Estimating the early-life exposure to two perfluorinated compounds (PFOS and PFOA) using PBPK modelling and biomarker measurements

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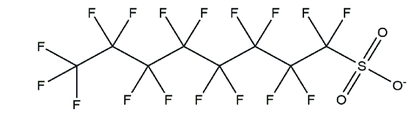
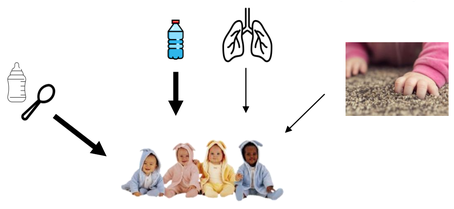
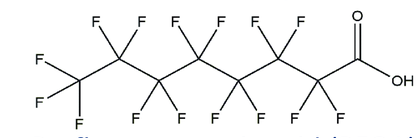
Context

Early-life exposure to per- and polyfluoroalkyl acids substances (PFAS) is a major concern in health risk. Several studies have shown that PFAS can cross the placental barrier and are suspected to induce adverse effects in children such as cardiometabolic, and neurodevelopmental disorders, or impact in the immune response.

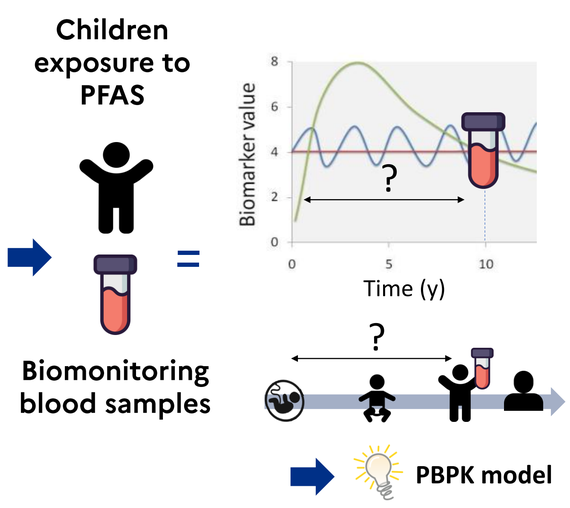


Perfluorooctane sulfonate (PFOS)





Perfluorooctanoic acid (PFOA)



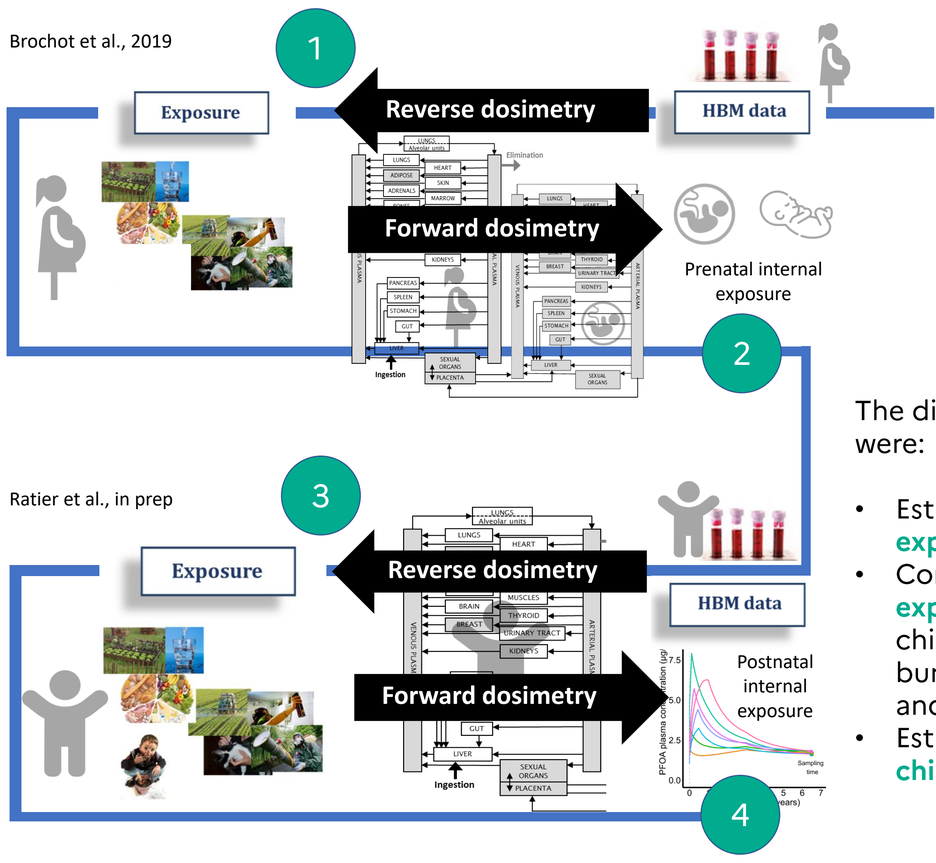
Aims

Our work aims to estimate children exposure to PFOA and PFOS using a Physiologically-Based Pharmacokinetic (PBPK) modelling approach and to determine the main factors that influence internal exposure.

A lifetime model for PFAS was updated to simulate the internal PFAS exposures during the *in utero* life and childhood, and to include individual characteristics and exposure scenarios.

Materials and methods

Our approach was applied on the HELIX cohort, involving 1,239 mother-child pairs from 6 European countries with measured PFOA and PFOS plasma concentrations at two sampling times: during pregnancy and in childhood (6 to 10 y.o).
Bayesian inference was used to estimate the exposures and performed with the GNU MCSim software (version 6.2.0).



The different steps of our workflow were:

- Estimation of the **prenatal exposure**
- Construction of **individual exposure scenarios** for each child based on her/his body burden at birth, breastfeeding, and diet
- Estimation of the **early childhood exposure**

Results

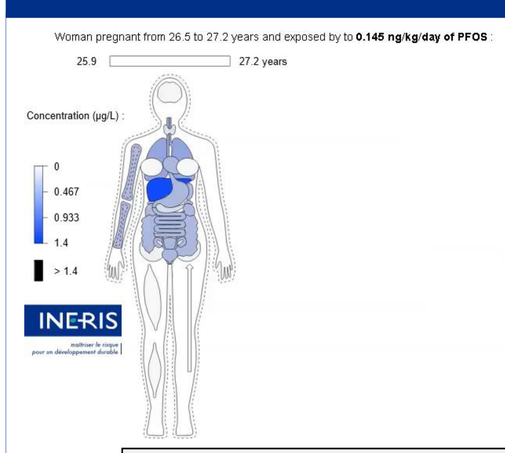


Figure 1. Visualisation of internal PFOS concentrations in the different organs for one HELIX pregnant woman and her foetus over time, performed with the VICKY tool (View Chemical Kinetics in the body) developed at Ineris.

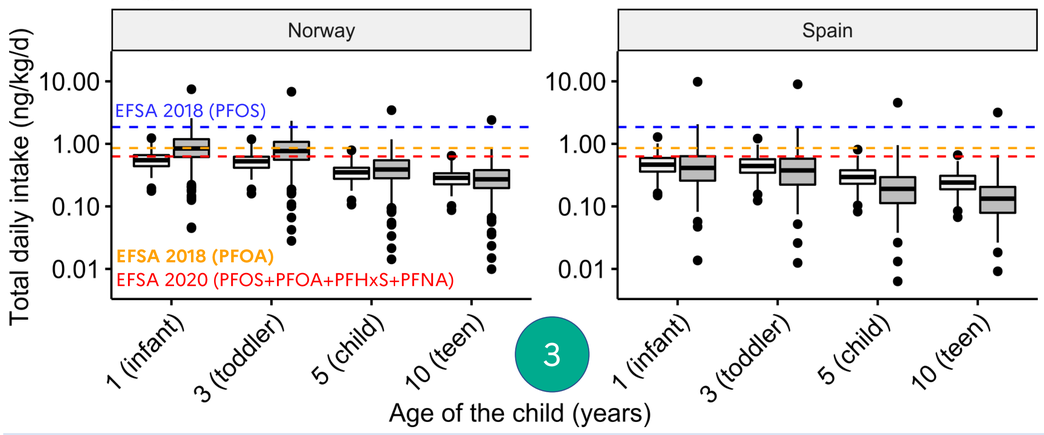


Figure 2. PFOA and PFOS total daily intakes (DI) estimated for the HELIX children at several ages (years) in Norway and Spain.

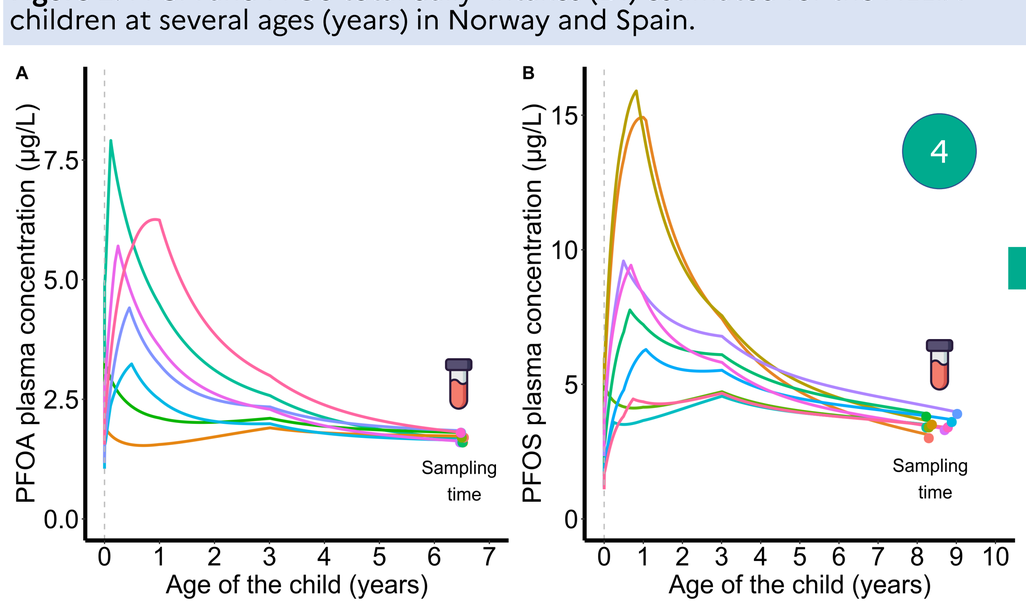


Figure 3. Example of PFOA (A) and PFOS (B) toxicokinetic profiles during early life incorporating individual scenarios exposure. The dots stand for the children sampling time.

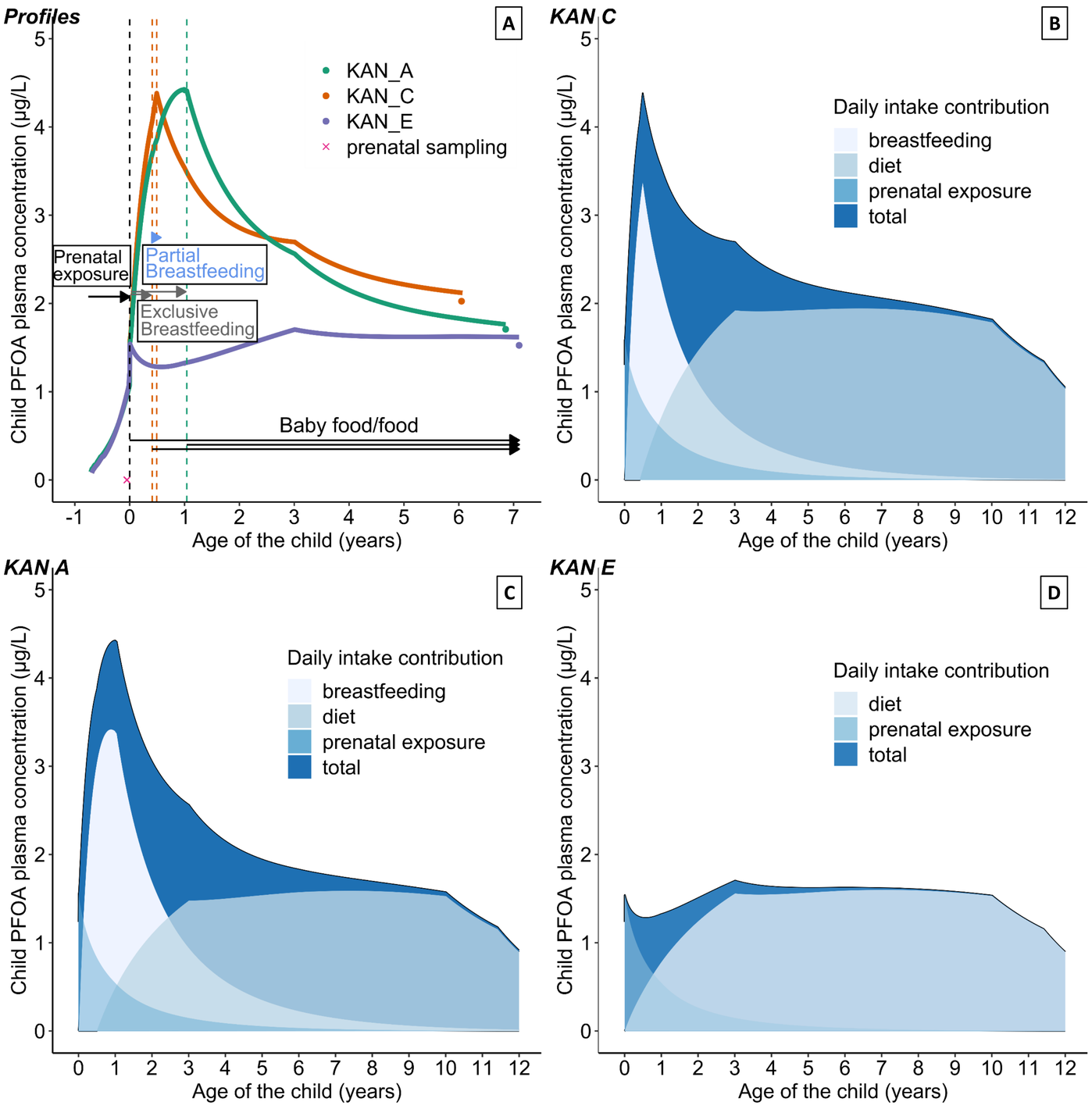


Figure 4. Example of PFOA toxicokinetic profiles for three HELIX children from Lithuania with variations of the breastfeeding duration (A), and PFOA plasma concentration (µg/L) simulated for the individuals KAN_C, KAN_A and KAN_E over childhood (B, C, D) depending on prenatal exposure, diet exposure, breastfeeding exposure when applicable and total exposure.

Discussion and conclusion

Our approach based on PBPK modelling and HBM data demonstrates the possibility to simulate individualized internal exposures, that could be accounted to refine risk assessment in early-life. Our model predictions show that children with similar levels at the same age can exhibit very different internal exposure during their first three years. Combine with HBM data, the use of PBPK models for the early-life, where measured biomarkers are scarce, will help risk assessors in providing more information on the exposure profile and the related sources of exposure.

Brochot et al., 2019. Prediction of maternal and foetal exposures to perfluoroalkyl compounds in a Spanish birth cohort using toxicokinetic modelling. *Toxicology and Applied Pharmacology*, 379, 14.
Ratier et al. In prep. Estimating the dynamic early life exposure PFOA and PFOS of the HELIX children: emerging profiles via breastfeeding and aged-intake fraction

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