



HAL
open science

Targeted and non-targeted lipidomic analysis of adipose tissue from general population to identify metabolic perturbations related to phthalate exposure

Axel Raux, Celia Pérez-Díaz, Hanne Frederiksen, Francisco Miguel Pérez-Carrascosa, Yann Guitton, Germán Cano-Sancho, Juan Pedro Arrebola

► **To cite this version:**

Axel Raux, Celia Pérez-Díaz, Hanne Frederiksen, Francisco Miguel Pérez-Carrascosa, Yann Guitton, et al.. Targeted and non-targeted lipidomic analysis of adipose tissue from general population to identify metabolic perturbations related to phthalate exposure. 16èmes Journées Scientifiques du RFMF, Jun 2024, Saint Malo, France. <hal-04905386>

HAL Id: hal-04905386

<https://hal.science/hal-04905386v1>

Submitted on 22 Jan 2025

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons CC BY 4.0 - Attribution - International License

Targeted and non-targeted lipidomic analysis of adipose tissue from general population to identify metabolic perturbations related to phthalate exposure



Axel RAUX^{a,b}, Celia PÉREZ-DÍAZ^{c,d}, Hanne FREDERIKSEN^{e,f}, Francisco Miguel PÉREZ-CARRASCOSA^c, Yann GUITTON^{a,b}, German CANO-SANCHO^a, Juan-Pedro ARREBOLA^{c,d,g}



^a Oniris, INRAE, LABERCA UMR1329, 44037 Nantes, France

^b INRAE, MetaboHUB-Grand-Ouest

^c Granada University. Department of Preventive Medicine and Public Health, Pharmacy School. Campus de Cartuja s/n, 18071, Granada, Spain

^d Instituto de Investigación Biosanitaria (ibs.GRANADA). Avda. de Madrid, 15. Pabellón de Consultas Externas 2, 2ª Planta, 18012, Granada, Spain

^e Department of Growth and Reproduction. Copenhagen Univ Hosp, Rigshospitalet, Blegdamsvej 9, 2100, Copenhagen, Denmark.

^f International Center for Research and Research Training in Endocrine Disruption of Male Reproduction and Child Health (EDMaRC), Copenhagen Univ Hosp, Rigshospitalet, Blegdamsvej 9, 2100, Copenhagen, Denmark

^g Consortium for Biomedical Research in Epidemiology and Public Health (CIBERESP), Instituto de Salud Carlos III, C/ Monforte de Lemos 3-5, Pabellón 11. Planta 0, 28029, Madrid, Spain



INTRODUCTION

Phthalates are ubiquitous chemical environmental pollutants classified as endocrine disruptors, they are used as plasticizers in different industry applications. In the last decades, some restrictive policies have reduced their use in the industry, but it remains high. They have been associated with obesity, oxidative stress, diabetes or cancer. Adipose tissue dysfunction plays a relevant role in metabolic disorders, however few studies have applied lipidomic analysis to explore the potential associations between environmental chemicals and dysfunctional phenotypes. Neither have these changes been related to different diseases in the long term.

The **objective** of this study was to develop and apply a lipidomic workflow to explore the associations between exposure to phthalates and altered lipid profiles in adipose tissue of general population.

RESULTS AND DISCUSSION

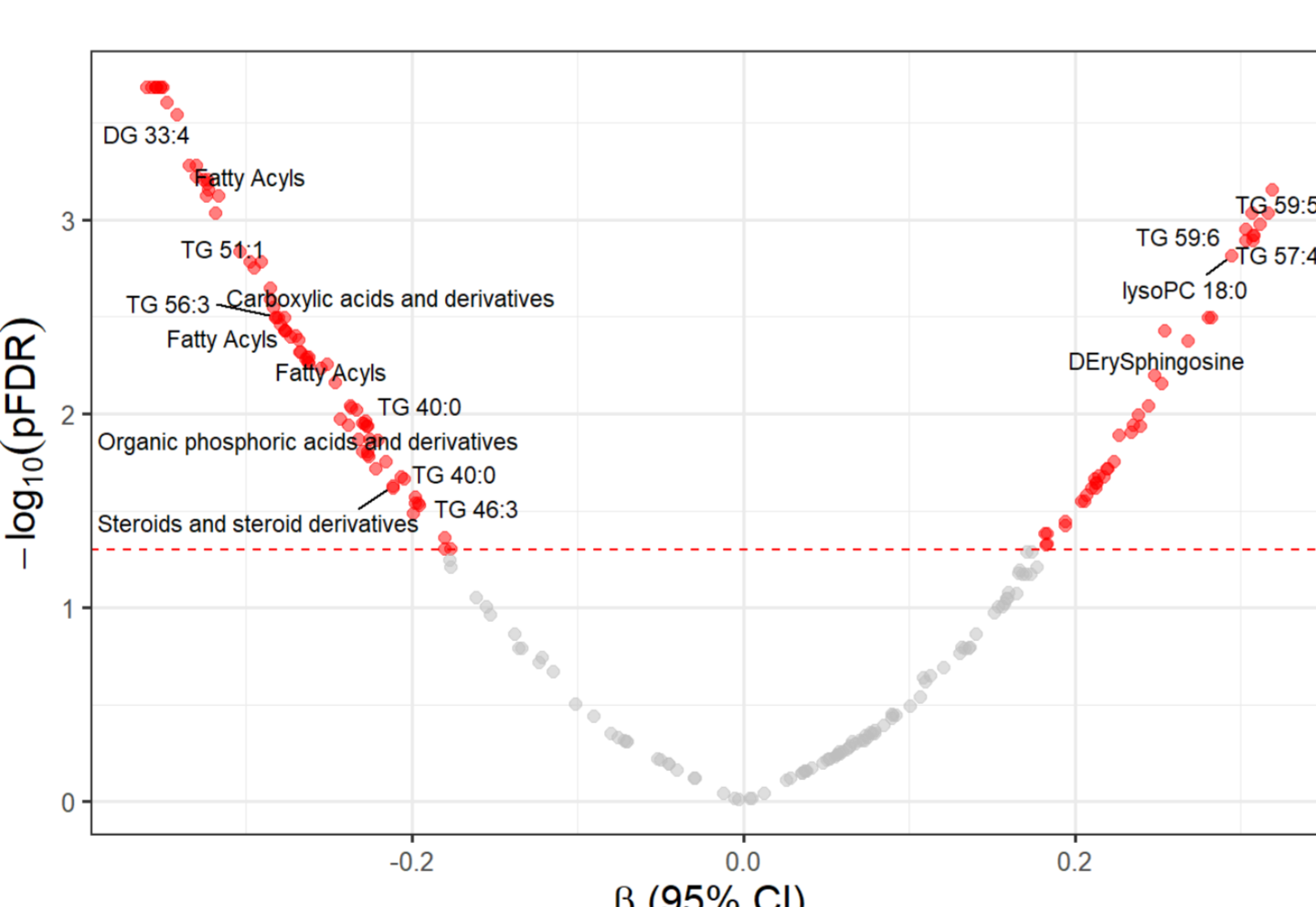
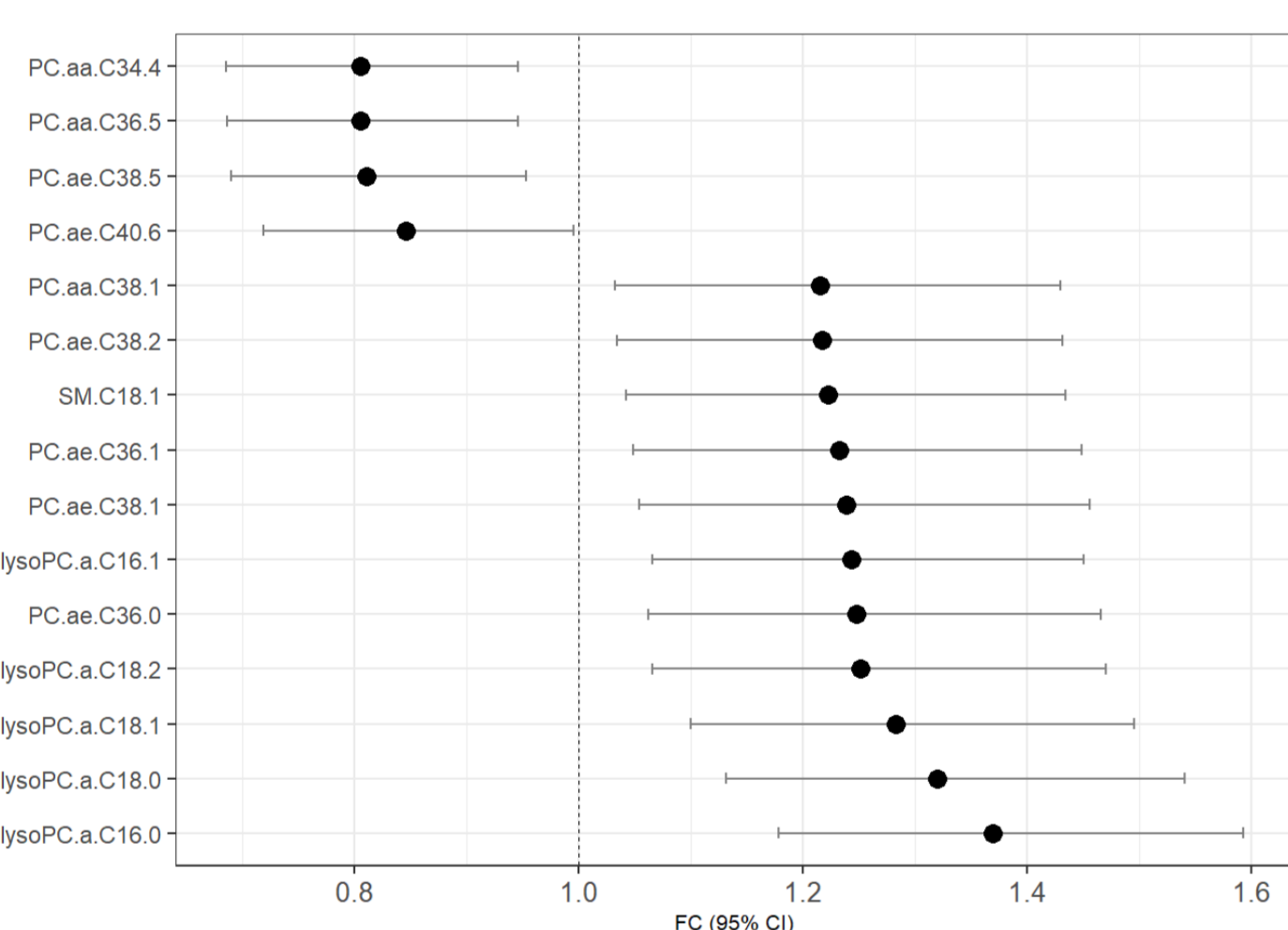
Low molecular weight phthalates MnBP and MiBP (Σ MxBP) were associated with a specific lipidomic profil

Targeted metabolomics:

15 metabolites were selected based on PLSDA-VIP and all of them were statistically associated with Σ MxBP in adjusted regression models.

Non-targeted metabolomics:

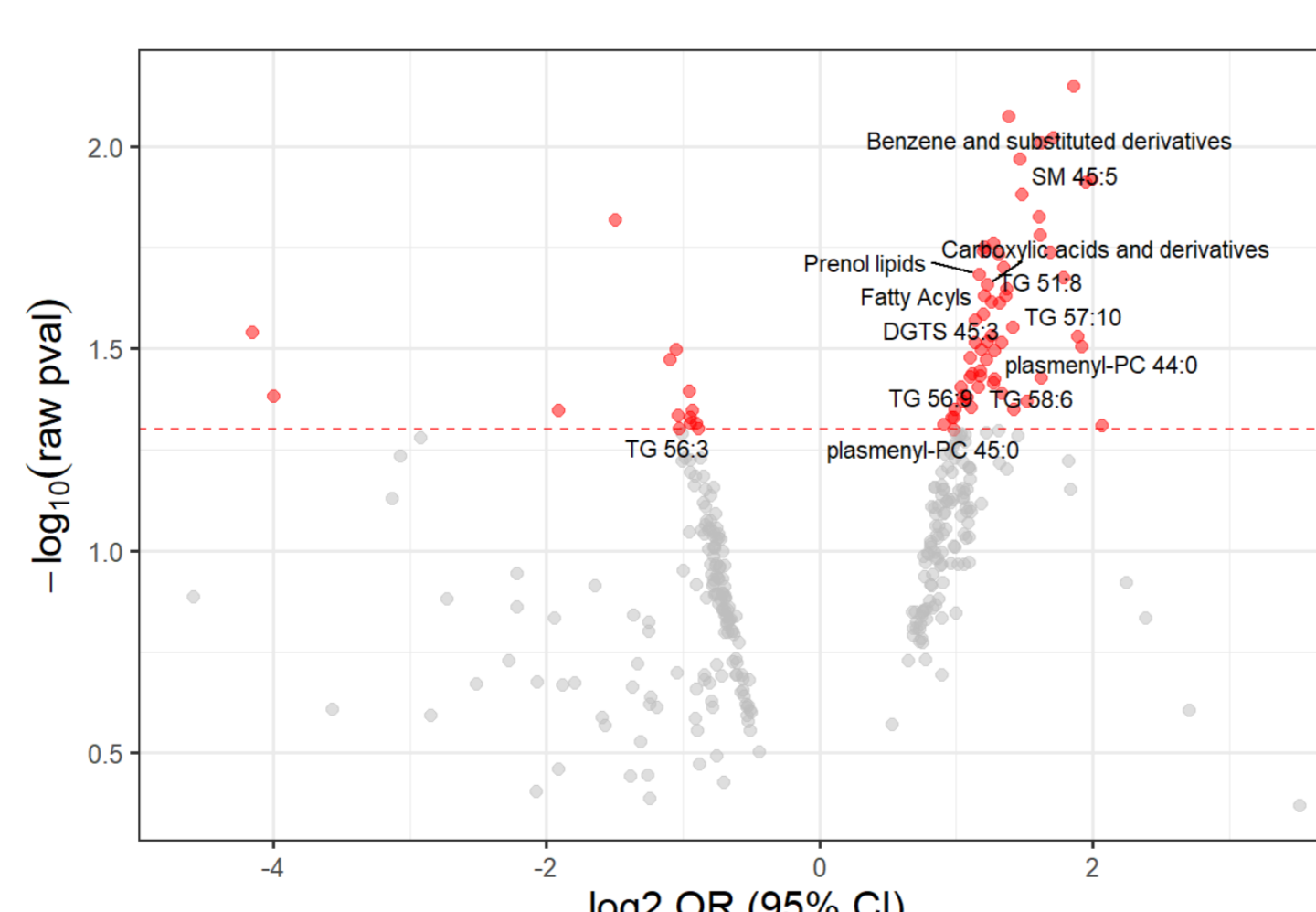
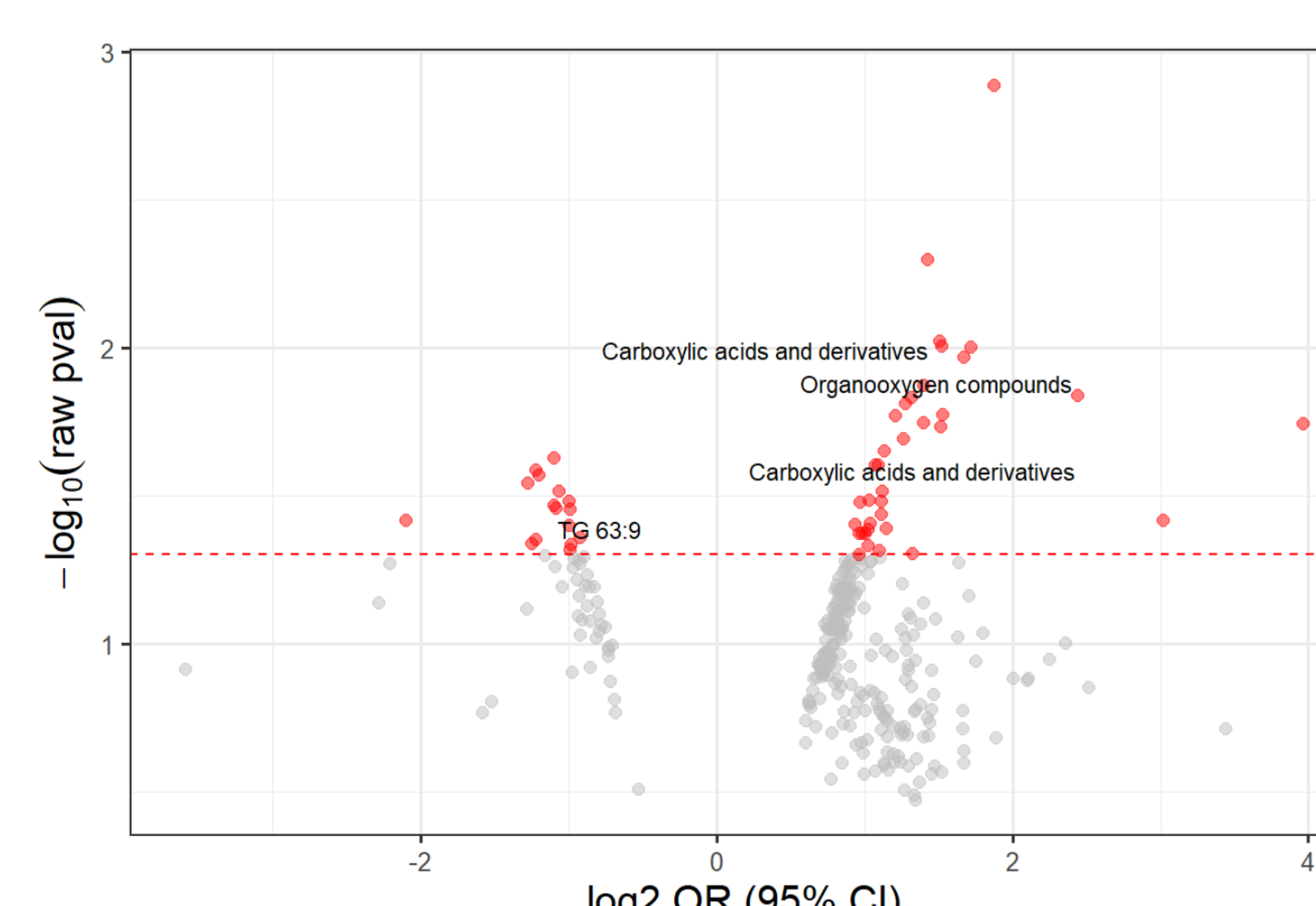
216 signals were selected based on PLSDA-VIP and a total of 119 were statistically associated with Σ MxBP, 17 of them were annotated as fatty acids.



Non-targeted lipidomics revealed a lipid signature in fat associated with hypercholesterolaemia at 20-years

Elevated LDL levels:

Reduced HDL levels:

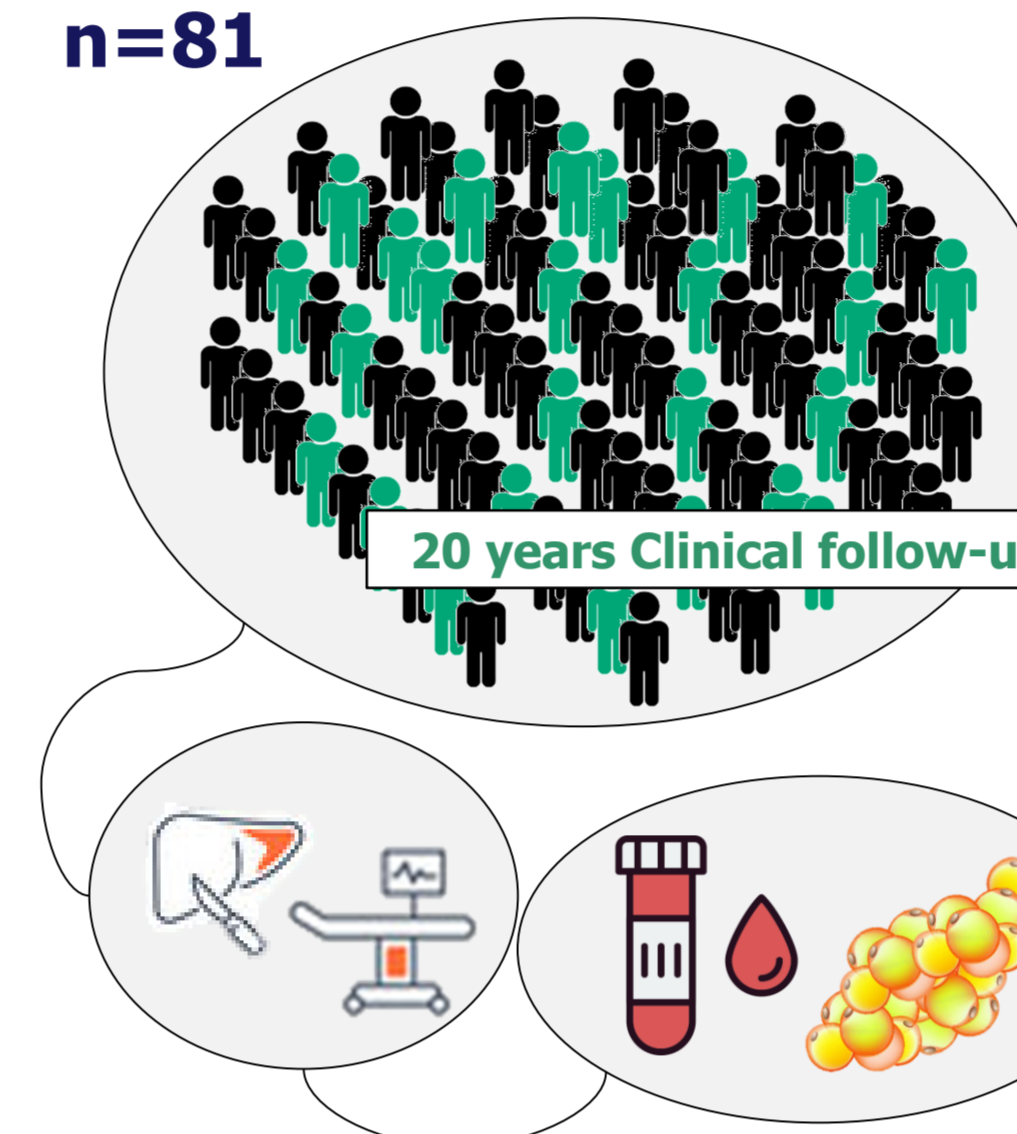


In the non-targeted multivariable logistic analysis, different associations were found between signals and plasma lipid alterations at 20 years of follow-up. Seven of the positive associations found between the signals and the high levels of LDL were also found for the signals and the phthalates.

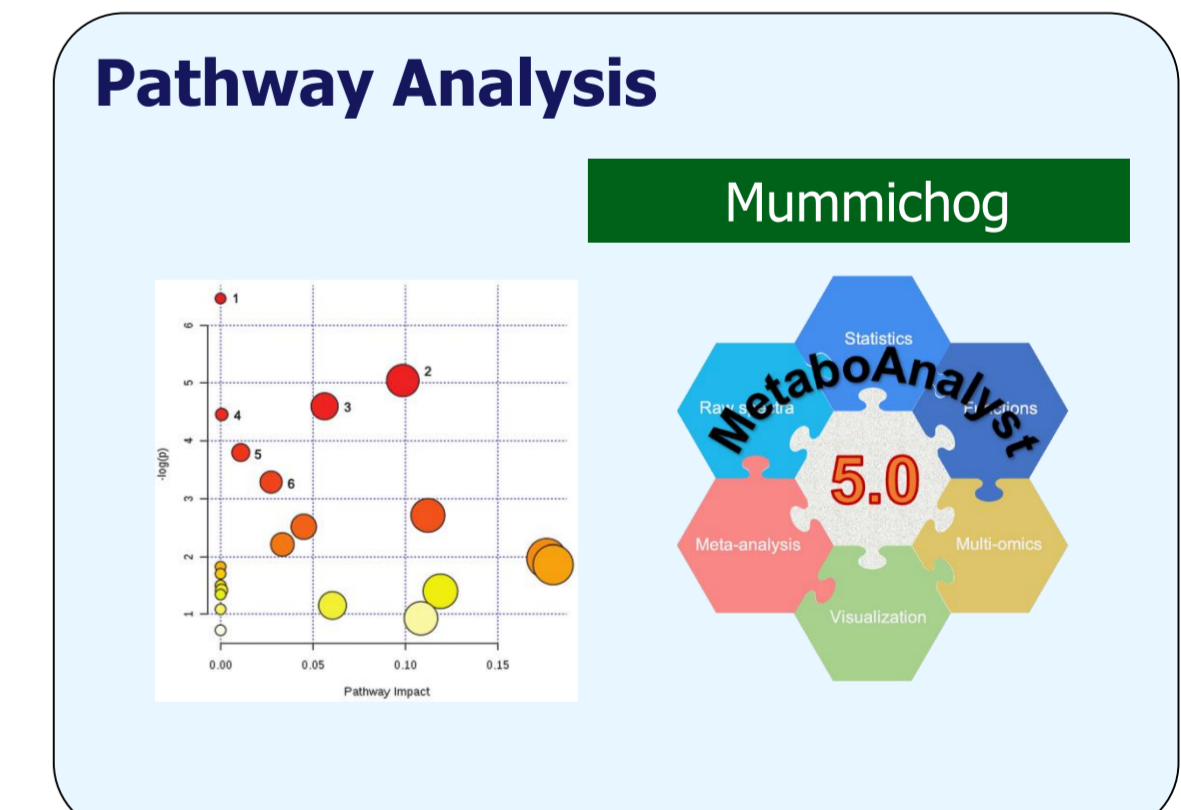
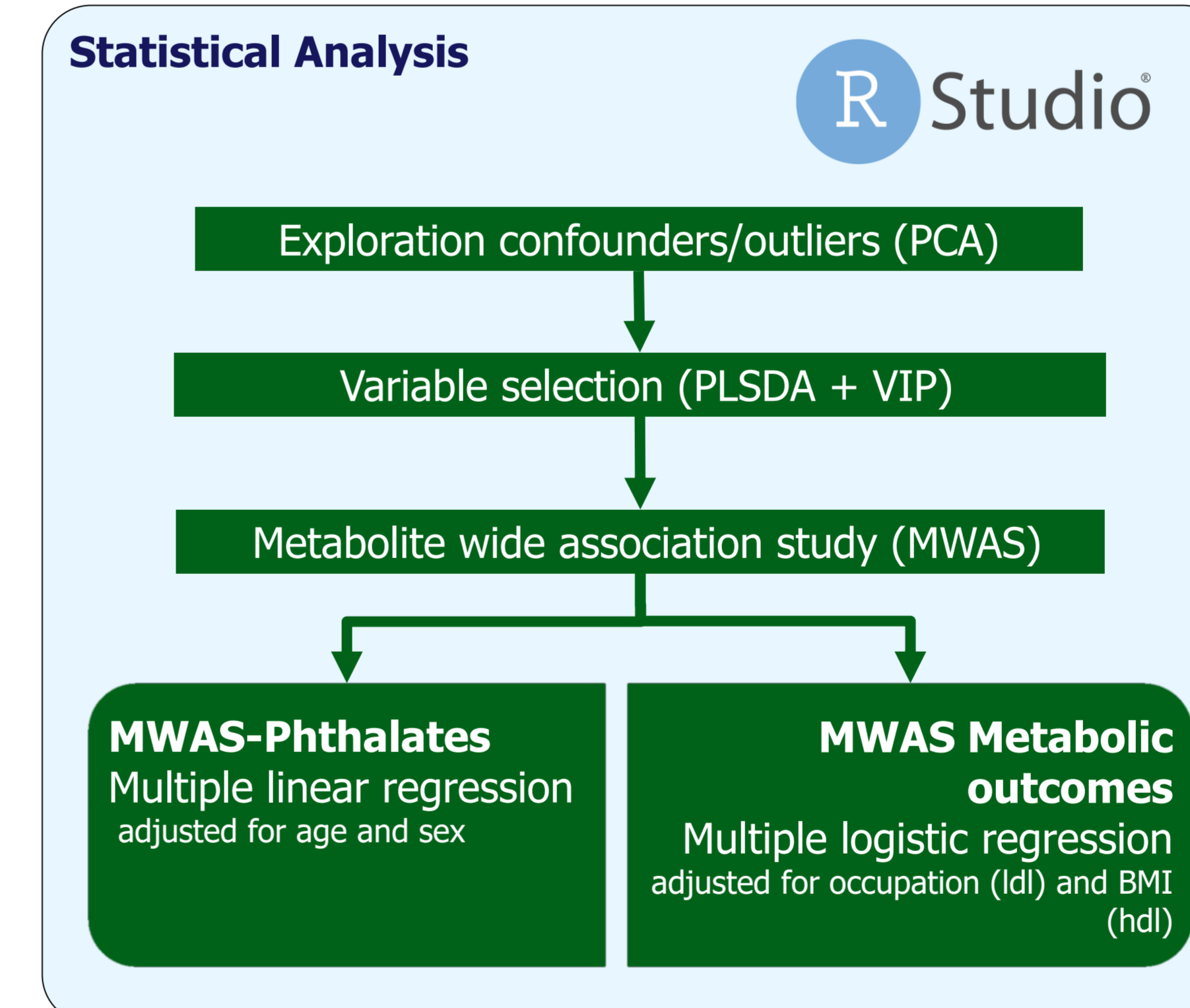
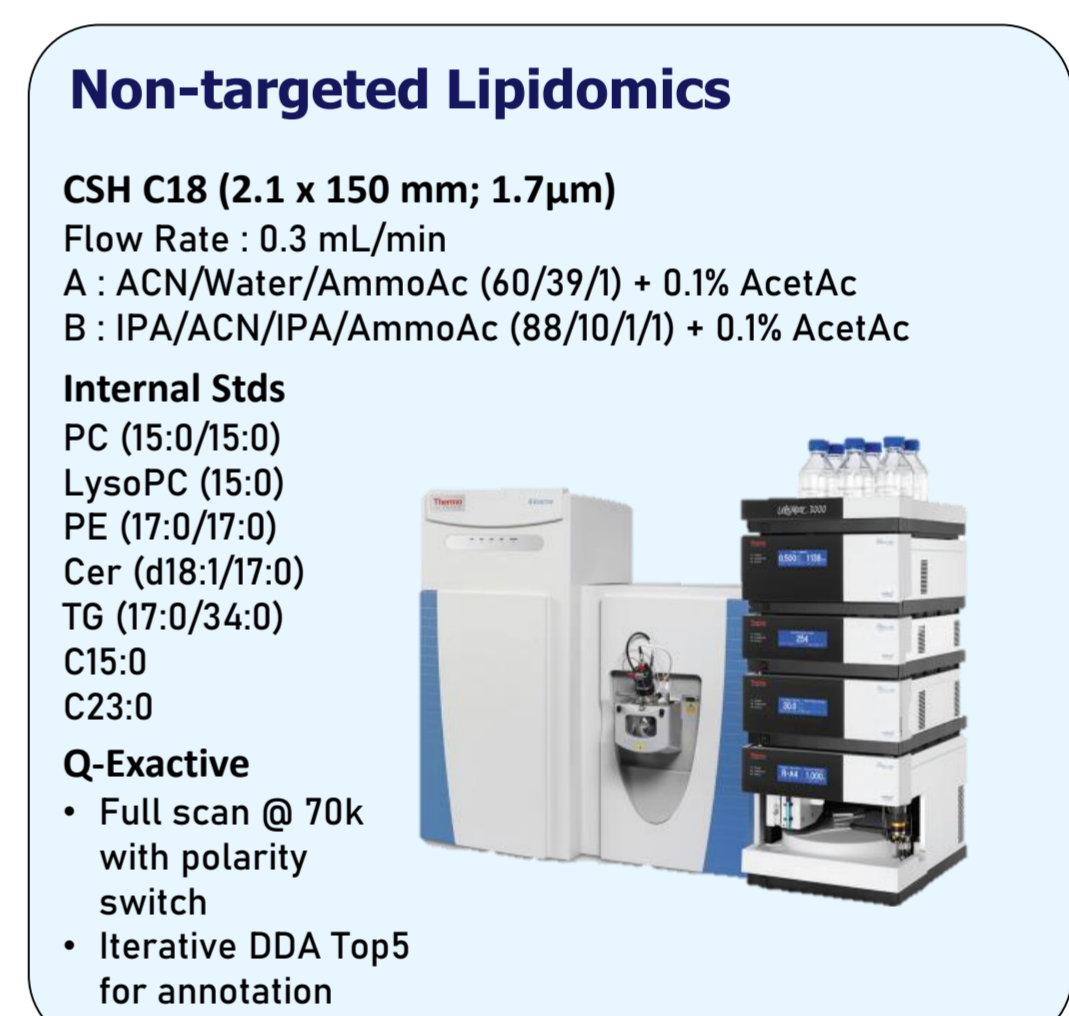
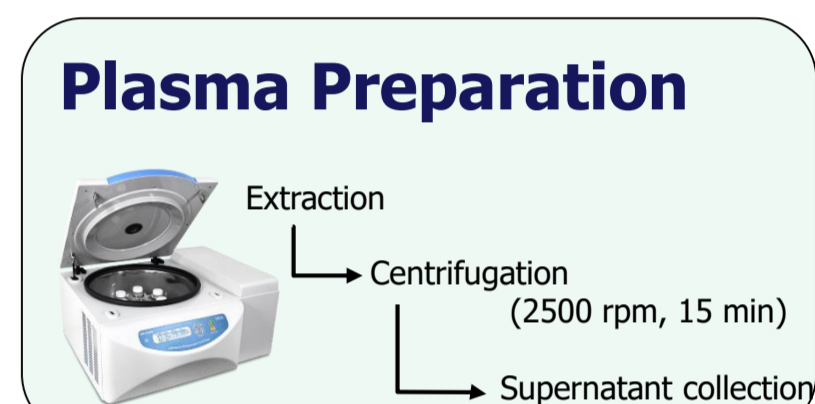
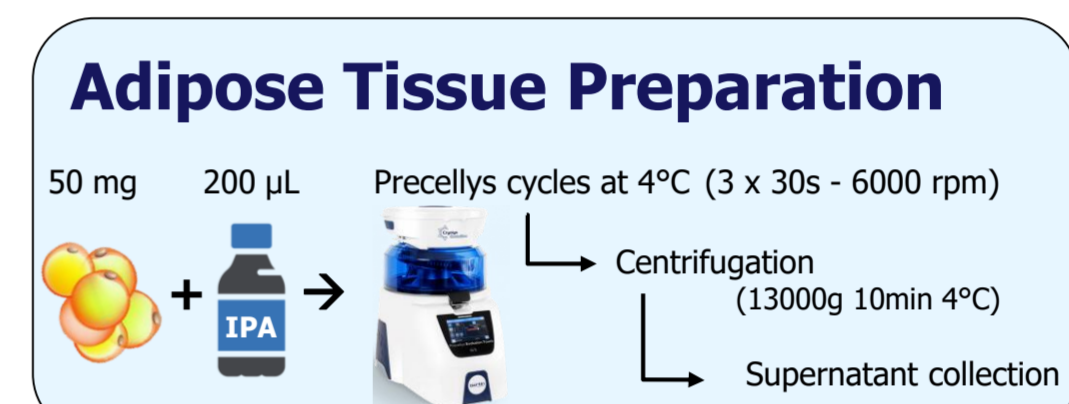
No previous studies have examined the relationship of phthalates to levels of adipose tissue metabolites and whether these are related to any long-term disease. Therefore, this study is pioneering and its results open the door to further study in this regard.

EXPERIMENTAL

GraMo sub-cohort (Spain) n=81



	Granada No. 22	Motril No. 59	P-value
Age [Median (IQR)]	49.00 (41.00 - 57.00)	49.00 (37.00 - 59.50)	0.94
BMI [Median (IQR)]	27.80 (25.30 - 31.96)	27.80 (24.33 - 30.26)	0.81
Sex [n (%)]			0.81
Women	11 (50.0)	32 (54.2)	
Men	11 (50.0)	27 (45.8)	
Residence area [n (%)]			< 0.0001
Urban	5 (22.7)	3 (5.1)	
Semi-rural	1 (4.5)	45 (76.3)	
Rural	16 (72.7)	11 (18.6)	



CONCLUSION

In conclusion, our study showed associations between the serum levels of low molecular weight phthalate metabolites (MnBP and MiBP) with a distinctive lipid signature in adipose tissue measured by targeted and non-targeted analysis.

Likewise, some lipids associated with elevated LDL levels and reduced HDL levels at 20 years follow-up. Some lipids were simultaneously associated to phthalate metabolites and prospective hypercholesterolemia at 20 years follow-up, suggesting a potential mediating role. The results of this preliminary study should be considered with caution due to the modest sample size and further confirmatory studies will be required on gain insight on the relationship between phthalates and adipose tissue-related metabolic diseases.

The authors also thank Biogenouest (Western France life science and environment core facility network supported by the Conseil Régional des Pays de la Loire) for supporting MELISA platform (UMR1329), NANTES, France. The authors from the MELISA platform acknowledge the French National Infrastructure for Metabolomics and Fluxomics MetaboHUB-ANR-11-INBS-0010 (www.metabohub.fr) and the Corsaire metabolomics core facility (Biogenouest). CPR also thanks to INRAE ALIMH for their international mobility grant within the IB20204.