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: $\text{Ridge} = \text{RSS} + \frac{1}{n} \times \lambda \times \sum_{j=1}^{p} \beta_j^2$, where RSS is the residual sum of squares, $n$ is the sample size, $\lambda$ 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 | cfMT (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                              | 0            | 30.6/28.6/40.7 | 0            | 31.2/29.1/39.7   | 0            | 31.1/29.1/39| 0            | 31.4/27.8/40.8 | 0            |
| **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                           | 0            | 51.8/23.0/24.9/0.3 | 0       | 53.0/23.3/23.6/0.1 | 0            | 52.9/23.3/23.7/0.1 | 0       | 55.6/21.4/22.7/0.2 | 0            |
| Newly diagnosed T2D, n                            | 68 (8.2)                                     | 0            | 57 (8.9)       | 114          | 59 (8.1)         | 0            | 59 (8.1)     | 0            | 68 (8.3)    | 0            |
| Fasting plasma glucose, mmol/L                    | 5.4 ± 5.0                                    | 0            | 5.5 ± 5.0      | 0            | 5.5 ± 5.0        | 0            | 5.5 ± 5.0    | 0            | 5.4 ± 5.0   | 0            |
| 2-hour post-load glucose, mmol/L                  | 6.5 ± 5.2                                    | 39           | 7.1 ± 5.3      | 33           | 6.8 ± 5.3        | 39           | 6.9 ± 5.3    | 39           | 6.6 ± 5.9    | 39           |
| MSGC0M, mmol/L                                   | 6.6 (5.7-6.7)                                |              |                |              |                   |              |              |              |             |              |
| SDGCOm, mmol/L                                   | 0.84 [0.68-1.19]                             |              |                |              |                   |              |              |              |             |              |
| CVGCM, %                                         | 14.0 ± 11.6                                  |              |                |              |                   |              |              |              |             |              |
| T1GCM, %                                         | 99.8 ± 100.0                                 |              |                |              |                   |              |              |              |             |              |
| HbA1c, %                                         | 5.5 [5.3-5.9]                                |              |                |              |                   |              |              |              |             |              |
| HbA1c, mmol/mol                                   | 37.0 ± 3.8                                   |              |                |              |                   |              |              |              |             |              |
| Diabetes medication use, n                        | 106 (12.8)                                   | 0            | 90 (14.0)      | 0            | 98 (13.5)        | 0            | 99 (13.6)    | 0            | 102 (12.5)  | 0            |
| Insulin                                          | 21 (2.5)                                     |              |                |              |                   |              |              |              |             |              |
| Metformin                                        | 100 (12.1)                                   |              |                |              |                   |              |              |              |             |              |
| Sulfonylureas                                     | 21 (2.5)                                     |              |                |              |                   |              |              |              |             |              |
| GLP-1 analogs                                    | 4 (0.5)                                      |              |                |              |                   |              |              |              |             |              |
| DPP-4 inhibitors                                 | 1 (0.1)                                      |              |                |              |                   |              |              |              |             |              |
| SGLT-2 inhibitors                                | 1 (0.1)                                      |              |                |              |                   |              |              |              |             |              |
| **Lifestyle factors**                             |                                               |              |                |              |                   |              |              |              |             |              |
| BMI, kg/m²                                        | 27.2 ± 4.4                                   |              |                |              |                   |              |              |              |             |              |
| Waist circumference (men), cm                    | 102.4 ± 11.8                                 |              |                |              |                   |              |              |              |             |              |
| Waist circumference (women), cm                  | 90.7 ± 12.2                                  |              |                |              |                   |              |              |              |             |              |
| 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 ± 6.2                                   |              |                |              |                   |              |              |              |             |              |
| 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                               | 0            | 39.5/48.2/12.3 | 0            | 38.3/49.1/12.6   | 0            | 38.4/49.0/12.5| 0            | 38.8/48.7/12.5 | 0            |
| **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                          | 132.3 ± 18.0                                 |              |                |              |                   |              |              |              |             |              |
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, MSGCGM, mean sensor glucose, SDCGM, standard deviation; CVCGM, coefficient of variation; TIRCGM, 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; CWSmean, mean circumferential wall stress; CWSpuls, pulsatile circumferential wall stress.

| Outcome measures | cf-PWV, m/s | carDC, 10^-3/kPa | cIMT, µm | ABI | ABI < 0.9, n | CWSmean, kPa | CWSpuls, kPa |
|------------------|-------------|------------------|---------|-----|--------------|-------------|-------------|
| Office diastolic BP, mmHg | 75.1 ± 10.2 | 0.15 ± 0.6 | 890.5 ± 152.8 | 1.14 ± 0.11 | 24.0 | 44.0 [37.9-50.6] | 22.5 [19.1-27.0] |
| Mean arterial pressure, mmHg | 97.0 ± 10.8 | 0.15 ± 0.6 | 890.5 ± 152.8 | 1.14 ± 0.11 | 24.0 | 44.0 [37.9-50.6] | 22.5 [19.1-27.0] |
| Mean heart rate, beats/minute | 61.0 ± 8.7 | 0.15 ± 0.6 | 890.5 ± 152.8 | 1.14 ± 0.11 | 24.0 | 44.0 [37.9-50.6] | 22.5 [19.1-27.0] |
| Antihypertensive medication use, n | 290 (35.2) | 0.15 ± 0.6 | 890.5 ± 152.8 | 1.14 ± 0.11 | 24.0 | 44.0 [37.9-50.6] | 22.5 [19.1-27.0] |
| Total-to-HDL cholesterol ratio | 3.5 [2.8-4.3] | 0.15 ± 0.6 | 890.5 ± 152.8 | 1.14 ± 0.11 | 24.0 | 44.0 [37.9-50.6] | 22.5 [19.1-27.0] |
| Triglycerides, mmol/L | 1.3 [0.9-1.8] | 0.15 ± 0.6 | 890.5 ± 152.8 | 1.14 ± 0.11 | 24.0 | 44.0 [37.9-50.6] | 22.5 [19.1-27.0] |
| Lipid-modifying medication use, n | 205 (24.8) | 0.15 ± 0.6 | 890.5 ± 152.8 | 1.14 ± 0.11 | 24.0 | 44.0 [37.9-50.6] | 22.5 [19.1-27.0] |
| Albuminuria, n | 63 (7.9) | 0.15 ± 0.6 | 890.5 ± 152.8 | 1.14 ± 0.11 | 24.0 | 44.0 [37.9-50.6] | 22.5 [19.1-27.0] |
# 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<sub>CGM</sub>, mmol/L | Median [IQR] | 5.8 [5.5 – 6.1] | 6.2 [5.8 – 6.6] | 7.5 [6.8 – 8.7] |
| 5<sup>th</sup> – 95<sup>th</sup> percentile | 5.15 - 6.54 | 5.25 - 7.60 | 5.73 – 11.85 |
| SD<sub>CGM</sub>, mmol/L | Median [IQR] | 0.72 [0.61 – 0.87] | 0.89 [0.73 – 1.12] | 1.55 [1.16 – 1.98] |
| 5<sup>th</sup> – 95<sup>th</sup> percentile | 0.48 - 1.28 | 0.60 - 1.61 | 0.79 - 3.13 |
| CV<sub>CGM</sub>, % | Median [IQR] | 12.6 [10.7 – 14.9] | 14.7 [12.2 – 17.5] | 19.3 [16.1 – 24.1] |
| 5<sup>th</sup> – 95<sup>th</sup> percentile | 8.51 - 20.57 | 10.13 – 24.08 | 12.42 – 33.36 |
| TIR<sub>CGM</sub>, % | Median [IQR] | 100.0 [99.5 – 100.0] | 99.8 [98.5 – 100.0] | 91.8 [79.1 – 98.3] |
| 5<sup>th</sup> – 95<sup>th</sup> 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<sub>CGM</sub>, mean sensor glucose; SD<sub>CGM</sub>, standard deviation; CV<sub>CGM</sub>, coefficient of variation; TIR<sub>CGM</sub>, 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\(_{\text{CGM}}\)) with arterial outcome variables

| Model      | B (95% CI)                  | P value | VIF  |
|------------|-----------------------------|---------|------|
| **Carotid femoral pulse wave velocity (cf-PWV), m/s (n=643)** |                |         |      |
| 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\(_{\text{CGM}}\) | 0.270 (-0.125; 0.666) | 0.180   | 2.918|
| **Carotid distensibility coefficient (carDC), 10^-3/kPa (n=725)** |                |         |      |
| 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\(_{\text{CGM}}\) | -0.071 (-1.204; 1.063) | 0.903   | 3.070|
| **Carotid intima-media thickness (cIMT), µm (n=726)** |                |         |      |
| 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\(_{\text{CGM}}\) | -1.648 (-33.984; 30.688) | 0.920   | 3.071|
| **Ankle-brachial index (ABI) (n=816)** |                |         |      |
| 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\(_{\text{CGM}}\) | -0.017 (-0.039; 0.005) | 0.121   | 3.001|
| **Mean circumferential wall stress (CWS\(_{\text{mean}}\)), kPa (n=725)** |                |         |      |
| 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\(_{\text{CGM}}\) | -1.126 (-3.271; 1.019) | 0.303   | 3.070|
| **Pulsatile circumferential wall stress (CWS\(_{\text{puls}}\)), kPa (n=725)** |                |         |      |
| 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\(_{\text{CGM}}\) | -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\(_{\text{CGM}}\). Crude: SD\(_{\text{CGM}}\). 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\(_{\text{CGM}}\): 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 |
|----------------|---------------------|-------------|
| **Carotid femoral pulse wave velocity (cf-PWV), m/s (n=643)** |                     |             |
| 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       |
| **Carotid distensibility coefficient (carDC), 10^{-3}/kPa (n=725)** |                     |             |
| 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       |
| **Carotid intima-media thickness (cIMT), μm (n=726)** |                     |             |
| 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       |
| **Ankle-brachial index (ABI) (n=816)** |                     |             |
| 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       |
| **Mean circumferential wall stress (CWS_{mean}), kPa (n=725)** |                     |             |
| 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       |
| **Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=725)** |                     |             |
| 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\textsubscript{CGM}) with arterial outcome variables

| Model     | B (95\%CI)          | P value |
|-----------|---------------------|---------|
|           | Carotid femoral pulse wave velocity (cf-PWV), m/s (n=643) |         |
| 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   |
|           | Carotid distensibility coefficient (carDC), 10\(^{-3}\)kPa (n=725) |         |
| 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   |
|           | Carotid intima-media thickness (cIMT), µm (n=726) |         |
| 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   |
|           | Ankle-brachial index (ABI) (n=816) |         |
| 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   |
|           | Mean circumferential wall stress (CWS\textsubscript{mean}), kPa (n=725) |         |
| 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   |
|           | Pulsatile circumferential wall stress (CWS\textsubscript{puls}), kPa (n=725) |         |
| 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\textsubscript{CGM}. Crude: TIR\textsubscript{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% (TIRCGM≥70%) with arterial outcome variables

| Model | B (95% CI) | P value |
|-------|------------|---------|
| **Carotid femoral pulse wave velocity (cf-PWV), m/s (n=643)** | | |
| 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 |
| **Carotid distensibility coefficient (carDC), 10^-3 kPa (n=725)** | | |
| 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 |
| **Carotid intima-media thickness (cIMT), µm (n=726)** | | |
| 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 |
| **Ankle-brachial index (ABI) (n=816)** | | |
| 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 |
| **Mean circumferential wall stress (CWS\_mean), kPa (n=725)** | | |
| 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 |
| **Pulsatile circumferential wall stress (CWS\_puls), kPa (n=725)** | | |
| 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 TIRCGM. Crude: TIRCGM≥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 | Type 2 diabetes status |
|------------------|-----|-----|-----------------|------------------------|
| 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 |
|------------------|-----------|---------|-----------|---------|
|                  | cIMT, men (n=375) |         | cIMT, women (n=351) |         |
| 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 |
|-------|------------|------------|------------|------------|
| cf-PWV, m/s | | | | |
| 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<sub>CGM</sub> | 0.249 (-0.373; 0.872) | 0.432 | 0.367 (-0.247; 0.982) | 0.239 |
| carDC, 10⁻³/kPa | | | | |
| 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<sub>CGM</sub> | 0.965 (-0.779; 2.708) | 0.278 | -0.575 (-2.254; 1.103) | 0.499 |
| cIMT, µm | | | | |
| 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<sub>CGM</sub> | 18.148 (-31.489; 67.784) | 0.473 | -7.393 (-56.083; 41.297) | 0.765 |
| ABI | | | | |
| 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<sub>CGM</sub> | -0.013 (-0.045; 0.019) | 0.425 | -0.017 (-0.055; 0.020) | 0.363 |
| CWS<sub>mean</sub>, kPa | | | | |
| 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<sub>CGM</sub> | -0.955 (-4.083; 2.172) | 0.549 | -1.763 (-5.421; 1.895) | 0.343 |
| CWS<sub>pulse</sub>, kPa | | | | |
| 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<sub>CGM</sub> | -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<sub>CGM</sub>: additionally adjusted for mean sensor glucose.
ESM Table 10. Multivariable-adjusted associations of daily glucose variability (expressed as SD<sub>CGM</sub>) with arterial outcome variables after adjustment for glucose metabolism status, HbA<sub>1c</sub>, or fasting plasma glucose instead of mean sensor glucose

| Model                  | B (95% CI)       | P value |
|------------------------|------------------|---------|
| **Carotid femoral pulse wave velocity** (cf-PWV), m/s (n=643) |                  |         |
| Model 2 + GMS          | 0.260 (-0.058; 0.579) | 0.109   |
| Model 2 + HbA<sub>1c</sub> | 0.244 (-0.081; 0.569) | 0.140   |
| Model 2 + FPG          | 0.294 (-0.014; 0.603) | 0.061   |
| **Carotid distensibility coefficient** (carDC), 10<sup>-3</sup>/kPa (n=725) |                  |         |
| Model 2 + GMS          | 0.827 (-0.062; 1.716) | 0.068   |
| Model 2 + HbA<sub>1c</sub> | 0.792 (-0.116; 1.700) | 0.087   |
| Model 2 + FPG          | 0.687 (-0.157; 1.531) | 0.111   |
| **Carotid intima-media thickness** (cIMT), µm (n=726) |                  |         |
| Model 2 + GMS          | 22.231 (-3.061; 47.524) | 0.085   |
| Model 2 + HbA<sub>1c</sub> | 2.242 (-23.487; 27.972) | 0.864   |
| Model 2 + FPG          | 9.738 (-14.259; 33.735) | 0.426   |
| **Ankle-brachial index** (ABI) (n=816) |                  |         |
| Model 2 + GMS          | -0.009 (-0.026; 0.008) | 0.307   |
| Model 2 + HbA<sub>1c</sub> | -0.013 (-0.031; 0.004) | 0.141   |
| Model 2 + FPG          | -0.009 (-0.025; 0.008) | 0.290   |
| **Mean circumferential wall stress** (CWS<sub>mean</sub>), kPa (n=725) |                  |         |
| Model 2 + GMS          | -0.670 (-2.349; 1.010) | 0.434   |
| Model 2 + HbA<sub>1c</sub> | 0.408 (-1.307; 2.123) | 0.641   |
| Model 2 + FPG          | 0.275 (-1.321; 1.871) | 0.735   |
| **Pulsatile circumferential wall stress** (CWS<sub>puls</sub>), kPa (n=725) |                  |         |
| Model 2 + GMS          | -0.868 (-1.853; 0.117) | 0.084   |
| Model 2 + HbA<sub>1c</sub> | -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<sub>CGM</sub>. Model 2 + represents the fully adjusted model that was additionally adjusted for glucose metabolism status (GMS), HbA<sub>1c</sub>, or fasting plasma glucose (FPG).
ESM Table 11. Multivariable-adjusted associations of $SD_{\text{CGM}}$ with arterial outcome variables, additionally adjusted for physical activity and Dutch healthy diet adherence

| Model                     | B (95% CI)       | $P$ value |
|---------------------------|------------------|-----------|
| **Carotid femoral pulse wave velocity (cf-PWV), m/s (n=487)** |                  |           |
| 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$_{\text{CGM}}$ | 0.461 (-0.014; 0.935) | 0.057    |
| **Carotid distensibility coefficient (carDC), 10$^{-3}$/kPa (n=519)** |                  |           |
| 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$_{\text{CGM}}$ | 0.866 (-0.461; 2.194) | 0.200    |
| **Carotid intima-media thickness (cIMT), µm (n=520)** |                  |           |
| 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$_{\text{CGM}}$ | -10.304 (-49.368; 28.760) | 0.605    |
| **Ankle-brachial index (ABI) (n=562)** |                  |           |
| 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$_{\text{CGM}}$ | -0.021 (-0.047; 0.005) | 0.114    |
| **Mean circumferential wall stress (CWS$_{\text{mean}}$), kPa (n=519)** |                  |           |
| 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$_{\text{CGM}}$ | -0.040 (-2.688; 2.607) | 0.976    |
| **Pulsatile circumferential wall stress (CWS$_{\text{puls}}$), kPa (n=519)** |                  |           |
| 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$_{\text{CGM}}$ | -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 $SD_{\text{CGM}}$. Crude: $SD_{\text{CGM}}$. 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$_{\text{CGM}}$: 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<sub>CGM</sub> 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 |
|-------|-----------|---------|
| Carotid femoral pulse wave velocity (cf-PWV), m/s (n=638) | | |
| 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<sub>CGM</sub> | 0.225 (-0.169; 0.618) | 0.263 |
| Carotid distensibility coefficient (carDC), 10<sup>-3</sup>/kPa (n=720) | | |
| 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<sub>CGM</sub> | -0.015 (-1.167; 1.138) | 0.980 |
| Carotid intima-media thickness (cIMT), µm (n=721) | | |
| 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<sub>CGM</sub> | 1.648 (-31.181; 34.477) | 0.922 |
| Ankle-brachial index (ABI) (n=811) | | |
| 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<sub>CGM</sub> | -0.012 (-0.034; 0.009) | 0.258 |
| Mean circumferential wall stress (CWS<sub>mean</sub>), kPa (n=720) | | |
| 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<sub>CGM</sub> | -1.300 (-3.472; 0.872) | 0.240 |
| Pulsatile circumferential wall stress (CWS<sub>puls</sub>), kPa (n=720) | | |
| 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<sub>CGM</sub> | -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<sub>CGM</sub>. Crude: SD<sub>CGM</sub>. 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<sub>CGM</sub>: 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 |
|------------------------|-------------------|-----------|
| Carotid intima-media thickness (cIMT), $\mu m$ (n=649) |                  |           |
| 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     |
| Ankle-brachial index (ABI) (n=728) |                  |           |
| 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 |
|-------|-----------|---------|
| **Carotid femoral pulse wave velocity (cf-PWV), m/s (n=641)** | | |
| 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 |

| **Carotid distensibility coefficient (carDC), 10^{-3}/kPa (n=724)** | | |
| 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 |

| **Carotid intima-media thickness (cIMT), µm (n=725)** | | |
| 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 |

| **Ankle-brachial index (ABI) (n=814)** | | |
| 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 |

| **Mean circumferential wall stress (CWS_{mean}), kPa (n=724)** | | |
| 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 |

| **Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=724)** | | |
| 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\textsubscript{CGM}) with arterial outcome variables after exclusion of individuals with CGM data gaps**

| Model | B (95% CI) | P value |
|-------|------------|---------|
| Carotid femoral pulse wave velocity (cf-PWV), m/s (n=591) | | |
| 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\textsubscript{CGM} | 0.368 (-0.095; 0.831) | 0.119 |
| Carotid distensibility coefficient (carDC), 10^-3/kPa (n=672) | | |
| 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\textsubscript{CGM} | 0.139 (-1.102; 1.380) | 0.826 |
| Carotid intima-media thickness (cIMT), μm (n=673) | | |
| 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\textsubscript{CGM} | -2.126 (-37.762; 33.510) | 0.907 |
| Ankle-brachial index (ABI) (n=749) | | |
| 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\textsubscript{CGM} | -0.026 (-0.051; 0.000) | 0.047 |
| Mean circumferential wall stress (CWS\textsubscript{mean}), kPa (n=672) | | |
| 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\textsubscript{CGM} | -1.027 (-3.396; 1.341) | 0.395 |
| Pulsatile circumferential wall stress (CWS\textsubscript{puls}), kPa (n=672) | | |
| 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\textsubscript{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\textsubscript{CGM}. Crude: SD\textsubscript{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\textsubscript{CGM}: additionally adjusted for mean sensor glucose.
ESM Table 16. Multivariable-adjusted associations of daily glucose variability (expressed as SD<sub>CGM</sub>) with arterial outcome variables after exclusion of individuals with a suboptimal CGM recording period

| Outcome Variable                                      | B (95%CI)                   | P value |
|-------------------------------------------------------|-----------------------------|---------|
| **Carotid femoral pulse wave velocity (cf-PWV), m/s (n=620)** |                             |         |
| 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<sub>CGM</sub>                           | 0.299 (-0.109; 0.706)       | 0.151   |
| **Carotid distensibility coefficient (carDC), 10⁻³kPa (n=698)** |                             |         |
| 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<sub>CGM</sub>                           | 0.066 (-1.116; 1.248)       | 0.913   |
| **Carotid intima-media thickness (cIMT), µm (n=699)**  |                             |         |
| 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<sub>CGM</sub>                           | 4.126 (-29.577; 37.829)     | 0.810   |
| **Ankle-brachial index (ABI) (n=785)**                 |                             |         |
| 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<sub>CGM</sub>                           | -0.019 (-0.041; 0.004)      | 0.109   |
| **Mean circumferential wall stress (CWS<sub>mean</sub>, kPa (n=698)** |                             |         |
| 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<sub>CGM</sub>                           | -1.544 (-3.759; 0.671)      | 0.172   |
| **Pulsatile circumferential wall stress (CWS<sub>puls</sub>, kPa (n=698)** |                             |         |
| Crude                                                 | 1.579 (0.707; 2.452)        | < 0.001 |
| Model 1                                                | 0.996 (0.133; 1.859)        | 0.024   |
| Model 2*                                               | -0.175 (-1.066; 0.656)      | 0.679   |
| Model 2 + MSG<sub>CGM</sub>                           | -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<sub>CGM</sub>. Crude: SD<sub>CGM</sub>. 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<sub>CGM</sub>: 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 |
|------------------------|-----------------------|---------|
| Carotid femoral pulse wave velocity (cf-PWV), m/s (n=418) | | |
| 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   |
| Carotid distensibility coefficient (carDC), 10^{-3}/kPa (n=500) | | |
| 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   |
| Carotid intima-media thickness (cIMT), µm (n=500) | | |
| 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   |
| Ankle-brachial index (ABI) (n=577) | | |
| 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   |
| Mean circumferential wall stress (CWS_{mean}), kPa (n=500) | | |
| 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   |
| Pulsatile circumferential wall stress (CWS_{puls}), kPa (n=500) | | |
| 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 |
|----------------------------|------------------|---------|
| **Carotid femoral pulse wave velocity (cf-PWV), m/s (n=643)** |                  |         |
| 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<sub>CGM</sub> | 0.087 (-0.091; 0.265) | 0.338   |
| **Carotid distensibility coefficient (carDC), 10<sup>-3</sup>/kPa (n=725)** |                  |         |
| 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<sub>CGM</sub> | 0.435 (-0.062; 0.933) | 0.086   |
| **Carotid intima-media thickness (cIMT), µm (n=726)** |                  |         |
| 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<sub>CGM</sub> | 9.398 (-4.793; 23.589) | 0.194   |
| **Ankle-brachial index (ABI) (n=816)** |                  |         |
| 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<sub>CGM</sub> | 0.004 (-0.0006 0.013) | 0.477   |
| **Mean circumferential wall stress (CWS<sub>mean</sub>), kPa (n=725)** |                  |         |
| 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<sub>CGM</sub> | 0.694 (-0.248; 1.635)  | 0.149   |
| **Pulsatile circumferential wall stress (CWS<sub>puls</sub>), kPa (n=725)** |                  |         |
| 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<sub>CGM</sub> | 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<sub>CGM</sub>. Crude: SD<sub>CGM</sub>. 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<sub>CGM</sub>: additionally adjusted for standard deviation.
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 |
|----------------|---------------|-------------------------|---------|-------------------------|---------|
| 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   |

Carotid femoral pulse wave velocity* (cf-PWV) (n=643)

| VIF            | SD (B, 95%CI) | SD_{CGM} (st.β, 95%CI) | P value | MSG_{CGM} (st.β, 95%CI) | P value |
|----------------|---------------|-------------------------|---------|-------------------------|---------|
| 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   |

Carotid distensibility coefficient* (carDC) (n=725)

| VIF            | SD (B, 95%CI) | SD_{CGM} (st.β, 95%CI) | P value | MSG_{CGM} (st.β, 95%CI) | P value |
|----------------|---------------|-------------------------|---------|-------------------------|---------|
| 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   |

Carotid intima-media thickness† (cIMT) (n=726)

| VIF            | SD (B, 95%CI) | SD_{CGM} (st.β, 95%CI) | P value | MSG_{CGM} (st.β, 95%CI) | P value |
|----------------|---------------|-------------------------|---------|-------------------------|---------|
| 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   |

Mean circumferential wall stress‡ (CWS_{mean}) (n=725)

| VIF            | SD (B, 95%CI) | SD_{CGM} (st.β, 95%CI) | P value | MSG_{CGM} (st.β, 95%CI) | P value |
|----------------|---------------|-------------------------|---------|-------------------------|---------|
| 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   |

Pulsatile circumferential wall stress* (CWS_{puls}) (n=725)

| VIF            | SD (B, 95%CI) | SD_{CGM} (st.β, 95%CI) | P value | MSG_{CGM} (st.β, 95%CI) | P value |
|----------------|---------------|-------------------------|---------|-------------------------|---------|
| 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.