ± 11.8	0	102.5 ± 11.9	0	102.5 ± 11.9	0	102.1 ± 11.5	0
Waist circumference (women), cm	90.7 ± 12.2	0	91.0 ± 11.9	0	90.7 ± 12.1	0	90.7 ± 12.1	0	90.4 ± 12.0	0
Physical activity, hours/week	12.3 [7.5-18.3]	95	12.0 [7.5-18.3]	63	12.3 [7.5-18.4]	81	12.3 [7.5-18.5]	81	12.3 [7.5-18.4]	92
Dutch healthy diet index, (range: 0-150)	83.6 ± 16.1	200	83.4 ± 16.1	114	83.6 ± 15.8	154	83.6 ± 15.9	154	83.6 ± 16.0	199
Alcohol use (none/low/high), n	145/529/151	0	114/410/119	0	130/465/130	0	130/466/130	0	143/523/150	0
Alcohol use (none/low/high), %	17.6/64.1/18.3		17.7/63.8/18.5		17.9/64.1/19.9		17.9/64.2/19.9		17.5/64.1/18.4	
Smoking (never/former/current), n	321/402/102	0	254/310/79	0	278/356/91	0	279/356/91	0	317/397/102	0
Smoking (never/former/current), %	38.9/48.7/12.4		39.5/48.2/12.3		38.3/49.1/12.6		38.4/49.0/12.5		38.8/48.7/12.5	
Cardiovascular risk factors										
History of CVD	125 (15.2)	2	102 (15.9)	2	109 (15.1)	2	109 (15.1)	2	122 (15.0)	2
Office systolic BP, mmHg	133.2 ± 18.0	0	133.6 ± 18.1	0	133.5 ± 18.1	0	133.5 ± 18.1	0	133.1 ± 18.0	0

Office diastolic BP, mmHg	75.1 ± 10.2	0	75.3 ± 10.5	0	75.2 ± 10.2	0	75.2 ± 10.2	0	75.0 ± 10.2	0
Mean arterial pressure, mmHg	97.0 ± 10.8	0	97.0 ± 10.8	0	97.2 ± 10.9	0	97.2 ± 10.9	0	97.0 ± 10.8	0
Mean heart rate, beats/minute	61.0 ± 8.7	0	61.1 ± 8.7	0	61.1 ± 8.6	0	61.1 ± 8.6	0	60.9 ± 8.7	0
Antihypertensive medication use, n	290 (35.2)	0	235 (36.5)	0	261 (36.0)	0	262 (36.1)	0	284 (34.8)	0
Total-to-HDL cholesterol ratio	3.5 [2.8-4.3]	0	3.5 [2.9-4.4]	0	3.5 [2.8-4.3]	0	3.5 [2.8-4.3]	0	3.5 [2.8-4.3]	0
Triglycerides, mmol/L	1.3 [0.9-1.8]	0	1.3 [0.9-1.8]	0	1.3 [0.9-1.8]	0	1.3 [0.9-1.8]	0	1.3 [0.9-1.7]	0
Lipid-modifying medication use, n	205 (24.8)	0	171 (26.6)	0	187 (25.8)	0	187 (25.8)	0	201 (24.6)	0
eGFR, mL/min/1.73 m ²	80.5 ± 13.7	0	80.5 ± 13.8	0	80.1 ± 13.7	0	80.1 ± 13.7	0	80.5 ± 13.7	0
Albuminuria, n	63 (7.9)	3	52 (8.1)	3	59 (8.2)	3	59 (8.1)	3	63 (7.8)	3
Outcome measures										
cf-PWV, m/s	8.8 ± 2.2	182	8.8 ± 2.2	0	8.8 ± 2.2	125	8.8 ± 2.2	125	8.8 ± 2.2	179
carDC, 10 ⁻³ /kPa	15.8 ± 6.0	100	16.0 ± 6.1	43	15.8 ± 6.0	0	15.8 ± 6.0	1	15.8 ± 6.0	99
cIMT, μm	890.5 ± 152.8	100	891.9 ± 151.6	43	890.5 ± 152.8	0	890.5 ± 152.7	0	891.0 ± 153.3	99
ABI	1.14 ± 0.11	8	1.14 ± 0.12	8	1.14 ± 0.11	7	1.14 ± 0.11	7	1.13 ± 0.11	0
ABI < 0.9, n	24 (2.9)		16 (2.5)		20 (2.8)		20 (2.8)		24 (2.9)	
CWS _{mean} , kPa	44.0 [37.9-50.6]	100	43.7 [37.7-50.6]	43	44.0 [37.9-50.6]	0	44.0 [37.9-50.6]	1	44.0 [37.9-50.6]	99
CWS _{puls} , kPa	22.5 [19.1-27.0]	100	22.4 [19.0-26.8]	43	22.5 [19.1-27.0]	0	22.5 [19.1-27.0]	1	22.5 [19.0-27.0]	99

Data are reported as mean ± SD, median [interquartile range], or number (percentage %) as appropriate. Data represent the study population of participants with complete data on determinant and confounders or on determinant, outcome and confounders (in case of cf-PWV; carDC, CWS; cIMT; and ABI).

NGM, normal glucose metabolism; PreD, prediabetes; T2D, type 2 diabetes; T1D, type 1 diabetes, MSG_{CGM}, mean sensor glucose, SD_{CGM}, standard deviation; CV_{CGM}, coefficient of variation; TIR_{CGM}, time in range; HbA1c glycated hemoglobin A1c; GLP-1 glucagon-like peptide-1; DPP-4 dipeptidase-4; SGLT2, sodium/glucose cotransporter 2; BMI, body mass index; CVD, cardiovascular disease; BP, blood pressure; HDL high-density lipoprotein; eGFR, estimated glomerular filtration rate; CWS_{mean}, mean circumferential wall stress; CWS_{puls}, pulsatile circumferential wall stress.

ESM Table 2. GMS-stratified distributions of CGM-derived indices in the ankle-brachial index study population

CGM-derived indices*		NGM (n=454)	PreD (n=175)	T2D (n=185)
MSG _{CGM} , mmol/L	Median [IQR]	5.8 [5.5 – 6.1]	6.2 [5.8 – 6.6]	7.5 [6.8 – 8.7]
	5 th – 95 th percentile	5.15 - 6.54	5.25 - 7.60	5.73 – 11.85
SD _{CGM} , mmol/L	Median [IQR]	0.72 [0.61 – 0.87]	0.89 [0.73 – 1.12]	1.55 [1.16 – 1.98]
	5 th – 95 th percentile	0.48 - 1.28	0.60 - 1.61	0.79 - 3.13
CV _{CGM} , %	Median [IQR]	12.6 [10.7 – 14.9]	14.7 [12.2 – 17.5]	19.3 [16.1 – 24.1]
	5 th – 95 th percentile	8.51 - 20.57	10.13 – 24.08	12.42 – 33.36
TIR _{CGM} , %	Median [IQR]	100.0 [99.5 – 100.0]	99.8 [98.5 – 100.0]	91.8 [79.1 – 98.3]
	5 th – 95 th percentile	95.91 – 100.0	87.96 – 100.0	24.18 – 100.0

GMS, glucose metabolism status; CGM, continuous glucose monitoring; NGM, normal glucose metabolism; PreD, prediabetes; T2D, type 2 diabetes; MSG_{CGM}, mean sensor glucose; SD_{CGM}, standard deviation; CV_{CGM}, coefficient of variation; TIR_{CGM}, time in range; IQR, interquartile range.

*Because of the small sample size (n=2), these values are not reported for individuals with type 1 diabetes.

ESM Table 3. Multivariable-adjusted associations of daily glucose variability (expressed as SD_{CGM}) with arterial outcome variables

Model	B (95%CI)	P value	VIF
<i>Carotid femoral pulse wave velocity (cf-PWV), m/s (n=643)</i>			
Crude	0.920 (0.636; 1.205)	< 0.001	1
Model 1	0.647 (0.384; 0.909)	< 0.001	1.044
Model 2*	0.413 (0.147; 0.679)	0.002	1.322
Model 2 + MSG _{CGM}	0.270 (-0.125; 0.666)	0.180	2.918
<i>Carotid distensibility coefficient (carDC), 10⁻³/kPa (n=725)</i>			
Crude	-0.822 (-1.615; -0.029)	0.042	1
Model 1	-0.184 (-0.917; 0.549)	0.622	1.036
Model 2*	0.684 (-0.052; 1.420)	0.068	1.291
Model 2 + MSG _{CGM}	-0.071 (-1.204; 1.063)	0.903	3.070
<i>Carotid intima-media thickness (cIMT), μm (n=726)</i>			
Crude	25.441 (5.286; 45.595)	0.013	1
Model 1	11.907 (-7.253; 31.066)	0.223	1.036
Model 2†	14.679 (-6.257; 35.615)	0.169	1.286
Model 2 + MSG _{CGM}	-1.648 (-33.984; 30.688)	0.920	3.071
<i>Ankle-brachial index (ABI) (n=816)</i>			
Crude	-0.020 (-0.033; -0.007)	0.003	1
Model 1	-0.023 (-0.036; -0.010)	< 0.001	1.048
Model 2†	-0.011 (-0.026; 0.003)	0.126	1.339
Model 2 + MSG _{CGM}	-0.017 (-0.039; 0.005)	0.121	3.001
<i>Mean circumferential wall stress (CWS_{mean}), kPa (n=725)</i>			
Crude	1.530 (0.183; 2.877)	0.026	1
Model 1	1.009 (-0.320; 2.338)	0.136	1.036
Model 2‡	0.077 (-1.313; 1.467)	0.913	1.287
Model 2 + MSG _{CGM}	-1.126 (-3.271; 1.019)	0.303	3.070
<i>Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=725)</i>			
Crude	1.551 (0.690; 2.413)	< 0.001	1
Model 1	1.014 (0.161; 1.867)	0.020	1.036
Model 2*	-0.202 (-1.019; 0.614)	0.627	1.291
Model 2 + MSG _{CGM}	-0.602 (-1.862; 0.658)	0.349	3.070

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated with 1 unit (mmol/L) increase of SD_{CGM}. Crude: SD_{CGM}. Model 1: adjusted for age, sex, and education level. Model 2: additionally adjusted for mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs. Model 2 + MSG_{CGM}: additionally adjusted for mean sensor glucose. VIF, variance inflation factor

ESM Table 4. Multivariable-adjusted associations of daily glucose variability (expressed as CV_{CGM}) with arterial outcome variables

Model	B (95%CI)	P value
<i>Carotid femoral pulse wave velocity (cf-PWV), m/s (n=643)</i>		
Crude	0.732 (0.443; 1.021)	< 0.001
Model 1	0.488 (0.223; 0.752)	< 0.001
Model 2*	0.303 (0.046; 0.559)	0.021
<i>Carotid distensibility coefficient (carDC), 10⁻³/kPa (n=725)</i>		
Crude	-0.790 (-1.587; 0.006)	0.052
Model 1	-0.160 (-0.893; 0.573)	0.669
Model 2*	0.274 (-0.436; 0.984)	0.449
<i>Carotid intima-media thickness (cIMT), μm (n=726)</i>		
Crude	18.784 (-1.497; 39.064)	0.069
Model 1	7.487 (-11.684; 26.659)	0.443
Model 2†	9.021 (-11.182; 29.223)	0.381
<i>Ankle-brachial index (ABI) (n=816)</i>		
Crude	-0.020 (-0.033; -0.006)	0.003
Model 1	-0.021 (-0.034; -0.008)	0.002
Model 2‡	-0.010 (-0.024; 0.004)	0.166
<i>Mean circumferential wall stress (CWS_{mean}), kPa (n=725)</i>		
Crude	0.494 (-0.863; 1.851)	0.475
Model 1	0.131 (-1.200; 1.462)	0.847
Model 2‡	-0.440 (-1.779; 0.899)	0.519
<i>Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=725)</i>		
Crude	0.919 (0.049; 1.789)	0.038
Model 1	0.436 (-0.419; 1.292)	0.317
Model 2*	-0.388 (-1.174; 0.398)	0.333

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated with 10% increase in CV_{CGM}. Crude: CV_{CGM}. Model 1: adjusted for age, sex, and education level. Model 2: additionally adjusted for mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs.

ESM Table 5. Multivariable-adjusted associations of time in range (TIR_{CGM}) with arterial outcome variables

Model	B (95%CI)	P value
<i>Carotid femoral pulse wave velocity (cf-PWV), m/s (n=643)</i>		
Crude	-0.303 (-0.424; -0.182)	< 0.001
Model 1	-0.247 (-0.356; -0.139)	< 0.001
Model 2*	-0.145 (-0.252; -0.038)	0.008
<i>Carotid distensibility coefficient (carDC), 10⁻³/kPa (n=725)</i>		
Crude	0.107 (-0.227; 0.441)	0.529
Model 1	0.028 (-0.277; 0.333)	0.857
Model 2*	-0.350 (-0.646; -0.055)	0.020
<i>Carotid intima-media thickness (cIMT), μm (n=726)</i>		
Crude	-9.743 (-18.211; -1.276)	0.024
Model 1	-7.380 (-15.336; 0.576)	0.069
Model 2†	-8.144 (-16.563; 0.275)	0.058
<i>Ankle-brachial index (ABI) (n=816)</i>		
Crude	0.005 (-0.001; 0.010)	0.118
Model 1	0.006 (0.001; 0.012)	0.026
Model 2‡	0.002 (-0.005; 0.008)	0.620
<i>Mean circumferential wall stress (CWS_{mean}), kPa (n=725)</i>		
Crude	-0.785 (-1.349; -0.220)	0.007
Model 1	-0.564 (-1.116; -0.013)	0.045
Model 2‡	-0.179 (-0.739; 0.380)	0.530
<i>Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=725)</i>		
Crude	-0.552 (-0.915; -0.190)	0.003
Model 1	-0.433 (-0.788; -0.079)	0.017
Model 2*	0.049 (-0.280; 0.378)	0.768

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated with 10% increase in TIR_{CGM}. Crude: TIR_{CGM}. Model 1: adjusted for age, sex, and education level. Model 2: additionally adjusted for mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs.

ESM Table 6. Multivariable-adjusted associations of time in range above 70% (TIR_{CGM}≥70%) with arterial outcome variables

Model	B (95%CI)	P value
<i>Carotid femoral pulse wave velocity (cf-PWV), m/s (n=643)</i>		
Crude	-1.943 (-2.707; -1.179)	< 0.001
Model 1	-1.732 (-2.416; -1.048)	< 0.001
Model 2*	-1.098 (-1.745; -0.451)	0.001
Model 2 + HbA1c	-0.775 (-1.504; -0.047)	0.037
<i>Carotid distensibility coefficient (carDC), 10⁻³/kPa (n=725)</i>		
Crude	0.618 (-1.513; 2.749)	0.569
Model 1	0.455 (-1.482; 2.393)	0.645
Model 2*	-1.759 (-3.583; 0.066)	0.059
Model 2 + HbA1c	-1.828 (-3.886; 0.230)	0.082
<i>Carotid intima-media thickness (cIMT), μm (n=726)</i>		
Crude	-69.366 (-123.377; -15.354)	0.012
Model 1	-62.914 (-113.401; -12.426)	0.015
Model 2†	-63.722 (-115.422; -12.023)	0.016
Model 2 + HbA1c	-48.116 (-106.285; 10.054)	0.105
<i>Ankle-brachial index (ABI) (n=816)</i>		
Crude	0.055 (0.018; 0.091)	0.003
Model 1	0.063 (0.028; 0.099)	0.001
Model 2‡	0.041 (0.004; 0.077)	0.030
Model 2 + HbA1c	0.045 (0.004; 0.086)	0.037
<i>Mean circumferential wall stress (CWS_{mean}), kPa (n=725)</i>		
Crude	-4.480 (-8.087; -0.872)	0.015
Model 1	-3.400 (-6.909; 0.108)	0.057
Model 2‡	-1.394 (-4.834; 2.047)	0.427
Model 2 + HbA1c	-2.242 (-6.119; 1.635)	0.257
<i>Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=725)</i>		
Crude	-2.686 (-5.006; -0.365)	0.023
Model 1	-2.224 (-4.481; 0.203)	0.053
Model 2*	0.523 (-1.502; 2.549)	0.612
Model 2 + HbA1c	0.374 (-1.911; 2.659)	0.748

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated with 10% increase in TIR_{CGM}. Crude: TIR_{CGM}≥70%. Model 1: adjusted for age, sex, and education level. Model 2: additionally adjusted for mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs. Model 2 + HbA1c: additionally adjusted for HbA1c.

ESM Table 7. P values for interaction for sex, age, and type 2 diabetes status for the associations between SD_{CGM} and arterial outcome variables

Outcome	Sex	Age	Diabetes status ^a	Type 2 diabetes status ^b
cf-PWV*	0.41	0.10	0.57	0.41
carDC*	0.07	0.69	0.96	0.93
cIMT†	0.044	0.94	0.34	0.36
ABI†	0.68	0.80	0.86	0.15
CWS _{mean} ‡	0.06	0.60	0.54	0.46
CWS _{puls} *	0.07	0.67	0.99	0.90

All models were adjusted for age, education level, mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs.

a For the associations with ‘SD_{CGM}*diabetes status’ as interaction term, the associations were additionally adjusted for diabetes status. Bold denotes statistical significance; b For the associations with ‘SD_{CGM}*type 2 diabetes status’ as interaction term, the associations were additionally adjusted for type 2 diabetes status. Bold denotes statistical significance.

ESM Table 8. Sex-stratified associations of daily glucose variability (expressed as SD_{CGM}) with carotid intima-media thickness

Model	B (95%CI)	P value	B (95%CI)	P value
	<i>cIMT, men (n=375)</i>		<i>cIMT, women (n=351)</i>	
Crude	3.693 (-23.829; 31.215)	0.792	51.562 (21.871; 81.254)	0.001
Model 1	-7.205 (-33.606; 19.197)	0.592	39.873 (11.918; 67.829)	0.005
Model 2	1.003 (-27.653; 29.659)	0.945	33.853 (2.814; 64.891)	0.033
Model 2 + MSG _{CGM}	-7.146 (-51.779; 37.487)	0.753	1.448 (-46.749; 49.644)	0.953

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated with 1 unit (mmol/L) increase of SD_{CGM}. Crude: SD_{CGM}. Model 1: adjusted for age and education level. Model 2: additionally adjusted for office systolic blood pressure, body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs. Model 2 + MSG_{CGM}: additionally adjusted for mean sensor glucose.

ESM Table 9. Diabetes status-stratified associations of daily glucose variability (expressed as SD_{CGM}) with arterial outcome measures

Model	B (95%CI)	P value	B (95%CI)	P value
<i>cf-PWV, m/s</i>	<i>No diabetes (n=481)</i>		<i>Diabetes (n=162)</i>	
Crude	1.031 (0.450; 1.613)	0.001	0.271 (-0.260; 0.802)	0.316
Model 1	0.483 (-0.057; 1.023)	0.079	0.345 (-0.148; 0.839)	0.169
Model 2*	0.505 (-0.008; 1.017)	0.054	0.276 (-0.171; 0.723)	0.224
Model 2 + MSG_{CGM}	0.249 (-0.373; 0.872)	0.432	0.367 (-0.247; 0.982)	0.239
<i>carDC, $10^{-3}/kPa$</i>	<i>No diabetes (n=553)</i>		<i>Diabetes (n=172)</i>	
Crude	-1.096 (-2.794; 0.602)	0.205	0.947 (-0.375; 2.270)	0.159
Model 1	0.820 (-0.727; 2.368)	0.298	0.576 (-0.733; 1.884)	0.386
Model 2*	1.164 (-0.278; 2.605)	0.113	0.868 (-0.322; 2.058)	0.152
Model 2 + MSG_{CGM}	0.965 (-0.779; 2.708)	0.278	-0.575 (-2.254; 1.103)	0.499
<i>cIMT, μm</i>	<i>No diabetes (n=553)</i>		<i>Diabetes (n=173)</i>	
Crude	69.320 (26.604; 112.037)	0.002	4.316 (-30.835; 39.467)	0.809
Model 1	36.178 (-4.282; 76.638)	0.080	13.354 (-19.747; 46.455)	0.427
Model 2†	37.967 (-3.157; 79.091)	0.070	13.855 (-19.914; 47.625)	0.419
Model 2 + MSG_{CGM}	18.148 (-31.489; 67.784)	0.473	-7.393 (-56.083; 41.297)	0.765
<i>ABI</i>	<i>No diabetes (n=629)</i>		<i>Diabetes (n=187)</i>	
Crude	-0.026 (-0.053; 0.001)	0.060	-0.014 (-0.040; 0.011)	0.289
Model 1	-0.023 (-0.049; 0.004)	0.091	-0.015 (-0.041; 0.011)	0.252
Model 2†	-0.013 (-0.039; 0.014)	0.354	-0.007 (-0.035; 0.020)	0.588
Model 2 + MSG_{CGM}	-0.013 (-0.045; 0.019)	0.425	-0.017 (-0.055; 0.020)	0.363
<i>CWS_{mean}, kPa</i>	<i>No diabetes (n=553)</i>		<i>Diabetes (n=172)</i>	
Crude	-1.280 (-3.991; 1.431)	0.354	-0.032 (-2.661; 2.124)	0.981
Model 1	-1.523 (-4.232; 1.187)	0.270	-0.434 (-2.992; 2.124)	0.738
Model 2‡	-1.508 (-4.094; 1.078)	0.253	-0.196 (-2.741; 2.349)	0.879
Model 2 + MSG_{CGM}	-0.955 (-4.083; 2.172)	0.549	-1.763 (-5.421; 1.895)	0.343
<i>CWS_{puls}, kPa</i>	<i>No diabetes (n=553)</i>		<i>Diabetes (n=172)</i>	
Crude	0.549 (-1.203; 2.300)	0.539	-0.344 (-1.970; 1.282)	0.677
Model 1	-0.558 (-2.295; 1.179)	0.528	-0.315 (-1.961; 1.330)	0.706
Model 2*	-0.876 (-2.412; 0.660)	0.263	-0.725 (-2.218; 0.768)	0.339
Model 2 + MSG_{CGM}	-0.698 (-2.556; 1.160)	0.461	-1.069 (-3.211; 1.072)	0.326

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated with 1 unit (mmol/L) increase of SD_{CGM} . Crude: SD_{CGM} . Model 1: adjusted for age, sex, and education level. Model 2: additionally adjusted for mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of *cf-PWV* and *ABI* only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs. Model 2 + MSG_{CGM} : additionally adjusted for mean sensor glucose.

ESM Table 10. Multivariable-adjusted associations of daily glucose variability (expressed as SD_{CGM}) with arterial outcome variables after adjustment for glucose metabolism status, HbA_{1c}, or fasting plasma glucose instead of mean sensor glucose

Model	B (95%CI)	P value
<i>Carotid femoral pulse wave velocity (cf-PWV), m/s (n=643)</i>		
Model 2 + GMS	0.260 (-0.058; 0.579)	0.109
Model 2 + HbA _{1c}	0.244 (-0.081; 0.569)	0.140
Model 2 + FPG	0.294 (-0.014; 0.603)	0.061
<i>Carotid distensibility coefficient (carDC), 10⁻³/kPa (n=725)</i>		
Model 2 + GMS	0.827 (-0.062; 1.716)	0.068
Model 2 + HbA _{1c}	0.792 (-0.116; 1.700)	0.087
Model 2 + FPG	0.687 (-0.157; 1.531)	0.111
<i>Carotid intima-media thickness (cIMT), μm (n=726)</i>		
Model 2 + GMS	22.231 (-3.061; 47.524)	0.085
Model 2 + HbA _{1c}	2.242 (-23.487; 27.972)	0.864
Model 2 + FPG	9.738 (-14.259; 33.735)	0.426
<i>Ankle-brachial index (ABI) (n=816)</i>		
Model 2 + GMS	-0.009 (-0.026; 0.008)	0.307
Model 2 + HbA _{1c}	-0.013 (-0.031; 0.004)	0.141
Model 2 + FPG	-0.009 (-0.025; 0.008)	0.290
<i>Mean circumferential wall stress (CWS_{mean}), kPa (n=725)</i>		
Model 2 + GMS	-0.670 (-2.349; 1.010)	0.434
Model 2 + HbA _{1c}	0.408 (-1.307; 2.123)	0.641
Model 2 + FPG	0.275 (-1.321; 1.871)	0.735
<i>Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=725)</i>		
Model 2 + GMS	-0.868 (-1.853; 0.117)	0.084
Model 2 + HbA _{1c}	-0.130 (-1.138; 0.879)	0.801
Model 2 + FPG	-0.147 (-1.084; 0.791)	0.759

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated with 1 unit (mmol/L) increase of SD_{CGM}. Model 2 + represents the fully adjusted model that was additionally adjusted for glucose metabolism status (GMS), HbA_{1c}, or fasting plasma glucose (FPG)

ESM Table 11. Multivariable-adjusted associations of SD_{CGM} with arterial outcome variables, additionally adjusted for physical activity and Dutch healthy diet adherence

Model	B (95%CI)	P value
<i>Carotid femoral pulse wave velocity (cf-PWV), m/s (n=487)</i>		
Crude	0.970 (0.639; 1.301)	< 0.001
Model 1	0.669 (0.356; 0.981)	< 0.001
Model 2*	0.487 (0.169; 0.804)	0.003
Model 3	0.487 (0.169; 0.805)	0.003
Model 3 + MSG_{CGM}	0.461 (-0.014; 0.935)	0.057
<i>Carotid distensibility coefficient (carDC), $10^{-3}/kPa$ (n=519)</i>		
Crude	-0.895 (-1.806; 0.017)	0.054
Model 1	-0.256 (-1.112; 0.601)	0.558
Model 2*	0.628 (-0.219; 1.475)	0.146
Model 3	0.641 (-0.209; 1.490)	0.139
Model 3 + MSG_{CGM}	0.866 (-0.461; 2.194)	0.200
<i>Carotid intima-media thickness (cIMT), μm (n=520)</i>		
Crude	18.139 (-5.039; 41.317)	0.125
Model 1	3.957 (-18.619; 26.534)	0.731
Model 2†	6.775 (-18.133; 31.683)	0.593
Model 3	7.294 (-17.684; 32.271)	0.566
Model 3 + MSG_{CGM}	-10.304 (-49.368; 28.760)	0.605
<i>Ankle-brachial index (ABI) (n=562)</i>		
Crude	-0.025 (-0.040; -0.009)	0.002
Model 1	-0.029 (-0.044; -0.013)	< 0.001
Model 2‡	-0.014 (-0.031; 0.003)	0.115
Model 3	-0.014 (-0.031; 0.003)	0.112
Model 3 + MSG_{CGM}	-0.021 (-0.047; 0.005)	0.114
<i>Mean circumferential wall stress (CWS_{mean}), kPa (n=519)</i>		
Crude	2.785 (1.184; 4.386)	0.001
Model 1	1.952 (0.348; 3.556)	0.017
Model 2‡	1.242 (-0.445; 2.928)	0.149
Model 3	1.227 (-0.465; 2.918)	0.155
Model 3 + MSG_{CGM}	-0.040 (-2.688; 2.607)	0.976
<i>Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=519)</i>		
Crude	2.024 (0.978; 3.071)	< 0.001
Model 1	1.414 (0.367; 2.462)	0.008
Model 2*	0.110 (-0.888; 1.109)	0.828
Model 3	0.059 (-0.938; 1.056)	0.908
Model 3 + MSG_{CGM}	-0.605 (-2.161; 0.951)	0.445

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated 1 unit (mmol/L) increase of SD_{CGM} . Crude: SD_{CGM} . Model 1: adjusted for age, sex, and education level. Model 2: additionally adjusted for mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs. Model 3: additionally adjusted for physical activity and Dutch healthy diet adherence. Model 3 + MSG_{CGM} : additionally adjusted for mean sensor glucose.

Of note, the alcohol component of the Dutch healthy diet adherence index was subtracted from the sum score prior to performing the regression analyses to avoid multicollinearity.

ESM Table 12. Multivariable-adjusted associations of SD_{CGM} with arterial outcome variables, additionally adjusted for history of cardiovascular disease, estimated glomerular filtration rate, and urinary albumin excretion

Model	B (95%CI)	P value
<i>Carotid femoral pulse wave velocity (cf-PWV), m/s (n=638)</i>		
Crude	0.885 (0.599; 1.171)	< 0.001
Model 1	0.609 (0.347; 0.871)	< 0.001
Model 2*	0.390 (0.124; 0.656)	0.004
Model 3	0.315 (0.048; 0.583)	0.021
Model 3 + MSG_{CGM}	0.225 (-0.169; 0.618)	0.263
<i>Carotid distensibility coefficient (carDC), $10^{-3}/kPa$ (n=720)</i>		
Crude	-0.832 (-1.631; -0.033)	0.041
Model 1	-0.187 (-0.925; 0.551)	0.620
Model 2*	0.668 (-0.072; 1.409)	0.077
Model 3	0.697 (-0.061; 1.455)	0.071
Model 3 + MSG_{CGM}	-0.015 (-1.167; 1.138)	0.980
<i>Carotid intima-media thickness (cIMT), μm (n=721)</i>		
Crude	25.173 (4.872; 45.474)	0.015
Model 1	11.635 (-7.671; 30.942)	0.237
Model 2†	14.680 (-6.391; 35.751)	0.172
Model 3	15.638 (-5.910; 37.187)	0.155
Model 3 + MSG_{CGM}	1.648 (-31.181; 34.477)	0.922
<i>Ankle-brachial index (ABI) (n=811)</i>		
Crude	-0.021 (-0.034; -0.008)	0.002
Model 1	-0.024 (-0.037; -0.011)	< 0.001
Model 2†	-0.012 (-0.027; 0.002)	0.094
Model 3	-0.007 (-0.022; 0.007)	0.333
Model 3 + MSG_{CGM}	-0.012 (-0.034; 0.009)	0.258
<i>Mean circumferential wall stress (CWS_{mean}), kPa (n=720)</i>		
Crude	1.430 (0.079; 2.782)	0.038
Model 1	0.911 (-0.423; 2.245)	0.180
Model 2‡	-0.036 (-1.431; 1.359)	0.960
Model 3	-0.129 (-1.556; 1.297)	0.859
Model 3 + MSG_{CGM}	-1.300 (-3.472; 0.872)	0.240
<i>Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=720)</i>		
Crude	1.528 (0.661; 2.395)	0.001
Model 1	0.989 (0.131; 1.846)	0.024
Model 2*	-0.215 (-1.036; 0.605)	0.607
Model 3	-0.306 (-1.143; 0.532)	0.474
Model 3 + MSG_{CGM}	-0.787 (-2.062; 0.488)	0.226

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated 1 unit (mmol/L) increase of SD_{CGM} . Crude: SD_{CGM} . Model 1: adjusted for age, sex, and education level. Model 2: additionally adjusted for mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs. Model 3: additionally adjusted for history of cardiovascular disease, estimated glomerular filtration rate, and urinary albumin excretion. Model 3 + MSG_{CGM} : additionally adjusted for mean sensor glucose.

ESM Table 13. Multivariable-adjusted associations of SD_{CGM} with arterial structure adjusted for ambulatory systolic blood pressure instead of office systolic blood pressure

Model	B (95%CI)	P value
<i>Carotid intima-media thickness (cIMT), μm (n=649)</i>		
Crude	29.322 (7.349; 51.294)	0.009
Model 1	15.560 (-5.410; 36.530)	0.146
Model 2	18.314 (-4.281; 40.909)	0.112
Model 2 + MSG_{CGM}	8.592 (-25.341; 42.525)	0.619
<i>Ankle-brachial index (ABI) (n=728)</i>		
Crude	-0.026 (-0.040; -0.012)	< 0.001
Model 1	-0.030 (-0.044; -0.016)	< 0.001
Model 2	-0.019 (-0.034; -0.004)	0.015
Model 2 + MSG_{CGM}	-0.021 (-0.043; 0.001)	0.062

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated 1 unit (mmol/L) increase of SD_{CGM} . Crude: SD_{CGM} . Model 1: adjusted for age, sex, and education level. Model 2: additionally adjusted for ambulatory systolic blood pressure and heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs. Model 2 + MSG_{CGM} : additionally adjusted for mean sensor glucose.

ESM Table 14. Multivariable-adjusted associations of SD_{CGM} with arterial outcome variables after exclusion of individuals with type 1 diabetes

Model	B (95%CI)	P value
<i>Carotid femoral pulse wave velocity (cf-PWV), m/s (n=641)</i>		
Crude	0.910 (0.619; 1.200)	< 0.001
Model 1	0.629 (0.362; 0.896)	< 0.001
Model 2*	0.402 (0.132; 0.673)	0.004
Model 2 + MSG_{CGM}	0.256 (-0.146; 0.658)	0.211
<i>Carotid distensibility coefficient (carDC), $10^{-3}/kPa$ (n=724)</i>		
Crude	-0.831 (-1.627; -0.034)	0.041
Model 1	-0.187 (-0.923; 0.549)	0.618
Model 2*	0.679 (-0.058; 1.416)	0.071
Model 2 + MSG_{CGM}	-0.068 (-1.203; 1.067)	0.906
<i>Carotid intima-media thickness (cIMT), μm (n=725)</i>		
Crude	25.389 (5.144; 45.634)	0.014
Model 1	11.724 (-7.511; 30.960)	0.232
Model 2†	14.708 (-6.267; 35.682)	0.169
Model 2 + MSG_{CGM}	-1.779 (-34.168; 30.610)	0.914
<i>Ankle-brachial index (ABI) (n=814)</i>		
Crude	-0.017 (-0.030; -0.003)	0.014
Model 1	-0.020 (-0.033; -0.007)	0.003
Model 2†	-0.007 (-0.022; 0.007)	0.313
Model 2 + MSG_{CGM}	-0.011 (-0.033; 0.011)	0.328
<i>Mean circumferential wall stress (CWS_{mean}), kPa (n=724)</i>		
Crude	1.527 (0.174; 2.880)	0.027
Model 1	1.026 (-0.308; 2.360)	0.132
Model 2‡	0.103 (-1.289; 1.495)	0.884
Model 2 + MSG_{CGM}	-1.170 (-3.317; 0.977)	0.285
<i>Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=724)</i>		
Crude	1.532 (0.667; 2.397)	0.001
Model 1	0.999 (0.143; 1.855)	0.022
Model 2*	-0.209 (-1.027; 0.610)	0.617
Model 2 + MSG_{CGM}	-0.596 (-1.858; 0.666)	0.354

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated with 1 unit (mmol/L) increase of SD_{CGM} . Crude: SD_{CGM} . Model 1: adjusted for age, sex, and education level. Model 2: additionally adjusted for mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs. Model 2 + MSG_{CGM} : additionally adjusted for mean sensor glucose.

ESM Table 15. Multivariable-adjusted associations of daily glucose variability (expressed as SD_{CGM}) with arterial outcome variables after exclusion of individuals with CGM data gaps

Model	B (95%CI)	P value
<i>Carotid femoral pulse wave velocity (cf-PWV), m/s (n=591)</i>		
Crude	0.984 (0.671; 1.297)	< 0.001
Model 1	0.734 (0.446; 1.022)	< 0.001
Model 2*	0.501 (0.207; 0.796)	0.001
Model 2 + MSG_{CGM}	0.368 (-0.095; 0.831)	0.119
<i>Carotid distensibility coefficient (carDC), $10^{-3}/kPa$ (n=672)</i>		
Crude	-0.628 (-1.470; 0.214)	0.144
Model 1	-0.043 (-0.821; 0.736)	0.914
Model 2*	0.909 (0.127; 1.691)	0.023
Model 2 + MSG_{CGM}	0.139 (-1.102; 1.380)	0.826
<i>Carotid intima-media thickness (cIMT), μm (n=673)</i>		
Crude	20.012 (-1.404; 41.428)	0.067
Model 1	8.587 (-11.835; 29.009)	0.409
Model 2†	12.413 (-9.973; 34.798)	0.277
Model 2 + MSG_{CGM}	-2.126 (-37.762; 33.510)	0.907
<i>Ankle-brachial index (ABI) (n=749)</i>		
Crude	-0.023 (-0.037; -0.008)	0.002
Model 1	-0.026 (-0.040; -0.011)	< 0.001
Model 2†	-0.015 (-0.031; 0.001)	0.071
Model 2 + MSG_{CGM}	-0.026 (-0.051; 0.000)	0.047
<i>Mean circumferential wall stress (CWS_{mean}), kPa (n=672)</i>		
Crude	1.751 (0.311; 3.192)	0.017
Model 1	1.254 (-0.165; 2.672)	0.131
Model 2‡	0.180 (-1.309; 1.670)	0.812
Model 2 + MSG_{CGM}	-1.027 (-3.396; 1.341)	0.395
<i>Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=672)</i>		
Crude	1.693 (0.773; 2.614)	< 0.001
Model 1	1.230 (0.315; 2.145)	0.008
Model 2*	-0.011 (-0.886; 0.864)	0.980
Model 2 + MSG_{CGM}	-0.277 (-1.668; 1.114)	0.696

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated with 1 unit (mmol/L) increase of SD_{CGM} . Crude: SD_{CGM} . Model 1: adjusted for age, sex, and education level. Model 2: additionally adjusted for mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs. Model 2 + MSG_{CGM} : additionally adjusted for mean sensor glucose.

ESM Table 16. Multivariable-adjusted associations of daily glucose variability (expressed as SD_{CGM}) with arterial outcome variables after exclusion of individuals with a suboptimal CGM recording period

Model	B (95%CI)	P value
<i>Carotid femoral pulse wave velocity (cf-PWV), m/s (n=620)</i>		
Crude	0.931 (0.642; 1.221)	< 0.001
Model 1	0.649 (0.381; 0.917)	< 0.001
Model 2*	0.425 (0.151; 0.698)	0.002
Model 2 + MSG_{CGM}	0.299 (-0.109; 0.706)	0.151
<i>Carotid distensibility coefficient (carDC), $10^{-3}/kPa$ (n=698)</i>		
Crude	-0.711 (-1.519; 0.098)	0.085
Model 1	-0.017 (-0.765; 0.730)	0.964
Model 2*	0.782 (0.028; 1.537)	0.044
Model 2 + MSG_{CGM}	0.066 (-1.116; 1.248)	0.913
<i>Carotid intima-media thickness (cIMT), μm (n=699)</i>		
Crude	26.580 (6.011; 47.149)	0.011
Model 1	12.627 (-6.950; 32.204)	0.206
Model 2†	16.739 (-4.712; 38.190)	0.126
Model 2 + MSG_{CGM}	4.126 (-29.577; 37.829)	0.810
<i>Ankle-brachial index (ABI) (n=785)</i>		
Crude	-0.020 (-0.034; -0.007)	0.003
Model 1	-0.024 (-0.037; -0.010)	0.001
Model 2†	-0.011 (-0.026; 0.004)	0.163
Model 2 + MSG_{CGM}	-0.019 (-0.041; 0.004)	0.109
<i>Mean circumferential wall stress (CWS_{mean}), kPa (n=698)</i>		
Crude	1.514 (0.155; 2.872)	0.029
Model 1	0.944 (-0.396; 2.285)	0.167
Model 2‡	0.097 (-1.316; 1.510)	0.893
Model 2 + MSG_{CGM}	-1.544 (-3.759; 0.671)	0.172
<i>Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=698)</i>		
Crude	1.579 (0.707; 2.452)	< 0.001
Model 1	0.996 (0.133; 1.859)	0.024
Model 2*	-0.175 (-1.006; 0.656)	0.679
Model 2 + MSG_{CGM}	-0.619 (-1.923; 0.685)	0.352

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated with 1 unit (mmol/L) increase of SD_{CGM} . Crude: SD_{CGM} . Model 1: adjusted for age, sex, and education level. Model 2: additionally adjusted for mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs. Model 2 + MSG_{CGM} : additionally adjusted for mean sensor glucose.

ESM Table 17. Multivariable-adjusted associations of daily glucose variability (expressed as SD_{CGM}) with arterial outcome variables after exclusion of individuals who underwent CGM as part of a ‘catch-up visit’

Model	B (95%CI)	P value
<i>Carotid femoral pulse wave velocity (cf-PWV), m/s (n=418)</i>		
Crude	0.724 (0.337; 1.107)	< 0.001
Model 1	0.408 (0.062; 0.754)	0.021
Model 2*	0.188 (-0.160; 0.536)	0.289
Model 2 + MSG_{CGM}	-0.200 (-0.673; 0.273)	0.406
<i>Carotid distensibility coefficient (carDC), $10^{-3}/kPa$ (n=500)</i>		
Crude	-0.728 (-1.882; 0.425)	0.215
Model 1	0.147 (-0.904; 1.198)	0.784
Model 2*	0.521 (-0.513; 1.555)	0.323
Model 2 + MSG_{CGM}	-0.355 (-1.758; 1.047)	0.619
<i>Carotid intima-media thickness (cIMT), μm (n=500)</i>		
Crude	42.209 (12.158; 72.261)	0.006
Model 1	22.183 (-5.946; 50.312)	0.122
Model 2†	27.960 (-2.331; 58.251)	0.070
Model 2 + MSG_{CGM}	4.808 (-36.285; 45.902)	0.818
<i>Ankle-brachial index (ABI) (n=577)</i>		
Crude	0.000 (-0.019; 0.019)	0.998
Model 1	-0.004 (-0.022; 0.015)	0.684
Model 2†	0.011 (-0.009; 0.031)	0.266
Model 2 + MSG_{CGM}	-0.002 (-0.028; 0.025)	0.902
<i>Mean circumferential wall stress (CWS_{mean}), kPa (n=500)</i>		
Crude	-0.767 (-2.710; 1.176)	0.438
Model 1	-0.987 (-2.909; 0.936)	0.314
Model 2‡	-1.740 (-3.697; 0.217)	0.081
Model 2 + MSG_{CGM}	-1.867 (-4.531; 0.797)	0.169
<i>Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=500)</i>		
Crude	0.434 (-0.824; 1.692)	0.498
Model 1	-0.139 (-1.382; 1.105)	0.827
Model 2*	-0.872 (-2.060; 0.315)	0.150
Model 2 + MSG_{CGM}	-0.473 (-2.088; 1.142)	0.565

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated with 1 unit (mmol/L) increase of SD_{CGM} . Crude: SD_{CGM} . Model 1: adjusted for age, sex, and education level. Model 2: additionally adjusted for mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs. Model 2 + MSG_{CGM} : additionally adjusted for mean sensor glucose.

ESM Table 18. Multivariable-adjusted associations of mean sensor glucose with arterial outcome variables

Model	B (95%CI)	P value
<i>Carotid femoral pulse wave velocity (cf-PWV), m/s (n=643)</i>		
Crude	0.437 (0.315; 0.560)	< 0.001
Model 1	0.298 (0.184; 0.412)	< 0.001
Model 2*	0.177 (0.057; 0.297)	0.004
Model 2 + SD _{CGM}	0.087 (-0.091; 0.265)	0.338
<i>Carotid distensibility coefficient (carDC), 10⁻³/kPa (n=725)</i>		
Crude	-0.423 (-0.759; -0.087)	0.014
Model 1	-0.143 (-0.456; 0.171)	0.372
Model 2*	0.412 (0.089; 0.734)	0.012
Model 2 + SD _{CGM}	0.435 (-0.062; 0.933)	0.086
<i>Carotid intima-media thickness (cIMT), μm (n=726)</i>		
Crude	14.612 (6.085; 23.139)	0.001
Model 1	7.526 (-0.670; 15.722)	0.072
Model 2†	8.847 (-0.330; 18.024)	0.059
Model 2 + SD _{CGM}	9.398 (-4.793; 23.589)	0.194
<i>Ankle-brachial index (ABI) (n=816)</i>		
Crude	-0.005 (-0.011; 0.000)	0.068
Model 1	-0.008 (-0.014; -0.002)	0.006
Model 2†	-0.002 (-0.009; 0.004)	0.507
Model 2 + SD _{CGM}	0.004 (-0.0006 0.013)	0.477
<i>Mean circumferential wall stress (CWS_{mean}), kPa (n=725)</i>		
Crude	1.096 (0.528; 1.664)	< 0.001
Model 1	0.823 (0.256; 1.390)	0.005
Model 2‡	0.317 (-0.293; 0.927)	0.308
Model 2 + SD _{CGM}	0.694 (-0.248; 1.635)	0.149
<i>Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=725)</i>		
Crude	0.905 (0.542; 1.268)	< 0.001
Model 1	0.657 (0.293; 1.020)	< 0.001
Model 2*	0.029 (-0.330; 0.388)	0.873
Model 2 + SD _{CGM}	0.230 (-0.323; 0.784)	0.414

Regression coefficients (B) indicate the mean difference (95% confidence interval) associated with 1 unit (mmol/L) increase of MSG_{CGM}. Crude: SD_{CGM}. Model 1: adjusted for age, sex, and education level. Model 2: additionally adjusted for mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, and use of antihypertensive and lipid-modifying drugs. Model 2 + SD_{CGM}: additionally adjusted for standard deviation.

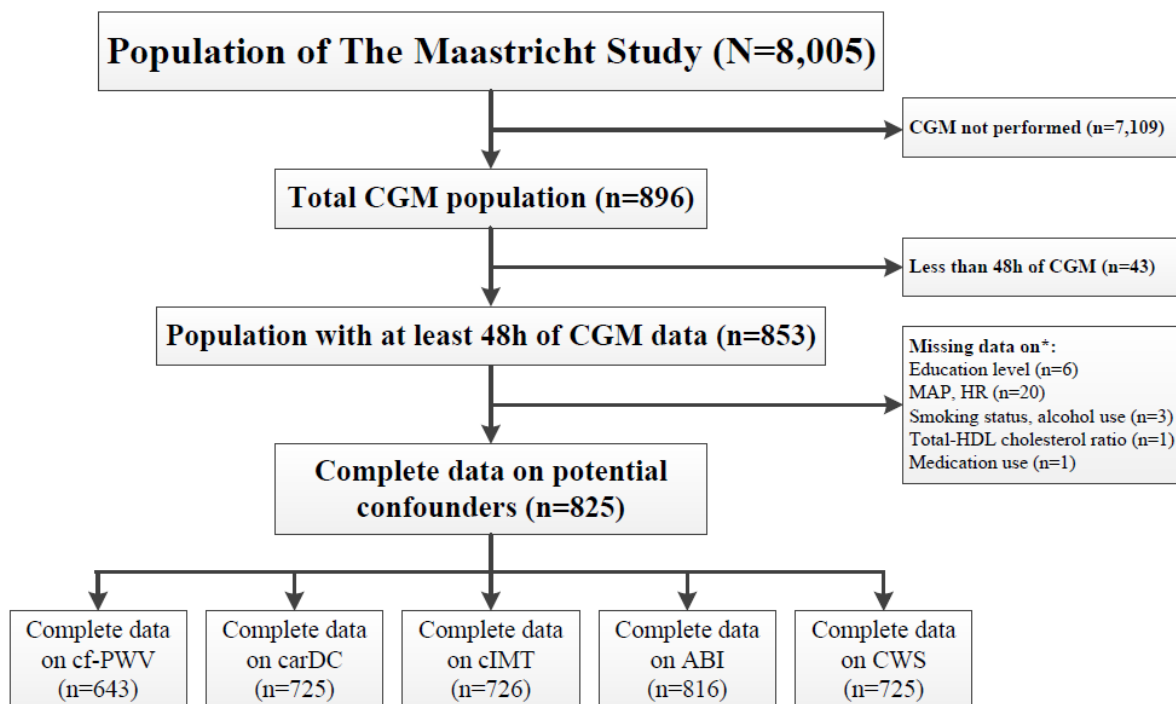
ESM Table 19. Regression coefficients of standard deviation and mean sensor glucose in the fully adjusted models with arterial outcome variables estimated with different degrees of penalization

VIF	SD (B, 95%CI)	SD _{CGM} (st.β, 95%CI)	P value	MSG _{CGM} (st.β, 95%CI)	P value
<i>Carotid femoral pulse wave velocity* (cf-PWV) (n=643)</i>					
Model 2 + MSG _{CGM} (λ=0)	0.259 (-0.127; 0.771)	0.070 (-0.037; 0.190)	0.198	0.055 (-0.086; 0.174)	0.426
Halfway (λ=0.04)	0.246 (-0.113; 0.723)	0.065 (-0.031; 0.183)	0.192	0.054 (-0.065; 0.174)	0.378
Model 2 (λ=0.11)	0.250 (-0.067; 0.663)	0.065 (-0.018; 0.167)	0.160	0.059 (-0.043; 0.164)	0.272
<i>Carotid distensibility coefficient* (carDC) (n=725)</i>					
Model 2 + MSG _{CGM} (λ=0)	-0.087 (-1.154; 1.088)	-0.008 (-0.106; 0.102)	0.864	0.095 (-0.024; 0.205)	0.110
Halfway (λ=0.04)	-0.069 (-1.179; 1.055)	-0.006 (-0.106; 0.095)	0.904	0.089 (-0.017; 0.201)	0.086
Model 2 (λ=0.12)	-0.035 (-1.065; 1.023)	-0.003 (-0.097; 0.092)	0.952	0.088 (-0.014; 0.184)	0.102
<i>Carotid intima-media thickness† (cIMT) (n=726)</i>					
Model 2 + MSG _{CGM} (λ=0)	-0.871 (-35.641; 31.033)	-0.003 (-0.128; 0.109)	0.954	0.080 (-0.038; 0.201)	0.196
Halfway (λ=0.04)	-0.215 (-34.456; 32.768)	-0.001 (-0.128; 0.120)	0.986	0.075 (-0.045; 0.204)	0.206
Model 2 (λ=0.12)	-1.872 (-32.526; 30.975)	-0.007 (-0.123; 0.111)	0.916	0.078 (-0.038; 0.207)	0.198
<i>Ankle-brachial index† (ABI) (n=816)</i>					
Model 2 + MSG _{CGM} (λ=0)	-0.017 (-0.047; 0.007)	-0.086 (-0.232; 0.038)	0.184	0.042 (-0.057; 0.147)	0.438
Halfway (λ=0.04)	-0.009 (-0.021; 0.001)	-0.045 (-0.105; 0.007)	0.104	0.003 (-0.040; 0.042)	0.898
Model 2 (λ=0.11)	-0.006 (-0.014; 0.000)	-0.033 (-0.071; 0.002)	0.060	-0.008 (-0.032; 0.017)	0.548
<i>Mean circumferential wall stress‡ (CWS_{mean}) (n=725)</i>					
Model 2 + MSG _{CGM} (λ=0)	-1.138 (-3.408; 1.304)	-0.061 (-0.181; 0.073)	0.344	0.085 (-0.045; 0.220)	0.186
Halfway (λ=0.04)	-1.131 (-3.278; 1.165)	-0.060 (-0.172; 0.063)	0.312	0.090 (-0.039; 0.202)	0.160
Model 2 (λ=0.12)	-1.077 (-3.067; 1.218)	-0.059 (-0.169; 0.066)	0.318	0.082 (-0.044; 0.204)	0.180
<i>Pulsatile circumferential wall stress* (CWS_{puls}) (n=725)</i>					
Model 2 + MSG _{CGM} (λ=0)	-0.673 (-1.785; 0.707)	-0.057 (-0.150; 0.058)	0.354	0.049 (-0.065; 0.144)	0.420
Halfway (λ=0.04)	-0.594 (-1.790; 0.788)	-0.049 (-0.148; 0.066)	0.350	0.045 (-0.065; 0.146)	0.434
Model 2 (λ=0.12)	-0.532 (-1.702; 0.643)	-0.045 (-0.145; 0.053)	0.374	0.042 (-0.055; 0.138)	0.410

Regression coefficients (B) indicate the median difference (95% confidence interval) associated with 1 unit (mmol/L) increase of SD_{CGM}. Standardized regression coefficients (st.β) indicate the median difference (95% confidence interval) associated with 1 SD higher SD_{CGM} or MSG_{CGM}. All coefficients were estimated by use of ridge regression. We pragmatically chose the level of penalization based on the λ required to reduce the variance inflation factor (VIF) of Model 2 + MSG_{CGM} back to the VIF of Model 2 (or halfway back). Point estimates and 95% confidence intervals were calculated by use of 1,000 bootstrap estimates.

The associations were adjusted for age, sex, educational level, mean arterial pressure (*), office systolic blood pressure (†) or brachial pulse pressure (‡), heart rate (in case of cf-PWV and ABI only), body mass index, smoking status, alcohol use, total-to-HDL cholesterol levels, use of antihypertensive and lipid-modifying drugs, and the other CGM-assessed index.

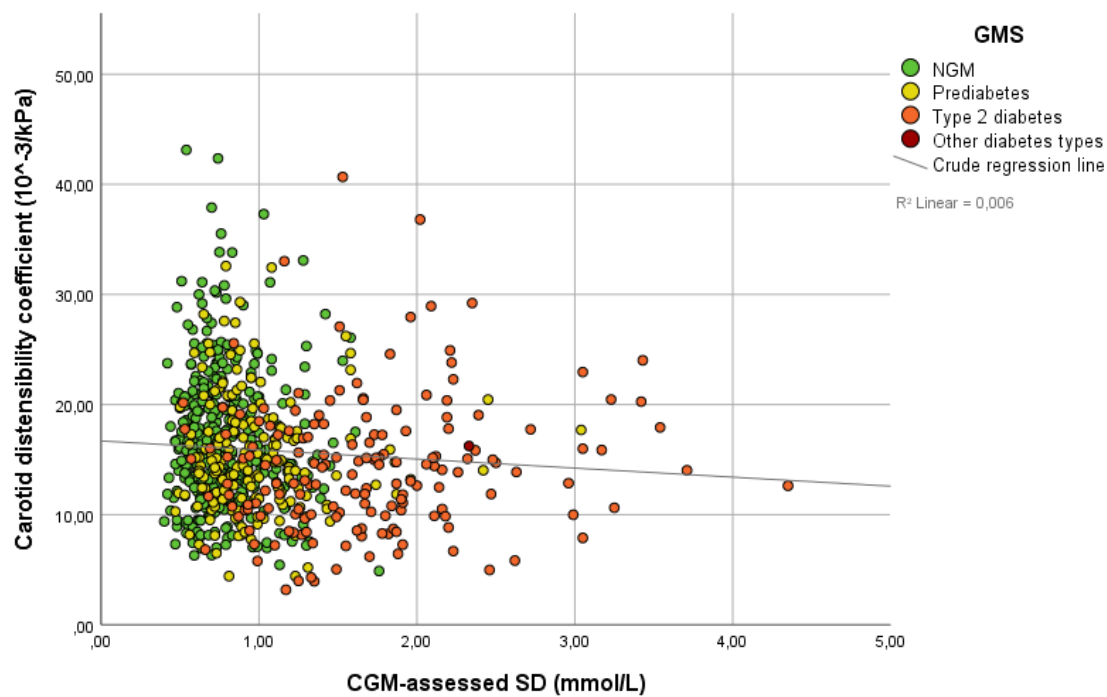
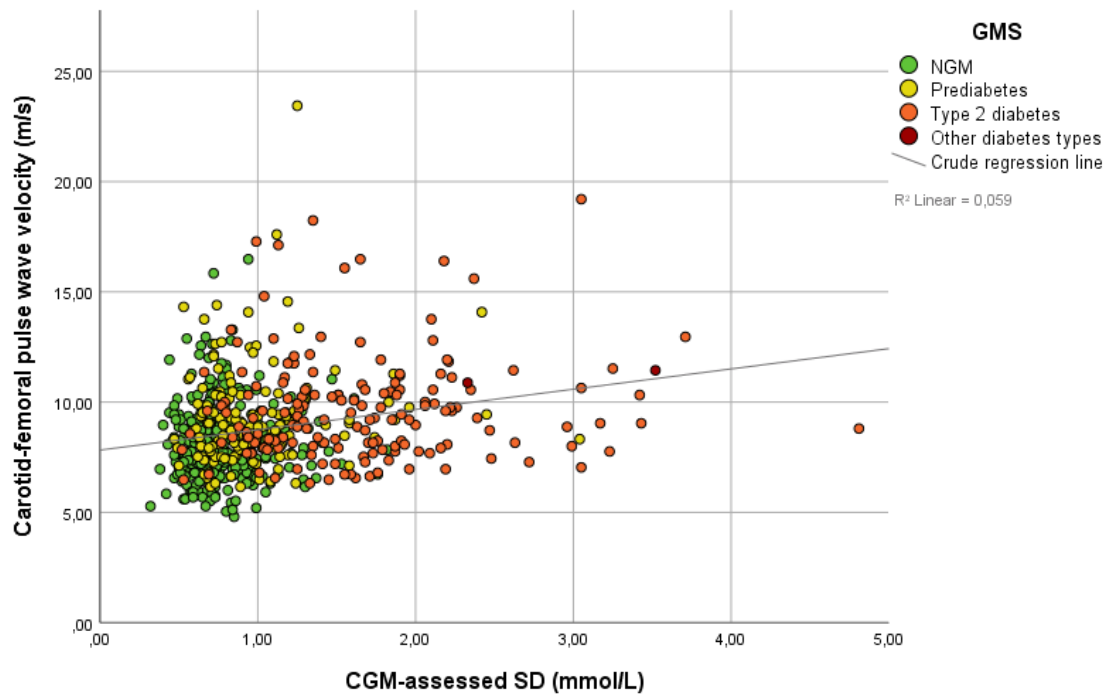
ESM Figure 1. Flowchart delineating the derivation of the study populations



CGM, continuous glucose monitoring; MAP, mean arterial pressure; HR, heart rate; HDL, high-density lipoprotein; cf-PWV, carotid-femoral pulse wave velocity; carDC, carotid distensibility coefficient; cIMT, carotid intima-media thickness; ABI, ankle-brachial index; CWS, circumferential wall stress.

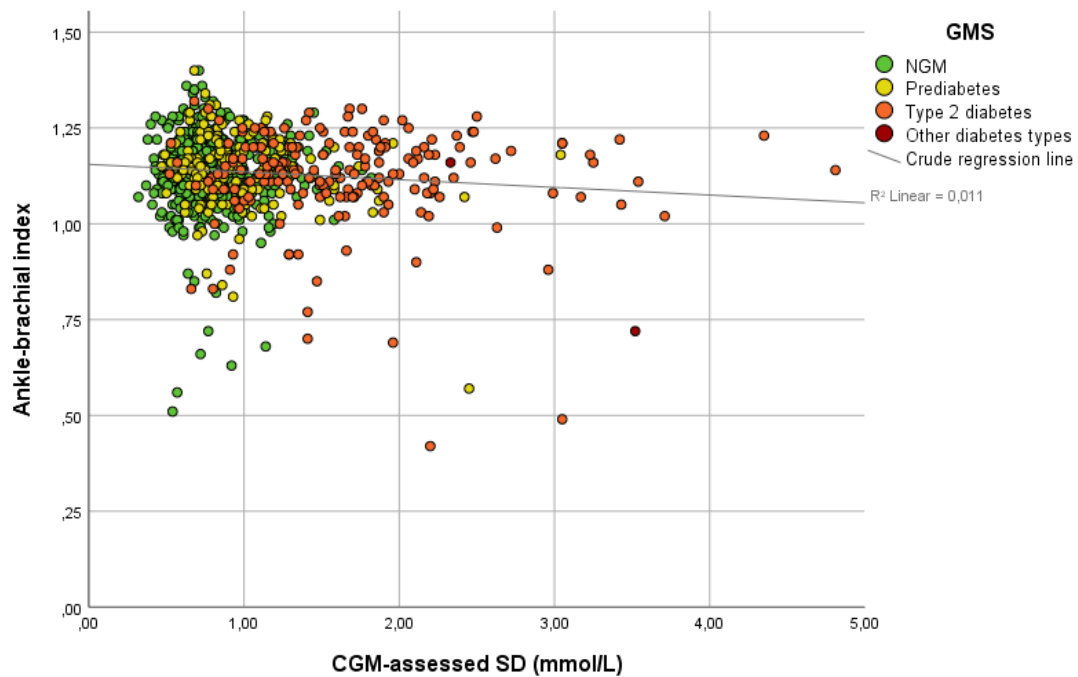
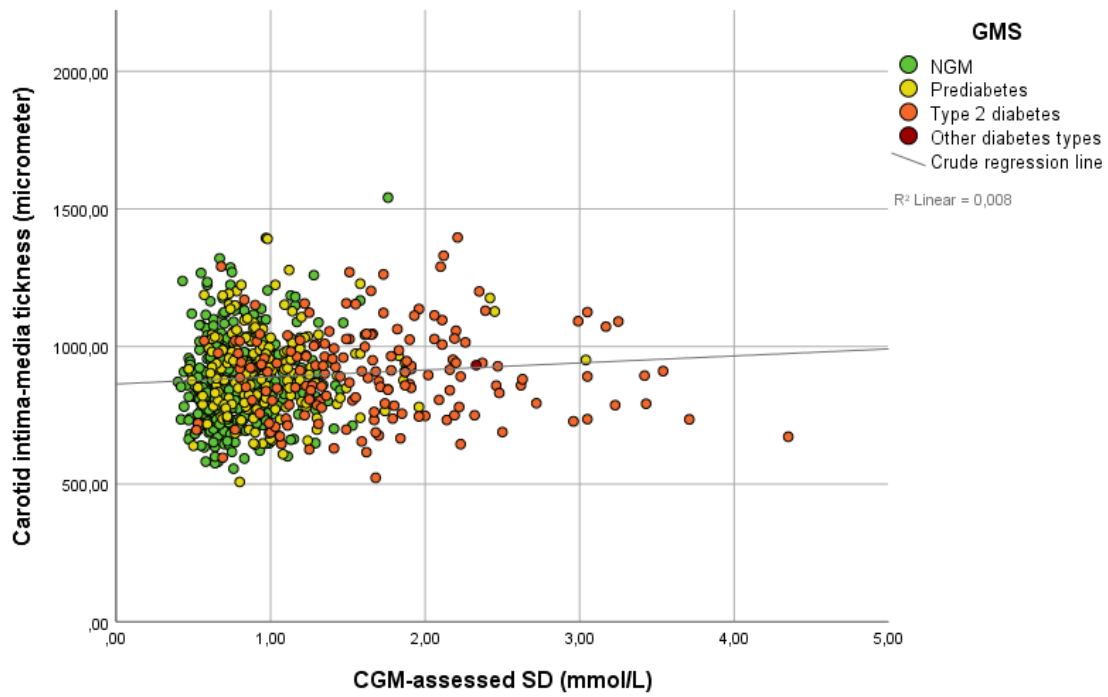
* Not mutually exclusive.

ESM Figure 2. GMS-highlighted scatter plots of the associations of CGM-assessed SD (SD_{CGM}) with carotid-femoral pulse wave velocity and carotid distensibility coefficient



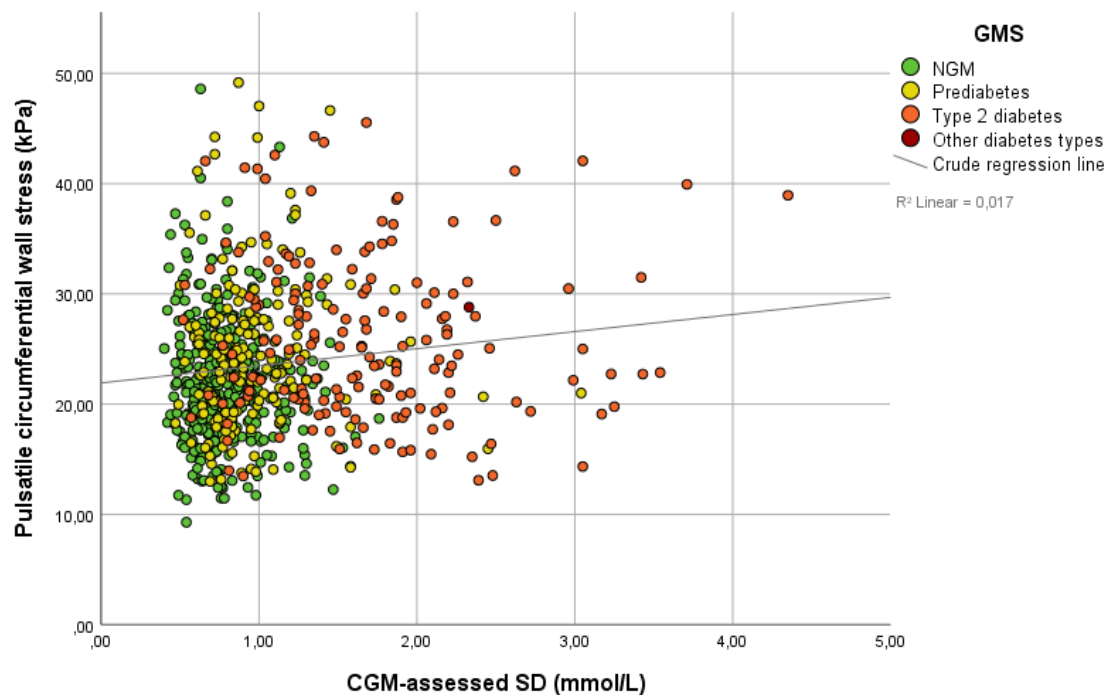
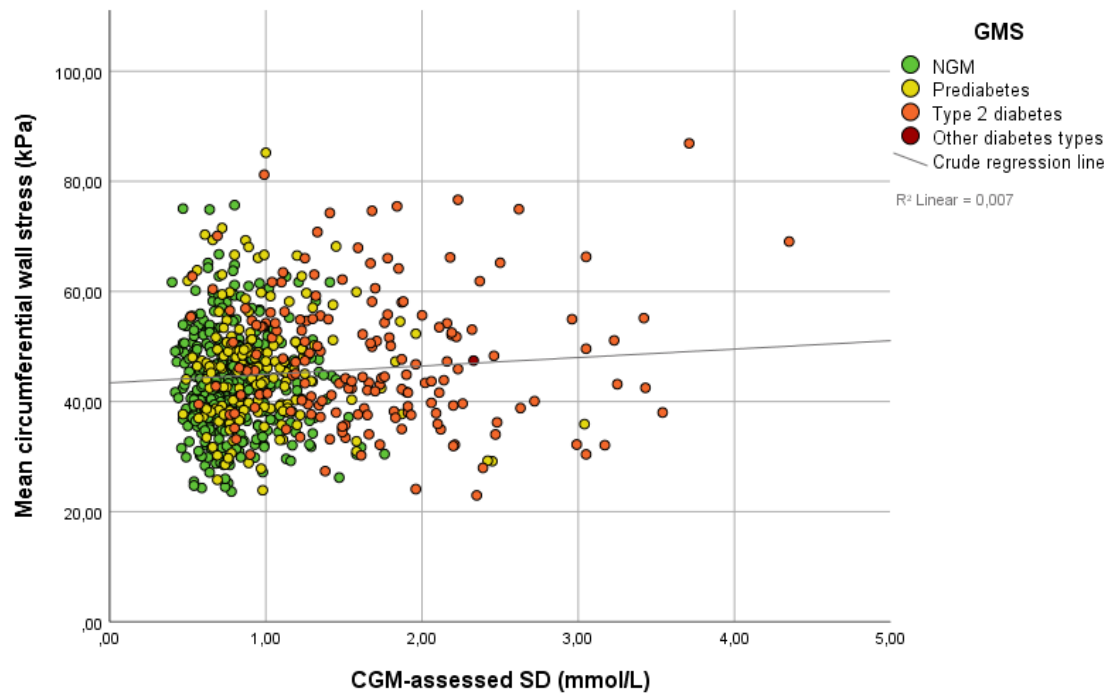
CGM, continuous glucose monitoring; SD, standard deviation; GMS, glucose metabolism status; NGM, normal glucose metabolism.

ESM Figure 3. GMS-highlighted scatter plots of the associations of CGM-assessed SD (SD_{CGM}) with carotid intima-media thickness and ankle-brachial index



CGM, continuous glucose monitoring; SD, standard deviation; GMS, glucose metabolism status; NGM, normal glucose metabolism.

ESM Figure 4. GMS-highlighted scatter plots of the associations of CGM-assessed SD (SD_{CGM}) with mean and pulsatile circumferential wall stress



CGM, continuous glucose monitoring; SD, standard deviation; GMS, glucose metabolism status; NGM, normal glucose metabolism.