## ESM Table 1. Baseline characteristics of attenders and non-attenders of the ET2DS at Year 10

| Characteristic               | Attenders | Non-Attenders | T or X² (p-value) |
|------------------------------|-----------|---------------|-------------------|
| **Demographic:**             |           |               |                   |
| Age (years)                  | 581       | 485           | -5.077 (<0.001)   |
| Sex males (n %)              | 581       | 485           | 0.069 (0.793)     |
| SIMD rank:                   |           |               | 14.725 (0.005)    |
| 1st quintile                 | 56 (9.6)  | 71 (14.6)     |                   |
| 2nd quintile                 | 116 (20.0)| 92 (19.0)     |                   |
| 3rd quintile                 | 92 (15.8) | 96 (19.8)     |                   |
| 4th quintile                 | 103 (17.7)| 91 (18.8)     |                   |
| 5th quintile                 | 214 (36.8)| 135 (27.8)    |                   |
| **Educational attainment:**  |           |               | 8.234 (0.041)     |
| University/ college          | 109 (18.8)| 62 (12.8)     |                   |
| Professional/ technical      | 169 (29.1)| 138 (28.5)    |                   |
| Secondary school             | 300 (51.6)| 281 (57.9)    |                   |
| Primary School               | 3 (0.5)   | 4 (0.8)       |                   |
| **Employment status:**       |           |               | 21.438 (0.001)    |
| Full-time                    | 47 (8.1)  | 28 (5.8)      |                   |
| Part-time                    | 54 (9.3)  | 23 (4.7)      |                   |
| Unemployed                   | 7 (1.2)   | 2 (0.4)       |                   |
| Retired                      | 443 (76.2)| 421 (86.8)    |                   |
| Homemaker                    | 15 (2.6)  | 4 (0.8)       |                   |
| Other                        | 15 (2.6)  | 7 (1.4)       |                   |
| **Vascular related:**        |           |               |                   |
| Systolic blood pressure (mmHg)| 132.06 ± 14.7| 134.79 ± 18.2| -2.651 (0.008)    |
| Diastolic blood pressure (mmHg)| 69.36 ± 8.5| 68.69 ± 9.6  | 1.198 (0.231)     |
| Hypertension (n)             | 580       | 484           | 8.161 (0.004)     |
| Total cholesterol (mmol/l)   | 578       | 479           | 0.739 (0.462)     |
| High density lipoprotein (mmol/l)| 1.31 ± 0.4| 1.27 ± 0.4   | 1.975 (0.049)     |
| Serum triglycerides (mmol/l) | 581       | 485           | -1.601 (0.110)    |
| Retinopathy (n)              | 575       | 469           | 3.318 (0.069)     |
| Stroke (n)                   | 581       | 485           | 6.621 (0.010)     |
| TIA (n)                      | 581       | 485           | 1.291 (0.256)     |
| Smoking status (n)           | 581       | 485           | 9.456 (0.009)     |
| - Current                    | 70 (12.0) | 84 (17.3)     |                   |
|                                      | Former       | Never        | Analysis       | P-Value    |
|--------------------------------------|--------------|--------------|----------------|------------|
| Total cigarettes smoked              | 577          | 1.66 ± 5.81  | 484            | 3.14 ± 8.02| 6.874 (<0.001) |
| Alcohol units                        | 581          | 9.85 ± 14.5  | 485            | 8.00 ± 14.5| 2.081 (0.038)  |
| Diabetes related:                    |              |              |                |            |
| Duration (median years (IQR))        | 581          | 8.19 ± 9.8   | 485            | 10.33 ± 13.9| -2.857 (0.004) |
| HbA1c (median (IQR))                 | 578          | 7.37 ± 1.1   | 479            | 7.45 ± 1.2 | -1.133 (0.258) |
| Plasma Glucose (mmol/L)              | 574          | 7.48 ± 1.9   | 475            | 7.66 ± 2.3 | -1.406 (0.160) |
| Medication status (n)                | 581          |              | 485            |            |
| - Insulin ± oral                     | 89 (15.3)    | 97 (20.0)    |                |            |
| - Oral                               | 365 (62.8)   | 316 (65.2)   |                |            |
| - Diet controlled                    | 127 (21.9)   | 72 (14.8)    |                |            |
| Obesity related:                     |              |              |                |            |
| Body mass index (kg/m2)              | 581          | 31.06 ± 5.5  | 484            | 31.86 ± 5.9| -2.273 (0.023) |
| Waist circumference (cm)             | 580          | 106.01 ± 12.7| 481            | 107.95 ± 12.9| -2.463 (0.014) |
| Waist to hip ratio                   | 580          | 0.96 ± 0.1   | 481            | 0.96 ± 0.1 | -1.004 (0.315) |
| Body fat (%)                         | 574          | 37.67 ± 7.7  | 478            | 38.60 ± 7.4| -2.010 (0.045) |
| Inflammatory related:                |              |              |                |            |
| Fibrinogen (median ng/ml)            | 580          | 3.57 ± 0.7   | 483            | 3.74 ± 0.8 | -3.677 (<0.001) |
| CRP (median mg/ml)                   | 569          | 3.15 ± 4.5   | 473            | 4.77 ± 7.4 | -4.161 (<0.001) |
| IL-6 (median pg/ml)                  | 580          | 3.45 ± 3.2   | 484            | 4.49 ± 3.8 | -4.771 (<0.001) |
| TNFα (median pg/ml)                  | 579          | 1.26 ± 1.7   | 484            | 1.47 ± 1.3 | -2.184 (0.029) |
| Psychological:                       |              |              |                |            |
| MMSE <24                             | 581          | 18 (3.1)     | 485            | 29 (6.0)   | 5.247 (0.022)  |
| HADS A                               | 581          | 5.29 ± 3.7   | 484            | 6.24 ± 4.1 | -3.922 (<0.001) |
| HADS D                               | 581          | 3.47 ± 2.7   | 484            | 4.32 ± 3.0 | -4.785 (<0.001) |

Total attenders n = 581 (max). Total non-attenders n = 485 (max). Analysis is a two-tailed independent t-test or Pearson's chi squared. Values are means ± SD, median (interquartile range) or n (%). SIMD, Scottish Index of Multiple Deprivation; HbA1c, haemoglobin A1c; CRP, c-reactive protein; IL-6, interleukin-6; TNFα, tumour necrosis factor α; TIA, transient ischaemic attack; MMSE, Mini Mental State Exam; HADS A, Hospital Anxiety and Depression Scale-Anxiety subscale; Hospital HADS B, Hospital Anxiety and Depression Scale-Depression subscale.
ESM Table 2. Association between baseline inflammatory markers and cognitive decline as measured by individual cognitive tests and g at year 10

| Inflammation marker | g          | LM         | lnTMTB      | Faces       | MR          | DST         | BVFT        | LNS         |
|---------------------|------------|------------|-------------|-------------|-------------|-------------|-------------|-------------|
|                     | Standardised Beta (SE) |           |             |             |             |             |             |             |
| Fibrinogen + age and sex | -0.111** (0.048) | -0.024 (0.049) | 0.150*** (0.048) | -0.063 (0.049) | -0.099* (0.049) | -0.125** (0.049) | -0.067 (0.050) | -0.069 (0.049) |
| + baseline cognition score | -0.059* (0.031) | -0.001 (0.041) | 0.088* (0.040) | -0.036 (0.041) | -0.061 (0.038) | -0.115*** (0.036) | -0.052 (0.033) | -0.071 (0.043) |
| + baseline diabetes covariates | -0.049 (0.049) | 0.008 (0.041) | 0.082* (0.040) | -0.022 (0.041) | -0.051 (0.039) | -0.107*** (0.036) | -0.045 (0.033) | -0.061 (0.043) |
| + baseline cardiovascular covariates | -0.035 (0.032) | 0.034 (0.042) | 0.063 (0.041) | -0.006 (0.042) | -0.033 (0.040) | -0.086*** (0.037) | -0.032 (0.034) | -0.050 (0.044) |
| lnCRP + age and sex | -0.101** (0.045) | -0.027 (0.046) | 0.116** (0.046) | -0.031 (0.046) | -0.078 (0.046) | -0.137*** (0.046) | -0.092* (0.047) | -0.058 (0.046) |
| + baseline cognition score | -0.055 (0.029) | -0.008 (0.039) | 0.072* (0.037) | -0.018 (0.038) | -0.028 (0.036) | -0.111** (0.034) | -0.056 (0.031) | -0.051 (0.041) |
| + baseline diabetes covariates | -0.045 (0.029) | 0.005 (0.040) | 0.065 (0.038) | -0.011 (0.039) | -0.023 (0.037) | -0.099** (0.034) | -0.049 (0.031) | -0.049 (0.041) |
| + baseline cardiovascular covariates | -0.029 (0.030) | 0.031 (0.041) | 0.050 (0.039) | 0.003 (0.040) | -0.010 (0.038) | -0.087** (0.035) | -0.035 (0.032) | -0.049 (0.0741) |
| lnIL-6 + age and sex | -0.152** (0.042) | -0.096* (0.043) | 0.166*** (0.043) | -0.049 (0.043) | -0.176*** (0.043) | -0.154*** (0.044) | -0.080 (0.044) | -0.089* (0.044) |
| + baseline cognition score | -0.064* (0.028) | -0.069 (0.036) | 0.095** (0.036) | -0.013 (0.036) | -0.127*** (0.034) | -0.091*** (0.033) | -0.017 (0.029) | -0.071 (0.038) |
| + baseline diabetes covariates | -0.052 (0.028) | -0.057 (0.037) | 0.089* (0.036) | 0.007 (0.037) | -0.119** (0.035) | -0.076* (0.033) | -0.011 (0.030) | -0.063 (0.039) |
| + baseline cardiovascular covariates | -0.039 (0.029) | -0.042 (0.038) | 0.076* (0.037) | 0.021 (0.038) | -0.111*** (0.036) | -0.061 (0.034) | 0.006 (0.031) | -0.052 (0.040) |
| lnTNF-α + age and sex | -0.055 (0.042) | -0.027 (0.042) | 0.083 (0.042) | -0.048 (0.042) | -0.053 (0.043) | -0.046 (0.042) | 0.004 (0.043) | -0.037 (0.043) |
| + baseline cognition score | -0.023 (0.027) | -0.023 (0.036) | 0.059 (0.035) | -0.035 (0.035) | -0.010 (0.034) | -0.084** (0.031) | 0.016 (0.028) | 0.001 (0.037) |
| + baseline diabetes covariates | -0.015 (0.027) | -0.014 (0.036) | 0.050 (0.035) | -0.023 (0.035) | -0.001 (0.034) | -0.073* (0.031) | 0.019 (0.029) | 0.008 (0.037) |
| + baseline cardiovascular covariates | -0.015 (0.027) | -0.018 (0.036) | 0.061 (0.035) | -0.024 (0.036) | -0.003 (0.034) | -0.083** (0.031) | 0.016 (0.029) | 0.014 (0.038) |

*p<0.05 **p<0.01 ***p<0.001.
Data for g (general cognitive ability) have been imputed, for remaining cognitive tests are non-imputed. Diabetes covariates; duration of diabetes, HbA1c and medication status.
Cardiovascular covariates: hypertension, smoking, HDL cholesterol, serum triglycerides, alcohol units, anxiety and depression scores. LM, Logical Memory; MR, Matrix Reasoning; DST, Digit Symbol Test; lnTMTB, Trail Making Test B (natural log transformed); BVFT, Borkowski Verbal Fluency Test; CRP, c-reactive protein; IL-6, interleukin-6; TNF-α, tumour necrosis factor α.