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Linking blood oxylipin profiles to internal POPs exposure levels in women undergoing in vitro fertilization

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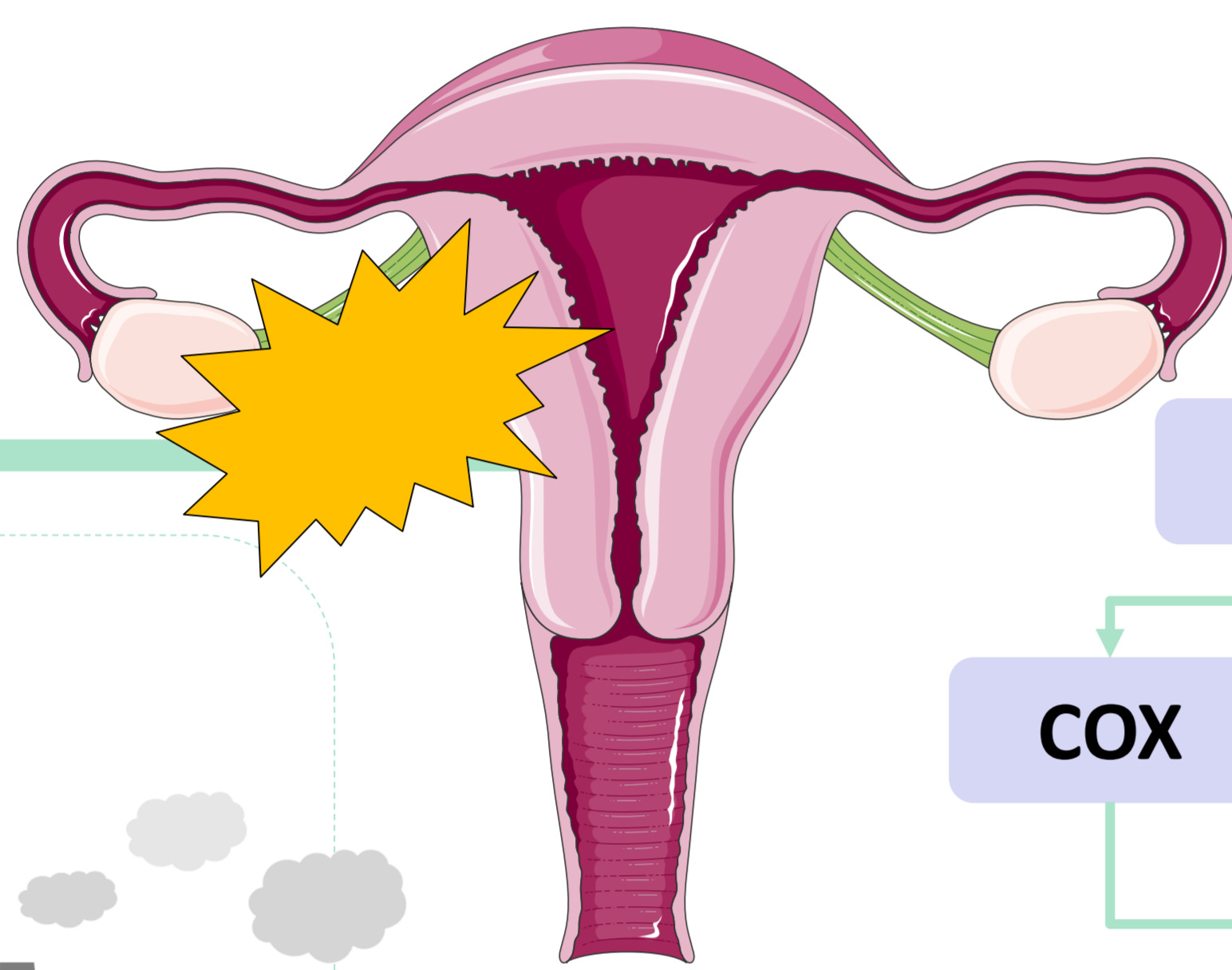
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Introduction and objectives

The impact of environmental pollutants on gynecological disorders is mediated by inflammation and oxidative stress, but little is known about the interaction of oxylipins, bioactive lipids derived from polyunsaturated fatty acids that play an important upstream role in regulating of these biological processes. **The aim** of this study was to explore factors influencing the levels of oxylipins and their precursor fatty acids in the serum of women undergoing in vitro fertilization (IVF), including internal exposure to chemical pollutants and underlying gynecological disorders in infertile women.



Arachidonic Acid

COX

5/15-LOX

P450

Inflammation

Reproductive disorders

PFAS

PCBs

Chemical exposome

Parts of the figure were drawn by using pictures from Servier Medical Art

Methods

Study population (n=100 women attending IVF) CHU Nantes



Fertile women (n=24)

Infertile (n=76)

Endometriosis

Polycystic ovaries

Ovarian Insufficiency

Unexplained

Laboratory Analysis

Free fatty acids

30 μ L serum
+ ISTD
+ heptane and cold drifting agent
Liquid/liquid extraction
Evaporation of organic phase
+ re-suspension with ethyl acetate



Agilent 5973 - GC-FID/MS
Column FAMEWAX 30 m x 0.25 mm, 0.25 μ m

Oxylipin profiling

200 μ L serum
+ ISTD
Protein precipitation (ice Methanol)
Extraction on SPE in 96-well plate, elution with methanol
Evaporation
+re-suspension with methanol



Waters Xevo TQ-S - ESI
Column BEH C18 100 x 2.1 mm, 1.7 μ m

Results

Figure 1. The most abundant free fatty acids in serum were C18:1, C18:2 and C18:0, followed by arachidonic acid (C20:4-w6). The oxylipins thromboxane B2 (TXB2), 5-HETE, 15-HETE and prostaglandin D2 (PGD2) presented the largest concentrations in serum (1B). Arachidonic acid (C20:4-w6) was positively associated with PGE2 and negatively correlated with PGD2, 8-iso-PGA2 and 5-HETE (1C).

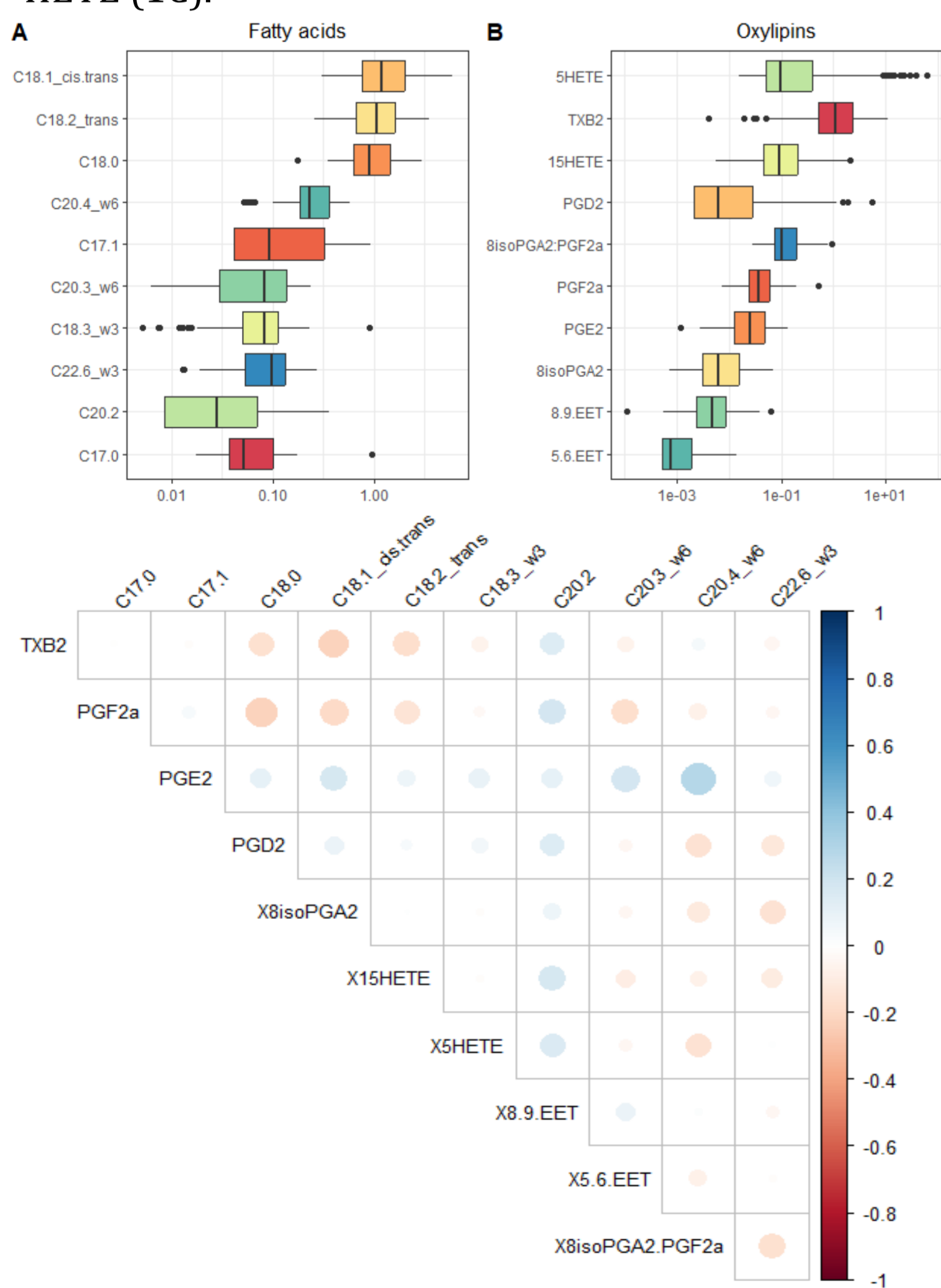


Figure 2. The associations between oxylipins and organochlorinated chemicals like the polychlorinated biphenyls or pesticides were statistically non-significant (2A). The fluorinated pollutant, perfluoroundecanoic acid (PFUnA) was negatively associated with 5-HETE, 15-HETE, PGD2 and 8-iso-PGA2 (2B). The levels of anti-müllerian hormone (AMH) were not associated with the oxylipin levels (2C). Significant values are depicted with white circles ($p < 0.05$).

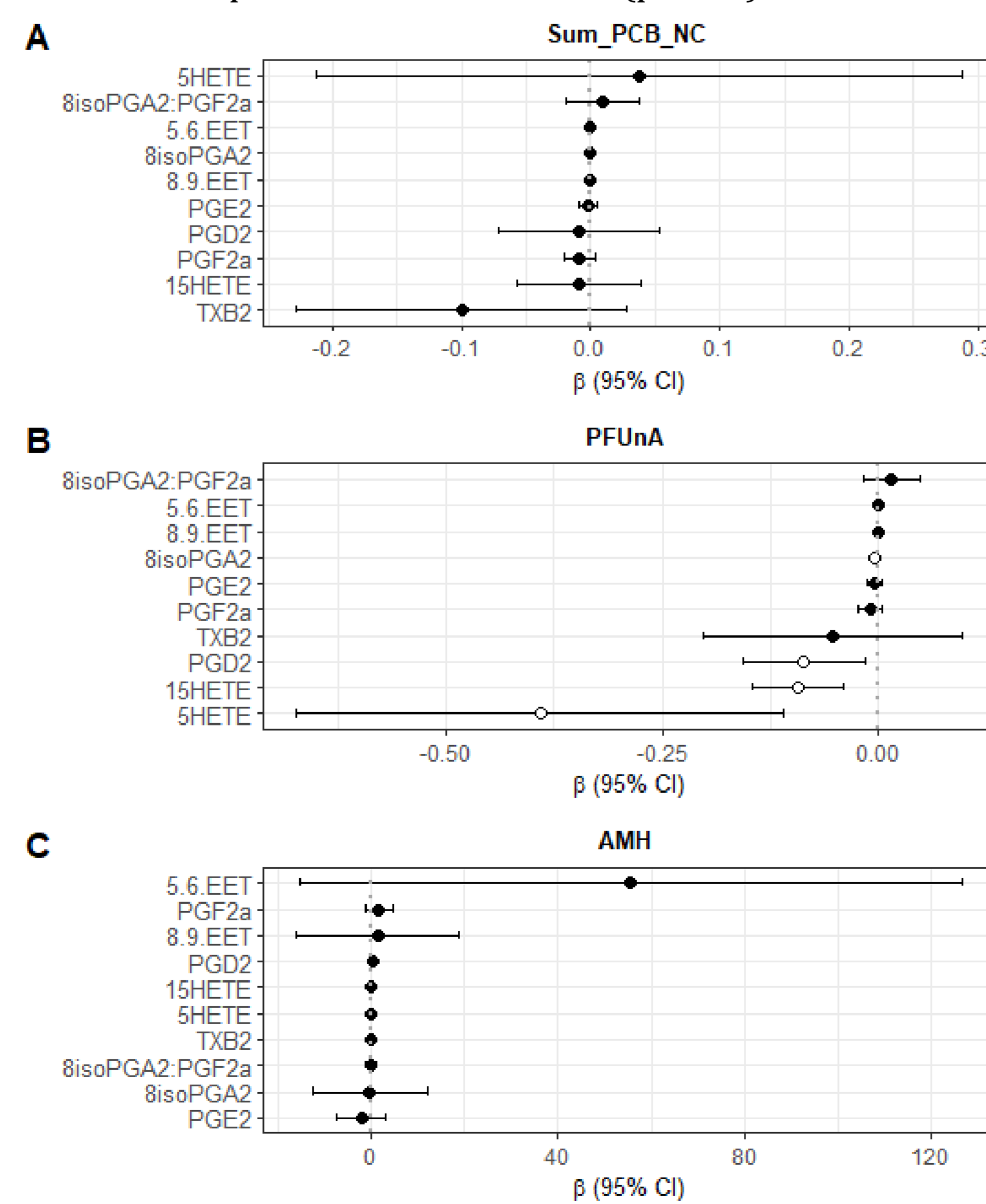
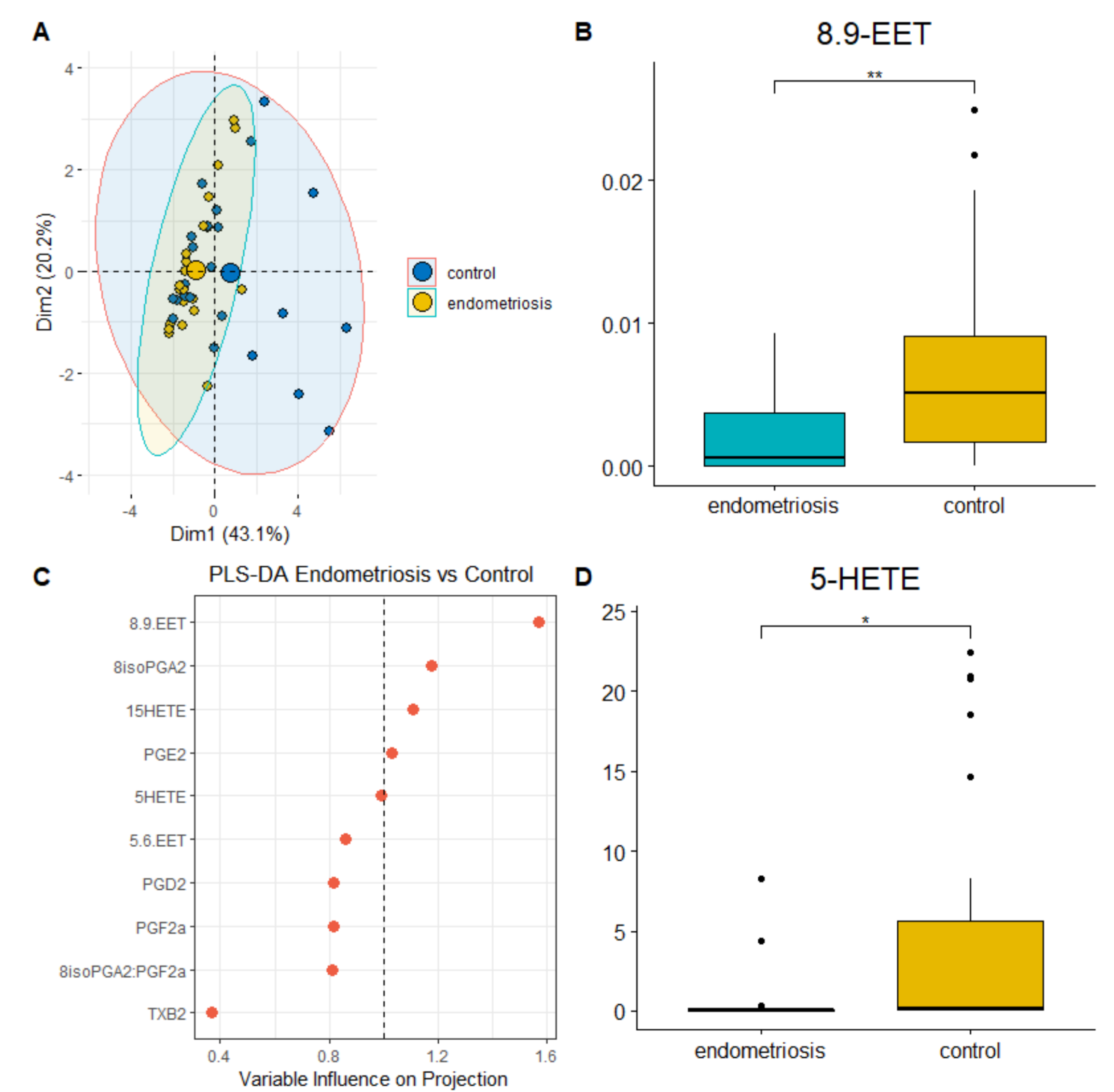


Figure 3. The levels of oxylipins poorly discriminated the groups of women attending IVF (3A) Infertile women with endometriosis showed lower levels of oxylipins 8.9-EET and 5-HETE than fertile women used as control (3B-D). Fertile women showed profiles of oxylipins similar to those of infertile women with polycystic ovaries and no associations were found between endometriosis status and levels of PFUnA. (Data not shown).



Acknowledgements :



Conclusions

Infertile women showed a specific profile of oxylipins when compared with fertile women. Further research will be conducted to better understand the potential role of oxylipins on the functional associations between environmental pollutants and gynecological disorders.