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ARISING FROM A. J. Nihart et al. *Nat. Med.* https://doi.org/10.1038/s41591-024-03453-1 **(2025)**

Human exposure to microplastics and nanoplastics (MNPs) is an emerging concern with potential implications for health. As awareness of this issue grows, it has prompted increasing scientific attention toward understanding if, and how, MNPs accumulate in human tissues. In a recent study, Nihart et al.[1] used the analytical technique of pyrolysis gas chromatography–mass spectrometry (Py-GC–MS) to detect MNPs in human liver, kidney and brain, reporting the highest concentrations in the brain, with polyethylene as the predominant polymer. The study as reported appears to face methodological challenges, such as limited contamination controls and lack of validation steps, which may affect the reliability of the reported concentrations. In this Matters Arising, we highlight methodological limitations that have general relevance for advancing robust and reproducible MNP detection in human biomonitoring studies.

Lack of procedural controls and quality assurance measures

Detecting MNPs in human tissues poses important analytical challenges due to the widespread presence of plastic contaminants and the complexity of biological matrices. International best-practice guidelines, such as ISO 24187:2023 and OECD test protocols, emphasize the need for comprehensive and consistent quality assurance and quality control (QA/QC) procedures. These include the systematic use of procedural blanks, field blanks, matrix contamination assessments and validated protocols for tissue digestion and polymer recovery. Such measures are essential to differentiate true tissue-derived MNPs from contamination introduced during sampling, sample preparation or detection[2]. In the study by Nihart et al., the absence of reported QA/QC procedures makes it difficult to evaluate the extent to which contamination from reagents, labware or airborne particulates may have influenced the findings, all of which are well-documented sources of false positives in MNP analysis[3]. Moreover, the tissue samples in the study were collected across different years and locations, raising uncertainty about whether harmonized, contamination-minimizing protocols were consistently applied. In environmental MNP research, such variability has been shown to substantially impact results[4]. This reflects a broader challenge across studies investigating MNPs, highlighting the need to standardize sampling, sample preparation, detection, QA/QC procedures and their documentation to ensure credible and reproducible findings in human biomonitoring.

Nihart et al.[1] used a 10% potassium hydroxide digestion at 40 °C for 72 h, followed by centrifugation and ethanol washing to remove tissue matrix components and isolate MNPs for Py-GC–MS analysis, a step commonly referred to as enrichment or concentration. However, potassium hydroxide digestion is known to be suboptimal for lipid-rich tissues such as the brain[2,5], with incomplete tissue removal often resulting in residual particulates that can be misidentified as synthetic polymers. Indeed, the study reports digestion efficiencies below 90% for several brain samples (see Supplementary Fig. 5 in ref. 1), suggesting that a significant fraction of undigested material may have remained, potentially biasing the reported results. The study does not report polymer-spiking experiments to validate recovery efficiency, limits of detection and quantification, or identification accuracy, nor does it describe the approach used to assess the possible impact of the extraction method on particle integrity[2]. This limitation highlights the importance of stepwise evaluation of sample preparation workflows using certified reference materials that reflect relevant particle size, type and morphology, and allow recovery measurements to validate each enrichment stage with high efficiency and minimal artifacts[6].

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Limitations of Py-GC–MS for MNP detection in tissues

Py-GC–MS is a well-established tool for identifying and quantifying pure polymers, but its specificity is limited when applied to complex biological samples. The consistent predominance of polyethylene across all organs, time points and individuals in the study by Nihart et al.[1] is notable, as environmental exposure studies often demonstrate greater diversity in polymer types, which suggests the possibility of analytical artifacts. Many biological lipids, especially long-chain fatty acids, produce pyrolysis products that mimic polyethylene mass fragments[7]. In the absence of adequate analytical expertise, procedural precision and robust QA/QC protocols, this resemblance may lead to misclassification. Recommended practices include verifying polymer identity by using multiple diagnostic mass fragments or marker ions (that is, distinctive ion signals characteristic of specific polymers) and verifying consistent retention time patterns. These patterns reflect the expected positions of polymer peaks relative to adjacent compounds (for example, alkanes) in the chromatogram, which help differentiate polymers from similarly fragmented biological compounds. The authors noted that such marker ions were absent, raising concerns that the observed polyethylene signals may have come from residual fatty acids rather than synthetic polyethylene. This possibility is reinforced by the lipid-rich nature of brain tissue (~60% lipid by dry weight)[8], compared to the liver and kidneys (<5%)[9,10]. Incomplete digestion, as indicated by the reported efficiencies, could result in lipid interference disproportionately affecting brain samples, possibly contributing to the higher MNP concentrations observed, despite the blood–brain barrier's role in restricting exogenous particle entry[11]. Furthermore, the reported increase in MNP concentrations over time may not reflect true bioaccumulation but could instead result from variability in lipid content or sample handling. For instance, rising global obesity rates have been linked to increased lipid accumulation in human brain and liver tissues[12,13], potentially influencing analytical outcomes over a multiyear sample series.

The detection of MNPs in human tissues continues to face substantial methodological challenges, compounded by the lack of harmonized reporting standards across the field and their limited implementation in scientific journals. Studies quantifying MNPs in biological matrices should follow rigorous QA/QC protocols, including clear false-positive identification strategies, consistent use of sampling and processing blanks, contamination-controlled procedures and validated digestion and recovery methods using well-characterized reference materials. Given the complexity of human tissue matrices, the use of Py-GC–MS requires particular caution. In the absence of more targeted methods, accurate polymer identification should rely on multiple analytical approaches to ensure specificity, alongside characterization of size and shape. The challenges reported by Nihart et al.[1] illustrate broader, ongoing gaps in analytical rigor within the field. As human biomonitoring of MNPs advances, it is essential for the scientific community to adopt harmonized practices that promote transparency, reproducibility and confidence in reported findings. Notably, findings that lack adequate validation may inadvertently shape public perception and regulatory discussions, despite underlying scientific uncertainties. Ensuring methodological robustness is therefore critical for producing reliable data to support risk assessments, inform policy decisions and guide future research.

Online content

Any methods, additional references, Nature Portfolio reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41591-025-04045-3.

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Author contributions

F.A.M. and D.M. conceived the work. All authors contributed to the writing of the article.

Competing interests

The authors declare no competing interests.

Additional information

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