TARGETED LIPIDOMICS (2)

Lipidomic patterns and the risk of T2D

Lipidomic patterns

- **First step: exploratory analysis:**

  1.PCA

- **Second step: hypothesis based analysis:**

  1. Scores of lipid metabolites

  2. Scores of lipid metabolite changes

- **Third step: Effects of intervention on lipid changes**

Lipidomic patterns

- **First step: exploratory analysis**:

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- **Second step: hypothesis based analysis:**

  1. Scores of lipid metabolites

  2. Scores of lipid metabolite changes

- **Third step: Effects of intervention on lipid changes**

FIRST STEP: PRINCIPAL COMPONENT ANALYSIS (PCA)

-Exploratory analysis

-207 known lipid metabolites were included

PCA

```
┌─────────────────────────────┐
│    207 factors generated    │
└─────────────────────────────┘
               │
               ▼
┌─────────────────────────────┐
│        Eigenvalues>2        │
└─────────────────────────────┘
               │
               ▼
┌─────────────────────────────┐
│     15 factors extracted    │
└─────────────────────────────┘
               │
               ▼
┌─────────────────────────────┐
│      Varimax rotation       │
│       (orthogonal)          │
└─────────────────────────────┘
```
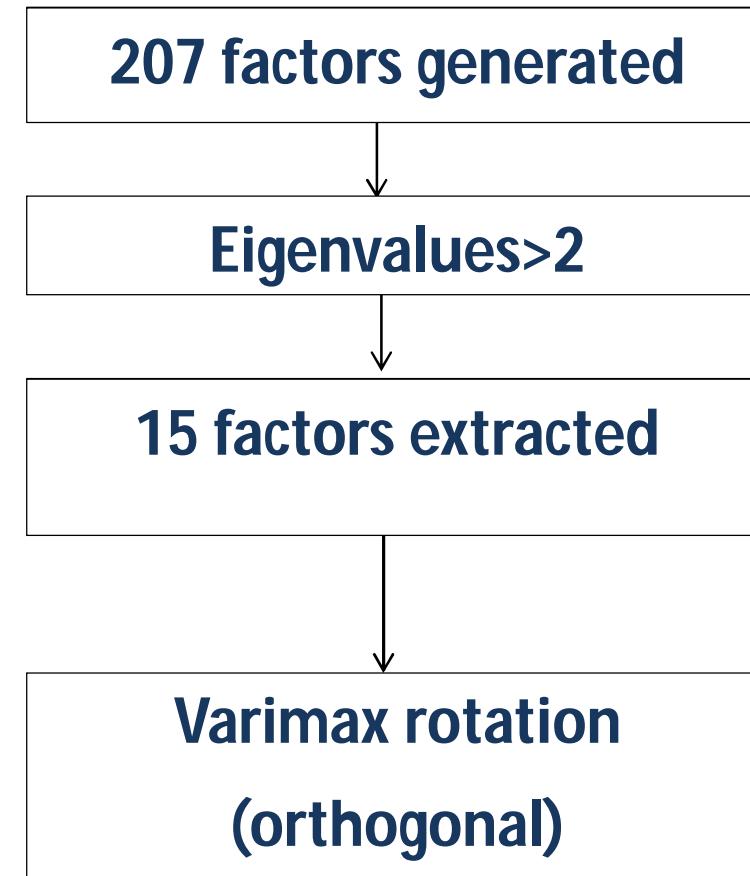
PCA

Factor	Eigenvalue	Difference	Proportion	Cumulative
Factor 1	53.35	21.57	0.26	0.26
Factor 2	31.78	7.94	0.16	0.42
Factor 3	23.83	9.59	0.12	0.53
Factor 4	14.24	4.30	0.07	0.59
Factor 5	9.94	1.60	0.05	0.64
Factor 6	8.33	1.96	0.04	0.68
Factor 7	6.37	0.49	0.03	0.71
Factor 8	5.89	1.18	0.03	0.74
Factor 9	4.70	0.93	0.03	0.76
Factor 10	3.77	0.87	0.02	0.78
Factor 11	2.91	0.39	0.01	0.80
Factor 12	2.53	0.109	0.01	0.81
Factor 13	2.48	0.239	0.01	0.82
Factor 14	2.19	0.19	0.01	0.83
Factor 15	2.00	0.37	0.01	0.84

Factors showing inverse association:

	Quartiles of factors				Linear trend	Per SD
	Q1	Q2	Q3	Q4		
Factor 3	Ref.	0.60 (0.36-1.00)	0.74 (0.44-1.25)	**0.43 (0.25-0.75)**	**0.014**	**0.78(0.66-0.92)**
Factor 7	Ref.	**0.62 (0.39-0.97)**	**0.39 (0.23-0.66)**	**0.37 (0.21-0.65)**	**<0.001**	**0.67 (0.57-0.79)**
Factor 10	Ref.	0.82 (0.50-1.37)	**0.48 (0.28-0.80)**	**0.56 (0.33-0.96)**	**0.017**	**0.81 (0.69-0.95)**

Cox model adjusted for: age, sex, intervention group

Additionally adjusted for the rest of factors (1-15)

	Factor	Description	Components	Eigen value	Variance explained (%)
Inverse association with T2D	**3**	Lysophosphatidylcholines (LPCs) and Lysophosphatidylethanolamines (LPEs); Pcplasmalogens; sphingomyelines (SM); ceramides (CER), and cholesterol esters (CE)*	34:0pc, 18:1lpe, 14:0lpc, 22:6lpe, 20:4lpe, 18:2lpc, 20:5lpc, 16:1lpc, 20:4lpc, 22:6lpc, 16:0lpe, 22:0lpe, 20:0lpe, 18:0lpe, 18:1lpc, 18:0lpc, 20:3lpc, 16:0lpc	23.8	11.5
	7		40:6ps, 36:1peplasmalogen, 20:0lpe 51:3tag, 34:0pe, 53:2tag, 53:3tag, 55:3tag, 38:2pe	6.4	3
	10		14:0sm, 16:0ce, 16:0cer18:1, 16:0sm 16:1sm, 18:0ce, 18:0sm, 18:1sm, 18:2ce, 18:2sm, 20:0sm, 22:0cer18:1, 22:0sm, 22:1sm, 24:0cer18:1, 24:0sm, 24:1cer181 24:1sm, 32:0pc, 34:0pc, 34:1pcplasmalogen_a, 34:1pcplasmalogen_b, 342pc, 34:2pcplasmalogen, 34:3pc, 34:3pcplasmalogen, 36:0pc, 36:1pcplasmalogen, 36:1psplasmalogen, 36:2pc, 36:2pcplasmalogen, 36:2psplasmalogen, 36:3pc, 36:3pcplasmalogen, 36:4pca, 36:4pcplasmalogen, 38:2pc, 38:2pe 38:4pcplasmalogen, 38:6pcplasmalogen, 40:7pcplasmalogen, 54:10tag, cholesterol	3.8	1.8

*Excluding CE 16:1

Factors showing direct association:

	Quartiles of factors				Linear trend	Per SD
	Q1	Q2	Q3	Q4		
Factor 1	Ref.	1.39 (0.78-2.50)	**2.17 (1.26-3.72)**	**2.70 (1.58-4.59)**	**<0.001**	**1.34 (1.16-1.55)**
Factor 5	Ref.	1.27 (0.73-2.19)	1.22 (0.71-2.09)	**1.92 (1.15-3.23)**	0.062	1.16 (0.99-1.35)
Factor 11	Ref.	1.30 (0.75-2.26)	**1.80 (1.03-3.13)**	**2.08 (1.17-3.69)**	**0.009**	**1.25 (1.07-1.47)**

Cox model adjusted for: age, sex, intervention group

Additionally adjusted for the rest of factors (1-15)

	Factor	Description	Components	Eigen value	Variance explained (%)
Direct association with T2D	**1**	Triacylglycerides (TAGs) with≤4 double bonds; Diacylglycerides (DAGs); Phosphatidylethanolamines (PEs)	38:2pc, 16:1lpc, 36:1pc, 32:0pc, 38:4dag, 40:6pe, 36:2dag, 38:5dag, 16:1ce, 34:1pc 14:0ce, 52:7tag, 54:2tag, 52:6tag, 36:4pe, 38:3pc, 53:2tag, 51:3tag, 56:2tag, 34:3pc, 36:2pe, 40:6ps, 36:1pe, 34:2pe, 34:3dag 34:4pc, 34:0pe, 52:2tag, 55:2tag, 32:2pc, 50:4tag, 34:2dag, 50:5tag, 14:0lpc, 32:0pe, 34:1dag, 34:0dag, 56:1tag, 36:1dag, 32:1pc, 50:3tag, 48:4tag, 54:1tag, 51:2tag, 30:0pc, 30:1pc, 49:3tag 30:0dag, 52:1tag, 32:1dag, 52:0tag, 51:0tag, 50:2tag, 46:3tag, 48:3tag, 32:0dag, 50:1tag, 49:2tag, 44:2tag, 42:0tag, 49:1tag, 51:1tag, 45:1tag, 47:1tag, 50:0tag, 48:0tag, 47:2tag 44:1tag, 46:2tag, 48:2tag, 46:0tag, 44:0tag, 48:1tag, 46:1tag 18:2ce* 22:4ce* 16:0ce* 22:6ce* 20:4ce* 18:1ce*	53.3	25.8
	5		53:3tag, 34:1pc, 34:1dag, 54:1tag, 36:1dag, 54:4tag, 52:3tag, 36:1pc, 24:1cer181, 36:1pe, 53:2tag, 56:4tag, 55:2tag, 52:2tag, 55:3tag, 56:2tag, 36:2dag, 54:2tag, 56:3tag, 54:3tag	9.9	6.9
	11		40:6pe, 36:2pe, 38:4pe, 38:5pe, 36:3pe, 38:6pe, 34:2pe, 36:4pe	2.9	1.4

*Negative loading factors

Lipidomic patterns

- **First step: exploratory analysis**:

  1.PCA

- **Second step: hypothesis based analysis:**

  1. Scores of lipid metabolites

  2. Scores of lipid metabolite changes

- **Third step: Effects of intervention on lipid changes**

SECOND STEP (1):
SCORES OF LIPID SPECIES

-Hypothesis based analysis

-Guided by PCA, metabolites were grouped

according to their similar chemical characteristics.

BASELINE SCORES

1. **Lysophosphatidylcholines (LPC) and Lysophosphatidylethanolamines (LPE)**

2. **Phosphatidylcholine-plasmalogens (PC-pl)**

3. **Sphingomyelines (SM)**

4. **Cholesterol esters (excluding ce16:1)**

5. **Ceramides (CER)**

6. **Triacylglycerides (TAG) low number of double bounds (≤ 4)**

7. **Diacylglycerides (DAG)**

8. **Phosphatidylethanolamines (PE)**

Scores showing inverse association

	N	Q1	Quartiles of scores			Linear trend	Per SD
			Q2	Q3	Q4		
LPC_LPE	17	Ref.	0.89 (0.61-1.31)	**0.47 (0.30-0.72)**	**0.48 (0.31-0.74)**	**<0.001**	**0.74 (0.63-0.86)**
PC-pl	12	Ref.	0.72 (0.48-1.08)	0.70 (0.47-1.05)	**0.38 (0.24-0.61)**	**<0.001**	**0.75 (0.65-0.87)**
SM	11	Ref.	0.49 (0.32-0.75)	**0.58 (0.38-0.89)**	**0.32 (0.19-0.54)**	**<0.001**	**0.67 (0.56-0.80)**
CE	12	Ref.	0.77 (0.52-1.15)	0.68 (0.45-1.02)	**0.30 (0.18-0.48)**	**<0.001**	**0.67 (0.58-0.79)**
CER	4	Ref.	1.06 (0.69-1.62)	0.96 (0.62-1.47)	1.05 (0.69-1.61)	0.814	1.01 (0.87-1.18)
Inverse score	54	Ref.	**0.51 (0.34-0.76)**	**0.48 (0.33-0.72)**	**0.25 (0.15-0.40)**	**<0.001**	**0.63 (0.53-0.74)**

LPC:LysoPhosphatidylCholines; LPE:LysoPhosphatidylEthanolamines; PC-pl:PhosphatidylCholines-plasmalogens; CER:ceramides; SM:sphingomyelines; CE:cholesterol esters.

Cox model adjusted for: age, sex, intervention group

Scores showing inverse association

	N	Q1	Quartiles of scores			Linear trend	Per SD
			Q2	Q3	Q4		
LPC_LPE	17	Ref.	0.89 (0.61-1.31)	**0.47 (0.30-0.72)**	**0.48 (0.31-0.74)**	**<0.001**	**0.74 (0.63-0.86)**
PC-pl	12	Ref.	0.72 (0.48-1.08)	0.70 (0.47-1.05)	**0.38 (0.24-0.61)**	**<0.001**	**0.75 (0.65-0.87)**
SM	11	Ref.	0.49 (0.32-0.75)	**0.58 (0.38-0.89)**	**0.32 (0.19-0.54)**	**<0.001**	**0.67 (0.56-0.80)**
CE	12	Ref.	0.77 (0.52-1.15)	0.68 (0.45-1.02)	**0.30 (0.18-0.48)**	**<0.001**	**0.67 (0.58-0.79)**
Inverse score w/o CER	50	Ref.	**0.55 (0.36-0.82)**	**0.49 (0.33-0.73)**	**0.24 (0.14-0.39)**	**<0.001**	**0.60 (0.51-0.72)**

LPC:LysoPhosphatidylCholines; LPE:LysoPhosphatidylEthanolamines; PC-pl:PhosphatidylCholines-plasmalogens;

CER:ceramides; SM:sphingomyelines; CE:cholesterol esters.

Cox model adjusted for: age, sex, intervention group

Scores showing inverse association
Multivariable model

	N	Q1	Quartiles of scores			Linear trend	Per SD
			Q2	Q3	Q4		
LPC_LPE	17	Ref.	0.96 (0.65-1.42)	**0.48 (0.31-0.76)**	**0.55 (0.35-0.86)**	**0.001**	**0.75 (0.64-0.88)**
PC-pl	12	Ref.	0.76 (0.50-1.15)	0.76 (0.50-1.15)	**0.43 (0.26-0.71)**	**0.005**	**0.80 (0.69-0.94)**
SM	11	Ref.	**0.47 (0.31-0.74)**	**0.56 (0.36-0.88)**	**0.32 (0.19-0.53)**	**<0.001**	**0.70 (0.58-0.83)**
CE	12	Ref.	**0.90 (0.59-1.37)**	0.79 (0.52-1.20)	**0.37 (0.23-0.62)**	**0.002**	**0.72 (0.61-0.85)**
Inverse score w/o CER	50	Ref.	**0.54 (0.35-0.82)**	**0.52 (0.34-0.79)**	**0.27 (0.16-0.46)**	**<0.001**	**0.63 (0.52-0.75)**

LPC:LysoPhosphatidylCholines; LPE:LysoPhosphatidylEthanolamines; PC-pl:PhosphatidylCholines-plasmalogens;

CER:ceramides; SM:sphingomyelines; CE:cholesterol esters.

Cox model adjusted for: age, sex, intervention group, BMI, smoking, dyslipidemia and hypertension

Scores showing inverse association
Multivariable model+baseline glucose

	N	Quartiles of scores				Linear trend	Per SD
		Q1	Q2	Q3	Q4		
LPC_LPE	17	Ref.	1.32 (0.76-2.30)	0.50 (0.24-1.03)	0.80 (0.43-1.48)	0.122	0.84 (0.66-1.07)
PC-pl	12	Ref.	0.55 (0.29-1.04)	0.71 (0.40-1.29)	**0.40 (0.19-0.84)**	**0.028**	**0.78 (0.61-0.99)**
SM	11	Ref.	0.30 (0.15-0.58)	**0.49 (0.25-0.94)**	**0.25 (0.11-0.55)**	**0.001**	**0.70 (0.53-0.93)**
CE	12	Ref.	0.54 (0.28-1.05)	0.79 (0.43-1.47)	**0.31 (0.15-0.64)**	**0.010**	**0.64 (0.50-0.83)**
Inverse score w/o CER	50	Ref.	**0.46 (0.25-0.88)**	**0.50 (0.27-0.93)**	**0.29 (0.14-0.59)**	**<0.001**	**0.65 (0.50-0.85)**

LPC:LysoPhosphatidylCholines; LPE:LysoPhosphatidylEthanolamines; PC-pl:PhosphatidylCholines-plasmalogens;

CER:ceramides; SM:sphingomyelines; CE:cholesterol esters.

Cox model adjusted for: age, sex, intervention group, BMI, smoking, dyslipidemia, hypertension, baseline glucose and baseline glucose quadratic term

Scores showing direct association:

| | N | Q1 | Quartiles of factors | | | Linear trend | Per SD |
			Q2	Q3	Q4		
TAG	45	Ref.	**1.73 (1.06-2.82)**	**2.26 (1.41-3.63)**	**2.88 (1.82-4.55)**	**<0.001**	**1.52 (1.29-1.79)**
DAG	14	Ref.	1.19 (0.73-1.94)	**2.18 (1.37-3.45)**	**2.84 (1.81-4.43)**	**<0.001**	**1.57 (1.33-1.86)**
PE	12	Ref.	1.51 (0.95-2.39)	1.57 (0.98-2.50)	**2.55 (1.64-3.95)**	**<0.001**	**1.45 (1,23-1.70)**
Direct score	71	Ref.	1.26 (0.77-2.07)	**2.25 (1.42-3.58)**	**2.76 (1.76-4.31)**	**<0.001**	**1.55 (1.32-1.83)**

Cox model adjusted for: age, sex, intervention group

Scores showing direct association
Multivariable model

	N	Q1	Quartiles of factors			Linear trend	Per SD
			Q2	Q3	Q4		
TAG	45	Ref.	1.70 (1.04-2.79)	**2.08 (1.28-3.36)**	2.40 (1.50-3.83)	**<0.001**	**1.41 (1.19-1.66)**
DAG	14	Ref.	1.23 (0.74-2.03)	**1.92 (1.20-3.07)**	**2.42 (1.54-3.82)**	**<0.001**	**1.48 (1.24-1.76)**
PE	12	Ref.	1.45 (0.91-2.32)	1.48 (0.92-2.38)	**2.12 (1.35-3.32)**	**0.002**	**1.36 (1.16-1.59)**
Direct score	71	Ref.	1.28 (0.77-2.10)	**2.02 (1.26-3.23)**	**2.33 (1.48-3.68)**	**<0.001**	**1.44 (1.22-1.70)**

Cox model adjusted for: age, sex, intervention group, BMI, smoking, dyslipidemia and hypertension

Scores showing direct association
Multivariable model+baseline glucose

	N	Q1	Quartiles of factors			Linear trend	Per SD
			Q2	Q3	Q4		
TAG	45	Ref.	1.41 (0.66-3.03)	2.33 (1.11-4.86)	1.86 (0.88-3.91)	0.092	**1.34 (1.03-1.74)**
DAG	14	Ref.	1.27 (0.60-2,70)	1.94 (0.99-3.80)	**2.19 (1.16-4.15)**	**0.009**	**1.37 (1.07-1.75)**
PE	12	Ref.	1.66 (0.86-3.20)	0.83 (0.41-1.70)	1.48 (0.77-2.85)	0.377	1.23 (0.97-1.56)
Direct score	71	Ref.	0.87 (0.42-1.83)	1.55 (0.78-3.07)	1.82 (0.97-3.42)	**0.022**	**1.35 (1.05-1.74)**

Cox model adjusted for: age, sex, intervention group, BMI, smoking, dyslipidemia, hypertension, baseline glucose and baseline glucose quadratic term

Lipidomic patterns

- **First step: exploratory analysis:**

  1.PCA

- **Second step: hypothesis based analysis:**

  1. Scores of lipid metabolites

  2. Scores of lipid metabolite changes

- **Third step: Effects of intervention on lipid changes**

Baseline missing values

1y missing values

Replace by half of minimum detected

Replace by half of minimum detected

FOR EACH Metabolite *CHANGE* = **1y_metabolite - baseline metabolite**

Bloom's inverse normal transformation of **Metabolite** *CHANGE*

Scores of changes: Sum of implicated metabolite changes
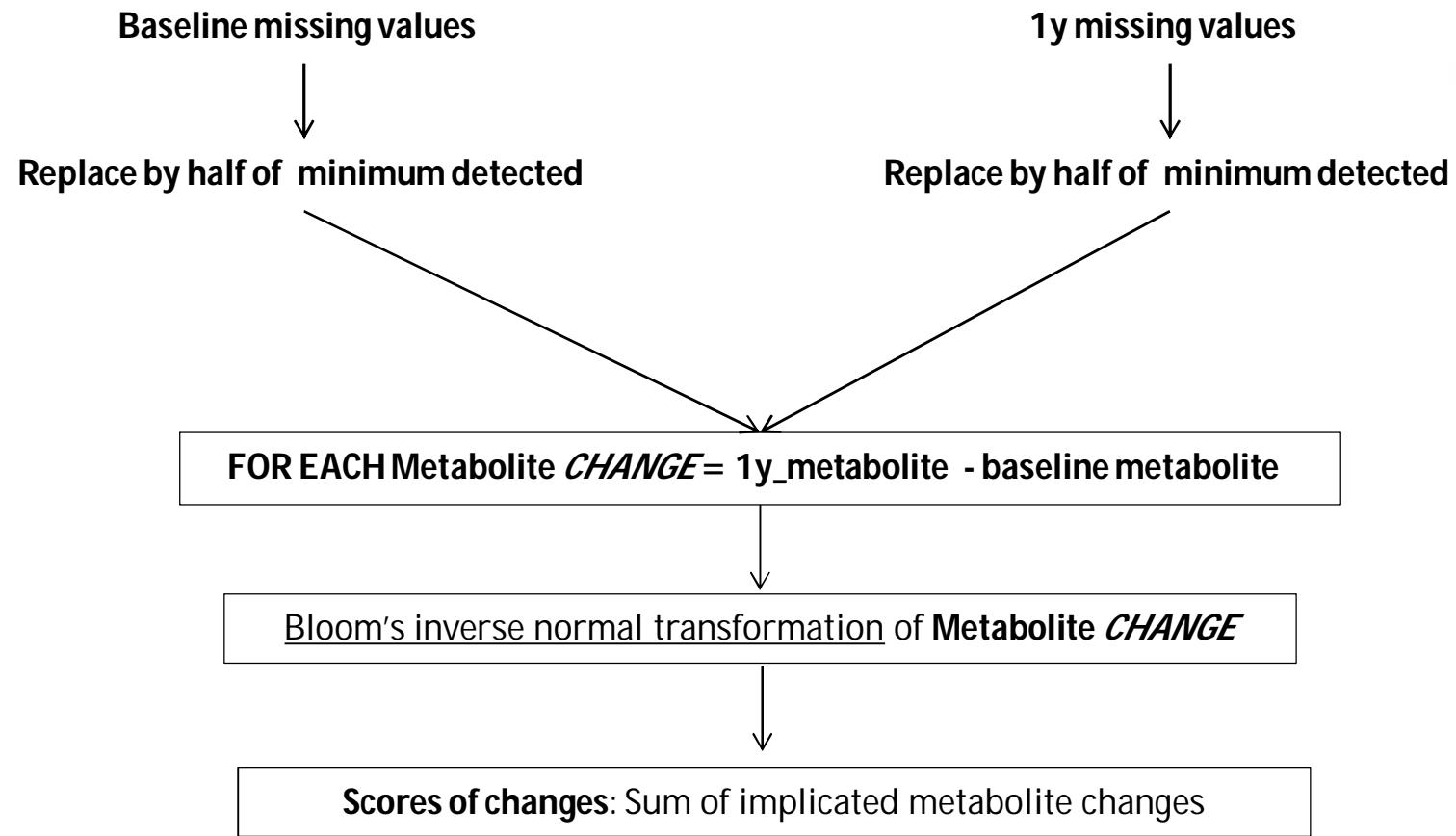
1y changes

Scores showing inverse association

	N	Q1	Quartiles of scores			Linear trend	Per SD
			Q2	Q3	Q4		
LPC_LPE	17	Ref.	0.92 (0.52-1.64)	0.86 (0.47-1.55)	0.75 (0.40-1.38)	0.311	0.87 (0.69-1.10)
PC-pl	12	Ref.	0.58 (0.33-1.03)	0.63 (0.36-1.09)	0.60 (0.33-1.08)	0.129	0.86 (0.71-1.05)
SM	11	Ref.	0.95 (0.54-1.70)	0.97 (0.55-1.72)	0.63 (0.34-1.19)	0.203	0.86 (0.70-1.06)
CE	12	Ref.	0.79 (0.45-1.38)	0.71 (0.40-1.25)	0.85 (0.47-1.53)	0.616	0.81 (0.64-1.01)
Inverse score w/o CER	50	Ref.	0.70 (0.39-1.23)	0.68 (0.37-1.22)	**0.49 (0.26-0.94)**	**0.039**	**0.76 (0.61-0.94)**

LPC:LysoPhosphatidylCholines; LPE:LysoPhosphatidylEthanolamines; PC-pl:PhosphatidylCholines-plasmalogens;
CER:ceramides; SM:sphingomyelines; CE:cholesterol esters.

Cox model adjusted for: age, sex, intervention group, **baseline score**

1y changes

Scores showing inverse association
Multivariable model

	N	Q1	Quartiles of scores			Linear trend	Per SD
			Q2	Q3	Q4		
LPC_LPE	17	Ref.	1.01 (0.55-1.87)	0.99 (0.53-1.83)	0.73 (0.36-1.44)	0257	0.86 (0.68-1.10)
PC-pl	12	Ref.	0.52 (0.28-0.95)	0.63 (0.36-1.12)	0.59 (0.33-1.08)	0.185	0.90 (0.74-1.10)
SM	11	Ref.	1.09 (0.59-1.99)	1.03 (0.56-1.88)	0.70 (0.36-1.36)	0.275	0.89 (0.72-1.11)
CE	12	Ref.	0.88 (0.49-1.60)	082 (0.45-1.47)	0.96 (0.52-1.78)	0.954	0.84 (0.67-1.06)
Inverse score w/o CER	50	Ref.	0.70 (0.39-1.26)	0.72 (0.39-1.32)	0.53 (0.27-1.04)	0.084	**0.78 (0.62-0.98)**

LPC:LysoPhosphatidylCholines; LPE:LysoPhosphatidylEthanolamines; PC-pl:PhosphatidylCholines-plasmalogens;

CER:ceramides; SM:sphingomyelines; CE:cholesterol esters.

Cox model adjusted for: age, sex, intervention group, **baseline score,** BMI, smoking, dyslipidemia and hypertension

1y changes

Scores showing inverse association
Multivariable model + baseline glucose

	N	Q1	Quartiles of scores			Linear trend	Per SD
			Q2	Q3	Q4		
LPC_LPE	17	Ref.	1.99 (0.89-4.75)	1.04 (0.45-2.49)	1.00 (0.38-2.62)	0.703	0.92 (0.67-1.26)
PC-pl	12	Ref.	0.75 (0.31-1.80)	0.80 (0.32-1.95)	0.62 (0.23-1.71)	0.451	0.85 (0.61-1.17)
SM	11	Ref.	1.23 (0.51-2.97)	1.87 (0.79-4.42)	0.68 (0.27-1.69)	0.693	0.89 (0.67-1.19)
CE	12	Ref.	1.13 (0.51-2.51)	0.78 (0.29-2.10)	1.06 (0.42-2.69)	0.916	0.81 (0.56-1.16)
Inverse score w/o CER	50	Ref.	1.16 (0.48-2.78)	1.35 (0.56-3.26)	0.64 (0.23-1.74)	0.474	0.81 (0.59-1.10)

LPC:LysoPhosphatidylCholines; LPE:LysoPhosphatidylEthanolamines; PC-pl:PhosphatidylCholines-plasmalogens;

CER:ceramides; SM:sphingomyelines; CE:cholesterol esters.

Cox model adjusted for: age, sex, intervention group, **baseline score,** BMI, smoking, dyslipidemia, hypertension, baseline glucose and baseline glucose quadratic term

1y changes

Scores showing direct association:

| | N | Q1 | Quartiles of factors | | | Linear trend | Per SD |
			Q2	Q3	Q4		
TAG	45	Ref.	0.88 (0.49-1.60)	1.02 (0.57-1.83)	1.55 (0.89-2.69)	0.102	**1.21 (1.00-1.46)**
DAG	14	Ref.	1.25 (0.70-2.23)	1.15 (0.66-2.00)	1.58 (0.90-2.78)	0.183	**1.20 (0.98-1.45)**
PE	12	Ref.	1.20 (0.68-2.10)	1.23 (0.69-2.21)	**1.84 (1.04-3.25)**	0.068	**1.25 (1.02-1.54)**
Direct score	71	Ref.	1.10 (0.62-1.97)	**1.01 (0.57-1.82)**	**1.58 (0.90-2.76)**	0.136	**1.23 (1.01-1.49)**

Cox model adjusted for: age, sex, intervention group, **baseline score**

1y changes
Scores showing direct association
Multivariable model

	N	Q1	Quartiles of factors			Linear trend	Per SD
			Q2	Q3	Q4		
TAG	45	Ref.	0.90 (0.50 -1.63)	1.03 (0.57-1.86)	1.46 (0.80-2.65)	0.216	1.19 (0.97-1.46)
DAG	14	Ref.	1.18 (0.65-2.16)	1.22 (0.69-2.15)	1.48 (0.82-2.68)	0.289	1.15 (0.94-1.98)
PE	12	Ref.	1.22 (0.69-2.16)	1.29 (0.71-2.35)	**1.84 (1.01-3.33)**	0.102	**1.25 (1.00-1.56)**
Direct score	71	Ref.	1.16 (0.64-2.10)	1.55 (0.55-1.83)	1.55 (0.85-2.84)	0.220	1.21 (0.98-1.48)

Cox model adjusted for: age, sex, intervention group, **baseline score,** BMI, smoking, dyslipidemia and hypertension

1y changes

Scores showing direct association
## Multivariable model+baseline glucose

	N	Q1	Quartiles of factors			Linear trend	Per SD
			Q2	Q3	Q4		
TAG	45	Ref.	0.99 (0.42-2.32)	1.22 (0.54-2.77)	1.58 (0.65-3.86)	0.331	1.22 (0.91-1.62)
DAG	14	Ref.	2.07 (0.85-5.04)	2.25 (0.91-5.57)	1.89 (0.75-4.77)	0.180	1.20 (0.91-1.57)
PE	12	Ref.	1.44 (0.65-3.23)	1.65 (0.68-3.96)	1.59 (0.64-3.98)	0.250	1.24 (0.91-1.67)
Direct score	71	Ref.	1.68 (0.72-3.89)	1.44 (0.64-3.26)	1.90 (0.75-4.79)	0.330	1.30 (0.93-1.64)

Cox model adjusted for: age, sex, intervention group, **baseline score,** BMI, smoking, dyslipidemia, hypertension, baseline glucose and baseline glucose quadratic term

Lipidomic patterns

- **First step: exploratory analysis:**

  1.PCA

- **Second step: hypothesis based analysis:**

  1. Scores of lipid metabolites

  2. Scores of lipid metabolite changes

- **Third step: Effects of intervention on lipid changes**

Inversely associated scores
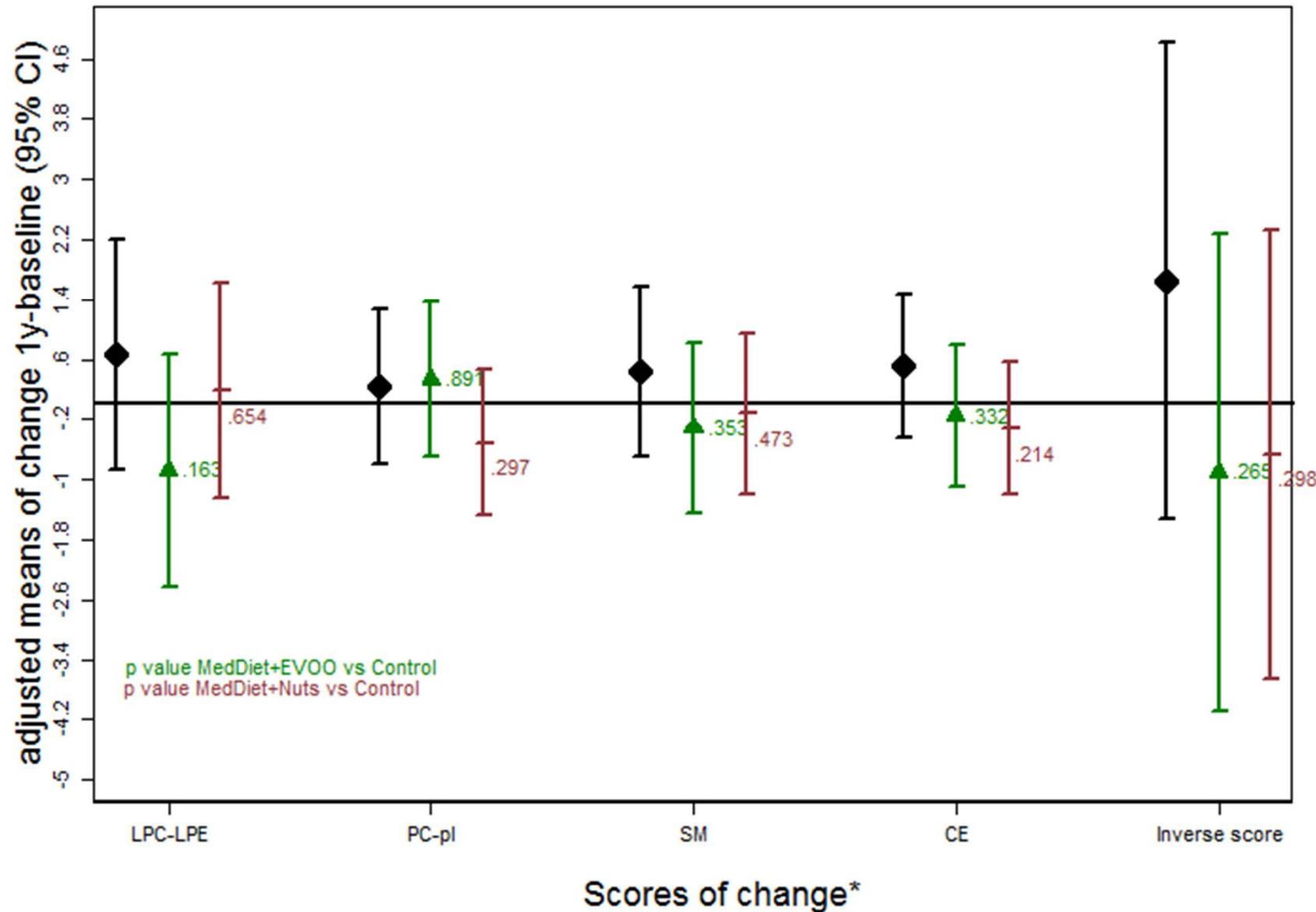
Directly associated scores
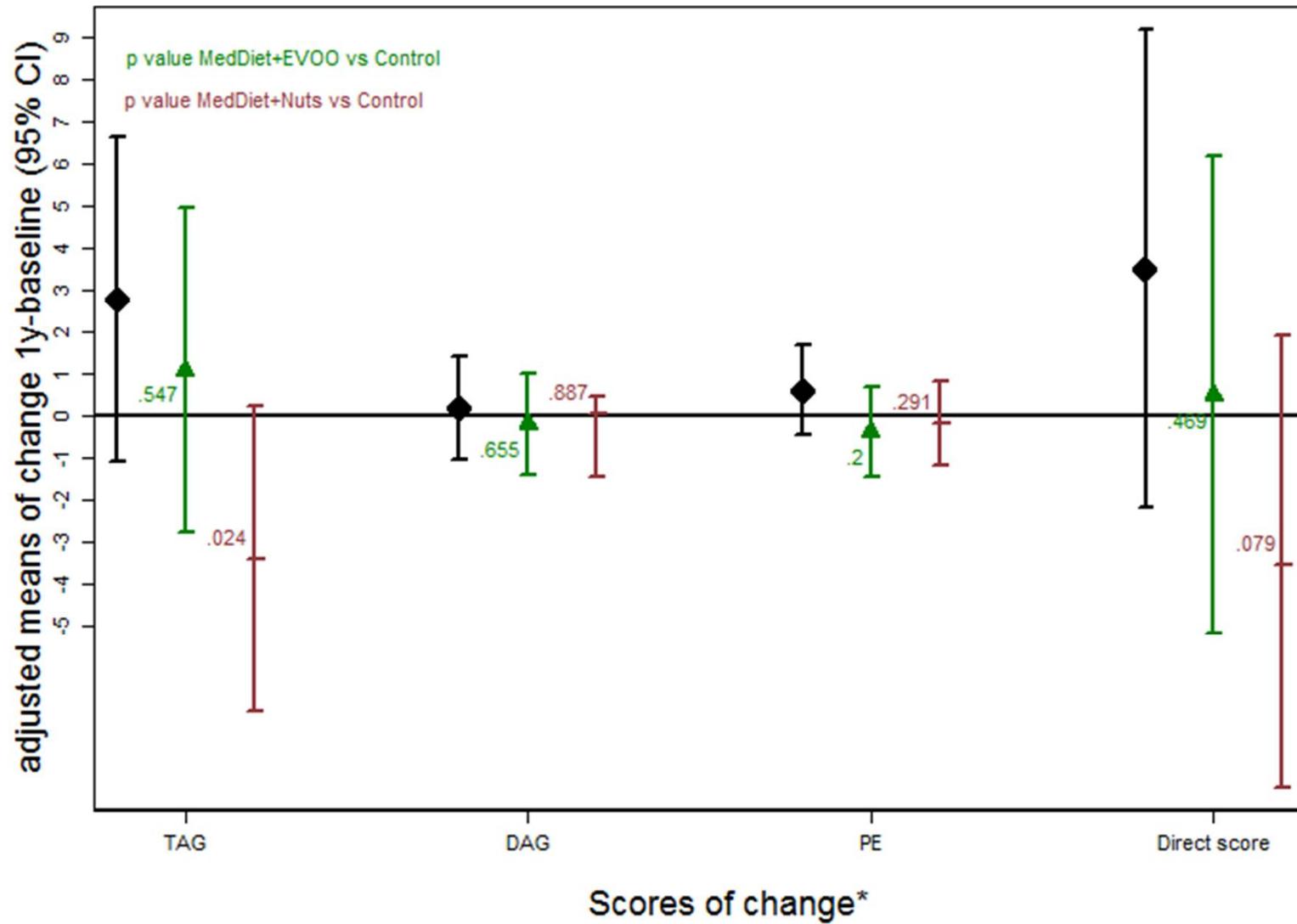
TARGETED LIPIDOMICS (2)

Lipidomic patterns and the risk of T2D

www.unav.es/preventiva

www.predimed.es

www.predimedplus.com

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