



SCHOOL OF PUBLIC HEALTH  
Department of Nutrition



# PREDIMED intervention signature:

## Metabolites describing MedDiet



Universidad  
de Navarra

[www.unav.es/preventiva](http://www.unav.es/preventiva)  
[www.predimed.es](http://www.predimed.es)  
[www.predimedplus.com](http://www.predimedplus.com)  
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*ciberobn*  
Centro de Investigación Biomédica en Red  
Fisiopatología de la Obesidad y Nutrición

## WORKING REPORT

### OBJECTIVE:

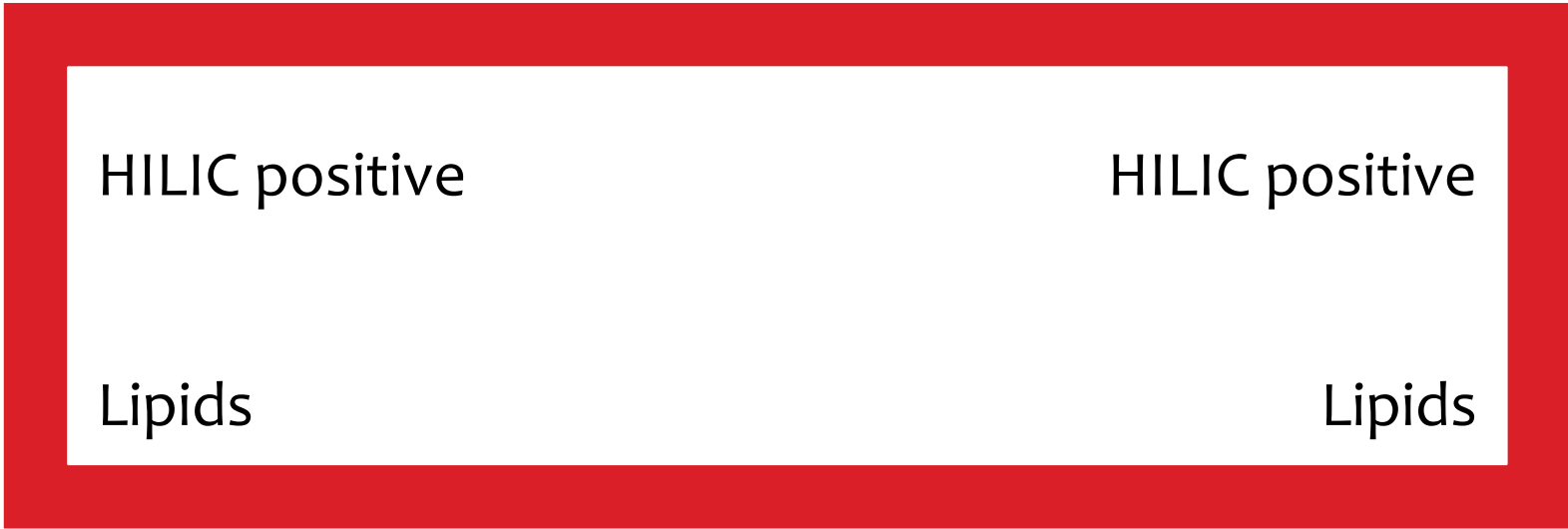
Describe the MedDiet intervention by the metabolites detected at year 1 of the PREDIMED trial.

- **Differential levels of metabolites MedDiet+EVOO vs control group**
- **Differential levels of metabolites MedDiet+Nuts vs control group**

WORKING REPORT

CVD project

T2D project



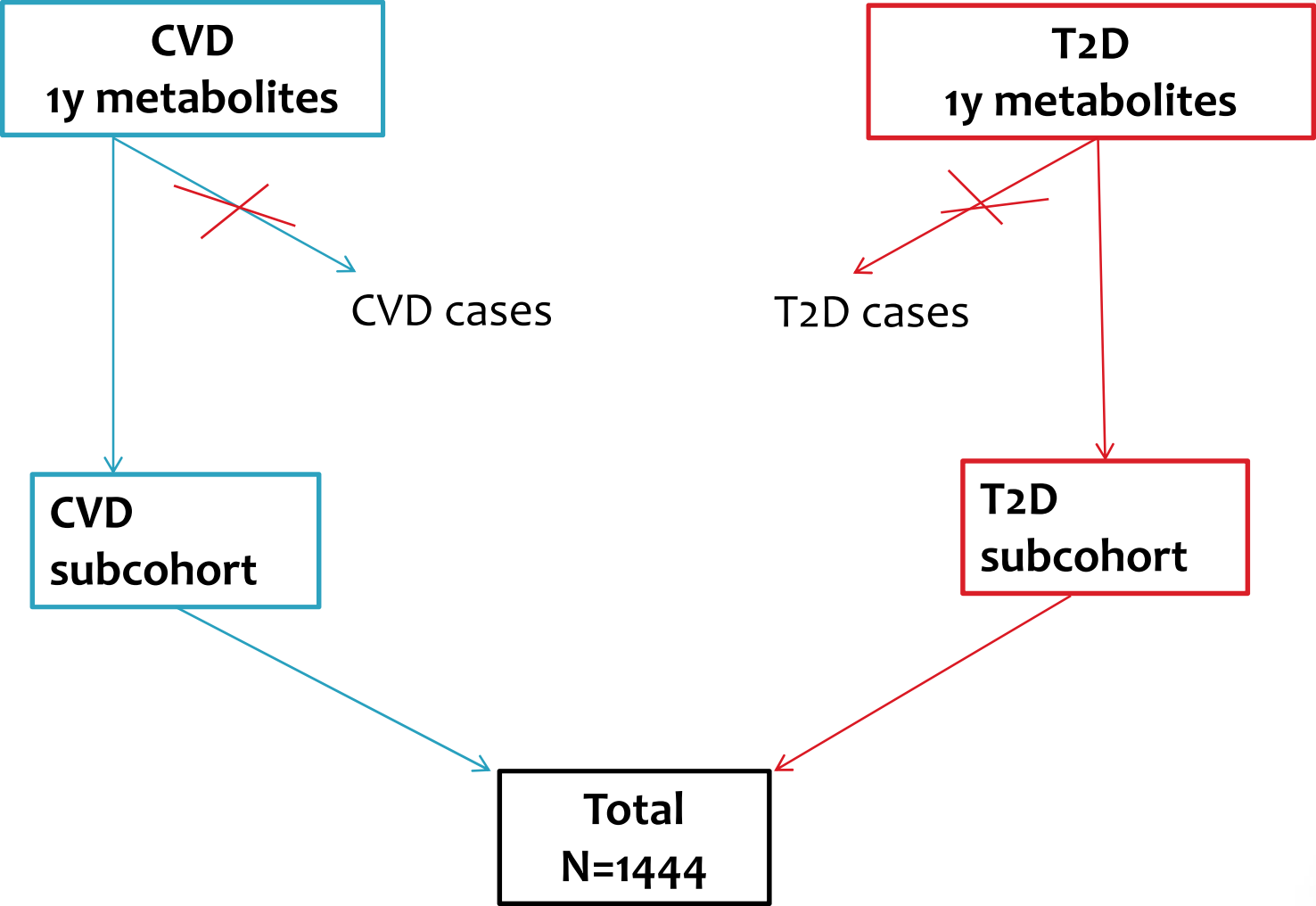
HILIC negative

HILIC negative



Shared metabolites

**WORKING REPORT**



## WORKING REPORT

### Simple first approach: Linear regression model for each metabolite

\*Replace missing values: half minimum detected (!=0)

**Dependent variable: 1y metabolite**

Independent variables:

**Baseline metabolite**

**Age**

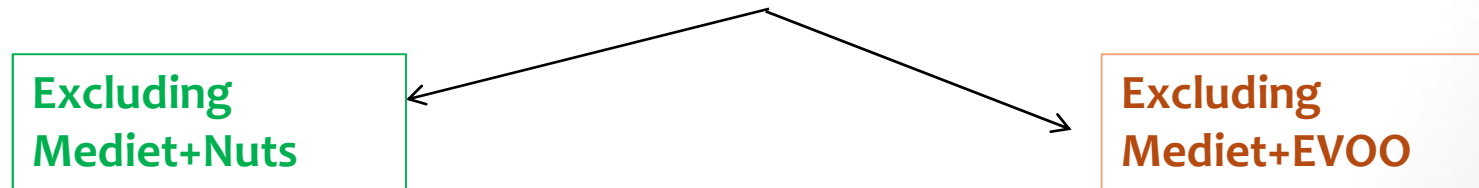
**Sex**

**CVD/T2D project measurement**

**INTERVENTION**

**Excluding  
Mediet+Nuts**

**Excluding  
Mediet+EVOO**



## MedDiet+EVOO vs control

Variable	coefficient	LCI	ULC	p
isoleucine1	-0.15	-0.25	-0.05	0.004
362pcplasmalogen1	0.1	0.03	0.17	0.006
181carnitine1	0.15	0.04	0.25	0.008
leucine1	-0.14	-0.24	-0.03	0.01
adenosine1	-0.15	-0.27	-0.03	0.015
18carnitine1	0.14	0.03	0.25	0.016
382pe1	0.1	0.02	0.17	0.016
340dag1	0.09	0.01	0.16	0.022
361peplasmalogen1	0.09	0.01	0.18	0.039
20carnitine1	0.11	0	0.23	0.044
364pcb1	-0.08	-0.15	0	0.044
161ce1	-0.07	-0.13	0	0.045
361pcplasmalogen1	0.08	0	0.16	0.046
383peplasmalogen1	0.11	0	0.21	0.046
hydroxyanthranilicacid1	-0.12	-0.24	0	0.048
valine1	-0.11	-0.21	0	0.049
406ps1	0.1	0	0.21	0.05
341pcplasmalogen1	0.06	0	0.12	0.06
4carnitine1	-0.09	-0.19	0	0.061
241sm1	0.06	0	0.13	0.063
320dag1	-0.1	-0.2	0.01	0.064
methylhistamine1	-0.1	-0.22	0.01	0.07
241ceramided1811	0.06	-0.01	0.13	0.08
142carnitine1	-0.1	-0.21	0.01	0.082
pipecolicacid1	0.11	-0.01	0.23	0.084
sarcosine1	-0.1	-0.21	0.02	0.091
342pcplasmalogen1	0.05	-0.01	0.12	0.091
tyrosine1	-0.08	-0.18	0.01	0.092
kynurenicacid1	-0.09	-0.19	0.02	0.094
180sm1	0.06	-0.01	0.13	0.097

Variable	coefficient	LCI	ULC	p
c181sm1	0.06	-0.01	0.13	0.104
histidine1	-0.09	-0.19	0.02	0.112
c3carnitine1	-0.08	-0.19	0.02	0.113
c200sm1	0.05	-0.01	0.12	0.114
c340pi1	0.07	-0.02	0.15	0.119
phosphocholine1	-0.09	-0.2	0.02	0.119
c384pc1	-0.06	-0.13	0.02	0.123
phenylalanine1	-0.08	-0.18	0.02	0.126
c205ce1	0.08	-0.02	0.19	0.133
c586tag1	-0.07	-0.16	0.02	0.14
lysine1	-0.08	-0.2	0.03	0.142
c226ce1	0.07	-0.02	0.16	0.149
c226lpc1	0.06	-0.02	0.14	0.158
c363pcplasmalogen1	0.05	-0.02	0.12	0.16
c384pe1	-0.06	-0.14	0.02	0.164
c182sm1	0.06	-0.02	0.14	0.166
c364dag1	-0.07	-0.17	0.03	0.168
c5carnitine1	-0.08	-0.18	0.03	0.172
c300dag1	-0.08	-0.19	0.04	0.177
alanine1	-0.07	-0.18	0.03	0.18
c226lpe1	0.05	-0.02	0.12	0.181
c343dag1	-0.06	-0.16	0.03	0.187
c181lpc1	0.05	-0.03	0.13	0.195
c420tag1	-0.08	-0.2	0.04	0.199
c4211peplasmalogen1	0.06	-0.03	0.15	0.209
c440tag1	-0.07	-0.19	0.04	0.212
c460tag1	-0.07	-0.19	0.04	0.215
cytosine1	-0.07	-0.19	0.04	0.218
taurine1	-0.08	-0.2	0.05	0.223
dimethylglycine1	-0.06	-0.15	0.04	0.226
c182ce1	0.06	-0.04	0.16	0.23
betaine1	0.06	-0.04	0.15	0.243
c342pe1	-0.05	-0.15	0.04	0.248

Variable	coefficient	LCI	ULC	p
carnitine1	0.07	-0.05	0.18	0.252
c224ce1	-0.06	-0.16	0.04	0.254
c181ce1	0.04	-0.03	0.11	0.254
c484tag1	-0.06	-0.17	0.04	0.256
sdma1	-0.05	-0.15	0.04	0.263
c480tag1	-0.06	-0.18	0.05	0.264
c546tag1	-0.06	-0.16	0.04	0.266
c543tag1	0.05	-0.04	0.13	0.269
c140sm1	0.04	-0.03	0.1	0.27
c340ps1	0.07	-0.05	0.18	0.271
c363pe1	-0.05	-0.14	0.04	0.272
c385pe1	-0.05	-0.13	0.04	0.278
creatine1	-0.05	-0.15	0.04	0.281
c181ohcarnitine1	0.06	-0.05	0.18	0.295
c365pcplasmalogen1	0.06	-0.05	0.17	0.295



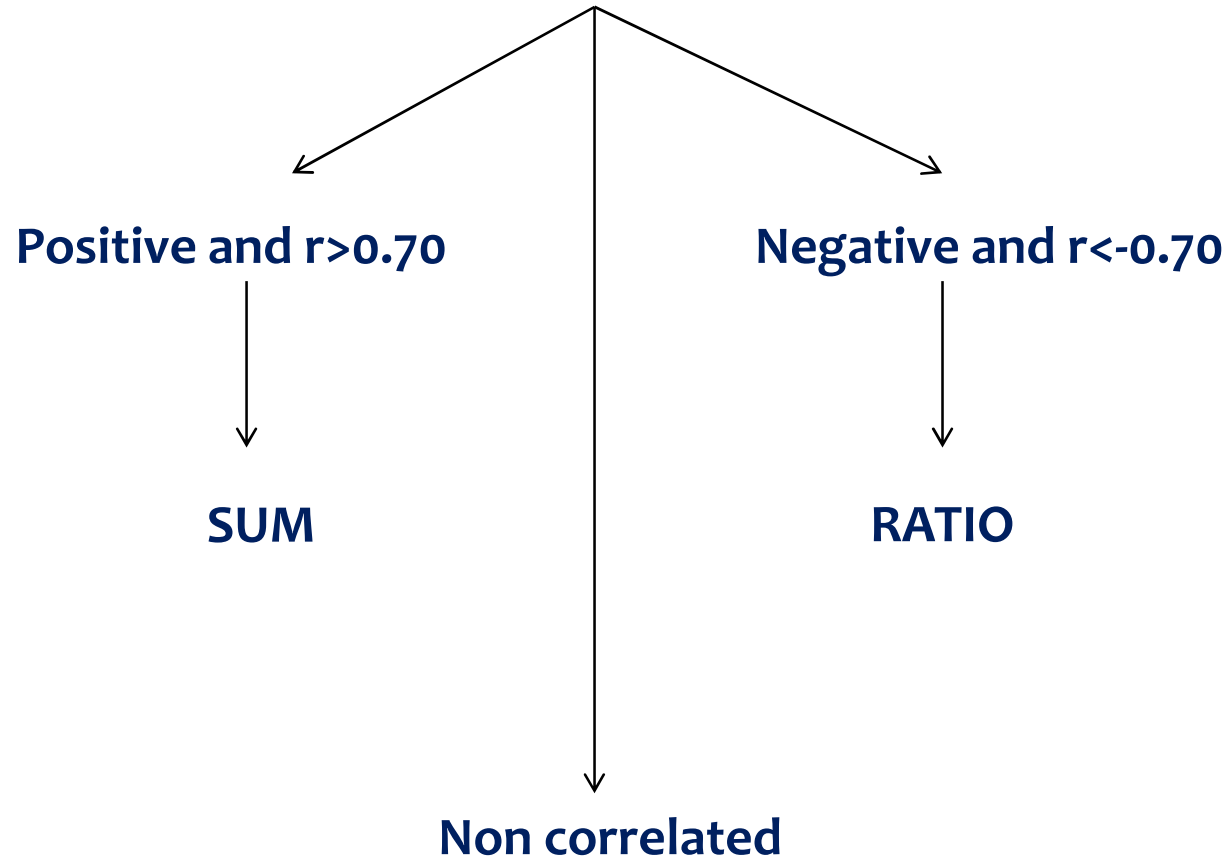
## MedDiet+Nuts vs control

Variable	coefficient	LCI	ULC	p
102carnitine1	0.12	0.06	0.18	0
161ce1	-0.07	-0.11	-0.04	0
364dag1	0.09	0.04	0.14	0
182carnitine1	0.08	0.03	0.14	0.002
182sm1	0.06	0.02	0.11	0.002
203ce1	-0.08	-0.12	-0.03	0.002
525tag1	0.08	0.03	0.13	0.002
pipecolicacid1	0.09	0.03	0.15	0.003
524tag1	0.07	0.02	0.11	0.003
343dag1	0.07	0.02	0.12	0.005
363psplasmalogen1	-0.06	-0.1	-0.02	0.005
545tag1	0.07	0.02	0.13	0.005
363dag1	0.06	0.01	0.1	0.009
343pcplasmalogen1	0.05	0.01	0.09	0.01
361psplasmalogen1	-0.05	-0.09	-0.01	0.01
406pc1	-0.05	-0.09	-0.01	0.013
343pc1	0.06	0.01	0.11	0.014
520tag1	-0.07	-0.13	-0.01	0.015
526tag1	0.05	0.01	0.09	0.017
364pca1	0.06	0.01	0.12	0.018
182lpc1	0.06	0.01	0.12	0.02
20carnitine1	0.07	0.01	0.12	0.021
5410tag1	0.05	0.01	0.09	0.022
182ce1	0.06	0.01	0.11	0.023
383peplasmalogen1	0.06	0.01	0.12	0.029
181carnitine1	0.06	0.01	0.12	0.03
364pcb1	-0.04	-0.08	0	0.032
382pe1	0.04	0	0.08	0.033
340pi1	0.04	0	0.09	0.035
544tag1	0.05	0	0.1	0.039
383pc1	-0.05	-0.09	0	0.04
361pc1	-0.04	-0.09	0	0.042
182lpe1	0.04	0	0.08	0.044
362psplasmalogen1	0.05	0	0.09	0.045
406ps1	-0.05	-0.11	0	0.049

Variable	coefficient	LCI	ULC	p
547tag1	0.04	0	0.08	0.051
341pc1	-0.04	-0.08	0	0.052
225ce1	-0.05	-0.1	0	0.055
xanthosine1	-0.05	-0.1	0	0.059
342pc1	0.04	0	0.08	0.063
18carnitine1	0.05	0	0.11	0.064
methylhistamine1	-0.06	-0.12	0	0.066
tryptophan1	0.05	0	0.09	0.07
362pcplasmalogen1	0.03	0	0.07	0.071
363pcplasmalogen1	0.03	0	0.07	0.072
548tag1	0.05	0	0.11	0.074
betaalanine1	0.05	-0.01	0.11	0.078
183ce1	0.04	-0.01	0.1	0.08
588tag1	-0.05	-0.1	0.01	0.083
321pc1	-0.04	-0.09	0.01	0.083
505tag1	0.05	-0.01	0.1	0.085
205lpc1	0.05	-0.01	0.1	0.088
362pc1	0.03	0	0.07	0.089
hydroxyanthranilicacid1	-0.05	-0.11	0.01	0.094
322pc1	0.04	-0.01	0.1	0.094
384pc1	-0.03	-0.08	0.01	0.094
51carnitine1	-0.04	-0.1	0.01	0.098
460tag1	-0.05	-0.11	0.01	0.099
586tag1	-0.04	-0.09	0.01	0.105
reatine1	-0.04	-0.09	0.01	0.106
204ce1	-0.03	-0.08	0.01	0.107
226ce1	-0.04	-0.09	0.01	0.108
161sm1	0.02	-0.01	0.06	0.122
480tag1	-0.04	-0.1	0.01	0.124
4carnitine1	-0.04	-0.08	0.01	0.131
386pc1	-0.03	-0.08	0.01	0.141
240sm1	0.03	-0.01	0.07	0.141
161lpc1	-0.04	-0.1	0.02	0.144
409pc1	-0.03	-0.08	0.01	0.146
363peplasmalogen1	0.03	-0.01	0.07	0.146
140sm1	-0.02	-0.05	0.01	0.149

Variable	coefficient	LCI	ULC	p
adenosine1	-0.04	-0.1	0.02	0.16
364pe1	-0.03	-0.08	0.01	0.162
440tag1	-0.04	-0.1	0.02	0.167
500tag1	-0.04	-0.09	0.02	0.171
320dag1	-0.04	-0.09	0.02	0.172
504tag1	0.03	-0.01	0.08	0.173
362pe1	0.03	-0.01	0.07	0.177
glutamine1	-0.04	-0.09	0.02	0.179
glutamate1	0.04	-0.02	0.09	0.181
546tag1	0.04	-0.02	0.09	0.181
384pcplasmalogen1	-0.03	-0.07	0.01	0.185
220sm1	0.03	-0.01	0.06	0.188
561tag1	-0.04	-0.09	0.02	0.188
valined81	0.04	-0.02	0.09	0.192
343peplasmalogen1	0.03	-0.02	0.08	0.193
pyroglutamicacid1	-0.04	-0.09	0.02	0.193
562tag1	-0.03	-0.08	0.02	0.195
otinine1	-0.02	-0.06	0.01	0.21
180lpe1	0.03	-0.02	0.07	0.219
ornithine1	0.03	-0.02	0.09	0.222
587tag1	-0.03	-0.09	0.02	0.224
382pc1	-0.03	-0.07	0.02	0.227
5811tag1	0.03	-0.02	0.09	0.232
420tag1	-0.04	-0.1	0.02	0.234
3carnitine1	-0.03	-0.08	0.02	0.234
569tag1	0.03	-0.02	0.09	0.234
240ceramided1811	0.02	-0.01	0.06	0.235
serine1	0.03	-0.02	0.08	0.236
224ce1	-0.03	-0.08	0.02	0.237
363pe1	0.03	-0.02	0.07	0.238
200sm1	0.02	-0.01	0.05	0.239
181ce1	-0.02	-0.06	0.01	0.241
140ce1	-0.02	-0.06	0.02	0.243
364peplasmalogen1	0.03	-0.02	0.08	0.246
549tag1	0.03	-0.02	0.08	0.248

**Correlations between metabolites**



## WORKING REPORT

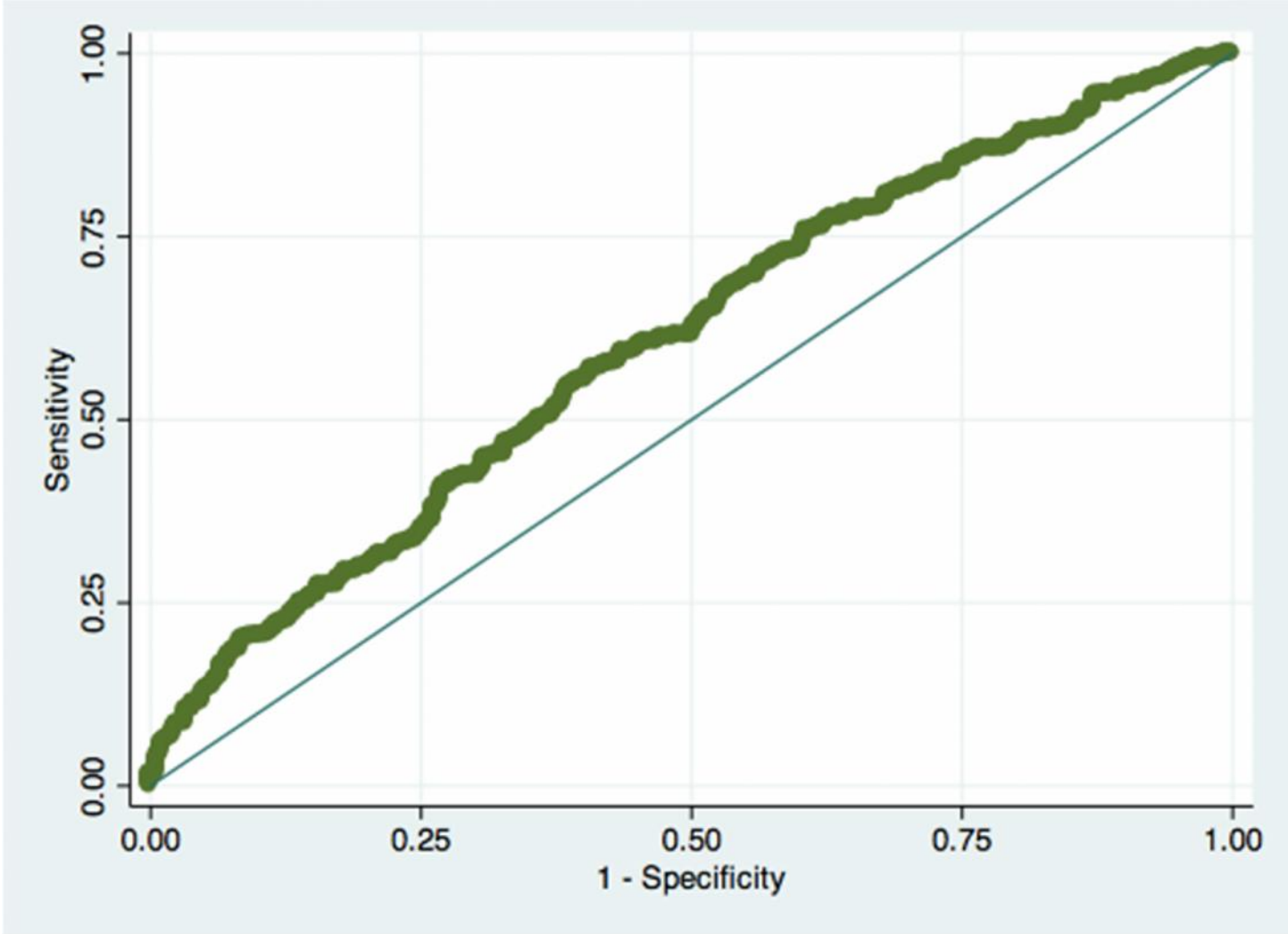
### Logistic regression model for MedDiet+EVOO vs control

- Sums of positively correlated metabolites
- Ratios of negatively correlated metabolites
- Non correlated
- CVD/T2D project measurement

MedDiet+EVOO vs control		coefficient	LCI	ULC	p
BCAA		-0.015	-0.089	0.059	0.682
PCP		-0.200	-0.448	0.049	0.115
<b>G1</b>		<b>0.085</b>	<b>0.016</b>	<b>0.154</b>	<b>0.016</b>
dag_tag		-0.025	-0.061	0.012	0.187
car		0.000	-0.075	0.075	0.991
sm		0.036	-0.011	0.082	0.13
G3		0.035	-0.013	0.084	0.154
G6		0.002	-0.046	0.050	0.924
181carnitine1		0.016	-0.230	0.262	0.898
362pcplasmalogen1		0.638	-0.189	1.465	0.13
18carnitine1		0.175	-0.034	0.384	0.101
adenosine1		-0.083	-0.252	0.086	0.333
hydroxyanthranilicacid1		-0.017	-0.189	0.154	0.842
20carnitine1		0.114	-0.079	0.307	0.246
methylhistamine1		0.001	-0.165	0.168	0.987
142carnitine1		-0.060	-0.274	0.155	0.584
181ohcarnitine1		0.014	-0.200	0.229	0.895
<b>sarcosine1</b>		<b>-0.252</b>	<b>-0.430</b>	<b>-0.073</b>	<b>0.006</b>
<b>pipecolicacid1</b>		<b>0.191</b>	<b>0.037</b>	<b>0.345</b>	<b>0.015</b>
histidine1		-0.031	-0.213	0.150	0.737
phenylalanine1		0.040	-0.262	0.343	0.794
phosphocholine1		-0.110	-0.283	0.063	0.211
lysine1		-0.119	-0.326	0.087	0.258
364dag1		-0.096	-0.359	0.167	0.472
alanine1		0.065	-0.145	0.275	0.546
224ce1		-0.131	-0.327	0.065	0.19
taurine1		-0.068	-0.239	0.104	0.44
cytosine1		0.000	-0.162	0.162	1
dimethylglycine1		-0.082	-0.272	0.107	0.395
arnitine1		0.085	-0.074	0.245	0.295
182ce1		0.008	-0.235	0.250	0.95
reatine1		-0.036	-0.207	0.135	0.679
betaine1		0.128	-0.082	0.338	0.233
sdma1		-0.093	-0.297	0.111	0.371

241ceramided181  
 C226lpe  
 406ps1  
 200sm1  
 241sm1  
 181ce1  
 342pcplasmalogen1  
 342dag1

# WORKING REPORT



**AUC: 0.603; CI95% 0.570-0.637**

## WORKING REPORT

### Logistic regression model for MedDiet+Nuts vs control

- Sums of positively correlated metabolites
- Ratios of negatively correlated metabolites
- Non correlated
- CVD/T2D project measurement

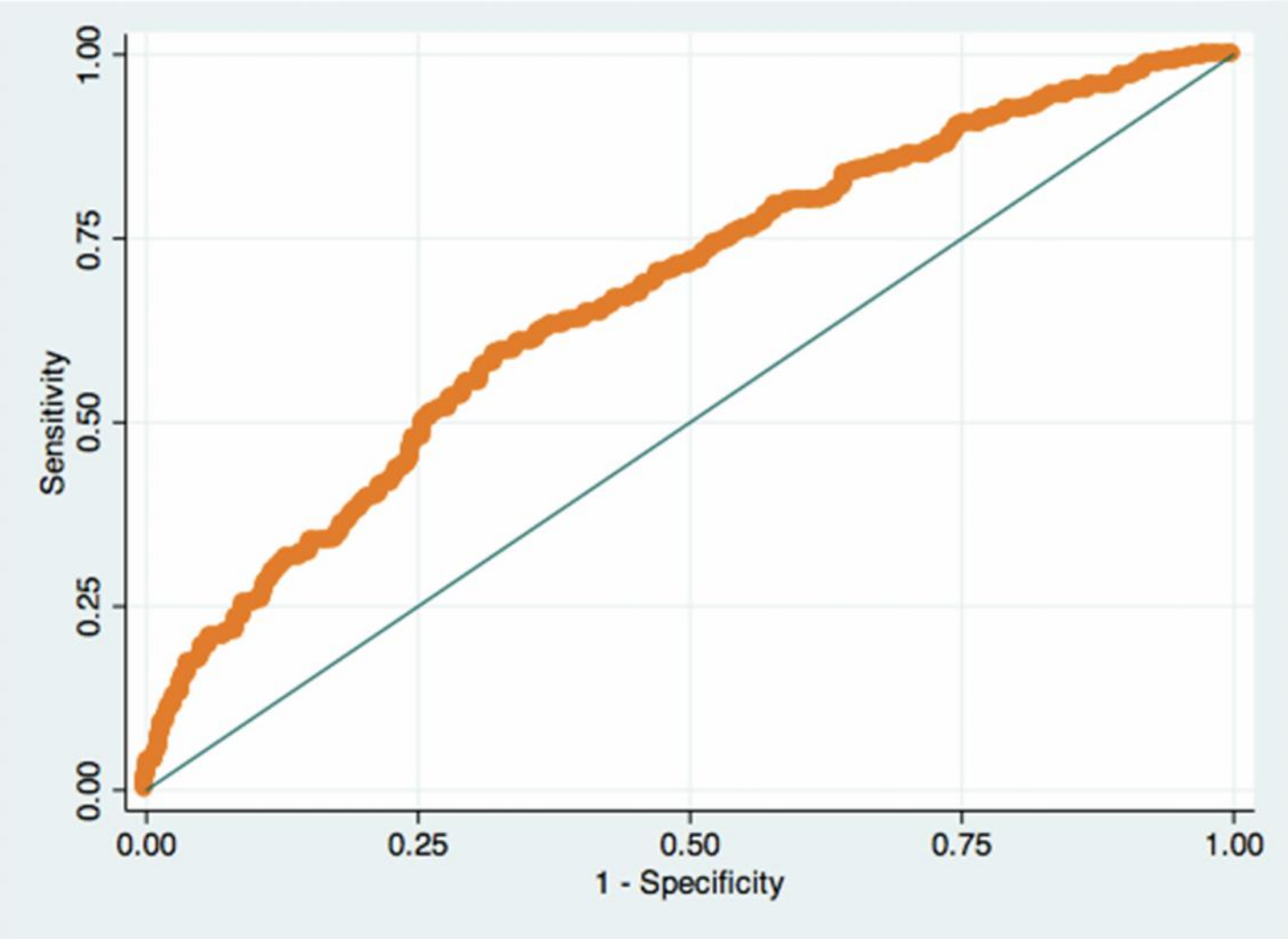


MedDiet+nuts vs control	coefficient	LCI	ULC	p
GN1	0.056	-0.059	0.172	0.339
GN2	-0.009	-0.047	0.030	0.660
<b>GN3</b>	<b>0.016</b>	<b>0.000</b>	<b>0.033</b>	<b>0.055</b>
<b>GN4</b>	<b>-0.022</b>	<b>-0.043</b>	<b>-0.001</b>	<b>0.042</b>
GN6	0.114	-0.023	0.252	0.103
<b>pipecolicacid1</b>	<b>0.300</b>	<b>0.136</b>	<b>0.464</b>	<b>0.000</b>
182carnitine1	-0.022	-0.298	0.254	0.875
363psplasmalogen1	-0.018	-0.203	0.167	0.847
181carnitine1	0.179	-0.086	0.444	0.184
20carnitine1	0.075	-0.108	0.259	0.419
51carnitine1	-0.155	-0.347	0.037	0.113
182ce1	0.142	-0.124	0.409	0.294
hydroxyanthranilicacid1	0.083	-0.095	0.260	0.361
<b>34opi1</b>	<b>0.271</b>	<b>0.004</b>	<b>0.537</b>	<b>0.047</b>
18carnitine1	0.041	-0.171	0.253	0.706
182lpc1	0.029	-0.287	0.346	0.856
383peplasmalogen1	0.134	-0.071	0.339	0.200
4carnitine1	-0.065	-0.278	0.149	0.551
reatine1	-0.079	-0.252	0.094	0.371
methylhistamine1	-0.048	-0.214	0.118	0.573
140sm1	0.064	-0.224	0.353	0.662
adenosine1	-0.041	-0.202	0.121	0.622
itrulline1	0.028	-0.150	0.205	0.761
205lpc1	-0.025	-0.284	0.234	0.850
serine1	0.115	-0.071	0.302	0.226
3carnitine1	0.034	-0.190	0.257	0.767
<b>301pc1</b>	<b>0.360</b>	<b>0.055</b>	<b>0.665</b>	<b>0.021</b>
cotinine1	-0.104	-0.271	0.064	0.225
glutamate1	0.036	-0.172	0.245	0.732
ornithine1	0.043	-0.162	0.249	0.679
224ce1	0.053	-0.156	0.262	0.620
161lpc1	-0.477	-0.723	-0.230	0.000
glutamine1	-0.095	-1.766	1.576	0.911
pyroglutamicacid1	-0.172	-1.836	1.492	0.839
methionine1	-0.012	-0.224	0.200	0.908
betaine1	0.046	-0.140	0.233	0.626

GN3:  
TAG  
DAG  
PC } >4 double b

GN4:  
Sphingomyelins  
CE>2 double b  
PC> 1 double b  
PC-plasmalogens  
PE-plasmalogens

# WORKING REPORT



**AUC: 0.667; CI95% 0.633-0.700**

**Working in new approaches (3<sup>rd</sup> T2D method):  
Expert in mathematics/statistics of the University of  
Navarra**

**-Classification models**

**- Other methods: discriminant...**



SCHOOL OF PUBLIC HEALTH  
Department of Nutrition



# PREDIMED intervention signature:

## Metabolites describing MedDiet



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