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## **Microplastic toxicity: A review of the role of marine sentinel species in assessing the environmental and public health impacts**

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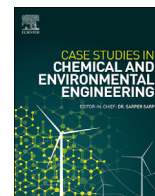
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## Microplastic toxicity: A review of the role of marine sentinel species in assessing the environmental and public health impacts



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## ABSTRACT

The ubiquity of plastics is a concern for the health of humans and marine ecosystems. Plastics and their composite endocrine disrupting chemicals (EDCs) are associated with adverse health outcomes in humans and marine species. With continued plastic production, waste mismanagement and global population increases, exposure effects will continue to escalate. The 'One Health' paradigm describes 'health' as a cross-species universal 'good'. Adverse outcomes from plastic exposure are shared cross-species, indicating common mechanisms of toxicity. Marine species with individuals ingesting naturally disparate levels of plastic present valuable opportunities for researchers in understanding the real-world impacts of plastic. Sampling from sentinels monitors dynamic exposures to the evolving plastics landscape, allowing transcriptomic and epigenetic adaptations to these exposures to be assessed. Advances in bioinformatics enable elucidation of shared biological pathways from plastic toxicity in a systems level context. This review examines microplastics in the marine environment, adverse health exposure outcomes, and the exploitation of marine sentinel species in this context to elucidate the impacts of plastics. Hierarchical priorities when selecting marine plastic sentinels are explored. Abundant seabirds such as the herring gull or the northern fulmar represent ideal marine plastic sentinels.

### 1. Plastics in the context of the marine environment

Plastics are high molecular weight polymers that are combined with additives during production that impart diverse qualities, e.g., plasticisers which soften plastic [1]. These additives are often endocrine disrupting chemicals (EDCs) [2]. Further, the strong polymeric carbon-carbon double bonds prohibit biodegradation [3]. Thus, plastics remain in the environment for thousands of years fragmenting into progressively smaller pieces e.g., to microplastics (5 mm–0.1 mm), and simultaneously leaching their resident plastic-derived EDCs into ecosystems [4]. Microplastic breakdown, uptake and exchange processes in marine ecosystems are summarised in Coyle et al., 2020 [5]. Plastics and their resident chemicals bioaccumulate in food webs and are associated with health problems in humans and other species [1].

The most recognisable plastic-derived EDC is the plastic precursor monomer bisphenol A (BPA) which covalently strengthens polyvinylchloride and other plastics [6]. Other plastic-derived EDCs like plasticisers and antioxidants are not covalently bonded to the polymer and

thus have more leaching potential than BPA [7]. Phthalate plasticisers are the most ubiquitous chemical that humans and wildlife interact with [8,9]. Table 1 summarises common plastic types and the EDCs they contain.

Understanding the environmental and health implications of population growth and waste mismanagement is an emerging concern. There has been a 205 times increase in plastic production from 1950 to 2016 [12], which is set to triple by 2060 [13]. Today, 80% of marine plastics originate from mismanaged terrestrial waste, mainly from coastal populations [14]. By 2023 50% of the world's population will reside in coastal areas [15]. Therefore, understanding the long-term impacts of plastics on marine ecosystem health is an urgent global issue.

Although plastic likely impacts all marine organisms, some species ingest more than others. As of 2020, a conservative 914 marine species were evidenced to encounter marine plastics [16]. Additionally, low trophic level phytoplankton and zooplankton commonly contain detectable levels of microplastics and plastic-derived EDCs, and these form the basis of marine food webs [17]. A variety of geographical, behavioural

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**Table 1**

**The most commonly produced plastic polymers and plastic-derived EDCs that they contain.** Other polymers including polystyrene compose the remaining 25.4% of plastic demand. Although polymer type can indicate the presence of certain EDCs, in reality all polymer types contain a broad suite of diverse EDCs. Adapted from Hermabessiere et al. (2017) [10].

Polymer	Demand distribution by resin types in 2019 (%) [11]	Common polymer uses	Plastic-derived EDCs
Polypropylene	19.3	Food packaging and wrappers, pipes	BPA, octylphenol (OP), nonylphenol (NP), brominated flame retardant
Polyethylene, low density	17.5	Reusable bags, containers, food packaging	BPA, OP, NP, brominated flame retardant
Polyethylene, high density	12.2	Toys, bottles, pipes	BPA, OP, NP, brominated flame retardant
Polyvinyl chloride	10	Window frames, cable insulation	Phthalates, BPA, NP
Polyurethane	7.9	Pillows, building insulation	Brominated flame retardant
Polyethylene terephthalate	7.7	Water and soft drink bottles	Phthalates

**Table 2**

Studies investigating plastic-derived EDCs in different species and tissues, the methodology utilised, the EDCs detected and study conclusions.

	Sample type, date and location	Study individuals	Methodology	Plastic-derived EDCs and metabolites detected	Study conclusions	Reference
Human	Urine, Denmark (2009, 2013 and 2017)	300 urine samples (100 samples/year) collected from young men	Isotope dilution TurboFlow liquid chromatography with tandem mass spectrometry (LC-MS/MS). Phthalates, BPA, and phthalate and BPA substitutes and their metabolites were analysed	Detected di-methyl phthalate (DMP), di-ethyl phthalate (DEP), butyl benzyl phthalate (BBP), di-butyl phthalate (DBP), DEHP, di-heptyl phthalate (DHpP), di-iso-nonyl phthalate (DiNP) and BPA levels decreased from 2009-2017. However, di-iso-decylphthalate (DiDP) increased and over 95% of samples contained phthalate metabolites. Phthalate substitutes di-2-ethylhexyl terephthalate (DEHTP) and di-iso-nonyl-cyclohexane-1,2-dicarboxylate (DINCH), and BPA substitutes like bisphenol-F (BPF) increased. DiBP, DnBP, DEHP, DEP and DiNP remained the most detected compounds.	Due to EU restrictions, many commonly studied plastic-derived chemicals have decreased in urine from 2009-2017. However, similarly toxic substitutes have increased over the same time period	[25]
	Urine, Slovenia (2011–2012)	155 children, 155 mothers and 71 fathers	Homogenisation and gas chromatography with tandem mass spectrometry (GC-MS/MS)	BPA in 94%, 88% and 81% of children, mothers and fathers' respective urine samples	Levels are typical of other EU countries	[24]
	Hair, Gdansk, Poland (2017)	15 adults and 27 teenagers	Methanol and ammonium acetate extraction and ultrasonication followed by high-performance liquid chromatography (HPLC)	BPA was detected at a mean concentration of 411.2 ng g <sup>-1</sup> dry weight (dw), NP at 4478.4 ng g <sup>-1</sup> dw and OP at 131.2 ng g <sup>-1</sup> dw	Questionnaire found high hair BPA levels associated with a diet rich in marine foods, hair dye use, and other lifestyle factors. Women had higher levels than men	[27]
	Blood, Turkey (2004)	Umbilical cord blood samples (n = 100) collected immediately after birth	Sodium acetate and glucuronidase incubation extraction followed by HPLC	Approximately 99% of cord blood samples contained detectable levels of BPA, DEHP and mono (2-ethylhexyl) phthalate (MEHP)	Cord blood BPA was associated with a decrease in stretched penile length and increased cord blood oestradiol levels in male newborns. DEHP was significantly inversely	[31]

(continued on next page)

and anatomical factors contribute to higher ingestion in some species. The foraging behaviour of procellariiform seabirds, e.g. the northern fulmar (Graphical Abstract) and shearwaters, means they confuse plastic for prey at higher rates than other species, and their anatomy prevents efficient plastic regurgitation resulting in longer retention times [18]. Additionally, species foraging in spatial areas called marine plastic waste 'hotspots' are at a higher risk of ingestion [3].

## 2. Plastics in the body – entry, accumulation and adverse health impacts

Plastics and their chemicals are incorporated into the body via three routes: ingestion, dermal absorption and inhalation. Ingestion through contaminated food and drink provides a major route for plastic components into the human body. On average, we ingest between 39,000 and 52,000 plastic particles annually [19]. BPA, NP, and di-(2-ethylhexyl) phthalate (DEHP) leach directly from consumer plastics such as plastic bottles [7,20]. Similarly, marine species ingest plastics and microplastics unwittingly, as well as trophic and seawater plastic-derived EDCs [3].

Plastic-derived EDCs are rapidly metabolised in the body, however steady state concentrations remain in tissues [21]. Phased enzymatic chemical reactions in the liver metabolise these EDCs facilitating excretion in the urine within 24 h [22]. High levels of their metabolites have been found in the urine of all recent human study participants [23–25]

Table 2 (continued)

	Sample type, date and location	Study individuals	Methodology	Plastic-derived EDCs and metabolites detected	Study conclusions	Reference
	Adipose, Italy (2003–2007)	16 samples adipose tissue, obtained from patients (3 males and 13 females) aged from 34 to 68 years during bariatric surgery	Lipid extraction and acetonitrile derivitization followed by gas chromatography- mass spectrometry (GC-MS)	NP was found at the highest level (mean 122 ng g <sup>-1</sup> fresh weight (fw). NP ethoxylates (NPEOs) were found in all samples. Total NPs ranged between 45 and 1131 ng g <sup>-1</sup> fw	correlated with anogenital index This study found higher average NP and OP concentrations compared to prior Spanish and Finnish studies	[21]
Seabird	Muscle, Aleutian Islands, Alaska (2009–2011, 2013–2015)	74 archipelago seabirds of ten species; Northern Fulmar ( <i>Fulmarus glacialis</i> ), Glaucous-winged Gull ( <i>Larus glaucescens</i> ), Common Murre ( <i>Uria aalge</i> ), Horned Puffin ( <i>Fratercula corniculata</i> ), Pelagic Cormorant ( <i>Phalacrocorax pelagicus</i> ), Pigeon Guillemot ( <i>Cepphus columba</i> ), Red-faced Cormorant ( <i>Phalacrocorax urile</i> ), Tufted Puffin ( <i>Fraterculacirrhata</i> ), Black-legged Kittiwake ( <i>Rissa tridactyla</i> ), Crested Auklet ( <i>Aethia cristatella</i> )	Tissue homogenisation and quencher extraction followed by phthalate analysis using liquid chromatography- mass spectrometry (LC-MS)	Phthalates detected in 100% of samples with concentrations of 3.64 ng/g to 539.64 ng/g per individual. DMP detected in 87.0% of samples. DEP in 99.1%, BBP in 93.0%, DBP in 83.5%, DEHP in 63.5%, and di-n-octyl phthalate (DnOP) in 77.4% of samples	Authors strain the requirement of more research into these contaminants and their effects	[30]
	Feather, Gdansk, Poland (2017)	13 male and female Herring gulls ( <i>Larus argentatus</i> ) (n = 26) specimens, including juvenile (n = 10) and mature (n = 16) birds	Methanol and ammonium acetate extraction and sonication, followed by HPLC	BPA detected at 145.1 ng g <sup>-1</sup> dw, NP at 37.7 ng g <sup>-1</sup> dw and OP at 162.0 ng g <sup>-1</sup> dw	Foraging location during moulting influenced phenol profiles and concentrations	[27]
	Preen oil, Queensland, Australia (2014)	Preen oil swabbed uropygial gland of 28 seabirds of 4 species; short-tailed shearwaters ( <i>Ardenna tenuirostris</i> ), wedge-tailed shearwaters ( <i>Ardenna pacifica</i> ), bridled terns ( <i>Onychoprion anaethetus</i> ) and sooty terns ( <i>Onychoprion fuscatus</i> )	Swabs were Soxhlet-extracted, and phthalate analysis was carried out with GC-MS	All samples were dominated by DBP and DEHP, with only small quantities of DMP detected in most. Highest phthalates detected from shearwaters	Phthalate levels were well correlated with plastic ingestion levels, and levels varied in seabird taxa that foraged in different ocean areas around Australia. Results of shearwater phthalate ingestion consistent with other reports of high levels of shearwater plastic ingestion	[29]
	Eggs, Norway (2012)	6 eggs sampled from Sklinna and 12 from Røst, of three species: Common eider ( <i>Somateria mollissima</i> ), European shag ( <i>Phalacrocorax aristotelis aristotelis</i> ), and European herring gull ( <i>Larus argentatus</i> )	Egg content was homogenised, and analysis not named	Phthalates were detected at levels above the limit of detection in all species, dominated by DEHP. DEHP ranged from 3 to 42 ng/g for each species. Every herring gull egg contained DEHP. AEs and BPA had extremely high mean concentrations in herring gulls at 254 ng/g. Shag eggs had the lowest levels of AEs	Other studies including piscivorous birds had higher concentrations of NP	[28]
Pinniped	Fur, Gdansk, Poland (2017)	Baltic grey seals ( <i>Halichoerus grypus</i> ); 5 mature females and their 12 pups	Methanol and ammonium acetate extraction and ultrasonication, followed by (HPLC)	BPA detected at 67.5 ng g <sup>-1</sup> dw, NP at 39.1 ng g <sup>-1</sup> dw and OP at 62.8 ng g <sup>-1</sup> dw	Authors suggested that AEs accumulate more than BPA in animal tissues and organs	[27]
Turtle	Liver, gonads muscle and adipose, collected along the Sicilian coasts, Italy (2016)	13 marine turtle specimens of two species; 1 <i>Dermochelys coriacea</i> and 12 <i>Caretta caretta</i> found dead	Homogenisation and acetonitrile extraction followed by phthalate analysis using LC-MS	DEP, BBP and DEHP detected. DBP was the most abundant phthalate in <i>C. caretta</i> liver and muscle (2600–19,000 ng/g). Higher contamination in <i>C. caretta</i>	<i>C. caretta</i> has potential as a biomonitor or sentinel of phthalates	[9]
Shark	Liver and muscle, Greenland, (2012–2014)	23 specimens of Greenland shark <i>Somniosus microcephalus</i>	Accelerated Solvent Extraction (ASE) followed by HPLC- fluorescence phenol detection	BPA, NP di-ethoxylate (NPE1-2EO) and 4-NP were detected in 72%, 87.5% and 75%, of samples respectively, with higher levels detected in liver tissue	Chronic exposure caused high muscle accumulation of phenols. The authors considered marine plastics a likely source and transport mechanism of phenols.	[26]

(see Table 2). Despite detoxification, negligible amounts of plastic-derived EDCs remain with chronic exposure, gradually bio-accumulating in body tissues. Plastic-derived EDCs and their metabolites are now ubiquitous in the tissues of humans and high trophic level

marine species [9,26–30]. These chemicals are also deposited into hair, feathers and fur during growth [27].

When sufficiently small, microplastics can be carried in the blood stream to distal tissues where they can elicit harmful effects. Polymers

<10 µm are the most toxic as they are translocated across cell membranes, including the placenta and blood-brain barrier [32]. Accumulation of microplastics in neural tissue has been associated with behavioural problems in fish [32]. In humans, small polymers primarily damage the lungs when chronically inhaled [33].

However, plastic-derived EDCs are associated with more adverse health outcomes than polymers alone. They are a global environmental and health problem due to their disruption of fundamental processes such as growth and development [34]. The recent rise in many human modern-day illnesses, e.g. infertility, cancers, and allergies, have been repeatedly attributed to the omnipresence of these chemicals [35–37]. EDCs often adversely affect wildlife populations as a whole, for example in reproductive output and sex ratio imbalances [38]. Adverse outcomes also commonly persist for generations, as EDCs transmit epigenetic transgenerational inheritance [39].

Plastic-derived EDCs commonly recovered from the bodies of humans and wildlife include BPA, phthalates and alkylphenol ethoxylates (AEs) (Table 2). In humans, BPA has been associated with decreased sperm count [36], developmental disorders [40], obesity [41] and

cardiovascular diseases [42]. Phthalates have been attributed to the development of endometriosis [43] and testicular dysgenesis syndrome [44]. AEs NP and OP have been implicated in human allergies [45].

The transcriptional outcomes of environmentally relevant levels of plastic-derived EDCs have been investigated in zebrafish models. BPA impacted transcriptional programs as associated with mitochondrial function, cell cycle, and transcription [46]. DEHP promoted non-alcoholic fatty liver disease development [47]. Similar changes were seen with NP, including perturbations in gene expression associated with oxidative stress [48].

### 3. Marine plastic sentinels for plastic human exposure

Sentinel species provide warnings of future environmental and health risks [49]. They exhibit behavior, habitats, niches and other characteristics that result in a measurable response to environmental stimuli [49]. The popular ‘canary in a coalmine’ example describes the historic use of canaries falling off their perch to signal to coalminers that carbon monoxide levels were rising [50]. An exaggerated response by sentinels to a stressor allows its impact to be detected more easily.

EDC research using wild sentinels is superior to laboratory models due to the context-specificity of biomarkers [51]. Studying gene expression and epigenetic profiles that have developed in a natural context provides a real-world understanding of adaptations to exposure. Inbreeding and influences unique to the caged laboratory environment are significant drawbacks to using inbred model laboratory species to model human disease [52]. Whereas, exploiting wild populations avoids these, and allows inclusion of indirect effects in the final model, e.g., changes in foraging behaviour. It also accounts for the complex mixture effects of ever-changing resident chemicals [25]. These benefits vastly outweigh difficulties in establishing causality [53].

Species that forage in different spatial areas with disparate contamination levels often possess distinct gene expression profiles and health status. When disparities in EDC exposure take place in a natural open system, it permits the normal development of biological responses as an adaptive mechanism. Different life-time exposures to EDCs lead to distinct epigenetic and transcriptomic profiles. For example, the turbot (*Pleuronichthys verticalis*) exhibited altered gene expression profiles in polluted water [54], and Arctic graylings exhibited altered transcriptomic profiles based on proximity to mining discharge [55].

Plastic indicator species may serve as useful sentinels. The stomach contents of dead indicator individuals permit assessment of marine plastic pollution levels [18,56]. An example is the northern fulmar, a robust and sensitive plastic indicator utilised by the EU in North Sea studies [18]. Sea turtles have served as marine plastic indicators on a global scale [56]. Indicators ingest plastic levels representative of their environment [57], and thus segregate into groups of high versus low plastic ingestion based on their differences in their foraging area or behaviour. These two groups of disparate plastic ingestion can be exploited for research into the biological effects of plastics in a natural context.

#### 3.1. The integrative thinking and tools that underpin sentinel microplastic research

Sentinel research is underpinned by species interconnectedness of biological processes, land, resources and genetics [58]. Most genes are shared between vertebrates, and humans for example share 71.4% of protein-coding genes with zebrafish [59]. As resources become further restrained due to population and pollution increases, species interconnectedness will become more obvious [58].

The use of sentinels is central to the coherent integrative thinking of ‘One Health’, which is relegating separated sectorial biology to the past [58]. ‘One Medicine’ emphasises the common scientific base in veterinary and human medicine [58]. The contributions of ecology have extended the paradigm of ‘One Medicine’ to ‘One Health’, reformulating ‘health’ as a cross-species universal ‘good’ [60]. This, in the age of ‘big

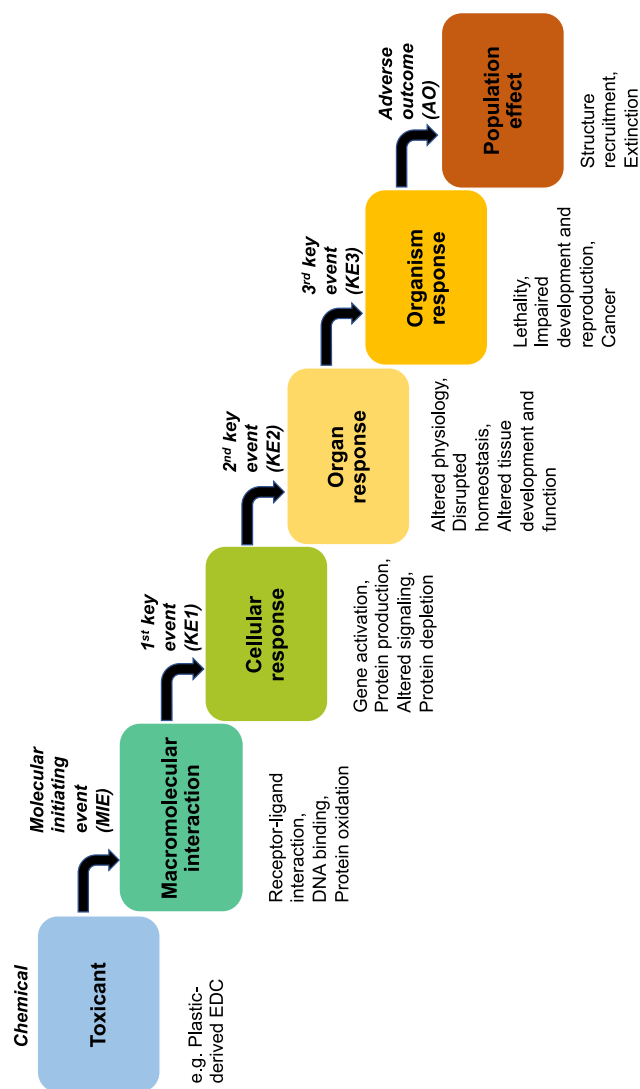


Fig. 1. Adverse Outcome Pathway Framework. Adapted from Huff et al., 2019 [48]. Prior scientific knowledge assists construction of the pathway, and each key event is an independent measurement at a particular level of organisation [62].



data' led to the genesis of Systems Biology, which integrates many diverse data types from multiple species to produce complex holistic models of biological systems that predict adverse health outcomes and assist in their mitigation [61].

Fundamentally underpinning the use of sentinels and the 'One Health' paradigm, are shared gene ontology and disease pathways shared cross-species. Risk with plastic-derived EDCs can be assessed using the Adverse Outcome Pathway (AOP) framework which defines an adverse outcome as the result of a molecular initiating event followed by a cascade of subsequent biological events [62] (Fig. 1). Tools like the AOP uncover the molecular mechanisms underpinning plastic toxicity, in a way that is applicable to both human and environmental health.

### 3.2. Considerations for choice of sentinel

#### 3.2.1. Species characteristics

Plastic high-ingestion species are exposed to high levels of plastic-derived EDCs. As global plastic waste production will likely increase threefold by 2060 [13], these species are ideal representatives for the future implications of increased plastic ubiquity. Due to EDC bioaccumulation in the tissues of their prey, species at upper trophic levels (including humans) are likewise highly exposed [63]. Chronic lifetime exposures are accumulated across the human lifespan, thus other long-lived sentinels are most valuable in mirroring this exposure. These characteristics are reflected in the Graphical Abstract northern fulmar example.

Species mobility is a fundamental consideration in sentinel species choice. High site fidelity is usually a preferred characteristic due to contaminant exposure only occurring in a well-studied limited locality [64]. This simplifies sampling, allowing omics and chemical profiles to be compared between populations across time to assess adaptations to

environmental change. However, this limits the pool of potential sentinels as many plastic high-ingestion and high trophic level species are mobile [27]. Further, it disregards the potential utility of wide-ranging plastic indicators such as the northern fulmar [18] and the sea turtle *C. caretta* [9]. To avail of these species, movement tracking is often required to map their foraging areas to infer the extent of plastic ingestion, as biomarkers of plastic exposure remain limited.

#### 3.2.2. Tissue availability

Preferred tissue sample type from humans and wild sentinels often differs due to ease of collection. Sampling methods that impact the wild individual minimally and sparingly are favoured to minimize stress and interference with results. Swift and infrequent sampling of small amounts of fur or a body feather does not impact health or movement/flight. The most diverse non-invasive sampling options are available when utilising seabird sentinels (Table 2).

More invasive blood sampling allows optimal cross-species comparisons as conjugated plastic-derived EDCs in blood may serve as a biomarker of plastic exposure in both humans and wildlife [31]. The establishment of biomarkers for plastic exposure in feathers or fur, as exists for persistent organic pollutants [65], would allow these preferable matrices to be utilised to indicate internal bioaccumulation levels. Plastic contamination must be avoided during sample storage to prevent interference with results [27].

Where available, recently deceased individuals are preferred for analysis. Available bycatch from long-line fisheries avoids sacrificing individuals for the study and provides whole tissues for investigation, including the liver and gonadal germ line cells [48]. This provides a superior insight into the impacts of chronic exposure. The protection status of certain species e.g. *C. caretta* [9], limits the availability of full

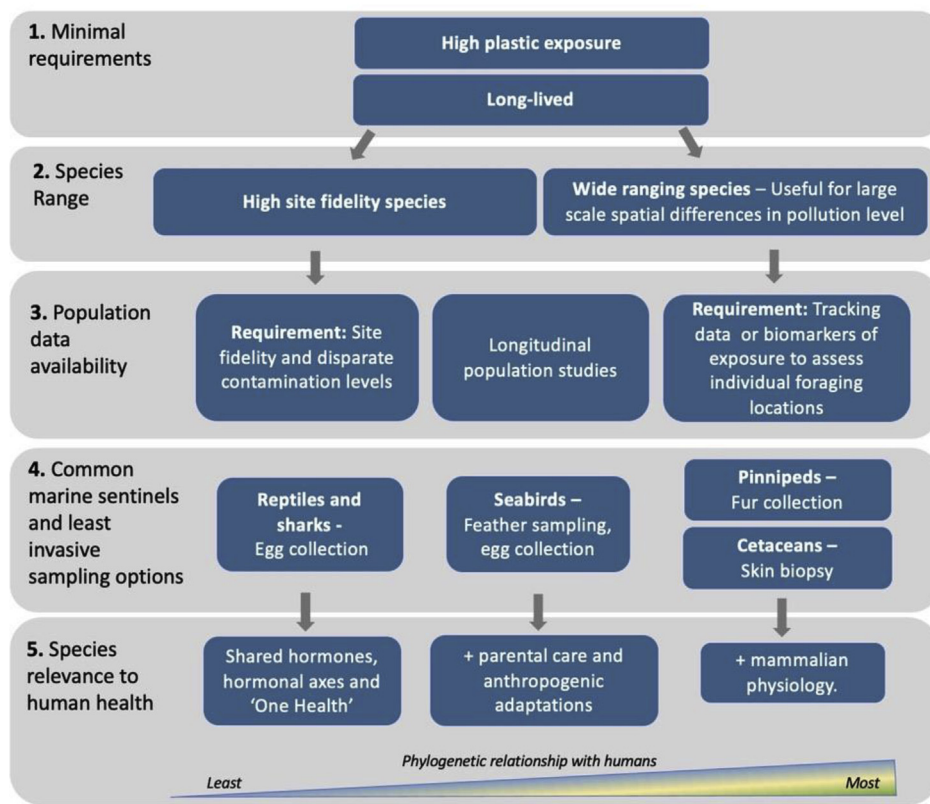


Fig. 2. Hierarchical priorities when choosing a marine plastic sentinel as a proxy for plastic exposure in humans and other species, or as an ecosystem monitoring tool. Priorities regarding species and population information are ranked from 1 being most pertinent to 5 being least.

bodies for analysis. However, many seabird scavenger species are abundant such as herring gulls [27] and northern fulmars [18], making them excellent potential sentinels for human plastic exposure (see summary in Fig. 2).

#### 4. Conclusions and future directions

Due to the ever-changing and complex nature of plastic and plastic-derived EDC exposure [25], it is becoming increasingly difficult to replicate these interactions in the laboratory. Practically all human populations are now exposed to uniformly high levels of mixtures of plastics and their chemicals [21,24,25,27,31], thus it is challenging to investigate the biological pathways to the adverse health outcomes they cause. Marine sentinels with disparate plastic ingestion levels serve as valuable natural models of plastic exposure.

When choosing a sentinel for human plastic exposure, plastic high-igestion, high trophic level and long-lived species are superior. Marine life such as seabirds [18] and sharks [26] have high site fidelity while maintaining a wide foraging range as they periodically return to the same breeding or laying grounds. This allows sampling over time across large marine areas and permits the exploitation of mobile marine species for health or environmental monitoring purposes. Establishing biomarkers of plastic exposure in noninvasively obtained tissues would simplify plastic sentinel studies.

Due to abundant and unprotected seabird species, commonplace bycatch makes available diverse tissue types to researchers [18,27]. This together with the diversity of seabirds species that are predators, ingest high plastic levels, and have a wide spread and site fidelity, makes certain seabirds attractive plastic sentinels [18,66]. Northern fulmars and herring gulls can be exploited to understand the adverse and chronic impacts of plastics on human and ecosystem health.

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#### 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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#### References

- [1] R.U. Halden, Plastics and health risks, *Annu. Rev. Publ. Health* 31 (2010) 179–194.
- [2] Å. Bergman, J.J. Heindel, S. Jobling, K. Kidd, T.R. Zoeller, W.H. Organization, *State of the Science of Endocrine Disrupting Chemicals 2012*, World Health Organization, 2013.
- [3] R.C. Thompson, Plastic debris in the marine environment: consequences and solutions, in: *Marine Nature Conservation in Europe 193, 2006*, pp. 107–115.
- [4] B. Worm, H.K. Lotze, I. Jubinville, C. Wilcox, J. Jambeck, Plastic as a persistent marine pollutant, *Annu. Rev. Environ. Resour.* 42 (2017) 1–26.
- [5] R. Coyle, G. Hardiman, K. O'Driscoll, Microplastics in the marine environment: a review of their sources, distribution processes and uptake into ecosystems, *Case Stud. Chem. Environ. Eng.* (2020), 100010.
- [6] A.M. Nelson, T.E. Long, A perspective on emerging polymer technologies for bisphenol-A replacement, *Polym. Int.* 61 (10) (2012) 1485–1491.
- [7] H.C. Erythropel, M. Maric, J.A. Nicell, R.L. Leask, V. Yargeau, Leaching of the plasticizer di(2-ethylhexyl)phthalate (DEHP) from plastic containers and the question of human exposure, *Appl. Microbiol. Biotechnol.* 98 (24) (2014) 9967–9981.
- [8] I. Markit, *Chemical Economics Handbook, Plasticizers* [WWW Document]. IHS, 2015.
- [9] D. Savoca, M. Arculeo, S. Barreca, S. Buscemi, S. Caracappa, A. Gentile, et al., Chasing phthalates in tissues of marine turtles from the Mediterranean sea, *Mar. Pollut. Bull.* 127 (2018) 165–169.
- [10] L. Hermabessiere, A. Dehaut, I. Paul-Pont, C. Lacroix, R. Jezequel, P. Soudant, et al., Occurrence and effects of plastic additives on marine environments and organisms: a review, *Chemosphere* 182 (2017) 781–793.
- [11] *Plastics Europe. Plastics - the Facts 2019, 2019.*
- [12] *PlasticsEurope Plastics, - the Facts 2018, 2018.*
- [13] L. Lebreton, A. Andrady, Future scenarios of global plastic waste generation and disposal, *Palgr Commun* 5 (2019).
- [14] J.R. Jambeck, R. Geyer, C. Wilcox, T.R. Siegler, M. Perryman, A. Andrady, et al., Plastic waste inputs from land into the ocean, *Science* 347 (6223) (2015) 768–771.
- [15] W.N. Adger, T.P. Hughes, C. Folke, S.R. Carpenter, J. Rockstrom, Social-ecological resilience to coastal disasters, *Science* 309 (5737) (2005) 1036–1039.
- [16] S. Kühn, J.A. Van Franeker, Quantitative overview of marine debris ingested by marine megafauna, *Mar. Pollut. Bull.* 151 (2020) 110858.
- [17] Y. Lv, Y. Pei, S. Gao, C. Li, Harvesting of a phytoplankton-zooplankton model, *Nonlinear Anal. R. World Appl.* 11 (5) (2010) 3608–3619.
- [18] J.A. van Franeker, S. Kuhn, Using Northern Fulmars as an Ecological Monitor of Marine Litter in Line with Indicators Set for MSFD Descriptor 10, Department for Environment, Food and Rural Affairs, 2019.
- [19] K.D. Cox, G.A. Covernton, H.L. Davies, J.F. Dower, F. Juanes, S.E. Dudas, Human consumption of microplastics, *Environ. Sci. Technol.* 53 (12) (2019) 7068–7074.
- [20] J.E. Loyo-Rosales, G.C. Rosales-Rivera, A.M. Lynch, C.P. Rice, A. Torrents, Migration of nonylphenol from plastic containers to water and a milk surrogate, *J. Agric. Food Chem.* 52 (7) (2004) 2016–2020.
- [21] T. Geens, H. Neels, A. Covaci, Distribution of bisphenol-A, triclosan and n-nonylphenol in human adipose tissue, liver and brain, *Chemosphere* 87 (7) (2012) 796–802.
- [22] D.R. Doerge, N.C. Twaddle, M.I. Churchwell, H.C. Chang, R.R. Newbold, K.B. Delclos, Mass spectrometric determination of p-nonylphenol metabolism and disposition following oral administration to Sprague-Dawley rats, *Reprod. Toxicol.* 16 (1) (2002) 45–56.
- [23] K.T. de Renzy-Martin, H. Frederiksen, J.S. Christensen, H.B. Kyhl, A.-M. Andersson, S. Husby, et al., Current exposure of 200 pregnant Danish women to phthalates, parabens and phenols, *Reproduction* 147 (4) (2014) 443–453.
- [24] J.S. Tratnik, T. Kosjek, E. Heath, D. Mazej, S. Čehič, S.P. Karakitsios, et al., Urinary bisphenol A in children, mothers and fathers from Slovenia: overall results and determinants of exposure, *Environ. Res.* 168 (2019) 32–40.
- [25] H. Frederiksen, O. Nielsen, H.M. Koch, N.E. Skakkebaek, A. Juul, N. Jørgensen, et al., Changes in urinary excretion of phthalates, phthalate substitutes, bisphenols and other polychlorinated and phenolic substances in young Danish men; 2009–2017, *Int. J. Hyg Environ. Health* 223 (1) (2020) 93–105.
- [26] N. Ademollo, L. Patrolocco, J. Rauseo, J. Nielsen, S. Corsolini, Bioaccumulation of nonylphenols and bisphenol A in the Greenland shark *Somniosus microcephalus* from the Greenland seawaters, *Microchem. J.* 136 (2018) 106–112.
- [27] I. Nehring, M. Staniszewska, L. Falkowska, Human hair, Baltic Grey Seal (*Halichoerus grypus*) fur and Herring Gull (*Larus argentatus*) feathers as accumulators of bisphenol A and alkylphenols, *Arch. Environ. Contam. Toxicol.* 72 (4) (2017) 552–561.
- [28] S. Huber, N.A. Warner, T. Nygård, M. Remberger, M. Harju, H.T. Uggerud, et al., A broad cocktail of environmental pollutants found in eggs of three seabird species from remote colonies in Norway, *Environ. Toxicol. Chem.* 34 (6) (2015) 1296–1308.
- [29] B.D. Hardesty, D. Holdsworth, A.T. Revill, C. Wilcox, A biochemical approach for identifying plastics exposure in live wildlife, *Methods Ecol. Evol.* 6 (1) (2015) 92–98.
- [30] V. Padula, A.H. Beaudreau, B. Hagedorn, D. Causey, Plastic-derived contaminants in Aleutian Archipelago seabirds with varied foraging strategies, *Mar. Pollut. Bull.* 158 (2020) 111435.
- [31] B. Sunman, K. Yurdakök, B. Kocer-Gumusel, Ö. Özyüncü, F. Akbıyık, A. Balci, et al., Prenatal bisphenol a and phthalate exposure are risk factors for male reproductive system development and cord blood sex hormone levels, *Reprod. Toxicol.* 87 (2019) 146–155.
- [32] K. Mattsson, E.V. Johnson, A. Malmendal, S. Linse, L.-A. Hansson, T. Cedervall, Brain damage and behavioural disorders in fish induced by plastic nanoparticles delivered through the food chain, *Sci. Rep.* 7 (1) (2017) 1–7.
- [33] J.C. Prata, Airborne microplastics: consequences to human health? *Environ. Pollut.* 234 (2018) 115–126.
- [34] A. Bergman, J. Heindel, S. Jobling, K. Kidd, R.T. Zoeller, State-of-the-science of endocrine disrupting chemicals, 2012, *Toxicol. Lett.* 211 (2012). S3-S.
- [35] J.M. Gray, S. Rasanayagam, C. Engel, J. Rizzo, State of the evidence 2017: an update on the connection between breast cancer and the environment, *Environ. Health* 16 (1) (2017) 94.
- [36] D. Santi, E. Magnani, M. Michelangeli, R. Grassi, B. Vecchi, G. Pedroni, et al., Seasonal variation of semen parameters correlates with environmental temperature and air pollution: a big data analysis over 6 years, *Environ. Pollut.* 235 (2018) 806–813.
- [37] E. Diamanti-Kandarakis, J.P. Bourguignon, L.C. Giudice, R. Hauser, G.S. Prins, A.M. Soto, et al., Endocrine-disrupting chemicals: an endocrine society scientific statement, *Endocr. Rev.* 30 (4) (2009) 293–342.
- [38] M.R. Lambert, G.S. Giller, L.B. Barber, K.C. Fitzgerald, D.K. Skelly, Suburbanization, estrogen contamination, and sex ratio in wild amphibian populations, *Proc. Natl. Acad. Sci. Unit. States Am.* 112 (38) (2015) 11881–11886.

- [39] C. Chamard-Jovenin, C. Thiebaut, A. Chesnel, E. Bresso, C. Morel, M. Smail-Tabbone, et al., Low-dose alkylphenol exposure promotes mammary epithelium alterations and transgenerational developmental defects, but does not enhance tumorigenic behavior of breast cancer cells, *Front. Endocrinol.* 8 (2017) 272.
- [40] S.E. Pinney, C.A. Mesaros, N.W. Snyder, C.M. Busch, R. Xiao, S. Aijaz, et al., Second trimester amniotic fluid bisphenol A concentration is associated with decreased birth weight in term infants, *Reprod. Toxicol.* 67 (2017) 1–9.
- [41] K.M. Junge, B. Leppert, S. Jahreis, D.K. Wissenbach, R. Feltens, K. Grützmann, et al., MEST mediates the impact of prenatal bisphenol A exposure on long-term body weight development, *Clin. Epigenet.* 10 (1) (2018) 58.
- [42] T. Wang, M. Xu, Y. Xu, J. Lu, M. Li, Y. Chen, et al., Association of bisphenol a exposure with hypertension and early macrovascular diseases in Chinese adults: a cross-sectional study, *Medicine* 94 (43) (2015).
- [43] L. Cobellis, G. Latini, C.D. Felice, S. Razzi, I. Paris, F. Ruggieri, et al., High plasma concentrations of di-(2-ethylhexyl)-phthalate in women with endometriosis, *Hum. Reprod.* 18 (7) (2003) 1512–1515.
- [44] N.E. Skakkebaek, E. Rajpert-De Meyts, K.M. Main, Testicular dysgenesis syndrome: an increasingly common developmental disorder with environmental aspects, *Hum. Reprod.* 16 (5) (2001) 972–978.
- [45] N. Couleau, J. Falla, A. Beillerot, E. Battaglia, M. d’Innocenzo, S. Plançon, et al., Effects of endocrine disruptor compounds, alone or in combination, on human macrophage-like THP-1 cell response, *PLoS One* 10 (7) (2015).
- [46] L. Renaud, WAd Silveira, E.S. Hazard, J. Simpson, S. Falcinelli, D. Chung, et al., The plasticizer bisphenol A perturbs the hepatic epigenome: a systems level analysis of the miRNome, *Genes-Basel.* 8 (10) (2017) 269.
- [47] M. Huff, W.A. da Silveira, O. Carnevali, L. Renaud, G. Hardiman, Systems analysis of the liver transcriptome in adult male zebrafish exposed to the plasticizer (2-ethylhexyl) phthalate (DEHP), *Sci. Rep.* 8 (1) (2018) 1–17.
- [48] M. Huff, W. da Silveira, E.S. Hazard, S.M. Courtney, L. Renaud, G. Hardiman, Systems analysis of the liver transcriptome in adult male zebrafish exposed to the non-ionic surfactant nonylphenol, *Gen. Comp. Endocrinol.* 271 (2019) 1–14.
- [49] N.R. Council, *Animals as Sentinels of Environmental Health Hazards*, National Academies Press, 1991.
- [50] T. Spencer, Effects of carbon monoxide on man and canaries, *Ann. Occup. Hyg.* 5 (1962) 231–234.
- [51] B. Sepers, K. Van Den Heuvel, M. Lindner, H. Viitaniemi, A. Husby, K. Van Oers, Avian ecological epigenetics: pitfalls and promises, *J. Ornithol.* (2019) 1–21.
- [52] E.M. Weber, J.A. Dallaire, B.N. Gaskill, K.R. Pritchett-Corning, J.P. Garner, Aggression in group-housed laboratory mice: why can’t we solve the problem? *Lab. Anim.* 46 (4) (2017) 157–161.
- [53] C. Carere, D. Costantini, A. Sorace, D. Santucci, E. Alleva, Bird populations as sentinels of endocrine disrupting chemicals, *Ann I Super Sanita* 46 (1) (2010) 81–88.
- [54] M.E. Baker, B. Ruggeri, L.J. Sprague, C. Eckhardt-Ludka, J. Lapira, I. Wick, et al., Analysis of endocrine disruption in Southern California coastal fish using an aquatic multispecies microarray, *Environ. Health Perspect.* 117 (2) (2009) 223–230.
- [55] N. Veldhoen, J.E. Beckerton, J. Mackenzie-Grieve, M.R. Stevenson, R.L. Truelson, C.C. Helbing, Development of a non-lethal method for evaluating transcriptomic endpoints in Arctic grayling (*Thymallus arcticus*), *Ecotoxicol. Environ. Saf.* 105 (2014) 43–50.
- [56] Q.A. Schuyler, C. Wilcox, K.A. Townsend, K.R. Wedemeyer-Strombel, G. Balazs, E. van Sebille, et al., Risk analysis reveals global hotspots for marine debris ingestion by sea turtles, *Global Change Biol.* 22 (2) (2016) 567–576.
- [57] M. De Cáceres, P. Legendre, M. Moretti, Improving indicator species analysis by combining groups of sites, *Oikos* 119 (10) (2010) 1674–1684.
- [58] J. Zinsstag, E. Schelling, D. Waltner-Toews, M. Tanner, From “one medicine” to “one health” and systemic approaches to health and well-being, *Prev. Vet. Med.* 101 (3–4) (2011) 148–156.
- [59] K. Howe, M.D. Clark, C.F. Torroja, J. Torrance, C. Berthelot, M. Muffato, et al., The zebrafish reference genome sequence and its relationship to the human genome, *Nature* 496 (7446) (2013) 498–503.
- [60] C. Degeling, Z. Lederman, M. Rock, Culling and the common good: re-evaluating harms and benefits under the one health paradigm, *Publ. Health Ethics* 9 (3) (2016) 244–254.
- [61] G. Hardiman, *An Introduction to Systems Analytics and Integration of Big Omics Data*, Multidisciplinary Digital Publishing Institute, 2020.
- [62] G.T. Ankley, R.S. Bennett, R.J. Erickson, D.J. Hoff, M.W. Hornung, R.D. Johnson, et al., Adverse outcome pathways: a conceptual framework to support ecotoxicology research and risk assessment, *Environ. Toxicol. Chem.* 29 (3) (2010) 730–741.
- [63] R. Ramos, V. Llabrés, L. Monclús, M. López-Béjar, J. González-Solís, Costs of breeding are rapidly buffered and do not affect migratory behavior in a long-lived bird species, *Ecology* 99 (9) (2018) 2010–2024.
- [64] K. Hicks, M. Servos, Site fidelity and movement of a small-bodied fish species, the rainbow darter (*Etheostoma caeruleum*): implications for environmental effects assessment, *River Res. Appl.* 33 (7) (2017) 1016–1025.
- [65] K. Lehnert, K. Ronnenberg, L. Weijs, A. Covaci, K. Das, V. Hellwig, et al., Xenobiotic and immune-relevant molecular biomarkers in harbor seals as proxies for pollutant burden and effects, *Arch. Environ. Contam. Toxicol.* 70 (1) (2016) 106–120.
- [66] A.L. Bond, J.F. Provencher, R.D. Elliot, P.C. Ryan, S. Rowe, I.L. Jones, et al., Ingestion of plastic marine debris by common and thick-billed murre in the northwestern Atlantic from 1985 to 2012, *Mar. Pollut. Bull.* 77 (1–2) (2013) 192–195.