Supplemental Material

Suppl. Table 1. Factors associated with oxidative stress cross-sectionally (defined by continuously modelled baseline D-ROM levels). Results of backwards variable selection with a generalized linear model.

Parameter	DIANA		ESTHER		Meta-analysis	
	ß	p	ß	p	ß	p
Sex	**58.32**	**<0.01**	**52.13**	**<0.01**	**55.17**	**<0.01**
Education						
Low	Ref		Ref		Ref	
Medium	1.45	0.80	4.30	0.512	2.66	0.54
High	-13.78	0.07	1.40	0.85	-5.81	0.27
BMI (kg/m²)						
< 25	Ref		Ref		Ref	
25 - < 30	0.74	0.91	-10.35	0.11	-4.93	0.29
30 - < 35	3.53	0.61	-0.05	0.99	1.76	0.72
35 - < 40	7.62	0.39	6.37	0.48	7.02	0.27
≥ 40	**39.98**	**<0.01**	7.24	0.55	**26.59**	**0.00**
Smoking						
Never smoker	Ref		Ref		Ref	
Former smoker	5.26	0.30	1.84	0.70	3.46	0.32
Current smoker, smoking 0-15 g tobacco/d	**33.39**	**<0.01**	**26.13**	**0.01**	**30.09**	**<0.01**
Current smoker, smoking > 15 g tobacco/d	**31.64**	**0.00**	15.73	0.14	**24.65**	**<0.01**
HbA₁c (%)						
< 6	Ref		Ref		Ref	
6 - < 7	-5.21	0.4215	6.48	0.24	1.48	0.73
7 - < 8	2.27	0.77	**16.73**	**0.01**	**10.35**	**0.04**
≥ 8	-3.19	0.71	12.78	0.18	4.08	0.53
Diabetes medication						
No	Ref		Ref		Ref	
Oral anti-diabetics	**-16.20**	**0.00**	**-14.90**	**0.00**	**-15.50**	**<0.01**
Insulin	-10.85	0.11	-5.06	0.45	-7.95	0.09
History of stroke	-13.16	0.15	-10.96	0.09	**-11.71**	**0.03**
History of myocardial infarction	-1.06	0.91	12.92	0.09	7.45	0.20
Coronary heart disease	13.10	0.07	-0.80	0.88	4.24	0.33
Heart failure	**23.39**	**<0.01**	8.98	0.11	**15.10**	**<0.01**
History of cancer	**22.41**	**0.00**	7.35	0.23	**13.74**	**0.00**
Total cholesterol (mg/dL)						
< 200	Ref		Ref		Ref	
200 - < 280	**13.87**	**0.00**	**9.80**	**0.04**	**11.86**	**<0.01**
≥ 280	**17.84**	**0.01**	**20.00**	**0.01**	**18.77**	**<0.01**

Abbreviations: BMI, body mass index; HbA₁c, glycated haemoglobin A₁c

Suppl. Table 2. Factors associated with high oxidative stress cross-sectionally (defined by baseline D-ROM levels > 400 Carr U). Results of a logistic regression model.

Parameter	DIANA	ESTHER	Meta-Analysis
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Female sex	**4.85 (4.21; 5.59)**	**4.35 (3.68; 5.14)**	**4.64 (4.16; 5.16)**
Education			
Low	Ref	Ref	Ref
Medium	1.13 (0.96; 1.32)	1.11 (0.90; 1.37)	1.12 (0.99; 1.27)
High	**0.53 (0.42; 0.68)**	**0.62 (0.46; 0.83)**	**0.57 (0.47; 0.68)**
BMI (kg/m²)			
< 25	Ref	Ref	Ref
25 - < 30	1.18 (0.98; 1.43)	1.07 (0.86; 1.33)	1.13 (0.98; 1.31)
30 - < 35	**1.27 (1.04; 1.55)**	**1.46 (1.16; 1.84)**	**1.35 (1.16; 1.57)**
35 - < 40	**1.72 (1.33; 2.21)**	**1.54 (1.15; 2.05)**	**1.64 (1.35; 1.98)**
≥ 40	**3.17 (2.37; 4.23)**	**2.34 (1.61; 3.39)**	**2.83 (2.25; 3.55)**
Smoking			
Never smoker	Ref	Ref	Ref
Former smoker	**1.31 (1.13; 1.52)**	1.08 (0.92; 1.28)	**1.20 (1.08; 1.34)**
Current smoker, smoking 0-15 g tobacco/d	**3.17 (2.44; 4.14)**	1.32 (0.95; 1.82)	**2.23 (1.82; 2.74)**
Current smoker, smoking > 15 g tobacco/d	**2.70 (2.07; 3.52)**	**1.50 (1.06; 2.12)**	**2.17 (1.76; 2.68)**
HbA$_{1c}$ (%)			
< 6	Ref	Ref	Ref
6 - < 7	1.04 (0.86; 1.25)	1.09 (0.91; 1.31)	1.06 (0.93; 1.21)
7 - < 8	1.22 (0.97; 1.52)	**1.43 (1.14; 1.80)**	**1.32 (1.12; 1.54)**
≥ 8	1.24 (0.97; 1.60)	**1.61 (1.12; 2.21)**	**1.38 (1.13; 1.68)**
Diabetes medication			
No	Ref	Ref	Ref
Oral anti-diabetics	**0.59 (0.51; 0.69)**	**0.54 (0.45; 0.63)**	**0.57 (0.51; 0.63)**
Insulin	**0.69 (0.57; 0.83)**	**0.74 (0.60; 0.93)**	**0.71 (0.62; 0.82)**
History of stroke	0.82 (0.63; 1.06)	0.88 (0.70; 1.11)	0.85 (0.72; 1.02)
History of myocardial infarction	1.11 (0.85; 1.44)	**1.50 (1.17; 1.94)**	**1.31 (1.08; 1.56)**
Coronary heart disease	1.16 (0.95; 1.41)	0.95 (0.79; 1.15)	1.05 (0.91; 1.20)
Heart failure	**1.53 (1.28; 1.84)**	**1.32 (1.10; 1.58)**	**1.42 (1.25; 1.62)**
History of cancer	**1.89 (1.56; 2.29)**	1.17 (0.95; 1.43)	**1.50 (1.31; 1.73)**
Total cholesterol (mg/dL)			
< 200	Ref	Ref	Ref
200 - < 280	**1.26 (1.10; 1.44)**	**1.43 (1.21; 1.68)**	**1.32 (1.19; 1.47)**
≥ 280	**1.51 (1.24; 1.84)**	**1.59 (1.24; 2.04)**	**1.54 (1.32; 1.80)**

Abbreviations: BMI, body mass index; 95% CI, 95% confidence interval; HbA$_{1c}$, glycated haemoglobin A$_{1c}$.

Suppl. Table 3. Factors associated with oxidative stress longitudinally (defined by continuously modelled Δ D-ROM levels). Results of backwards variable selection with a generalized linear model.

Parameter	Diana		Esther		Meta-analysis	
	ß	p	ß	p	ß	p
Age (years)						
< 60	Ref		Ref		Ref	
60 - < 70	0.59	0.93	15.69	0.05	6.96	0.19
70 - < 80	2.60	0.71	**19.74**	**0.02**	9.68	0.07
≥ 80	5.06	0.61	**28.06**	**0.01**	15.62	0.03
Female sex	**15.01**	**0.01**	**14.65**	**0.00**	**14.79**	**<0.01**
BMI (kg/m²)						
< 25	Ref		Ref		Ref	
25 - < 30	-0.03	1.00	-3.59	0.53	-3.37	0.45
30 - < 35	-2.74	0.71	-0.96	0.87	-1.67	0.72
35 - < 40	17.89	0.07	4.94	0.53	10.10	0.10
≥ 40	**26.378**	**0.02**	7.36	0.52	**16.94**	**0.03**
Smoking						
Never smoker	Ref		Ref		Ref	
Former smoker	2.95	0.59	0.81	0.85	1.61	0.63
Current smoker, smoking 0-15 g tobacco/d	14.38	0.17	6.94	0.48	10.43	0.15
Current smoker, smoking >15 g tobacco/d	17.57	0.12	17.56	0.07	**17.56**	**0.02**
Alcohol consumption						
Abstainer	Ref		Ref		Ref	
Low consumption	3.71	0.47	4.52	0.27	4.21	0.19
Moderate consumption	-7.06	0.56	4.51	0.66	-0.38	0.96
High consumption	**42.47**	**0.04**	-0.87	0.96	14.35	0.25
Physical activity (active)	-0.46	0.94	**-9.31**	**0.01**	**-6.77**	**0.03**
Diabetes medication						
No	Ref		Ref		Ref	
Oral anti-diabetics	-5.13	0.37	3.31	0.43	0.32	0.96
Insulin	4.32	0.58	**14.26**	**0.02**	**10.45**	**0.03**
Time since diabetes diagnosis (years)						
< 5	Ref		Ref		Ref	
5 - < 10	-1.20	0.84	-6.26	0.23	-4.13	0.29
10 - < 20	10.53	0.09	**-12.03**	**0.03**	-1.76	0.67
≥ 20	1.99	0.84	-12.41	0.18	-5.738	0.397
Baseline D-ROM (per 10 Carr Units)	**-3.66**	**<0.01**	**-5.46**	**<0.01**	**-4.71**	**<0.01**

Abbreviations: BMI, body mass index.

Suppl. Table 4. Factors associated with high oxidative stress longitudinally (defined by D-ROM levels > 400 Carr U at follow-up). Results of a logistic regression model.

Parameter	DIANA	ESTHER	Meta-Analysis
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age (years)			
< 60	Ref	Ref	Ref
60 - < 70	1.08 (0.84; 1.39)	**2.24 (1.28; 3.92)**	1.22 (0.97; 1.54)
70 - < 80	**1.35 (1.05; 1.74)**	**2.50 (1.42; 4.40)**	**1.50 (1.19; 1.88)**
≥ 80	**1.67 (1.16; 2.42)**	2.02 (1.00; 4.10)	**1.74 (1.26; 2.41)**
Female sex	**2.10 (1.72; 2.57)**	**2.24 (1.28; 3.92)**	**2.12 (1.75; 2.56)**
BMI (kg/m²)			
< 25	Ref	Ref	Ref
25 - < 30	0.86 (0.66; 1.10)	1.05 (0.76; 1.45)	0.93 (0.76; 1.14)
30 - < 35	**0.73 (0.56; 0.96)**	0.88 (0.63; 1.24)	**0.79 (0.64; 0.97)**
35 - < 40	**1.82 (1.25; 2.63)**	**2.08 (1.40; 3.09)**	**1.94 (1.48; 2.54)**
≥ 40	**1.91 (1.21; 3.03)**	1.61 (0.94; 2.75)	**1.78 (1.25; 2.52)**
Smoking			
Never smoker	Ref	Ref	Ref
Former smoker	**1.23 (1.01; 1.50)**	**1.52 (1.20; 1.94)**	**1.34 (1.15; 1.56)**
Current smoker, smoking 0-15 g tobacco/d	1.21 (0.83; 1.77)	**1.76 (1.07; 2.90)**	**1.39 (1.03; 1.88)**
Current smoker, smoking >15 g tobacco/d	**2.22 (1.45; 3.38)**	0.80 (0.45; 1.43)	**1.56 (1.11; 2.19)**
Alcohol consumption			
Abstainer	Ref	Ref	Ref
Low consumption	1.07 (0.89; 1.29)	0.99 (0.79; 1.24)	1.04 (0.90; 1.20)
Moderate consumption	**0.45 (0.29; 0.69)**	0.78 (0.42; 1.46)	**0.54 (0.38; 0.77)**
High consumption	**3.38 (1.60; 7.14)**	1.08 (0.45; 2.61)	**2.09 (1.18; 3.70)**
Physical activity (active)	1.09 (0.89; 1.35)	**0.68 (0.55; 0.84)**	0.86 (0.75; 1.00)
Diabetes medication			
No	Ref	Ref	Ref
Oral anti-diabetics	**0.73 (0.59; 0.89)**	1.17 (0.92; 1.49)	0.89 (0.76; 1.04)
Insulin	1.11 (0.83; 1.48)	1.34 (0.96; 1.87)	1.20 (0.97; 1.45)
Time since diabetes diagnosis (years)			
< 5	Ref	Ref	Ref
5 - < 10	**1.41 (1.14; 1.75)**	1.24 (0.97; 1.58)	**1.33 (1.34; 1.57)**
10 - < 20	**1.43 (1.15; 1.79)**	0.89 (0.64; 1.24)	**1.24 (1.03; 1.48)**
≥ 20	1.33 (0.93; 1.89)	1.13 (0.72; 1.75)	1.25 (0.95; 1.65)
Baseline D-ROM (per 10 Carr Units)	**1.21 (1.19; 1.23)**	**1.20 (1.18; 1.22)**	**1.21 (1.19; 1.22)**

Abbreviations: BMI, body mass index; 95% CI, 95% confidence interval; D-ROM; Diacron`s reactive oxygen metabolites.

Suppl. Table 5. Factors associated with oxidative stress cross-sectionally (defined by continuously modelled baseline D-ROM levels) in a model adjusted for CRP

Parameter	DIANA		ESTHER		Meta-Analysis	
	ß	p	ß	p	ß	p
Sex	**55.95**	**<0.01**	**48.13**	**<0.01**	**51.92**	**<0.01**
Education						
Low	Ref		Ref		Ref	
Medium	3.69	0.50	3.77	0.55	3.72	0.37
High	-7.53	0.30	4.75	0.49	-0.99	0.84
BMI (kg/m²)						
< 25	Ref		Ref		Ref	
25 - < 30	-0.96	0.88	**-12.83**	**0.04**	-7.10	0.11
30 - < 35	-0.84	0.90	-10.37	0.12	-5.58	0.23
35 - < 40	-1.08	0.90	-8.72	0.32	-4.79	0.43
≥ 40	**23.10**	**0.02**	-10.37	0.37	9.13	0.22
Smoking						
Never smoker	Ref		Ref		Ref	
Former smoker	2.07	0.67	2.32	0.61	2.20	0.51
Current smoker, smoking 0-15 g tobacco/d	**27.98**	**0.00**	17.32	0.08	**23.04**	**0.00**
Current smoker, smoking >15 g tobacco/d	**20.92**	**0.02**	12.32	0.22	**17.06**	**0.01**
Total cholesterol (mg/dL)						
< 200						
200 - < 280	**11.46**	**0.01**	8.17	0.06	**9.82**	**0.00**
≥ 280	**14.04**	**0.04**	**18.20**	**0.02**	**15.90**	**0.00**
HbA$_{1c}$ (%)						
< 6	Ref		Ref		Ref	
6 - < 7	-7.24	0.234	6.54	0.21	0.74	0.85
7 - < 8	-2.00	0.78	11.31	0.08	5.51	0.25
≥ 8	-4.26	0.61	5.36	0.55	0.72	0.98
Diabetes medication						
No	Ref		Ref		Ref	
Oral anti-diabetics	**-15.73**	**0.00**	**-11.555**	**0.01**	**-13.48**	**<0.01**
Insulin	-11.28	0.08	-1.61	0.80	-6.36	0.16
History of stroke	-8.57	0.33	-9.47	0.13	-9.17	0.07
History of myocardial infarction	3.72	0.68	10.99	0.12	8.20	0.14
Coronary heart disease	9.39	0.19	-3.16	0.55	1.26	0.76
Heart failure	**17.09**	**0.01**	7.11	0.18	**11.24**	**0.01**
History of cancer	**23.02**	**0.00**	6.39	0.27	**12.87**	**0.01**
CRP (mg/L)						
≤ 3	Ref		Ref		Ref	
> 3 - ≤ 10	**30.80**	**<0.01**	**33.32**	**<0.01**	**32.08**	**<0.01**
> 10	**61.02**	**<0.01**	**66.06**	**<0.01**	**63.77**	**<0.01**

Abbreviations: BMI, body mass index; CRP, C-reactive protein; HbA$_{1c}$, glycated haemoglobin A$_{1c}$.

Suppl. Table 6. Factors associated with oxidative stress longitudinally (defined by continuously modelled Δ D-ROM levels) in a model adjusted for CRP

Parameter	DIANA		ESTHER		Meta-analysis	
	ß	p	ß	p	ß	p
Age (years)						
< 60						
60 - < 70	0.41	0.95	15.51	0.06	6.75	0.20
70 - < 80	2.43	0.73	**18.77**	**0.02**	9.14	0.09
≥ 80	3.18	0.75	**27.21**	**0.01**	14.18	0.05
Gender	**14.18**	**0.01**	**14.80**	**0.00**	**14.56**	**<0.01**
BMI (kg/m²)						
< 25						
25 - < 30	-1.12	0.88	-4.29	0.45	-3.08	0.49
30 - < 35	-4.62	0.54	-3.45	0.58	-3.93	0.41
35 - < 40	14.83	0.13	2.13	0.79	7.24	0.24
≥ 40	**25.03**	**0.03**	2.88	0.80	14.15	0.08
Smoking						
Never smoker						
Former smoker	1.53	0.78	0.70	0.87	1.01	0.76
Current smoker, smoking 0-15 g tobacco/d	11.11	0.29	5.06	0.61	7.90	0.28
Current smoker, smoking >15 g tobacco/d	17.84	0.11	17.59	0.07	**17.69**	**0.02**
Alcohol consumption						
Abstainer						
Low consumption	3.30	0.52	4.74	0.24	4.18	0.19
Moderate consumption	-5.67	0.63	4.88	0.63	0.40	0.96
High consumption	34.90	0.10	-1.48	0.92	11.30	0.37
Physical activity (active)	-0.94	0.87	**-8.58**	**0.02**	**-6.37**	**0.043**
Diabetes medication						
No						
Oral anti-diabetics	-5.79	0.30	3.47	0.41	0.18	0.96
Insulin	3.79	0.63	**13.69**	**0.03**	**9.88**	**0.04**
Time since diabetes diagnosis (years)						
< 5						
5 - < 10	-0.80	0.89	-5.91	0.25	-3.75	0.33
10 - < 20	11.93	0.05	**-11.58**	**0.04**	1.01	0.08
≥ 20	3.37	0.73	-10.93	0.25	-4.21	0.54
Baseline D-ROM (per 10 Carr Units)	**-3.74**	**<0.01**	**-5.67**	**<0.01**	**-4.86**	**<0.01**
CRP (mg/L)						
≤ 3						
> 3 - ≤ 10	**14.06**	**0.01**	7.17	0.09	**9.87**	**0.00**
> 10	-10.18	0.25	**14.41**	**0.05**	4.37	0.43

Abbreviations: BMI, body mass index; CRP, C-reactive protein; D-ROM; Diacron`s reactive oxygen metabolites.