

Per- and polyfluoroalkyl substances (PFAS) exposure and untargeted human metabolomics: a scoping review

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Highlights

- Comprehensive review of research studies on metabolomics of PFAS exposures in humans
- PFAS exposures are associated with disruption of amino acid, energy and lipid metabolism
- Research needs include prospective design, standardized reporting, and risk of bias
- Metabolic alterations associated with PFAS are implicated in cardiometabolic health

Background

What is known

- Recent developments on high-resolution phenotyping of non-targeted metabolic alterations at the molecular level
- Increasing concern on the potential health effects of per- and polyfluoroalkyl substances (PFAS): 4-8 yr half-lives in humans
- Human health risks reported in previous epidemiological studies



Cardiovascular disease; Cancer



Hypertension; Immunosuppression



Low birth weight; ADHD

Research gap

The **underlying biologic mechanisms**: how the exposures lead to these reported adverse health outcomes?

Purpose of this scoping review

To provide an assessment of the current evidence regarding **non-targeted metabolomics and associations with PFAS exposure in humans**.

❖ Evaluated the study methods, metabolites identified, and metabolic pathways reported to be associated with specific PFAS chemicals

❖ Identified knowledge gaps and made recommendations for future research

Materials and Methods

A scoping review

- 1) database searching (PubMed, Dimensions, Web of Science Core Collection as licensed at Yale, Embase via Ovid, Scopus)
- 2) citation chaining

Inclusion criteria

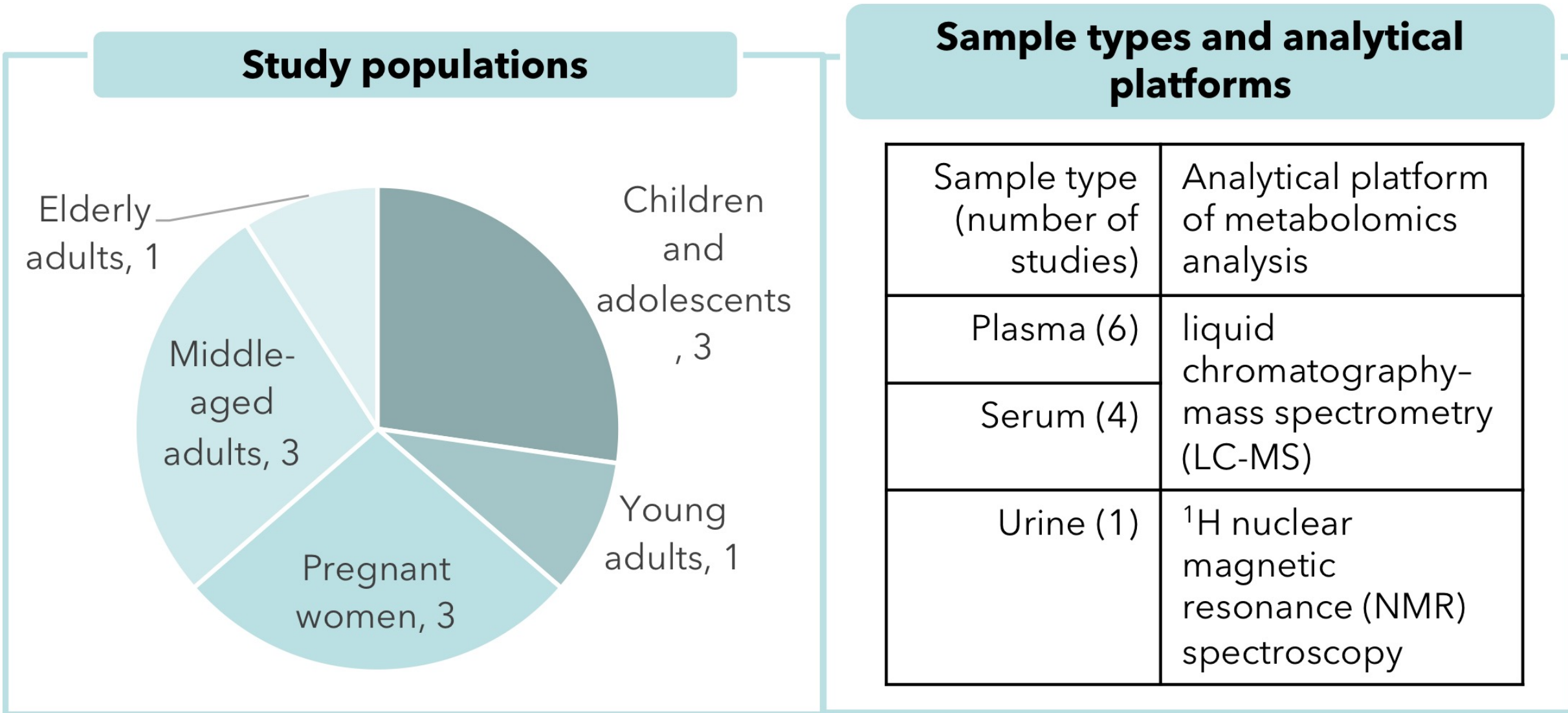
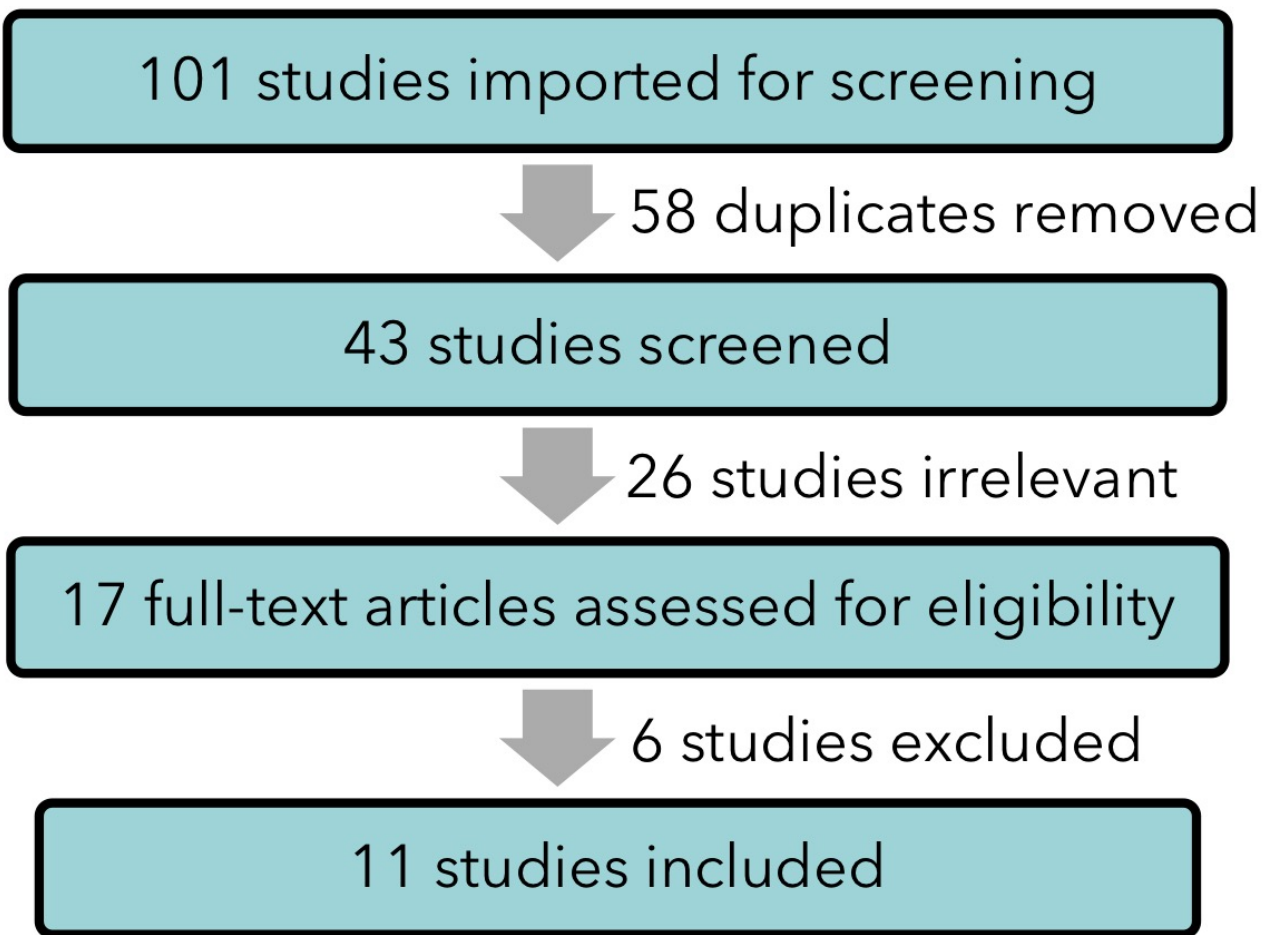
- 1) published epidemiological original articles
- 2) publication date range from the year 2000 to 1st April 2021
- 3) no language limit
- 4) with at least one type of PFAS measured in participants' biofluid samples
- 5) with non-targeted metabolomics applied in participants' biofluid samples

Data summary

- 1) study characteristics, measured PFAS types, sample collection, analytical platforms, statistical analysis, and main findings
- 2) focused on four most studied PFAS compounds (PFOS (n=11), PFOA (n=10), PFHxS (n=9), PFNA (n=5)) and PFAS mixtures which were reported in at least three studies

Data visualization

grouped based on chemical taxonomy in HMDB and metabolism category in KEGG database and ranked by the total number of studies regardless of associated PFAS types



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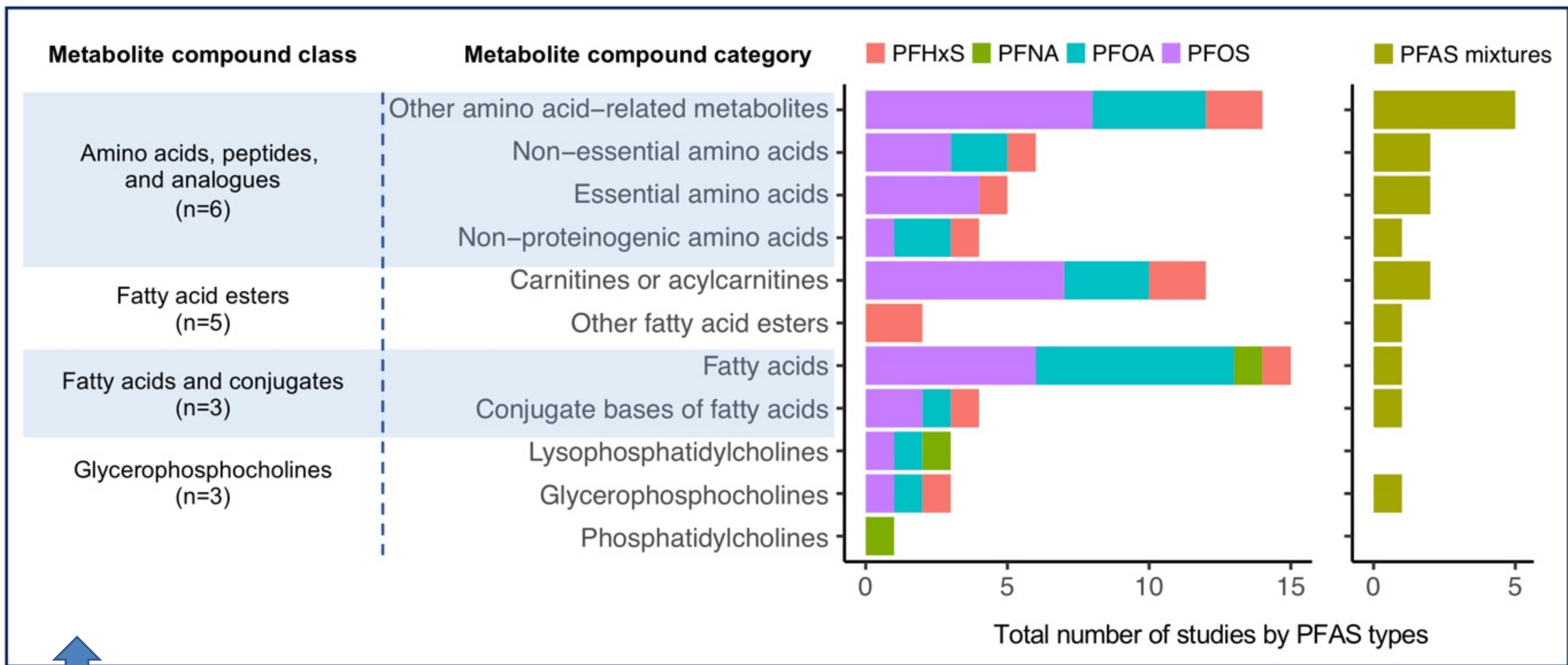
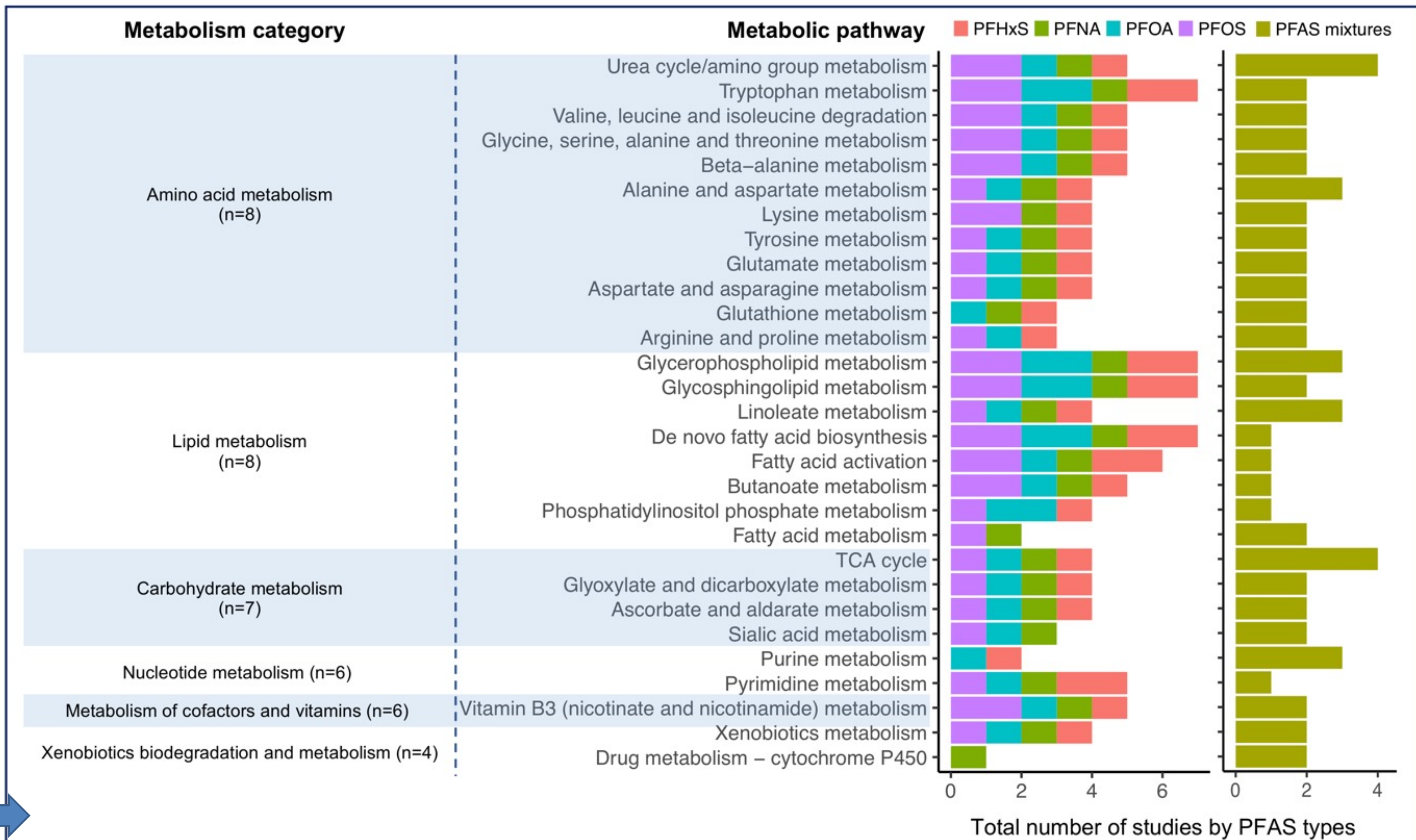


Figure 1. A summary of the commonly detected metabolite compound classes (in at least three studies) and categories associated with four individual PFAS compounds and PFAS mixtures.

Figure 2. A summary of the commonly detected metabolic pathways (in at least three studies) associated with four individual PFAS compounds and PFAS mixtures.



Conclusions

- There is growing interest in using non-targeted metabolomics to study the human physiological changes associated with PFAS exposure.
- Multiple PFAS were reported to be associated with alterations in amino acid and lipid metabolism, but these results are driven by one predominant type of pathway analysis thus require further confirmation.
- Standardizing research methods and reporting are recommended to facilitate result comparison.
- Future studies should consider potential differences in study methodology, use of prospective design, and confounding bias and measurement errors.