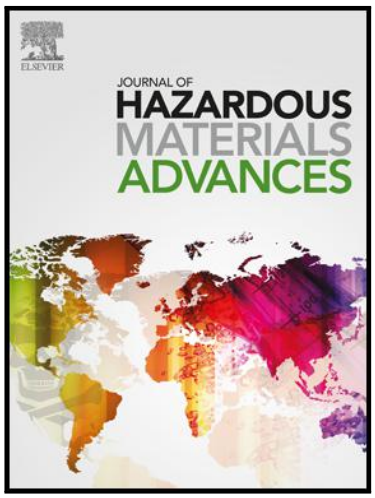
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# Co-occurrence, interactions, and combined ecological and human health risks of microplastics, pharmaceuticals and personal care products, antibiotics, and pesticides in aquatic environments: a critical review with evidence grading and quantitative synthesis

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**Highlights**

- 77 studies were graded as field, sorption or mixture-toxicity evidence.
- No included study measured microplastics with all three chemical classes.
- Ageing raised chemical sorption to microplastics 3.4-fold (95% CI 1.6-7.3).
- Dissolved organic matter and salinity often weakened sorption in water.
- Most synergy claims lacked a formal additive or independent-action null model.

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# Co-occurrence, interactions, and combined ecological and human health risks of microplastics, pharmaceuticals and personal care products, antibiotics, and pesticides in aquatic environments: a critical review with evidence grading and quantitative synthesis

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**Abstract**

Microplastics (MPs), pharmaceuticals and personal care products (PPCPs), antibiotics and pesticides share sources and receiving waters, yet evidence on their co-occurrence, interactions and combined risks is fragmented and often over-generalised. We conducted a critical review with a PRISMA 2020-guided search of Web of Science, ScienceDirect and PubMed (397 database records, plus citation and update searches; 77 included studies) and classified each study as Level 1 (field co-occurrence), Level 2 (laboratory interaction: sorption, desorption,

ageing, biofouling) or Level 3 (laboratory exposure toxicity), with plastisphere/antimicrobial resistance (AMR), treatment and modelling studies analysed separately. Of 72 core studies, 20 were field studies, 22 were Level 2 and 10 were Level 3; 58% originated from China and only three from Africa. No study measured MPs together with antibiotics, other PPCPs and pesticides, and only three field studies quantified MPs and a target chemical in the same study. Random-effects meta-analysis showed that ageing increased the sorption capacity of MPs for antibiotics, a pharmaceutical and a pesticide by 3.40-fold (95% CI 1.58-7.28; k =7 studies), but with a wide prediction interval (0.36-31.7). Salinity generally lowered antibiotic sorption, and dissolved organic matter either suppressed (up to 97%) or enhanced sorption depending on the sorbate. Only three of 10 core mixture-toxicity studies applied a formal null model; these mostly reported additive or antagonistic outcomes, whereas enhanced-toxicity claims came mainly from designs without a null model. Plastisphere enrichment of resistance genes was frequent but comparator-dependent. Human-health evidence remains largely modelled or in vitro. We propose an evidence-graded framework and priorities for field-realistic, four-class monitoring, null-model-based mixture testing and research in under-represented regions.

**Keywords:** Microplastics; Antibiotics; Pharmaceuticals and personal care products; Pesticides; Mixture toxicity; Evidence grading

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## 1. Introduction

### *1.1. Four contaminant classes, one exposure problem*

Microplastics (MPs), pharmaceuticals and personal care products (PPCPs), antibiotics and pesticides are routinely detected in surface water, sediment and groundwater (Bertrand et al., 2023; K'oreje et al., 2018; Xu et al., 2019). They have traditionally been studied by separate research communities, although they share agricultural runoff, municipal and hospital wastewater, livestock and aquaculture effluent and improper waste disposal as sources (Grung et al., 2015; Kushwaha et al., 2024; Micella et al., 2024). Here, antibiotics are treated as a distinct class because of their resistance-selection hazard, and "other PPCPs" refers to non-antibiotic pharmaceuticals, hormones and personal care ingredients, so that no compound is counted twice.

The scale of use explains why these classes co-occur. Global human antibiotic consumption increased by an estimated 65% between 2000 and 2015 (Klein et al., 2018), and across 67 countries with comparable data it increased by a further 16.3%, from 29.5 to 34.3 billion defined daily doses, between 2016 and 2023; without policy change, global consumption is projected to reach 75.1 billion defined daily doses by 2030 (Klein et al., 2024). Bacterial antimicrobial resistance (AMR) was associated with 4.95 million deaths and directly attributable to 1.27 million deaths in 2019 (Murray et al., 2022). A substantial fraction of many administered pharmaceuticals is excreted unchanged or as active metabolites, and conventional wastewater treatment plants (WWTPs) remove them incompletely (Mojiri et al., 2022; Keerthanan et al., 2021); for example, secondary effluents of four WWTPs in Tianjin contained 1441.6-4917.6 ng $L^{-1}$ of ten antibiotics (Wang et al., 2021c). Only a very small fraction of applied pesticides reaches target pests (Pimentel, 1995), and neonicotinoids, introduced commercially in the early 1990s, became the most widely used insecticide class worldwide (Jeschke et al., 2011; Wood and Goulson, 2017). Cumulative plastic production had reached

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about 8300 million tonnes by 2015, of which about 6300 million tonnes had become waste (Geyer et al., 2017); weathering and abrasion fragment this material into particles <5 mm (Thompson et al., 2004; Barnes et al., 2009; Andrady, 2011).

### *1.2. Co-occurrence, interaction and enhanced toxicity are different claims*

Much of the literature, including our original submission, moves quickly from co-occurrence to interaction to enhanced toxicity. These are distinct claims that require different evidence (Box 1). Co-occurrence is demonstrated by field detection of two or more classes in the same water body or sample. Interaction requires evidence that one contaminant changes the fate, transport or bioavailability of another, typically from controlled sorption, desorption or transformation experiments. Enhanced toxicity requires that a combined exposure produces a larger effect than predicted by an explicit additive reference model; an effect larger than that of either component alone is not, by itself, evidence of synergy (Kortenkamp et al., 2009; Cedergreen, 2014). The vector hypothesis-that MPs increase the transport and bioavailability of co-occurring chemicals-also needs to be weighed against competing natural sorbents and dilution; model-supported reinterpretation of empirical studies suggested that MPs are usually a minor pathway relative to natural organic matter and food for hydrophobic chemicals (Koelmans et al., 2016; Hartmann et al., 2017).

**Box 1. Definitions used in this review**

Co-occurrence: detection of two or more contaminant classes in the same water body, sampling campaign or sample (Level 1 evidence). Same-sample co-detection is stronger than co-detection at the catchment scale.

Interaction: a measured change in the fate of one contaminant caused by another, for example sorption of an antibiotic to MPs, desorption in digestive fluids, or MP-surface-catalysed transformation (Level 2 evidence).

Combined (mixture) effect: the biological response to simultaneous exposure (Level 3 evidence). It is classified against a reference model: concentration addition (CA; Loewe additivity) for similarly acting components or independent action (IA; Bliss independence) for dissimilarly acting components (Loewe and Muischnek, 1926; Bliss, 1939).

Additive: observed effect not different from the reference prediction. Synergistic: significantly greater than predicted (commonly a model deviation ratio, MDR >2). Antagonistic: significantly smaller than predicted (MDR <0.5) (Belden et al., 2007; Cedergreen, 2014). "Enhanced" is used here only descriptively when a study reported a larger combined effect without testing a reference model.

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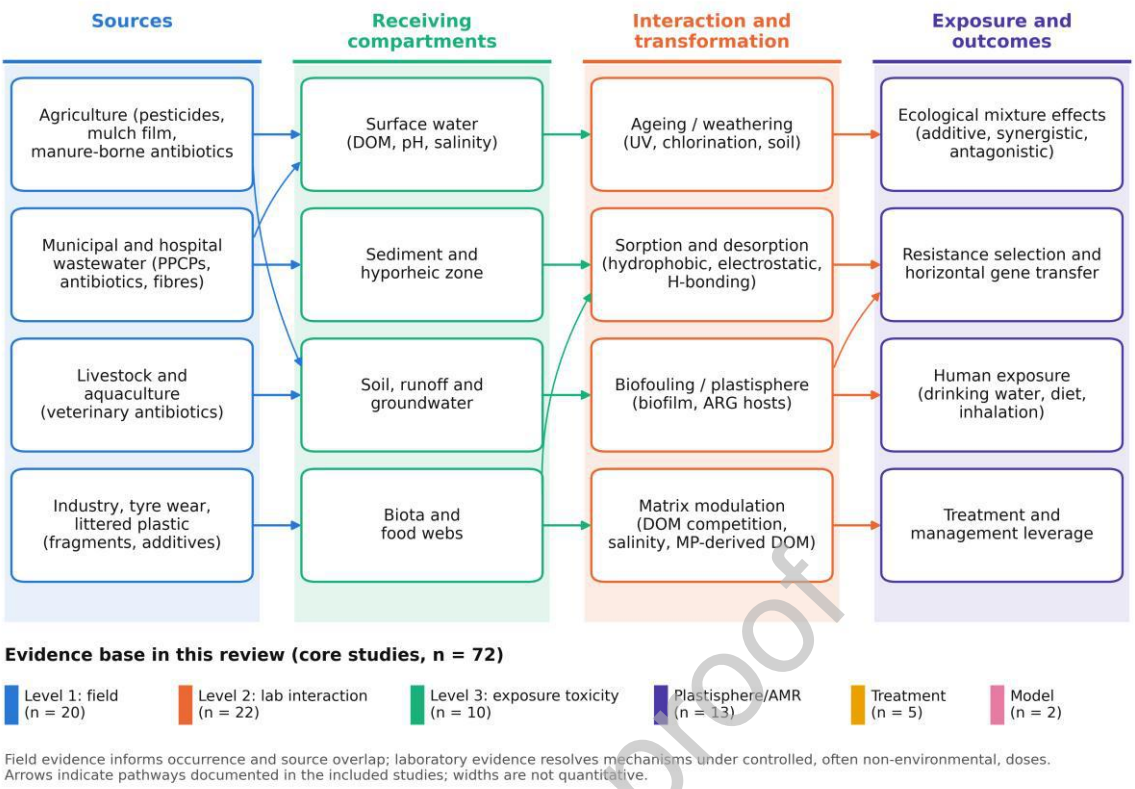



Fig. 1. Conceptual framework linking sources, receiving compartments, interaction and transformation processes, and exposure outcomes for microplastics (MPs), antibiotics, other pharmaceuticals and personal care products (PPCPs) and pesticides. The lower band shows the number of core studies in each evidence category. ARG, antibiotic resistance gene; DOM, dissolved organic matter.

### *1.3. Previous reviews and the remaining gap*

Several reviews have addressed parts of this problem (Table 1). Earlier syntheses focused on sorption of PPCPs or antibiotics to MPs (Atugoda et al., 2021; Wang et al., 2021d; Vieira et al., 2021; Torres et al., 2021; Stapleton et al., 2023). More recent reviews examined combined toxicity of MPs with antibiotics (Du et al., 2024; Zhang et al., 2024b; Tang, 2025), with pesticides (Derbalah and Takeda, 2025), or with broad groups of emerging contaminants (Bastante-Rabadán and Boltes, 2024; Ahmad Sabri et al., 2025; Banaee et al., 2026), and a PRISMA-guided review addressed pharmaceuticals and MPs together (Aib et al., 2025). Two gaps emerge from the comparison in Table 1. First, the closest review, Bastante-Rabadán and Boltes (2024), did cover MPs with antibiotics, other PPCPs and pesticides, but it combined aquatic and terrestrial studies, treated field evidence only partially and reported synergy or

antagonism as labelled by the primary authors rather than against a concentration addition or independent action model. We did not identify a review that separated field co-occurrence, laboratory interaction and laboratory mixture-toxicity evidence for the four classes. Second, although Bastante-Rabadán and Boltes (2024) noted that most mixture studies did not calculate interaction parameters, and Stapleton et al. (2023) reported that weathering and salinity strongly modify antibiotic sorption, these observations have not been quantified across contaminant classes or used to qualify vector claims. Our novelty claim is therefore restricted to these two points and is not based on the number of classes alone.

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**Table 1. Comparison of the present review with previous reviews on microplastics (MPs) and co-occurring antibiotics, other pharmaceuticals and personal care products (PPCPs) and pesticides.**

| Review | MPs | Antibiotics | Other PPCPs | Pesticides | Field co-occurrence | Mixture toxicity | AMR | Human health | Evidence grading / quantitative synthesis | Main focus |
|---|---|---|---|---|---|---|---|---|---|---|
| Atugoda et al. (2021) | ● | ◐ | ● | ○ | ◐ | ◐ | ◐ | ◐ | ○ | MP-PPCP sorption and vector transport |
| Wang et al. (2021d) | ● | ● | ○ | ○ | ◐ | ◐ | ● | ◐ | ○ | MP-antibiotic distribution, adsorption, toxicity |
| Vieira et al. (2021) | ● | ◐ | ● | ◐ | ○ | ○ | ○ | ○ | ○ | Adsorption modelling |
| Torres et al. (2021) | ● | ◐ | ◐ | ◐ | ○ | ○ | ○ | ○ | ○ | Sorption on degradable vs conventional MPs |
| Stapleton et al. (2023) | ● | ● | ○ | ○ | ○ | ○ | ◐ | ○ | ○ | Antibiotic sorption factors; weathering up to +171%, salinity up to -100% |
| Du et al. (2024) | ● | ● | ○ | ○ | ◐ | ● | ● | ○ | ○ | MP-antibiotic combined ecotoxicity, ARGs |
| Zhang et al. (2024b) | ● | ● | ○ | ○ | ● | ● | ◐ | ○ | ◐ | Occurrence, interaction factors, meta-analysis of combined toxicity by organism group, ecological risk |
| Bastante-Rabadán and Boltes (2024) | ● | ● | ● | ● | ◐ | ● | ◐ | ○ | ○ | Aquatic and terrestrial mixture toxicity; synergy/antagonism labels without CA/IA models |
| Aib et al. (2025) | ● | ● | ◐ | ○ | ○ | ◐ | ◐ | ● | ◐ | Sources, pathways and effects of pharmaceuticals and MPs; human exposure |
| Ahmad Sabri et al. (2025) | ● | ◐ | ● | ● | ◐ | ● | ◐ | ◐ | ○ | MPs with pharmaceuticals, PBDEs, PFAS, bisphenols, pesticides |
| Derbalah and Takeda (2025) | ● | ○ | ○ | ● | ◐ | ● | ○ | ◐ | ○ | Pesticide-MP interactions and remediation |
| Tang (2025) | ● | ● | ◐ | ◐ | ○ | ● | ● | ○ | ○ | Laboratory co-exposure toxicity in aquatic and terrestrial animals |
| Banaee et al. (2026) | ● | ◐ | ◐ | ● | ○ | ● | ○ | ◐ | ○ | Synergistic/antagonistic/additive patterns with metals, pesticides, pharmaceuticals, PAHs |
| Present review | ● | ● | ● | ● | ● | ● | ● | ● | ● | Four classes; PRISMA 2020 search; Level 1-3 evidence grading; null-model audit; realism meta-analysis; evidence-typed human health |

● dedicated synthesis; ◐ discussed without dedicated synthesis; ○ not addressed. Coverage was judged from the full text for Bastante-Rabadan and Boltes (2024), Aib et al. (2025) and Tang (2025), from the full text of the main sections for Ahmad Sabri et al. (2025) and Zhang Y. et al. (2024), and from titles, abstracts and section structure for the other reviews, which should be read as indicative. "Evidence grading" denotes explicit separation of field and laboratory evidence or a formal quantitative synthesis. AMR, antimicrobial resistance.

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### *1.4. Objectives*

This revised review aims to: (i) document the search, screening and evidence base transparently (PRISMA 2020); (ii) grade the evidence for co-occurrence, interaction and combined effects of MPs, antibiotics, other PPCPs and pesticides; (iii) quantify how environmental realism (ageing, biofouling, salinity and dissolved organic matter, DOM) modifies sorption to MPs; (iv) audit how mixture outcomes were classified; (v) re-evaluate human-health relevance by evidence type; and (vi) derive research priorities, including for under-represented regions. Treatment technologies are considered only where they bear on exposure.

## 2. Review methodology

### *2.1. Design*

In response to the reviewers' comments on the literature search, the search, screening, selection and reporting were carried out following the PRISMA 2020 guideline (Page et al., 2021). This is a critical review with a systematic, reproducible literature search; it was not registered and is not a full systematic review of every effect size. The full search strings, eligibility criteria, screening counts, extraction workbook, meta-analysis dataset and a PRISMA checklist are provided in the Supplementary Material (Tables S1-S12).

### *2.2. Information sources and search strategy*

Web of Science Core Collection, ScienceDirect and PubMed were searched from database inception to December 2025. The core Boolean structure combined four concept blocks: (microplastic* OR "plastic particle*" OR "plastic debris") AND (antibiotic* OR "antimicrobial resistance" OR pharmaceutical* OR "personal care product*" OR PPCP* OR pesticide*) AND (aquatic OR freshwater OR marine OR river* OR lake* OR sediment* OR wastewater) AND (co-occurrence OR coexist* OR interaction* OR mixture* OR "combined exposure" OR toxicity OR "risk assessment"). Focused strings addressed

sorption/desorption/ageing/biofouling, mixture toxicity and AMR-biofilm evidence (Table S1). Because strings that require all concept blocks miss eligible studies that name a specific compound or polymer rather than the class term, two further sources were used and are reported separately in the second arm of the PRISMA diagram (Fig. 2): (i) backward and forward citation searching of included studies and key reviews, together with targeted compound- and polymer-specific searches; and (ii) update searches from January to September 2026, carried out during revision. Google Scholar was used only to cross-check retrieval; its hits were not added to the identification counts.

### *2.3. Eligibility criteria*

Studies were included if they (i) were peer-reviewed primary studies (field monitoring, laboratory or mesocosm experiments, or exposure studies); (ii) reported measured contaminant parameters-occurrence or concentration, sorption/desorption, transformation, toxicity linked to measured exposures, bioaccumulation or resistance markers-for microplastics or at least one of the three chemical classes; (iii) concerned aquatic environments, aquatic organisms or water-connected matrices (wastewater, sludge, sediment, runoff); and (iv) were available in full text. Reviews, meta-analyses and other secondary syntheses, editorials, conference abstracts, studies without primary contaminant measurements, studies with no aquatic exposure pathway (soil-only systems or terrestrial organisms) and studies with no target contaminant class (e.g., PFAS or mercury without microplastics) were excluded (Table S2). Studies that measured microplastics together with a co-contaminant outside the three chemical classes (polycyclic aromatic hydrocarbons, metals, PFAS), or that were methodological rather than environmental, were retained as contextual evidence and analysed separately; they were not counted as evidence for the four target classes.

### *2.4. Selection process*

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Database searches yielded 397 records (Web of Science 155; ScienceDirect 148; PubMed 94). After removal of 8 duplicates, 389 records were screened by title and abstract and 328 were excluded, mainly reviews, meta-analyses and other secondary syntheses. Sixty-one reports were retrieved and assessed in full text; 8 were excluded for lacking primary contaminant measurements and 2 for having no aquatic exposure pathway, leaving 51 studies, which form the majority of the evidence base. Because every database string required the microplastic concept block, studies without a microplastic component (chemical-only field and treatment studies used as co-occurrence context) could not be retrieved by the database searches; these were identified by citation and targeted searching (21 reports), and studies published in 2026 by the update searches (14 reports). Of these 35 reports, 9 were excluded (no target contaminant class, 6; not a primary study, 1; no aquatic exposure pathway, 1; outside scope, 1), leaving 26 studies. Repeated downloads of the same article were consolidated before assessment, so each included study corresponds to one report. In total, 77 studies were included: 72 core studies on the four target classes and 5 contextual studies (Fig. 2; Tables S3 and S3b). Twelve included studies were published in 2026 and entered only through the update searches; none of them contributed to the ageing meta-analysis (Section 4.3).

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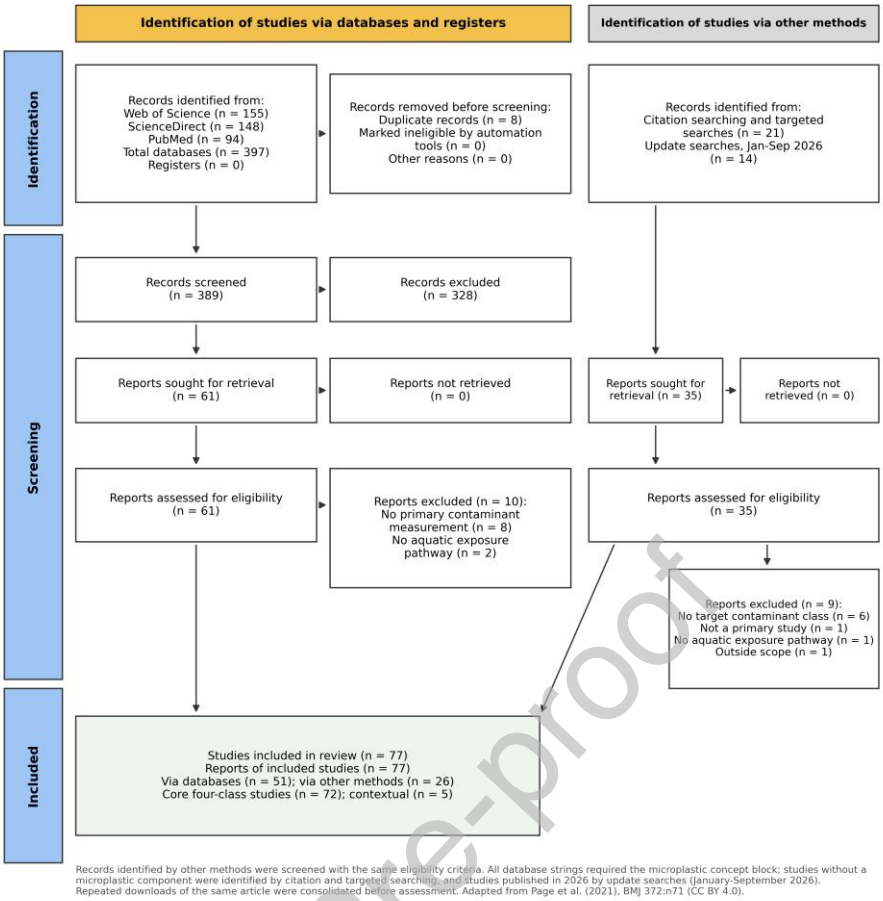



Fig. 2. PRISMA 2020 flow diagram of literature identification, screening and inclusion, with the database arm (left) and the other-methods arm (citation and targeted searching, and update searches from January to September 2026; right). Repeated downloads of the same article were consolidated before assessment. Adapted from Page et al. (2021).

### *2.5. Data extraction and evidence classification*

Data were extracted into a structured workbook with separate sheets for occurrence, interactions, effects and AMR, treatment and human-health evidence, recording the exact page, table or figure for each value (Table S4). Each study was assigned one primary evidence category (Table 2): Level 1, field co-occurrence or occurrence; Level 2, laboratory interaction (sorption, desorption, ageing, biofouling, transformation); Level 3, laboratory exposure toxicity; and supporting categories for plastisphere/AMR, treatment/removal and modelling. The levels describe what a study can demonstrate, not its quality, and were used to prioritise evidence as follows: statements about environmental occurrence rely on Level 1; statements

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about mechanisms rely on Level 2; statements about combined effects rely on Level 3 with an explicit reference model. For Level 3 studies we recorded the author classification (synergistic, additive, antagonistic), the reference model used, and whether single-component treatments were present. Country was assigned by study site for field studies and by the corresponding author's institution for laboratory and modelling studies.

**Table 2. Evidence classification framework applied to the 72 core studies.**

| Category | Definition | Core studies (n) | Examples | What it can support | What it cannot support |
|---|---|---|---|---|---|
| Level 1: field (co-)occurrence | Field or mesocosm detection of MPs and/or target chemicals; same-sample co-detection noted separately | 20 (3 with MPs + a target chemical) | (Yu et al., 2022; Song et al., 2026; Udensi et al., 2026; Bradley et al., 2017; Halbach et al., 2021) | Occurrence, co-occurrence, source overlap, seasonal dynamics | Interaction, causation or combined effects |
| Level 2: laboratory interaction | Controlled sorption, desorption, ageing, biofouling or transformation experiments | 22 | (Li et al., 2018; Wang et al., 2022b; Xu et al., 2018; Fatema and Farenhorst, 2022; Fan et al., 2023) | Mechanisms and direction of modifiers (ageing, DOM, salinity) | Field magnitude of the vector effect |
| Level 3: laboratory exposure toxicity | Single or combined exposure of organisms or microbial systems | 10 (3 with formal null model) | (Nugnes et al., 2022; Kühl et al., 2026; Mao et al., 2024; Wang et al., 2023; Zeng et al., 2025) | Effects under controlled doses; interaction class only with a reference model | Current field risk when doses exceed field levels |
| Plastisphere / AMR | Resistance genes, pathogens or gene transfer on MPs (field or laboratory) | 13 | (Xu et al., 2022; Wang et al., 2020a; Nguyen et al., 2026; Yu et al., 2023; Han et al., 2024) | Enrichment relative to a stated comparator | Contribution to clinical AMR burden |
| Treatment / removal | Removal of MPs, antibiotics or resistance markers in treatment systems | 5 | (Johnson et al., 2020; Chand et al., 2024; Long et al., 2019; Manoli et al., 2022) | Exposure reduction by barriers | Ecological or health outcomes |
| Model | Predictive or process models | 2 | (Wang et al., 2024b; Li et al., 2020) | Hypotheses and screening | Validation without field data |

Levels describe the type of claim a study can support, not its quality. Contextual studies (n = 5) on MPs with PAHs, metals or PFAS, and one methodological study, are analysed separately. DOM, dissolved organic matter.

### *2.6. Quantitative synthesis*

Where at least two studies reported comparable sorption parameters under a reference and a modified condition, we calculated the log response ratio, lnRR = ln(X_modified/X_reference) (Hedges et al., 1999), using the parameter reported with the most information in the order linear

Kd, Langmuir qmax, then equilibrium qe. Within-study variances were obtained by the delta method when standard deviations and replicate numbers were reported; otherwise the median coefficient of variation of records that did report dispersion was imputed. Multiple comparisons from one study (e.g., several polymers) were averaged so that each study contributed one effect. Studies were pooled with a DerSimonian-Laird random-effects model (DerSimonian and Laird, 1986) and Hartung-Knapp-Sidik-Jonkman confidence intervals, which perform better with few studies (IntHout et al., 2014); heterogeneity is reported as $I^2$, $\tau^2$ and the 95% prediction interval (Higgins et al., 2009). Sensitivity analyses included leave-one-out pooling, an unweighted study mean with bootstrap confidence intervals (10,000 resamples), exclusion of a ratio reported only approximately in the text, and pooling of parameter-homogeneous subsets (capacity parameters only; Langmuir qmax only). Contrasts supported by fewer than two independent studies (biofouling, salinity) or with opposite mechanistic directions (DOM) are presented descriptively. Acute toxicity data were summarised as the ratio of the 96-h LC50 in combination to that of the chemical alone. Analyses were performed in Python (NumPy, SciPy); code and data are provided in Table S6.

### *2.7. Evidence map and research geography*

Replacing the previous reliance on published bibliometric studies, we analysed the included studies directly by publication year, country, evidence category, contaminant-class combination and polymer type. The analysis is restricted to the included studies and is therefore a descriptive evidence map of the included corpus rather than a bibliometric analysis of the whole field, and we interpret it as such.

### *2.8. Verification of quantitative statements*

All quantitative statements retained from the original submission were checked against their cited sources. Statements that could not be traced were removed or replaced with values from included studies, and incorrect attributions were corrected (Table S10). In a second pass,

40 numerical values reported in Sections 4-6 were searched for in the text of their source articles and all 40 were located (Table S12).

### *2.9. Methodological limitations*

Several limitations should be noted. No formal risk-of-bias tool was applied; instead, the evidence levels, reference-model status and reporting of controls, replicates and dispersion were recorded for each study. Data were extracted by one reviewer with AI-assisted text extraction and checked against the original tables and figures, but an independent duplicate extraction was not performed. Only full-text articles accessible to the authors were included, which may under-represent studies published in regional journals and non-English languages. Most included studies (51 of 77) were identified by the database searches; the remaining 26 were chemical-only studies without a microplastic component, which the microplastic-based strings could not retrieve, or studies published in 2026, and were identified by citation, targeted and update searches (Section 2.4). The evidence base is therefore a screened selection rather than a complete census of the literature. Finally, the quantitative synthesis is restricted to sorption contrasts with sufficient comparable data; it is not a meta-analysis of toxicity or occurrence.

## 3. Characteristics of the evidence base

The 77 included studies were published between 2015 and 2026, and 57 (74%) appeared from 2022 onwards (Fig. 4a). Of the 72 core studies, 20 provided Level 1, 22 Level 2 and 10 Level 3 evidence; 13 addressed the plastisphere or AMR, 5 treatment and 2 modelling (Table 2). Microplastics were studied in 58 core studies, antibiotics in 32, pesticides in 21 and other PPCPs in 13 (Fig. S2). The most frequent combination was MPs with antibiotics (23 studies), followed by MPs alone (18) and MPs with pesticides (11); MPs with non-antibiotic PPCPs were studied in only two core studies, and four studies combined MPs with two or more chemical classes (Fig. 4b). Six studies measured two or more chemical classes without MPs

and eight a single chemical class. No included study measured MPs together with antibiotics, other PPCPs and pesticides. Polystyrene and polyethylene dominated laboratory interaction work, followed by polyvinyl chloride; biodegradable polymers and tyre-wear particles were rarely tested (Fig. S3). The 5 contextual studies addressed MP-sorbed polycyclic aromatic hydrocarbons or metals (Liang et al., 2021; Pirvu et al., 2025; Huang et al., 2023), a PFAS-PET mixture-toxicity design (Soltanighias et al., 2024) and an educational sorption module (Vinko et al., 2025); they informed methods and analogues but were not counted as evidence for the four target classes.

The evidence base is geographically concentrated (Fig. 3). China contributed 44 of 77 studies (57%) and 42 of 72 core studies (58%); Europe contributed 20 studies across 12 countries, North America 5, Latin America 4 and Africa 3 (Ghana, Nigeria and the South Africa-Lesotho Orange-Senqu basin). India contributed one study, and no included study originated from South-East Asia, the Middle East or Oceania. Laboratory interaction and AMR studies were almost entirely from China, Europe and North America, whereas the three African studies were all field occurrence studies.

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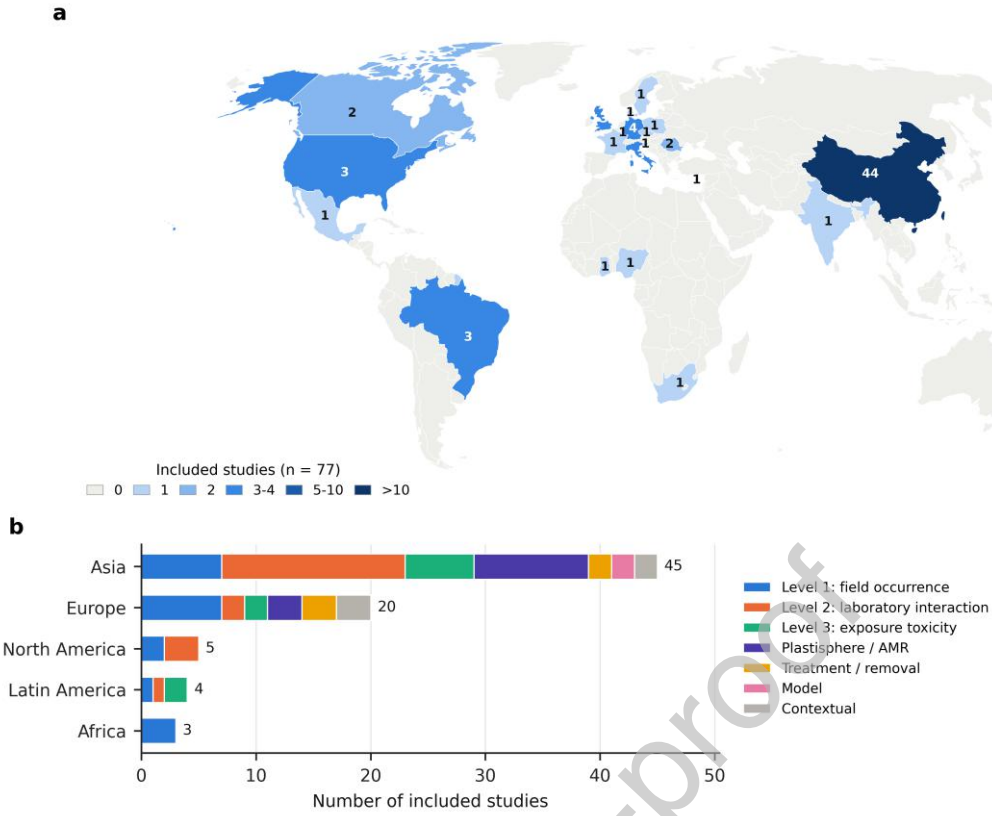



Fig. 3. Geographic distribution of the included studies (n = 77). (a) Number of studies per country, assigned by study site for field studies and by the corresponding author's institution for laboratory and modelling studies (one study from the Taiwan region is counted with China). (b) Studies per region by evidence category.

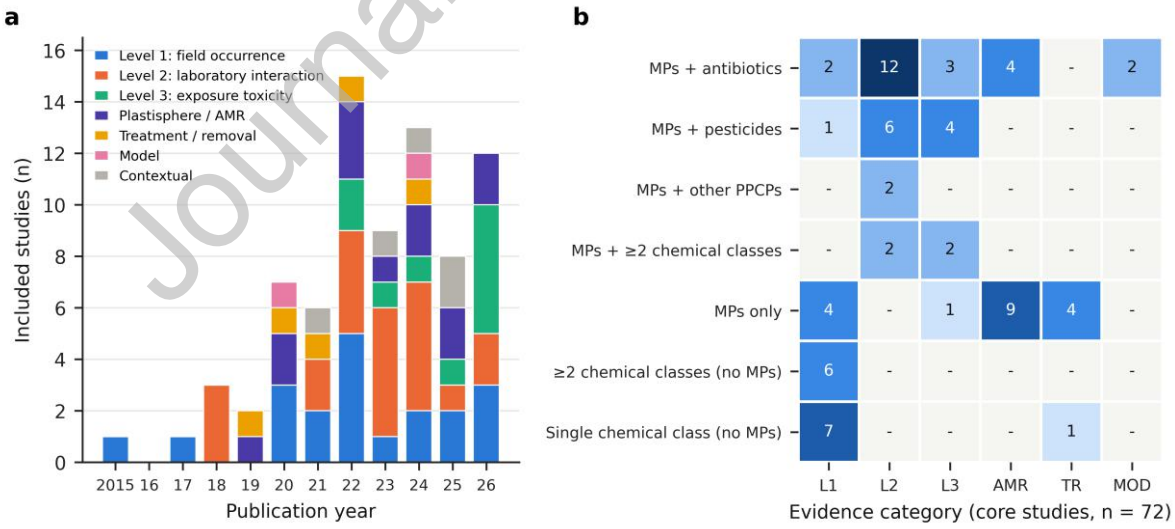



Fig. 4. Evidence map. (a) Included studies by publication year and evidence category (n = 77). (b) Core studies (n = 72) by contaminant-class combination and evidence category; L1, field occurrence; L2, laboratory interaction; L3, exposure toxicity; AMR, plastisphere/antimicrobial resistance; TR, treatment; MOD, model.

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## 4. Sources, co-occurrence and interaction mechanisms

### *4.1. Shared sources and field co-occurrence (Level 1)*

Field studies consistently show that wastewater-impacted and agricultural waters carry complex chemical mixtures. U.S. streams contained a median of 70 detected organic compounds per site (range 4-161) and summed concentrations up to 102,847 ng $L^{-1}$ (Bradley et al., 2017); high-throughput monitoring of 323 PPCPs and pesticides in Chinese surface water detected azithromycin up to 3493.2 ng $L^{-1}$ and dinotefuran up to 755.6 ng $L^{-1}$ in the same samples (Du et al., 2025). Pharmaceuticals and pesticides co-occurred in Danish streams (Nanusha et al., 2022) and in German wastewater and bank-filtration systems (Wode et al., 2015; Köke et al., 2022). Pesticide exposure is strongly event-driven: in small German agricultural streams the median summed pesticide concentration rose from 0.07 μg $L^{-1}$ in dry weather to 0.7 μg $L^{-1}$ after rainfall, with up to 41 pesticides in one sample (Halbach et al., 2021), and biocides reached surface waters through distinct wastewater and building-runoff pathways (Galle et al., 2020). Pesticide transformation products dominated water and sediment of a French agricultural pond (Slaby et al., 2022), and natural estrogens and their metabolites contributed most of the calculated estrogenic activity in WWTP effluent and river water (Tang et al., 2020b). Antibiotics and resistance genes were widespread in the Pearl and Liaohe river basins (Tang et al., 2020a; Gao et al., 2022a), in Tianjin effluent-receiving waters (Wang et al., 2021c), and at mg $L^{-1}$ levels in hospital effluent and landfill leachate in Ghana, although none were detected in boreholes, tap water or sachet water (Opoku et al., 2025).

Microplastic field studies show equally wide ranges: 5-152 MPs $m^{-3}$ in the Amazon mainstem but up to 74,550 MPs $m^{-3}$ in urban tributaries (Rico et al., 2023), 1-69.75 items $L^{-1}$ (site means) in the Orange-Senqu basin (Graham et al., 2024) and 1.78 ± 0.84 items $L^{-1}$ in the Huangpu River (Xu et al., 2022). WWTPs retained 79.3-97.8% of MPs in Xiamen (Long et al., 2019) and 99.98% in an advanced Swedish plant with sand filtration (Chand et al., 2024), and

bank filtration reduced MP concentrations by more than 84% between river and groundwater (Loui et al., 2026).

Crucially, true co-detection of MPs and target chemicals in the same study is rare. Only three of the 20 Level 1 studies quantified MPs and a target chemical together: antibiotics accumulated on MPs deployed in a mariculture area (Yu et al., 2022) and in WWTP ponds (Song et al., 2026), and MPs and organochlorine pesticides shared hotspots in the Nworie River, Nigeria (Udensi et al., 2026). The remaining field studies measured MPs or chemicals, not both. Field co-occurrence of all four classes is therefore inferred from overlapping sources rather than demonstrated, and should be stated as such.

### *4.2. Sorption mechanisms across classes (Level 2)*

Sorption of antibiotics to pristine MPs is generally modest and polymer-dependent. In freshwater, linear Kd values for five antibiotics on five polymers ranged from 6.19 to 756 L $kg^{-1}$, with polyamide sorbing amoxicillin and tetracycline far more strongly than PE, PP, PS or PVC (Li et al., 2018). Electrostatic attraction favours cationic over anionic pharmaceuticals on negatively charged polymer surfaces (Razanajatovo et al., 2018), and electrostatic interaction, hydrogen bonding and cation bridging dominate for ionisable antibiotics such as oxytetracycline, with maximum sorption near pH 5 (Zhang et al., 2018). Non-antibiotic PPCPs show similar polymer dependence: UV-aged PS and poly(butylene adipate-co-terephthalate) sorbed 23.91 and 27.65 mg $g^{-1}$ diclofenac (Liang et al., 2023), and sorbed fractions of diclofenac, atenolol, ibuprofen and acetaminophen on PE, PS and PVC were not explained by particle size or hydrophobicity (Tseng et al., 2022). Chemically aged plastics sorbed more of a 66-compound PPCP panel than virgin plastics (Yao et al., 2023).

Pesticide sorption depends strongly on hydrophobicity. MPs sorbed more than 50% of DDT but less than 6% of the current-use herbicides 2,4-D, atrazine and glyphosate (except glyphosate on PVC in low-ionic-strength solutions), and adding 5% MPs to river sediment did

not change pesticide sorption, whereas ash and charcoal did (Fatema and Farenhorst, 2022). Aged PE sorbed up to 350.4 μg $g^{-1}$ atrazine and 327.8 μg $g^{-1}$ imidacloprid through hydrophobic interaction (Wu et al., 2025); organochlorine pesticides reached equilibrium with PS within 6 h (Qmax 1.02-29.7 μg $g^{-1}$) (Cojocaru et al., 2024); and poly-parameter linear free-energy relationships and QSPR models predicted sorption of neutral compounds, including atrazine and diuron, to polar and non-polar polymers (Xu et al., 2021; Li et al., 2020). Earlier studies outside our search results also reported sorption of neonicotinoids and other insecticides to conventional and biodegradable MPs (Li et al., 2021; Šunta et al., 2020; Wang et al., 2024a). Herbicide anions (glyphosate, 2,4-D) sorbed only 5-10% to virgin or aged acrylonitrile butadiene styrene, whereas the surfactant cation of the same ionic-liquid formulations sorbed strongly (Lisiecka et al., 2024). These results caution against generalising "MPs as pesticide vectors" to polar, current-use pesticides.

### *4.3. Environmental realism: ageing, biofouling, salinity, DOM and desorption*

As recommended by the reviewers, we evaluated the vector hypothesis along four environmental-realism contrasts (Table 3; Fig. 5): pristine versus aged MPs, clean versus biofouled surfaces, freshwater versus saline water, and DOM-free versus DOM-rich water.

Ageing. Across seven studies (11 comparisons) covering tetracycline, oxytetracycline, erythromycin, diclofenac and chlorpyrifos, ageing by UV, chlorination, soil exposure, anaerobic microbial processes or beach weathering increased sorption capacity by a pooled 3.40-fold (95% CI 1.58-7.28; $p = 0.008$) (Gao et al., 2022b; Wang et al., 2022b; Hu et al., 2024; Costa et al., 2024; Zhang et al., 2018; Liang et al., 2023; Han et al., 2024). The direction was consistent, but magnitude varied greatly ($I^2 = 99\%$; prediction interval 0.36-31.7), from 1.32-fold for UV-B-aged PET and chlorpyrifos (Costa et al., 2024) to about 10-fold for beach-weathered PS foam and oxytetracycline (Zhang et al., 2018). The pooled estimate was robust to omission of any single study (2.82-3.97-fold), to unweighted pooling (3.39; 1.99-6.04) and

to exclusion of the approximate erythromycin ratio (2.94; 1.27-6.83) (Fig. S1). Because studies reported different sorption parameters, we also pooled parameter-homogeneous subsets: capacity parameters only, excluding the linear Kd study (2.82; 1.31-6.04; k = 6), and Langmuir qmax only (2.90; 0.32-26.6; k = 3). The point estimates were similar, but the qmax-only interval included 1, and only two studies reported dispersion for both conditions, so the pooled ratio should be read as an indication of direction and order of magnitude rather than a precise effect size (Table S6). The prediction interval implies that in a new setting ageing could leave sorption practically unchanged; site-specific ageing state therefore needs to be measured rather than assumed.

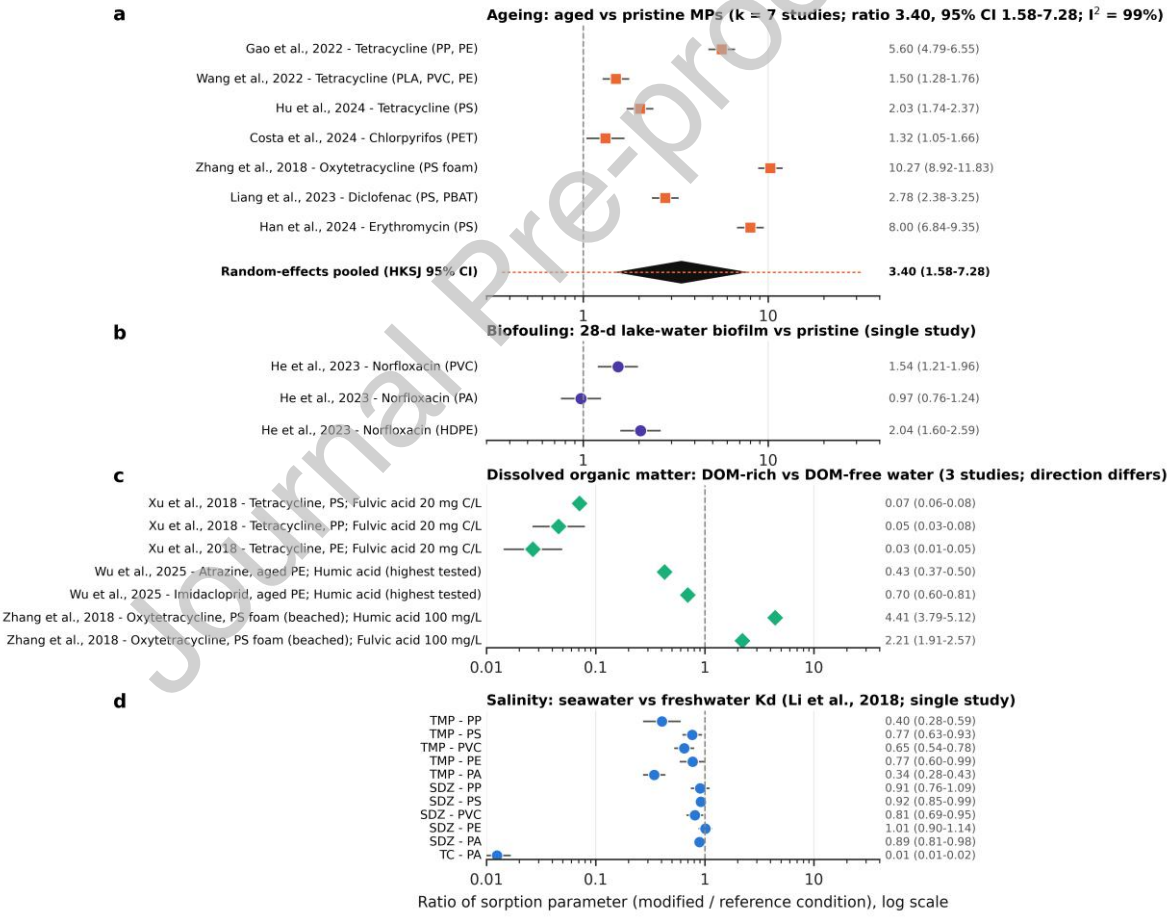



Fig. 5. Environmental-realism synthesis of sorption to microplastics. (a) Random-effects meta-analysis of aged versus pristine MPs (study-level ratios with 95% CI; diamond, pooled estimate with Hartung-Knapp-Sidik-Jonkman 95% CI; dashed line, 95% prediction interval). (b) Biofilm-coated versus pristine MPs. (c) DOM-rich versus DOM-free water. (d) Seawater versus freshwater. Panels (b)-(d) are descriptive because they contain fewer than two independent studies or opposite mechanistic directions.

Biofouling. Biofilms grown for 28 days in lake water increased Langmuir capacity for norfloxacin on PVC (1.54-fold) and HDPE (2.04-fold) but not on polyamide (0.97-fold) (He et al., 2023), and phytoplankton-derived biofilms increased or decreased antibiotic adsorption depending on the algal species and fouling level (Kiki et al., 2023). Biofilms also change fate beyond sorption: tetracycline biodegraded more slowly on PLA and PVC plastispheres (17.3% and 16.7% in 28 days) than on mineral biofilms (24%) (Wang et al., 2022a), whereas antibiotics accumulated over 12 months on MPs deployed in WWTP ponds reflected biofilm chemistry more than biomass (Song et al., 2026).

Salinity. In the only study that compared freshwater and seawater directly, Kd declined in 10 of 11 antibiotic-polymer pairs (median ratio 0.77; tetracycline on polyamide 0.012), and ciprofloxacin and amoxicillin showed no measurable sorption in seawater (Li et al., 2018). This agrees with Stapleton et al. (2023), who reported salinity-driven reductions of up to 100%.

DOM. DOM effects were direction-dependent, so no pooled estimate is given. Fulvic acid at 20 mg C $L^{-1}$ reduced tetracycline sorption to PE, PP and PS by 93-97% (Xu et al., 2018), humic acid reduced atrazine and imidacloprid sorption to aged PE by up to 57% and 30% (Wu et al., 2025), but humic and fulvic acids increased oxytetracycline sorption to beach-weathered PS 2.2-4.4-fold through π-π bridging (Zhang et al., 2018). In natural waters with typical DOC, MPs may therefore be a minor sorbent for some antibiotics (Xu et al., 2018), consistent with the natural-sorbent comparison above (Fatema and Farenhorst, 2022) and with model-based assessments (Koelmans et al., 2016).

Desorption and changing exposure conditions. Vector claims require desorption in the receiving compartment. Sulfamethoxazole desorbed from tyre-wear particles by 62.7-65.2% in simulated human gastric and intestinal fluids, increasing to 71.5-79.8% after photo-ageing and to 87.2% in sequential gastric-intestinal digestion, with human fluids exceeding fish intestinal fluid (Fan et al., 2023); faster desorption under gut conditions has also been reported for

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persistent organic pollutants (Bakir et al., 2014). Soil-exposed MPs sorbed more tetracycline but also desorbed more in soil DOM (Wang et al., 2022b). Antibiotics altered heteroaggregation and sedimentation of nanoplastics with minerals in filtered pond water (Zhou et al., 2026), and MP transport through riverbeds depended on polymer density and hydraulic regime (Loui et al., 2026). Together, these results show that ageing can increase sorption, but DOM, salinity, biofouling and desorption can offset or reverse the net vector effect. Conclusions that MPs enhance persistence and biological effects should therefore be conditional on these factors.

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**Table 3. Environmental-realism framework for the vector role of microplastics: quantitative synthesis of paired laboratory comparisons.**

| Contrast | Evidence (studies; comparisons) | Result (ratio modified/reference) | Interpretation | References |
|---|---|---|---|---|
| Pristine vs aged MPs | 7; 11 | Pooled 3.40 (95% CI 1.58-7.28); $I^2$ = 99%; prediction interval 0.36-31.7; study range 1.32-10.3 | Ageing (UV, chlorination, soil, microbial, beach weathering) consistently increases sorption, but magnitude is highly setting-specific | (Gao et al., 2022b; Wang et al., 2022b; Hu et al., 2024; Costa et al., 2024; Zhang et al., 2018; Liang et al., 2023; Han et al., 2024) |
| Clean vs biofouled surfaces | 2; 3 quantified | 0.97-2.04 (norfloxacin); direction species-dependent for phytoplankton biofilms | Biofilms can increase or leave unchanged sorption and slow biodegradation of sorbed antibiotics | (He et al., 2023; Kiki et al., 2023; Wang et al., 2022a) |
| Freshwater vs saline water | 1; 11 | Median 0.77 (0.012-1.01); no sorption of ciprofloxacin and amoxicillin in seawater | Salinity generally reduces antibiotic sorption; vector role likely weaker in estuarine and marine waters | (Li et al., 2018; Stapleton et al., 2023) |
| DOM-free vs DOM-rich water | 3; 7 | 0.03-0.07 (fulvic acid, tetracycline); 0.43-0.70 (humic acid, pesticides); 2.2-4.4 (humic/fulvic acid, oxytetracycline on weathered PS) | Direction depends on sorbate and DOM; not pooled. DOM often out-competes MPs as a sorbent | (Xu et al., 2018; Wu et al., 2025; Zhang et al., 2018) |
| MPs vs natural sorbents | 1; 4 pesticides | 5% MP addition to sediment: no change in sorption; ash/charcoal increased sorption | MPs are a minor sorbent for current-use pesticides relative to natural phases | (Fatema and Farenhorst, 2022; Koelmans et al., 2016) |
| Single vs multiple sorbates | 2 (qualitative) | Competitive sorption in 7-antibiotic and 66-PPCP panels | Competition rarely quantified; single-sorbate capacities overestimate field loadings | (Kiki et al., 2023; Yao et al., 2023) |
| Sorbed vs desorbed (gut fluids) | 1; 4 | Desorption 62.7-65.2% (pristine) to 71.5-87.2% (aged) | Ageing increases bioaccessibility of sorbed antibiotic; high laboratory loadings | (Fan et al., 2023) |

Ratios >1 indicate higher sorption (or desorption) under the modified condition. Pooled estimate: DerSimonian-Laird random effects with Hartung-Knapp-Sidik-Jonkman CI; sensitivity analyses in Fig. S1 and Table S6.

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### *4.4. Microplastic-derived dissolved organic matter and surface-mediated transformation*

MPs also act chemically rather than only as passive sorbents. DOM leached from PVC sequestered 28.5% of seven antibiotics in the dark, about three times more than solid PVC (10.1%), and under sunlight enhanced photodegradation by up to 88.9% while generating transformation products toxic to Microcystis aeruginosa (Ahlonsou et al., 2026). DOM from UV-aged PET and PS bound chloramphenicol and carbamazepine, with binding determined more by the pharmaceutical than by the DOM source (Yan et al., 2024). Photo-aged PVC catalysed hydrolysis of cefazolin through hydrogen bonding to the β-lactam carbonyl, but not of cephalexin (Wang et al., 2021a). These processes can shorten persistence, contrary to the common assumption that sorption to MPs always prolongs it.

### *4.5. A revised conceptual mass-balance framework*

Both reviewers questioned the necessity and parameterisation of the mass-balance equation in the original submission. We retain a revised version only as a structuring tool that makes explicit the terms that field studies would need to measure. Instead of a bimolecular term between contaminants, the revised form tracks the dissolved (C_i,w) and MP-sorbed (C_i,MP) fractions of chemical i and links them through sorption and desorption kinetics:

$$dC_{i,w}/dt = S_i - (k_{deg,i} + k_{vol,i})\, C_{i,w} - k_{a,i} \cdot M_{MP} \cdot C_{i,w} + k_{d,i} \cdot C_{i,MP} \cdot M_{MP} - k_{up,i}\, C_{i,w} \quad (1a)$$

$$dC_{i,MP}/dt = k_{a,i} \cdot C_{i,w} - k_{d,i} \cdot C_{i,MP} - k_{deg,MP,i} \cdot C_{i,MP} \quad (1b)$$

where S_i is the external input rate (μg $L^{-1}$ $d^{-1}$); k_deg,i and k_vol,i are first-order loss rate constants in water ($d^{-1}$); M_MP is the MP mass concentration (g $L^{-1}$); k_a,i (L $g^{-1}$ $d^{-1}$) and k_d,i ($d^{-1}$) are sorption and desorption rate constants whose ratio approximates Kd at equilibrium; C_i,MP is the sorbed concentration (μg $g^{-1}$); k_deg,MP,i captures surface-mediated transformation (Section 4.4); and k_up,i is net biological uptake. Ageing, biofouling, salinity and DOM enter through k_a,i and k_d,i (Table 3). Table S7 lists each parameter, its units and example values from the included studies. We stress that this framework has not been

parameterised or validated in any field system and is not used to generate quantitative predictions in this review; its purpose is to show that the MP pathway matters only when M_MP · Kd is large relative to natural sorbents, which the evidence in Sections 4.2-4.3 suggests is uncommon for polar antibiotics and current-use pesticides (Koelmans et al., 2016).

## 5. Combined ecological effects

### *5.1. Mixture-toxicity frameworks*

Mixture assessment requires a reference model. Concentration addition assumes a shared mode of action, independent action assumes independent modes, and the model deviation ratio (MDR; predicted/observed effect concentration) is commonly used to classify deviations, with MDR >2 indicating synergy and <0.5 antagonism (Loewe and Muischnek, 1926; Bliss, 1939; Belden et al., 2007). In the wider ecotoxicological literature, synergy exceeding a two-fold deviation is uncommon and concentrated in particular chemical groups (Cedergreen, 2014). For MP-chemical mixtures an additional complication is that MPs can change the freely dissolved concentration of the chemical, so an apparent interaction may reflect altered exposure rather than toxicodynamic synergy.

### *5.2. Demonstrated mixture interactions*

Table 4 summarises the combined-exposure studies. Only three core Level 3 studies applied a formal reference model. Using Bliss independence, PS microspheres combined with the neonicotinoid imidacloprid and the antiviral acyclovir produced mostly antagonistic genotoxicity in Ceriodaphnia dubia over 24 h and mostly additive effects on reproduction over 7 days (Nugnes et al., 2022). Using MDR, imidacloprid antagonised the chronic toxicity of pristine PE to Daphnia similis, while photo-aged PE mainly affected reproduction (Kiihl et al., 2026). Using the Abbott formula, PS combined with tetracycline yielded 10 antagonistic and 2 synergistic classifications in two submerged macrophytes, although sign conventions in the published indices require clarification (Mao et al., 2024). As a methodological comparator

outside the four classes, PFAS-PET mixtures analysed against an additive null model in Daphnia magna gave 59% additive and 41% synergistic outcomes and no antagonism (Soltanighias et al., 2024).

The remaining Level 3 studies reported enhanced effects without a reference model. PE lowered the 96-h LC50 of acetochlor in zebrafish from 0.76 to 0.42-0.47 mg $L^{-1}$ (Wang et al., 2023), PS and aged PS lowered the LC50 of atrazine from 1.577 to 1.197 and 1.024 mg $L^{-1}$, with co-exposure also degrading water quality (Zeng et al., 2025), MPs with the pyrethroid imiprothrin reduced cladoceran population growth by 53-65% (Sarma et al., 2026), and PE with sulfanilamide (Zhang et al., 2022), and PE with sulfamethoxazole in sulfate-reducing sludge (Yan et al., 2026) were described as intensifying stress. These ratios (0.55-0.76; Fig. 6b) indicate greater acute toxicity in combination, but without single-MP controls analysed under a null model they cannot be classified as synergistic.

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**Table 4. Demonstrated combined-exposure effects of microplastics with antibiotics, pharmaceuticals and pesticides (Level 3 evidence).**

| MP type | Chemical contaminant | Organism / system | Exposure design | Endpoint | Interaction (reference model) | Main finding | Reference |
|---|---|---|---|---|---|---|---|
| PS, 1.0 µm | Imidacloprid + acyclovir | Ceriodaphnia dubia | Binary/ternary mixtures at EC50-based ratios; 24 h and 7 d | Comet assay; reproduction | Antagonistic (24 h); additive (7 d) (Bliss IA) | Deviations from independence mostly antagonistic for genotoxicity and additive for reproduction | (Nugnes et al., 2022) |
| PE, pristine and UV-C aged (94 d) | Imidacloprid | Daphnia similis | Chronic factorial; PE up to 140 mg $L^{-1}$ | Survival; neonates | Antagonistic (MDR <0.5) | Imidacloprid attenuated pristine PE toxicity; aged PE mainly reduced reproduction (up to 69.8%) | (Kiihl et al., 2026) |
| PS, three sizes | Tetracycline | Hydrilla verticillata; Elodea nuttallii | 35-d factorial macrophyte community | Integrated physiological index | 10 antagonistic, 2 synergistic (Abbott) | Mostly antagonistic; published index conventions need clarification | (Mao et al., 2024) |
| PET fibres/fragments* | PFOS + PFOA* | Daphnia magna (2 genotypes) | Life-cycle factorial | Life-history traits | 59% additive, 41% synergistic (additive null) | Contextual benchmark of formal null-model reporting | (Soltanighias et al., 2024) |
| PE, virgin and aged | Acetochlor | Danio rerio | 96-h acute; 21-d sub-chronic | LC50; gut oxidative stress, microbiota | Enhanced (no null model) | LC50 0.76 to 0.42-0.47 mg $L^{-1}$; increased accumulation | (Wang et al., 2023) |
| PS, pristine and aged | Atrazine | Danio rerio | 96-h acute; long-term | LC50; tissue damage; liver transcriptome | Enhanced (no null model) | LC50 1.577 to 1.024-1.197 mg $L^{-1}$; co-exposure also degraded water quality | (Zeng et al., 2025) |
| MPs (20-40 mg $L^{-1}$) | Imiprothrin | C. dubia; Simocephalus vetulus | Life table and population growth | Lifespan; population growth | Enhanced (no null model) | Population growth 53-65% lower under combination | (Sarma et al., 2026) |
| PE (0.1-1% w/w) | Sulfanilamide | Vallisneria natans microcosm | Single and combined | Chlorophyll; ROL; microbiome; ARGs | Author-labelled synergy (no null model) | Reduced chlorophyll; altered N cycling; ARGs rose with antibiotic | (Zhang et al., 2022) |
| PE (100-800 particles $L^{-1}$) | Sulfamethoxazole | Sulfate-reducing sludge | Long-term continuous reactors | SMX removal; ROS; LDH | Enhanced stress (not classified) | SMX removal 37.1% to 30.5%; reversible after MP withdrawal | (Yan et al., 2026) |
| PS, pristine and UV-aged | Erythromycin | Escherichia coli biofilm | Factorial with 0.1-1.0 mg $L^{-1}$ | Resistance mutation frequency | Not classified | Mutation frequency $1.0 \times 10^{-7}$ (aged) vs $1.4 \times 10^{-8}$ (pristine) | (Han et al., 2024) |
| PVC-derived DOM | Seven antibiotics | Microcystis aeruginosa | Dark vs sunlight | Growth; chlorophyll | Not classified | Transformation products contributed to toxicity | (Ahlonsou et al., 2026) |

*Contextual comparator outside the four target classes. MDR, model deviation ratio; IA, independent action; ROL, radial oxygen loss; LDH, lactate dehydrogenase; SMX, sulfamethoxazole. "Enhanced" denotes a larger combined effect reported without an additive reference model.

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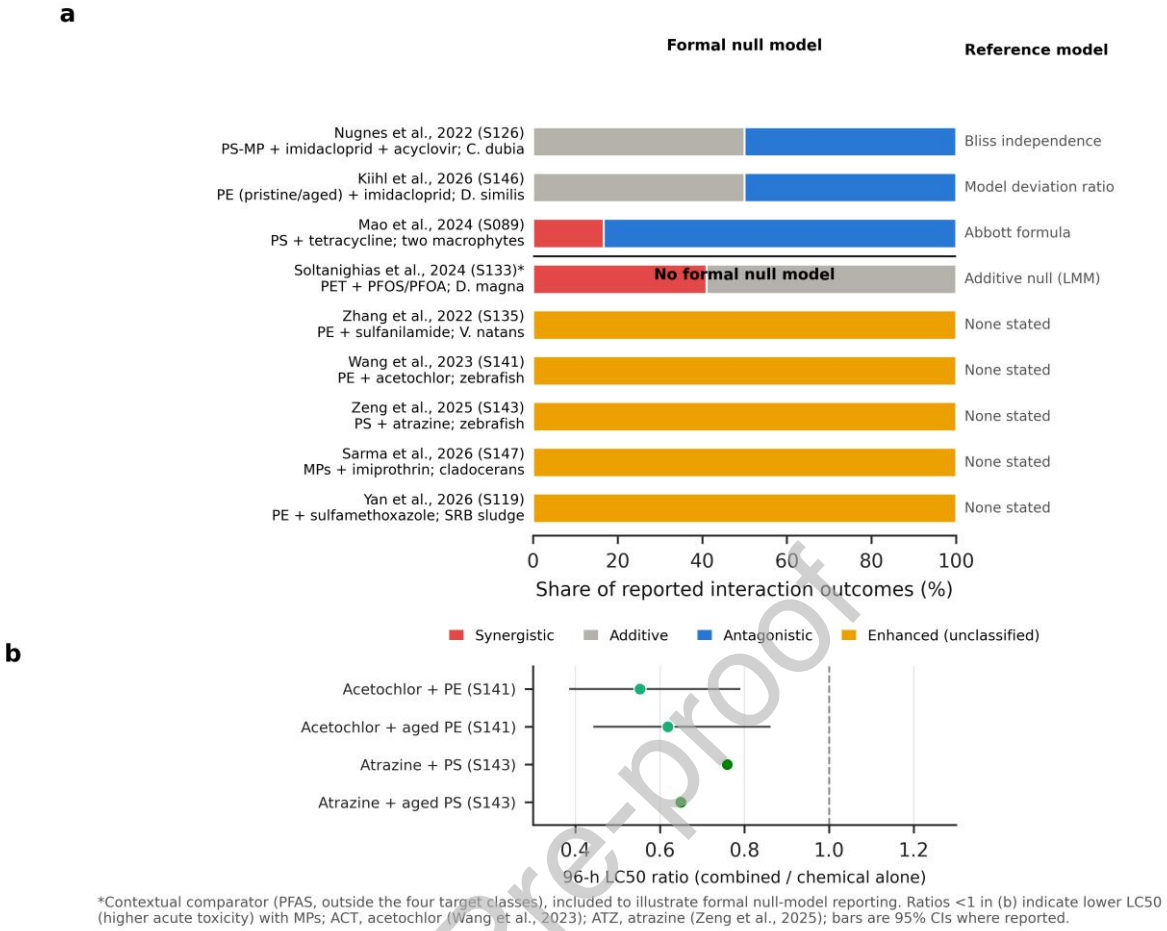



Fig. 6. Classification of combined-exposure outcomes. (a) Share of reported interaction outcomes per study, grouped by whether a formal null model (Bliss independence, model deviation ratio, Abbott formula or additive null) was applied. (b) Ratio of 96-h LC50 with MPs to that of the pesticide alone in zebrafish (95% CI where reported).

### *5.3. What the evidence supports*

The audit leads to three conclusions. First, the statement in our original abstract that mixture effects are "often more severe than predicted" is not supported: where a formal null model was used, additive and antagonistic outcomes predominated, consistent with Bastante-Rabadán and Boltes (2024)'s observation that most studies do not calculate interaction parameters. Second, MP concentrations used in Level 3 studies (typically mg $L^{-1}$) are orders of magnitude above field concentrations (Section 4.1), so these experiments demonstrate potential mechanisms rather than current field risk. Third, evidence is strongest for MP-antibiotic and MP-pesticide pairs; we found no Level 3 study of MPs combined with personal

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care products and only two studies involving non-antibiotic pharmaceuticals (Nugnes et al., 2022; Nugnes et al., 2026), one of which tested single substances only. MP-only exposures, such as particles released from single-use bags, also impaired zebrafish development at high doses (Kumar et al., 2026), underlining the need for MP-only controls in combined designs.

## 6. Antibiotics, microplastics and antimicrobial resistance

Environmental AMR is shaped by selection at sub-inhibitory antibiotic concentrations, co-selection by metals and biocides, and horizontal gene transfer in wastewater and receiving waters (Larsson and Flach, 2022; Bengtsson-Palme and Larsson, 2016). AMR was associated with 4.95 million deaths in 2019, with the highest attributable mortality rate in western sub-Saharan Africa (27.3 per 100,000) and the lowest in Australasia (6.5 per 100,000) (Murray et al., 2022), and 39 million cumulative deaths attributable to AMR are forecast for 2025-2050 (Naghavi et al., 2024). In the United States, about 2.8 million antibiotic-resistant infections and more than 35,000 deaths occur annually (CDC, 2019).

Evidence that MPs contribute to this burden is mixed and comparator-dependent (Fig. S4). Early observations of resistant bacteria on plastic debris (Laganà et al., 2019) have been followed by more controlled comparisons. MPs enriched resistance genes and class 1 and 2 integrons relative to river water in Jiaxing (Wang et al., 2020a), synthetic textile fibres carried more blaOXA-48 than cotton fibres (Nguyen et al., 2026), PLA and PVC plastispheres carried more resistance genes than mineral biofilms (Wang et al., 2022a), PE increased RP4 plasmid conjugative transfer 1.6-1.7-fold (Yu et al., 2023) and PS increased conjugation and transformation frequencies in municipal wastewater assays (Cheng et al., 2022). Real-world aged PET and PP increased normalised resistance-gene abundance during anaerobic sludge digestion (increases of 2.6-15.3% across treatments) more than pristine MPs (Liu et al., 2026), and UV-aged PS biofilms had a higher frequency of resistance mutation ($1.0 \times 10^{-7}$ versus $1.4 \times 10^{-8}$) under erythromycin exposure (Han et al., 2024). However, total resistance-gene

abundance was lower on MPs than in water in the Huangpu River, with enrichment confined to particular genes and plasmid-associated elements (Xu et al., 2022), and leaf biofilms carried more resistance-gene subtypes than PVC in a river-water bioreactor (Wu et al., 2019). Treatment systems are an important setting: in constructed wetlands, PS altered sulfamethoxazole removal while increasing sul1 and sul2 abundance (Zhang et al., 2024a), MP concentration and size shaped resistance-gene profiles (Liang et al., 2025), and full-scale plants showed compound-specific and sometimes negative apparent antibiotic removal with culturable resistant bacteria in final effluent (Wang et al., 2021b). Lake plastispheres share a core biofilm microbiome whose diversity increases with polymer degradation (Di Pippo et al., 2020). PE at 1 g $L^{-1}$ reduced UV inactivation of multidrug-resistant Escherichia coli by about 3 log units (Manoli et al., 2022), and field-deployed PE biofilms harboured culturable potential pathogens downstream of WWTP effluent (Woodford et al., 2025). Microplastics are therefore best described as a surface on which resistance can be enriched under some conditions, not as a demonstrated driver of the clinical AMR burden. This section has been shortened relative to the original submission to balance the treatment of the four contaminant classes.

**7. Human-health relevance**

Reviewer comments prompted us to replace the former Table 2, which listed therapeutic side effects of ciprofloxacin, tetracycline and other compounds at clinical doses, with an evidence-typed summary of human exposure (Table 5; Fig. 7). Therapeutic adverse effects are not evidence of risk at environmental concentrations, and we no longer present them as such.

Drinking water. MPs were detected in raw water at an average of 4.9 particles $L^{-1}$ but at only 0.00011 particles $L^{-1}$ in potable water from eight treatment works in England and Wales for the measured size range (Johnson et al., 2020), and riverbank filtration removed more than 84% of particles ≥32 μm (Loui et al., 2026). Pharmaceuticals present in hospital effluents and leachates in Ghana were not detected in boreholes, tap water or sachet water (Opoku et al.,

2025). The World Health Organization concluded that, on current evidence, MPs in drinking water do not indicate a health concern but that data on small particles and nanoplastics are insufficient (WHO, 2019).

Diet and food-web transfer. Antibiotic biomagnification in a subtropical river plankton food web was compound-specific (Tang et al., 2020a); pesticide transformation products accumulated in whole fish and were detected in fillets (e.g., imidacloprid-desnitro up to 0.64 ng $g^{-1}$ wet weight) (Slaby et al., 2022); and in a mariculture area the authors' hazard quotients suggested potential risk from antibiotics in seafood and on MPs, although the reported estimated daily intakes (≤1.5 µg $person^{-1}$ $d^{-1}$) are far below acceptable daily intakes (0.7-50 µg $kg^{-1}$ bw $d^{-1}$), indicating that unit harmonisation is needed before such quotients are interpreted (Yu et al., 2022) (Table S10). MP ingestion by fish was documented in field and mesocosm studies (Rochman et al., 2024; Graham et al., 2024), and trophic transfer of MPs via copepods has been shown experimentally (Domínguez-López et al., 2022); however, gut presence does not demonstrate translocation to edible tissue.

Inhalation and internal dose. None of the included studies addressed inhalation of MP-associated chemicals. Outside the four-class evidence base, MPs have been detected in human blood (Leslie et al., 2022) and lung tissue (Jenner et al., 2022), and their presence in carotid plaque was associated with cardiovascular events in an observational cohort (Marfella et al., 2024); such findings demonstrate internal exposure but not causation, and none measured co-sorbed antibiotics, PPCPs or pesticides. The WHO has highlighted dietary and inhalation exposure as priority knowledge gaps (WHO, 2022).

Mixture exposure and bioaccessibility. The only direct evidence on MP-mediated human exposure to a co-contaminant was in vitro: aged tyre-wear particles released up to 87.2% of sorbed sulfamethoxazole in simulated sequential digestion (Fan et al., 2023). Because the

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particles were loaded at concentrations far above environmental levels, this demonstrates bioaccessibility, not an absorbed dose.

Vulnerable populations. Two field studies modelled higher non-carcinogenic risk for children than adults from co-occurring MPs and organochlorine pesticides (Udensi et al., 2026) or MP-sorbed polycyclic aromatic hydrocarbons (Pirvu et al., 2025); in both, hazard quotients for most compounds remained below 1. Children are more vulnerable to developmental effects of synthetic chemicals generally (Landrigan et al., 2023; Wager and Thompson, 2025), but no included study measured outcomes in children, pregnant women or occupationally exposed groups.

Uncertainty. Human-health characterisation is limited by (i) absence of measured co-exposure in human-relevant matrices, (ii) reliance on default exposure factors and acceptable daily intakes derived for single compounds, (iii) analytical size cut-offs that exclude nanoplastics, (iv) use of laboratory loadings far above environmental levels, and (v) absence of mixture-specific toxicity reference values. We therefore classify current human-health risk from these combined exposures as plausible but unquantified.

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**Table 5. Evidence on human exposure to microplastics and co-occurring antibiotics, pharmaceuticals and pesticides, classified by evidence type.**

| Exposure pathway | Contaminant(s) | Evidence type | Key quantitative finding | Human-health relevance and limitation | Reference |
|---|---|---|---|---|---|
| Drinking water | MPs | Measured (raw and potable water) | 4.9 particles $L^{-1}$ raw; 0.00011 particles $L^{-1}$ potable | Very low measured exposure for the size range analysed; no nanoplastics | (Johnson et al., 2020) |
| Drinking water (source protection) | MPs | Measured (river-groundwater) | >84% reduction by bank filtration | Barrier efficiency for particles ≥32 µm only | (Loui et al., 2026) |
| Drinking water | Antibiotics, analgesics, antimalarials | Measured | 0.4-18.4 mg $L^{-1}$ in effluents/leachate; not detected in boreholes, tap or sachet water | Protective finding for drinking sources; high detection limits | (Opoku et al., 2025) |
| Aquatic food web | Antibiotics | Measured (plankton food web) | Compound-specific bioaccumulation and biomagnification | MPs not measured; no human dose estimated | (Tang et al., 2020a) |
| Seafood | Antibiotics in shellfish and on MPs | Modelled intake | Estimated intakes ≤1.5 µg person$^{-1}$ $d^{-1}$ vs ADIs 0.7-50 µg $kg^{-1}$ bw $d^{-1}$ | Authors' HQs require unit harmonisation; no adverse outcome measured | (Yu et al., 2022) |
| Fish consumption | Pesticides and transformation products | Measured (whole fish and fillet) | Imidacloprid-desnitro up to 0.64 ng $g^{-1}$ ww in fillet | Establishes a dietary pathway; no health outcome | (Slaby et al., 2022) |
| Ingestion (in vitro) | Sulfamethoxazole on tyre-wear particles | In vitro bioaccessibility | Desorption 65.2% (pristine) to 79.8% (aged) in gastric fluid; 87.2% sequential | Bioaccessibility, not absorbed dose; high loadings | (Fan et al., 2023) |
| Drinking water (modelled) | Organochlorine pesticides co-occurring with MPs | Modelled risk (children, adults) | HQ <1 for >95% of compounds; cancer risk $<10^{-6}$ | Single campaign; GC-FID identification | (Udensi et al., 2026) |
| Water contact (modelled) | PAHs sorbed to MPs (contextual) | Modelled risk (children) | Higher non-carcinogenic risk for children than adults | Outside four classes; illustrates vulnerable-group assessment | (Pirvu et al., 2025) |
| Resistance transfer | Pathogens and ARGs on MPs | Measured (environment) | Culturable potential pathogens on PE downstream of WWTPs; UV inactivation reduced by ~3 log at 1 g $L^{-1}$ PE | Plausible pathway; human infection not quantified | (Woodford et al., 2025; Manoli et al., 2022) |
| Internal dose (external evidence) | MPs | Measured in human tissue | Detection in blood and lung; plaque MPs associated with cardiovascular events | Observational; co-sorbed chemicals not measured | (Leslie et al., 2022; Jenner et al., 2022; Marfella et al., 2024) |

This table replaces the former Table 2, which listed therapeutic adverse effects at clinical doses. ADI, acceptable daily intake; HQ, hazard quotient; ww, wet weight; ARG, antibiotic resistance gene.

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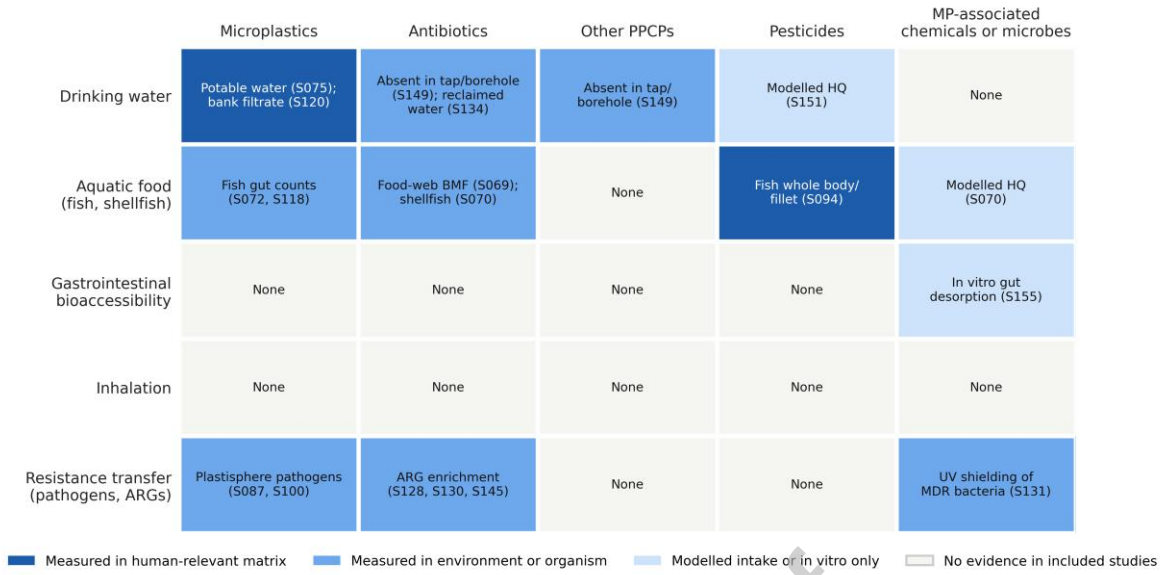



Fig. 7. Human exposure evidence matrix by pathway and contaminant class, showing the strongest evidence type available in the included studies (study identifiers as in Table S4). No included study addressed inhalation of MP-associated chemicals.

## 8. Evidence map and research geography

Our own evidence map (Figs. 3 and 4) replaces the journal-frequency table of the original submission (former Table 3), which was based on secondary bibliometric sources and did not have a reproducible method. The analysis shows rapid growth since 2022 driven by laboratory interaction and AMR studies, a strong concentration of evidence in China and Europe, and very limited evidence from Africa, Latin America and South and South-East Asia, where wastewater treatment coverage is lower and pesticide use is intensifying (Githaiga et al., 2023; K'oreje et al., 2018). Notably, the reported mg $L^{-1}$ pharmaceutical concentrations in Ghanaian hospital effluent and leachate (Opoku et al., 2025) and the MP-organochlorine hotspots in Nigeria (Udensi et al., 2026) were obtained with methods that have higher detection limits (HPLC-PDA, GC-FID) than those used in most Chinese and European studies, so geographic comparison of concentrations must account for analytical capacity. Because the included corpus is a screened subset of the literature, these proportions describe the evidence available for this review rather than global publication output.

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## 9. Knowledge gaps and research priorities

Table 6 distinguishes the interactions supported by field evidence from those that remain laboratory observations and lists the corresponding research priorities. The main priorities are:

- Four-class field monitoring. Co-located, same-sample measurement of MPs (including particles <20 μm) with antibiotics, other PPCPs and pesticides, including particle-bound chemical concentrations, across wet and dry seasons.
- Environmentally realistic interaction studies. Standardised factorial designs that combine aged and biofouled polymers, DOM and salinity gradients and competing contaminants, with desorption measured under relevant conditions.
- Null-model-based mixture testing. Full factorial designs with single-component controls and CA/IA analysis, reporting MDRs with confidence intervals and freely dissolved concentrations, at environmentally relevant MP doses.
- Human-relevant exposure. Measurement of co-contaminants in drinking water, edible tissues and air, bioaccessibility at realistic loadings, and attention to children and other vulnerable groups.
- Balanced and inclusive evidence. Expansion of research on non-antibiotic PPCPs and current-use pesticides, and investment in analytical capacity and monitoring in Africa, Latin America and South and South-East Asia.

Societal context. These materials underpin medicine, hygiene, food security and vector control (Dar et al., 2019), and more than 350,000 chemicals and mixtures are registered for production and use (Wang et al., 2020b). Elimination is not realistic; the management aim is to reduce unintended release and combined exposure through source control, advanced treatment and monitoring that is proportionate to the strength of the evidence.

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**Table 6. Interactions supported by field evidence versus those that remain laboratory observations, with research priorities.**

| Interaction or claim | Field evidence (Level 1) | Laboratory evidence (Levels 2-3) | Status | Priority |
|---|---|---|---|---|
| Co-occurrence of antibiotics, other PPCPs and pesticides | Yes (Bradley et al., 2017; Du et al., 2025; Nanusha et al., 2022; Wode et al., 2015) | Not applicable | Field-supported | Add MPs to multi-residue campaigns |
| Co-occurrence of MPs with a target chemical | Limited: 3 studies (Yu et al., 2022; Song et al., 2026; Udensi et al., 2026) | Not applicable | Partly field-supported | Same-sample, particle-bound measurements |
| Co-occurrence of all four classes | None | None | Not demonstrated | Four-class monitoring |
| Antibiotic accumulation on MPs | Yes, in deployments (Yu et al., 2022; Song et al., 2026) | Yes (Li et al., 2018; Zhang et al., 2018) | Field-supported | Link to desorption and uptake |
| Ageing increases sorption | Indirect (field-aged particles) (Zhang et al., 2018; Song et al., 2026) | Yes; 3.40-fold (Gao et al., 2022b; Wang et al., 2022b; Liang et al., 2023) | Laboratory-supported | Measure ageing state in the field |
| Salinity/DOM weaken sorption | No | Yes (Li et al., 2018; Xu et al., 2018; Wu et al., 2025) | Laboratory-supported | Estuarine gradient studies |
| MPs as dominant vector in natural waters | No | Contradicted for polar chemicals (Xu et al., 2018; Fatema and Farenhorst, 2022) | Not supported | Mass-balance field tests |
| Synergistic mixture toxicity | No | Rare under null models (Nugnes et al., 2022; Kiihl et al., 2026; Mao et al., 2024) | Not supported | Factorial CA/IA designs |
| Increased acute toxicity of pesticides with MPs | No | Yes, LC50 ratios 0.55-0.76 (Wang et al., 2023; Zeng et al., 2025) | Laboratory only | Environmentally relevant MP doses |
| ARG enrichment on MPs | Yes, gene-specific (Wang et al., 2020a; Xu et al., 2022) | Yes (Yu et al., 2023; Cheng et al., 2022; Liu et al., 2026) | Partly field-supported | Standardised comparators and normalisation |
| Human-health risk from combined exposure | No | In vitro/model only (Fan et al., 2023; Yu et al., 2022) | Not quantified | Human-relevant matrices; vulnerable groups |

CA, concentration addition; IA, independent action; DOM, dissolved organic matter; ARG, antibiotic resistance gene.

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## 10. Conclusions

Microplastics, antibiotics, other PPCPs and pesticides share sources and receiving waters, but the evidence that they interact and jointly increase risk is uneven. Field evidence supports co-occurrence of chemical classes in wastewater-impacted and agricultural waters, accumulation of antibiotics on MPs deployed in mariculture and WWTP settings, co-located MP and organochlorine pesticide hotspots, and enrichment of some resistance genes on riverine MPs. Laboratory evidence supports stronger sorption to aged MPs (3.4-fold on average, but highly variable), reduction of antibiotic sorption by salinity and often by DOM, MP-surface and MP-DOM-mediated transformation of antibiotics, gut-fluid desorption, and altered acute toxicity of some pesticides in the presence of MPs. Synergistic mixture toxicity, a dominant MP vector role in natural waters, MP-driven clinical AMR and quantified human-health risk remain unproven. No study has yet measured all four classes together. Integrated, null-model-based and field-realistic research, particularly in under-represented regions, is needed before combined risks can be quantified and managed.

**CRediT authorship contribution statement**

Edwin Hena Dawolo: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Visualization, Writing - original draft, Writing - review & editing. Songhe Zhang: Supervision, Writing - review & editing. Amin Khan, Solomon Joseph, Richard Vallah and Miatta Tisdell: Investigation, Writing - review & editing.

**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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## Data availability

The search strings, screening counts, study register, data-extraction workbook and meta-analysis dataset supporting this review are provided in the Supplementary Material and in the accompanying workbook (HAZADV_Reviewer_Guided_Data_Extraction.xlsx).

## Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used Claude (Anthropic) to assist in image improvement, some data verification. After using this tool, the authors reviewed, verified and edited the content as needed and take full responsibility for the content of the publication.

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## Appendix A. Supplementary data

Supplementary data to this article (Tables S1-S12, including Table S3b, and Figs. S1-S4) can be found online.

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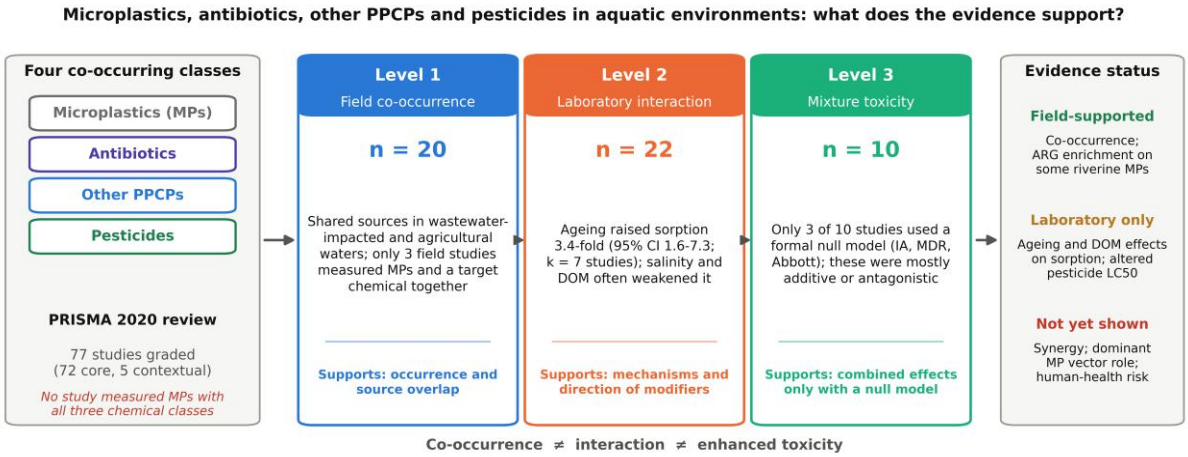
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## Graphical abstract




## Declaration of interests

☒ 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.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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