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# Microplastics shape the ecology of the human gastrointestinal intestinal tract

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**Abstract**

Microplastic particles are global pollutants which have been measured in drinking water, dust, and some food items. Concerns about population exposures and the resulting risks to human health are increasing. Because the gut can be considered one of the primary sites for microplastic exposure in the human body, here, we explore the possible impact of ingested microplastic particles on gastrointestinal ecology, providing some evidence for their active role as a driver of dysbiotic variation in the human gut microbiome. This further stresses the urgent need to quantitatively assess both oral exposure and hazards of microplastic in the human gut, enabling prediction of the levels of microplastic risk and outcomes of dysbiotic changes in the gut microbiome to be inferred.

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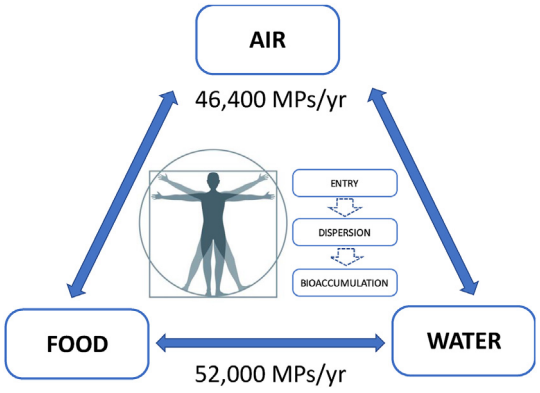
## Microplastics: origin; dispersion; and level of human exposure

Microplastic particles (MPs) are global pollutants [1], consisting of a range of different polymers and morphologies reflecting the wide range of sources they originate from. They predominantly arise through degradation (photochemical and biological) and abrasion of plastic across its life cycle ('secondary MPs'), although they can also be purposefully manufactured ('primary MPs') and intentionally added to a range of consumer products (e.g. facial cleaners, shower gels, or toothpaste) [2]. Trillions of MPs contaminate the global ocean surface, and MPs have been detected ubiquitously on our planet, including in ice cores from remote locations [3–6]. Current estimates report that 2.5 million tons of MPs enter the ocean every year, with a burden of 75,000 to 300,000 tons of MPs released into the environment each year in Europe alone [7]. The presence and persistence of MPs in the environment have been argued to be of concern, supported by evidence that ingestion of MPs by a range of biota under laboratory conditions leads to adverse effects [8]. In addition to potentially containing different mixtures of chemicals added during manufacture (e.g. plasticizers and additives), MPs can adsorb and concentrate environmental contaminants on their surface, including priority pollutants, such as organochlorine pesticides, and polycyclic aromatic hydrocarbons [9–11]. MPs may also harbor (and deliver) an eco-corona of different molecules, including a microbial community, known as the plastisphere, potentially being a vector for the dispersal of potential pathogens and, in parallel, a hotspot for the enrichment of antibiotic resistance genes [12,13].

Although traditionally recognized as a marine issue, evidence is growing to reveal a network of complex environmental MP pathways, which result in the contamination of water, food, air, and dust, and ultimately lead to human exposure via ingestion and/or inhalation [14]. Although there is a general lack of direct information on the total human MP exposome, some estimates combining the different routes of exposure can now be advanced. Indeed, it has been estimated that up to 52,000 MPs per year can be inadvertently ingested with water and food intake [15]. Bottled drinking water in single-use plastic, can contain, on average, a few thousand MPs per liter [16], although plastic-packaged foods provide a further source of ingested MPs [17]. In addition, terrestrial and aquatic trophic chains may become

**Figure 1**




**Microplastics can enter, disperse, and bioaccumulate in the human body, with potential health implications.** Urban environments, especially densely populated areas, are a major source of microplastics (MPs), which can be transported into the atmosphere and deposited, even far away, cycling to soil, water, and food. Based on recent estimates [15], up to 52,000 MPs per year can be inadvertently ingested with water and food intake, including through the use of disposable plastic bottles and plastic packaging for food. A roughly equivalent source of MP exposure is the atmospheric compartment with up to about 46,400 inhaled MPs per year that can reach the gut [25]. After uptake from the gut lumen, MPs can reach the lymphatic and/or circulatory systems, spreading throughout the body and potentially accumulating in secondary organs [28]. Once in the body, MPs may pose a risk to human health, through generation of reactive oxygen species, inducing inflammation and apoptosis, and driving dysbiotic changes in the gut microbiome, with cascading implications for human pathophysiology.

contaminated by MPs [18,19], resulting in direct contamination of the food we ingest [6].

Recent observations of airborne MPs indicate that the air we breathe may be an emerging route of MP exposure [20–23]. This is especially true in urban environments, particularly in densely populated areas, where different point sources, such as buildings and construction, vehicles (synthetic tires, brake pads), road paints, asphalt, among others, occur [24]. Indoor environments are even more contaminated than outdoor ones. Inhaled MPs that are too large to penetrate the central airways and distal lung (aerodynamic diameter >10 μm) deposit in the nasopharyngeal region, whilst those <10 μm can deposit in the thoracic region and are eliminated via the mucociliary escalator, reaching the gastrointestinal tract. Based on outdoor and indoor MP concentrations, indoor/outdoor activity patterns, and a conservative resting ventilation rate, an additional gastrointestinal burden of up to 46,453 MPs per year has been estimated from the atmospheric compartment [25] (see Figure 1).

## Microplastics in the human body: routes of entry; dispersion; and general toxicological outcomes

At present, inferences about the biodistribution of the fraction of MPs that are bioavailable in the human body and their toxicity can only be made from studies performed using experimental animal models [26,27]. Indeed, the inherent physicochemical heterogeneity of MPs can impact their toxicokinetics and dynamics.

Once in the body, MPs could follow particle distribution patterns and reach the lymphatic and/or circulatory systems, potentially accumulating in secondary organs, including the liver, kidney, spleen, heart, and brain, and impacting the immune system and health of cells [28]. In particular, as anticipated previously, the inhaled particles that deposit in the upper and central airways will be cleared mechanically (e.g. via coughing or sneezing) or via the mucociliary escalator, possibly leading to gastrointestinal exposure [29].

In the gut, particles can be taken up through different size-dependent pathways. Luminal particles up to a few microns in size can be phagocytosed by M cells of the Peyer's patches or dendritic cells, transferring the particles to the lymphoid tissues of the underlying mucosa [26]. Particles <130 μm in diameter may translocate paracellularly across loose junctions. Particle uptake via these processes is typically low, with 0.3% and 0.0002% of ingested particles translocating over 24 h for phagocytic and persorption processes, respectively [30]. After uptake from the gut lumen, MPs can be transported by lymph vessels and/or portal circulation, being distributed via systemic circulation throughout the body, potentially reaching secondary tissues [31,32]. Even if hypotheses have been advanced, to date, no evidence has been published on the presence of MPs in the human body, except for a single publication documenting fibrous MPs in lung tissue from a lung cancer sample population [33]. Very recently, few MP fragments have also been detected in the human placenta [34], but further research is needed to validate these findings before inferences for human health can be made.

MPs entering the body could lead to an array of toxicological impacts, depending on their size, shape, solubility, and surface charge (reviewed in the study reported by Wright and Kelly [29]). Historical studies suggest that high levels of respirable plastic (nylon) dust can cause chronic inflammation in the lower respiratory tract of synthetic textile workers [35–37], and recipients of plastic prosthetic implants experience localized chronic inflammation in response to wear particles [38–40]. This was found to be highly dependent on the chemical composition of the plastic, with polyethylene terephthalate being more inflammatory than polyethylene. In addition to inflammation, recent studies have measured the effects on oxidative stress, apoptosis, and cell proliferation (reviewed in the study reported by Hu and Palić [41]). Plastics may contain reactive oxygen species (owing to the history of polymerization and processing), the concentration of which can increase significantly after interaction with

ultraviolet light, the presence of transition metals, and microbial metabolism of organic contaminants, thus posing a hazard to cells and tissues, as a molecular initiating event leading to oxidative stress and inflammation.

## Impact of microplastics on the human gut ecology

Although it is a fact that our gut is one of the main sites of MP exposure in the human body, there is currently no published study exploring the real-life effects of MPs at environmentally relevant concentrations on the human intestinal microenvironment. However, the level of human gut exposure to MPs was indicated in a preliminary milestone study, albeit pilot in nature, on the presence of MPs in human stool [42]. Samples from eight healthy volunteers across the globe were analyzed for the presence of MPs. One hundred percent of the participants' stool contained MPs, ranging in size from 50 (instrumental detection limit) to 500 μm, at a mean concentration of 20 MPs/100 g of stool. The extrapolation has led others to approximate an average annual elimination of 73,000 (29,200−1,518,400) MPs per year [25], which is comparable to current estimates of external human exposure via ingestion and inhalation, as reported previously.

Although we have no direct information on the impact of such MP burden on the human gut microbiome, some hypotheses can now be advanced, mainly thanks to the availability of data from laboratory animal models exposed to known concentrations of MPs [43−45]. As per the available observations, high concentrations of MPs composed of polystyrene can affect gut ecology through direct and indirect mechanisms. Several local pathophysiological outcomes have also been observed — such as disruption of the intestinal barrier, induction of apoptosis, abnormal expression of mucin, and increased inflammation — which can alter, even profoundly, the ecology of the gastrointestinal tract, forcing dysbiotic shifts of the gut microbiome [45]. On the other hand, ingested MPs can have a direct impact on the diversity and composition of the gut microbiota. Indeed, once in the gut, MPs can select for specific microorganisms, which would be enriched on the MP surface, and, in parallel, can inhibit other intestinal groups, through the release of a series of different chemicals, such as plasticizers and additives and/or, eventually, the absorbed pollutants [13,46]. For instance, in mouse models exposed to very high, likely unrealistic MP concentrations (up to 1000 μg/l of MPs per day for a total of 5 or 6 weeks), the gut microbiome was significantly modified, with a decrease in the percentages of Bacteroidetes, Firmicutes, and Actinobacteria, and a corresponding increase in *Melainabacteria* and *Staphylococcus* [44,47]. Although these and other studies have provided important glimpses on the interaction processes between the gut microbiome and MPs, the results are mostly focused on model organisms and were obtained under laboratory conditions, exposing mice to MPs consisting of a single polymer and shape at concentrations that might not reflect actual exposure. In a recent study, Biagi et al. [48] explored the connections between microbiome composition and gastrointestinal plastic contamination in real-world conditions, that is, in live loggerhead sea turtles (Caretta caretta) rescued from the Northwestern Adriatic Sea. According to the authors, 48 operational taxonomic units showed increased abundance with an increasing plastic content in the feces. These include *Cetobacterium somerae*, a microorganism known to increase in response to exposure to organic pollutants, *Terrisporobacter petrolearius*, previously isolated from hydrocarbon-contaminated sites, and the pathogenic species *Vibrio fluvialis* and *Fusobacterium varium*. Conversely, other gut microbiome operational taxonomic units were negatively correlated with the presence of plastic in the gut and included common and even health-promoting gut microbiome components, such as *Akkermansia*, *Rikenella*, *Faecalicatena*, and *Clostridium*.

Taken together, these findings support the hypothesis that MPs may interact with intestinal ecology in the real world, promoting dysbiotic changes in the gut microbiome, with possible detrimental consequences on gut health. Indeed, as a carrier of pollutants and pathogenic species, MPs may facilitate their entrance and colonization of the gastrointestinal tract, directly shaping the gut microbiome. At the same time, the presence of MPs may indirectly lead to an environment less favorable to the survival of some endogenous symbiotic species, possibly owing to increased local inflammation and/or release of chemicals.

## Best practices for microplastic particle assessment in human and animal biological samples

For studying the impact of MPs on the ecology of the gastrointestinal tract, the adoption of robust and standardized methodologies for sampling and MP detection is mandatory. The collection of tissues and/or stool must avoid contamination with exogenous MP sources. To this aim, glass, aluminum, or stainless steel sampling apparatus should be used. During sampling, exposure to contaminated ambient air should be minimized. To control for such contamination, 'field blanks' should be collected and analyzed with samples. Any fixatives should be prefiltered and checked for MP contamination.

For MP detection, characterization, and quantification, robust and highly sensitive techniques must be used. MPs need to be classified by size, polymer, and shape at the least. Thermal degradation and desorption

techniques (e.g. pyrolysis or thermal desorption gas chromatography-mass spectrometry and variations thereof) can be used to determine bulk polymer composition, whilst vibrational microscopy and imaging techniques (e.g. Raman microscopy, attenuated total reflectance-Fourier transform infrared microscopy) can enable the collection of qualitative information on size and shape. However, for stool samples, which will be most relevant to microbiome linkages, the challenge will be in sample preparation, whereby organic matrix removal, such as via wet peroxide digestion, with minimum effects on MPs, is needed and must be carefully demonstrated.

## Conclusions and future perspective

The study by Biagi et al. [48] indicate that, under real-world conditions, MPs have the potential to affect the gut microbiome, shaping its compositional structure, both directly and indirectly, and facilitating dysbiotic transitions. This evidence, coupled with recent findings showing a relevant MP burden in the human gut, supports the importance of quantitatively assessing both the exposure and hazards of MPs in the human gut, allowing for the deduction of real-world risks and outcomes of dysbiotic gut microbiome changes.

It can be assumed that humans have been chronically exposed to MPs over their life course, since the mass production, use, and disposal of plastic began. In the current scenario where global plastic production is steadily increasing, MP emissions are expected to continue. This ubiquitous burden of MPs on a planetary scale generally highlights the urgent need to assess the level of human exposure and the consequent impacts on human health [49]. However, without quantitatively assessing both exposure and hazards, it is challenging to infer risk, disease pathways, and health outcomes. Furthermore, MP exposure should be considered in a broad exposome context, also taking into account the full range of particles to which we are exposed to. To this end, an exposome-based approach needs to be adopted, examining both external and internal (dose) exposure to MPs, in the context of the full complexity of exposure factors and in combination with clinical metadata and targeted toxicological assessments, starting from the gut, to advance our understanding of pathways indicative of acute health impairment and chronic disease development.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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