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The challenging use and interpretation of circulating biomarkers of exposure to persistent organic pollutants in environmental health: Comparison of lipid adjustment approaches in a case study related to endometriosis.

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**Abstract**

The gold-standard matrix for measuring the internal levels of persistent organic pollutants (POPs) is the adipose tissue, however in epidemiological studies the use of serum is preferred due to the low cost and higher accessibility. The interpretation of serum biomarkers is tightly related to the understanding of the underlying causal structure relating the POPs, serum lipids and the disease. Considering the extended benefits of using serum biomarkers we aimed to further examine if through statistical modelling we would be able to improve the use and interpretation of serum biomarkers in the study of endometriosis. Hence, we have conducted a systematic comparison of statistical approaches commonly used to lipid-adjust the circulating biomarkers of POPs based on existing methods, using data from a pilot case-control study focused on severe deep infiltrating endometriosis. The odds ratios (ORs) obtained from unconditional regression for those models with serum biomarkers were further compared to those obtained from adipose tissue. The results of this exploratory study did not support the use of blood biomarkers as proxy estimates of POPs in adipose tissue to implement in risk models for endometriosis with the available statistical approaches to correct for lipids. The current statistical approaches commonly used to lipid-adjust circulating POPs, do not fully represent the underlying biological complexity between POPs, lipids and disease (especially those directly or indirectly affecting or affected by lipid metabolism). Hence, further investigations are warranted to improve the use and interpretation of blood biomarkers under complex scenarios of lipid dynamics.

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