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Integrated Environmental Assessment and Management

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https://doi.org/10.1002/ieam.4743

Integrated Environmental Assessment and Management — Volume 00, Number 00—pp. 1–25
Received: 6 October 2022 | Revised: 4 January 2023 | Accepted: 18 January 2023

Health & Ecological Risk Assessment

Advancing exposure assessment approaches to improve wildlife risk assessment

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EDITOR'S NOTE:

This article is part of the special series from the SETAC workshop "Wildlife Risk Assessment in the 21st Century: Integrating Advancements in Ecology, Toxicology, and Conservation." The series presents contributions from a multidisciplinary, multi-stakeholder team providing examples of applications of emerging science focused on improving processes and estimates of risk for assessments of chemical exposures for terrestrial wildlife. Examples are considered relative to applications within an expanding risk assessment paradigm where improvements are suggested in decision-making and bridging various levels of biological organization.

Abstract

The exposure assessment component of a Wildlife Ecological Risk Assessment aims to estimate the magnitude, frequency, and duration of exposure to a chemical or environmental contaminant, along with characteristics of the exposed population. This can be challenging in wildlife as there is often high uncertainty and error caused by broad-based, interspecific extrapolation and assumptions often because of a lack of data. Both the US Environmental Protection Agency (USEPA) and European Food Safety Authority (EFSA) have broadly directed exposure assessments to include estimates of the quantity (dose or concentration), frequency, and duration of exposure to a contaminant of interest while considering "all relevant factors." This ambiguity in the inclusion or exclusion of specific factors (e.g., individual and species-specific biology, diet, or proportion time in treated or contaminated area) can significantly influence the overall risk characterization. In this review, we identify four discrete categories of complexity that should be considered in an exposure assessment—chemical, environmental, organismal, and ecological. These may require more data, but a degree of inclusion at all stages of the risk assessment is critical to moving beyond screening-level methods that have a high degree of uncertainty and suffer from conservatism and a lack of realism. We demonstrate that there are many existing and emerging scientific tools and cross-cutting solutions for tackling exposure complexity. To foster greater application of these methods in wildlife exposure assessments, we present a new framework for risk assessors to construct an "exposure matrix." Using three case studies, we illustrate how the matrix can better inform, integrate, and more transparently communicate the important elements of complexity and realism in exposure assessments for wildlife. Modernizing wildlife exposure assessments is long overdue and

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[Correction added on 20 April, 2023 after first online publication: Acknowledgment updated to include correct funding information.]

Published 23 January 2023 on wileyonlinelibrary.com/journal/ieam.

 DOI: 10.1002/ieam.4743

will require improved collaboration, data sharing, application of standardized exposure scenarios, better communication of assumptions and uncertainty, and postregulatory tracking. *Integr Environ Assess Manag* 2023;00:1–25. © 2023 SETAC

KEYWORDS: Exposure estimation; Risk assessment; Screening-level assessment; Uncertainty assessment; Wildlife

INTRODUCTION

Several authors have noted the lack of environmental realism in ecological risk assessments (Brühl & Zaller, 2019; Hill et al., 2000; Hope, 2009). For Wildlife Ecological Risk Assessment (WERA), data are often lacking, estimates of wildlife exposure tend to err on the conservative side, there is an overreliance on point estimates for toxicity reference values to determine if effect thresholds are met, and there is a lack of capacity to provide uncertainty metrics resulting in categorical or otherwise subjective use of hazard quotients. Current WERAs, therefore, have been structured to initially use simple conservative screening-level (lower tier) assessments which, if a hazard is identified, proceed to a more detailed, higher tier assessment. The use of conservatism, including application of arbitrary assessment or safety factors (10×, 100×), is frequently criticized as unscientific (Raimondo & Forbes, 2022), leading to regulatory and legal challenges. Regulatory, jurisdictional, and resource constraints can be a barrier to change (Topping et al., 2020). Critics for reform of ERA have advocated for a more integrated and holistic approach such as an "ecosystem reality check" (Burton et al., 2012; Topping et al., 2020) that aims to better harmonize and communicate multiple stages of the process throughout the life cycle of the risk assessment.

Exposure assessments are a critical component of the wildlife risk assessment process, with the aim of accurately estimating the quantity (dose or concentration), frequency, and duration of all exposure sources and pathways and any potential confounding sources of uncertainty. However, most prospective (lower tier) risk assessments used for screening chemicals and sites necessarily rely on vague species- and site-specific assumptions resulting in high uncertainty about true exposure conditions. More detailed site-specific retrospective assessments can better fill these gaps in ecotoxicological and environmental interactions but are more data intensive and are not generalizable. This often means that relatively few assessments proceed to more refined and realistic assessments (higher tier) when screening-level assessments indicate potential hazard issues and there is a general lack of transparency and standardization in decision-making for inclusion or exclusion of key factors that drive the exposure assessment. Overall, there is a considerable lag by regulatory bodies in incorporating and adapting recent scientific advances into exposure assessments for wildlife to address these concerns.

The overall aim of this review is to identify how exposure assessments for contaminants of environmental concern to wildlife may be improved and better incorporate the best available science. To accomplish this aim, our interdisciplinary team of scientists and risk assessment practitioners collectively (1) identified important shortcomings in current exposure assessment practices that prioritize simplicity over realism; (2) critically reviewed and evaluated promising approaches and solutions to address these shortcomings; (3) provided a new matrix framework and example case studies that illustrate better data integration, standardization, and transparency across tiered exposure assessments; and (4) provided recommendations for prioritization and modernization of wildlife exposure assessments to incorporate the latest science.

The simplicity paradox in wildlife exposure assessment

Because of resource and data limitations, most screening-level wildlife risk assessments rely on simplistic exposure scenarios involving one or a few model wildlife receptors to compare with toxicity point estimate thresholds derived with standard test species in the laboratory. Such lower tier assessments may, for example, rely on single upper bound concentrations in food items or other media, and ignore other exposure pathways, environmental degradation, animal movement, animal metabolism and elimination, and so on. Although unrealistic, screening-level exposure assessments can be useful in conservatively estimating upper bound exposures to wildlife for single chemicals or groups of chemicals sharing a common mode of action. If such screening-level exposure estimates are well below corresponding toxicity thresholds, current guidance suggests no further assessments are required and chemicals of lowest concern can be screened out.

In reality, many wildlife species range widely across variable habitats and are exposed to contaminants via multiple exposure routes (e.g., diet, drinking water, soil and/or sediment, dermal contact, inhalation; Figure 1). Although diet is generally assumed to be the major exposure pathway for wildlife, this assumption has rarely been tested. The relationship between dietary exposure estimates and internal concentrations suggests other exposure routes are important, for example, atmospheric inhalation sources from landfills (Sorais et al., 2020) and dermal exposure to pesticide sprays (Hernández-Jerez et al., 2019; Mineau, 2011). Moreover, assessing and regulating one chemical at a time often ignores the reality that wildlife are exposed to dynamic chemical mixtures over their lifetime and that contaminant concentrations and exposure conditions vary spatially and temporally across diverse habitats and across an organism's life cycle. The result is over- or underestimation of true exposure.

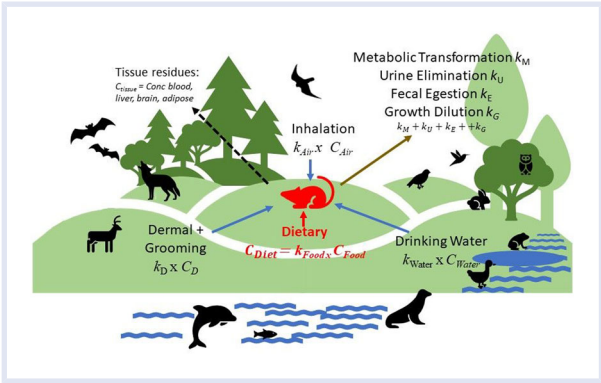

FIGURE 1 Contaminant exposure pathways for wildlife. Exposures have traditionally focused on diet-based estimates based on rates of uptake (*k*) and environmental concentrations (*C*). However, exposure is known to vary across individuals, species, and life stages and is driven by multiple pathways from diet, inhalation, dermal, and ingestion of water, soil, and sediment. Complementary measurements of internal concentrations are thus essential to understanding actual exposures and can be confirmed through analysis of tissue residues.

The simplistic approach to exposure assessment has dominated WERAs and remains attractive for its low cost and rapid completion. However, if chemicals are inappropriately screened out at a lower tier, there is no opportunity to revisit the assessment using more comprehensive and realistic methods. Given high environmental variation in contaminant distribution coupled with large individual and interspecific variation in species' life histories, behavior, diet, habitats, exposure routes, and community interactions that underpin natural ecosystems, the use of overly simplistic approaches is insufficient and often criticized as unscientific. Wildlife exposure assessments require modernization of the current approaches that use the best available science along with qualifiers to transparently communicate the uncertainty and risk.

In this article, we have identified four major categories of complexity in wildlife exposure assessments.

- *Chemical complexity*—Wildlife exposures are rarely limited to a single parent compound. They are typically exposed to contaminant mixtures as well as metabolites and transformation products.
- *Environmental complexity*—There is a high degree of spatial and temporal variation in contaminant concentrations and environmental conditions across diverse wildlife habitats and ecosystems.
- *Organismal complexity*—Estimating external exposure (e.g., daily dietary dose) does not account for species- or stage-specific differences in the dynamic uptake, bioaccumulation, biomagnification, biotransformation, and elimination processes occurring within the individual organism.
- *Ecological complexity*—Restricting assessments to a narrow set of "model" receptor species commonly overlooks the ecological and functional diversity among species and their life-history traits as well as indirect and community-level effects (e.g., loss of food or changes in habitat suitability).

Although not an exhaustive review, these critical issues must be addressed. Here we present and discuss these four categories of complexity in wildlife exposure assessments along with several promising proposals that incorporate the latest science (Table 1).

CHEMICAL COMPLEXITY

Complex mixtures

Wildlife risk assessments traditionally focus on a single compound or a narrow chemical group, although organisms are often exposed to complex mixtures from multiple natural and anthropogenic compounds, transformation products, and formulated products over their life span (Scholz et al., 2022; Topping et al., 2020). The co-occurrence of multiple compounds in a single source and the co-exposure to multiple sources leads to dynamic patterns of exposure to complex mixtures over time and space. For example, data on pesticide applications and monitoring of movements of amphibians, mammals, and birds in an agricultural landscape mosaic have revealed sequential exposures to different pesticide-active ingredients in the course of a year (Bro et al., 2015; Leeb et al., 2020; Lenhardt et al., 2015; Mayer et al., 2020). This phenomenon has prompted more experimental studies that include measuring wildlife responses to coexposures (e.g., Glinski et al., 2019).

There are no simple or easy solutions available to meet the challenge of estimating the magnitude of wildlife exposure to mixtures, but several complementary approaches have emerged. The "exposome" concept, originally developed in human health research, may be a promising way to refine exposure assessment to multiple compounds. The eco-exposome approach was defined by Scholz et al. (2022) as an extension of exposure science that "…represents the totality of internal exposure over a lifetime to individuals of a given species … including exposure to anthropogenic chemicals, their biotransformation products, and/or adducts." Several of the scientific and technical obstacles to applying the exposome concept to identify mixture components have been overcome by advances in analytical chemistry.

Sensitive analytical methods to determine the concentrations of a broad array of metals and metalloids have become the norm (e.g., ICP-MS), and similar methods are now available for many organic chemicals to measure multi-residues and metabolites with high resolution (e.g., mass spectrometry). Although targeted analytical chemistry is the approach most used to detect and quantify a set of predefined compound residues, non-target analytical screening methods to identify chromatographic peaks from multi-residues for unknown compounds and metabolites are rapidly developing (Scholz et al., 2022). Other advances in methods to extract, clean up, and concentrate chemicals in wildlife tissue and

 DOI: 10.1002/ieam.4743

TABLE 1 Simplicity and complexity challenges in wildlife exposure assessments and some promising solutions

Category	Static simplicity	Dynamic complexity	Solutions	Cross-cutting solutions
1. Chemical complexity	Single parent compound	Metabolites and transformation products	Target, nontarget, and metabolite multiresidue analysis	Spatially explicit modeling and explicit scenario-based simulations
		Mixtures and formulated products	Eco-exposome approach	
		Mobility and stability: Lipid and water solubility and physiochemical properties affecting recalcitrance	DEBTox models	
			Fate models using multimedia and physiochemical properties	Biomonitoring, environmental monitoring, and passive sampling
		Chemical properties	Assimilation efficiency values	
2. Environmental complexity	Single medium exposure source	Multiple exposure sources (soil, air, water)	National and regional monitoring programs	Use of available open-source data
		Temporal contaminant variation—acute and chronic exposure duration	Spatially and temporally explicit fate modeling	Optimization and improvement of experimental designs in applied research
			Spatial statistics	
	Single time point	Spatial contaminant variation	Land use and habitat characterization using GIS	
		Habitat variation	Habitat availability and suitability assessment	
		Climate and weather	Field studies under realistic conditions	
	Habitat uniformity	Multiple drivers and stressors	Scenario-based modeling	
3. Organismal complexity	Total daily intake	External versus internal dose	Species-specific estimates for dermal, inhalation, and preening exposures	Chemical activity (fugacity-based concentration)
		Genetics and individual variation	Maternal transfer and elimination pathways	
	Diet only	Multiple exposure routes (diet, dermal, respiration, maternal)	Linking internal vs. diet-based exposures	Uncertainty estimation
		Biotransformation and elimination	Bioaccumulation Assessment Tool (BAT)	Reduction in animal use
		Bioaccumulation/trophic magnification	Bioaccumulation, biomagnification, and trophic magnification factors (BAF, BMF, TMF)	
		Bioavailability	Physiologically based extraction tests (PBET)	
			Physiologically based toxicokinetic–toxicodynamic (PBTK-TD) modeling	
4. Ecological complexity	Model species receptors	Multispecies communities	Trait-based approaches (ecological and physiological)	Use of available open-source data
		Diet composition and foraging ecology	Life-history- and life-stage-specific exposure	Uncertainty estimation

(*Continued*)

TABLE 1 (*Continued*)

Category	Static simplicity	Dynamic complexity	Solutions	Cross-cutting solutions
	Single trophic position	Indirect effects	Cumulative lifetime exposure	Optimization and improvement of experimental designs in applied research
		Demography (sex and age)	Tracer data on foraging and dietary ecology	
		Seasonal phenology (e.g., reproduction, migration)	Dynamic energy budget modeling	
	Single life stage	Animal movement and habitat use	Tracking animal movement and spatial behavior	Use of available open-source data
		Life-history traits (e.g., reproductive strategy, age at first breeding, longevity)	Food web models	
	Taxonomy and body size extrapolation	Physiological variability (lipid content and body-size variability)		

environmental samples now enable the measurement of complex biological matrices, low mass or volumes, and with low detection limits.

Using advances in analytical chemistry, molecular biology, ecology, computational sciences, and statistics, mixture-related tools have been increasingly applied to wildlife. For instance, the DEBtox approach is a modeling framework based on the dynamic energy budget theory (Jager et al., 2010). The EuroMix methodology has been developed to provide methods and statistical tools (EuroMix toolbox) to perform mixture-risk assessment based on dietary exposure or a combination of dietary and nondietary sources (Beronius et al., 2020). Advances in assessment of mixture exposures have benefited from the adverse outcome pathway (AOP) concept to classify multiple compounds by mode of action and address toxicity outcomes based on exposure source. Within the framework of the eco-exposome approach, an Aggregate Exposure Pathway (AEP) is designed to characterize pathways from source to environmental media as well as external to internal concentrations, through linking individual and networks of AOPs (Scholz et al., 2022).

Surveys of known or suspected environmental releases of compounds concurrently with modeling can better capture the patterns of co-occurrence or sequential occurrence of compounds, thus allowing the identification of the mixtures of concern for wildlife exposure. For instance, the occurrence and frequency of exposure to multiple compounds can be characterized when dealing with released pulses of compounds (dynamics of pulses, features of mixtures in such pulses, time lapses that separate the pulses). Ultimately, such approaches can identify scenarios representing different magnitude, frequency, and duration of the exposure to multiple compounds to predict coexposure, sequential exposure, or ecological recovery (Weisner et al., 2021).

Chemical properties affecting exposure: Recalcitrance, lipid and water solubility, protein association

The environmental fate and behavior of contaminants in wildlife is controlled largely by the chemical properties affecting persistence, bioaccumulation potential, and inherent ability to partition between air, water, and organic phases (e.g., soil, sediment, lipid, protein, organic matter, etc.), often defined by partition coefficients. The current regulatory criteria and endpoints used in North America to classify a substance as bioaccumulative include a log octanol–water partition coefficient ($\log K_{OW}$) > 5 or a bioconcentration factor (BCF) or bioaccumulation factor (BAF) > 5000. This approach is useful for water-breathing aquatic organisms but not for air-breathing organisms (Gobas et al., 2009). For air breathers, the European Union considers chemicals to have significant bioaccumulation potential if the chemical has $\log K_{OW} > 5$ and log octanol–air partition coefficient $\log K_{OA} > 2$. Two of the inherent assumptions in the partition coefficient approach is that bioaccumulation of organic substances occurs predominantly in the lipids of organisms and that octanol is a good surrogate phase to

 DOI: 10.1002/ieam.4743

represent the solubility of chemicals in lipids. Consideration of chemicals with differing solubilities or sorptive capacities in lipids and octanol may be better represented by the lipid–octanol partition coefficient (K_{LO}; Seston et al., 2014). K_{LO} values of substances often vary with different types of lipids, specifically neutral (i.e., storage) and polar lipids (i.e., membrane or phospholipids; Seston et al., 2014).

When the lipid content in organisms is low, other organic matrices may become the main site of chemical bioaccumulation. Proteins, particularly albumin and structural proteins, can contribute substantially to the internal exposure and sorptive capacity for the chemical in the organism (Allendorf et al., 2021). For example, for ionogenic surfactants (e.g., PFAS), the sorptive capacity of proteins is much greater than that of lipids and should be assessed using distribution coefficients (Allendorf et al., 2021). deBruyn and Gobas (2007) found the sorptive capacity of animal protein can range from 1% to 10% that of lipid for a range of hydrophobic chemicals with a log $K_{OW} > 2$, but is substantially greater than 10% for chemicals with a lower log K_{OW}. For bioaccumulation assessments, a recommended nonspecific sorptive capacity of proteins for neutral hydrophobic organic chemicals is 5% that of lipid (deBruyn & Gobas, 2007). This illustrates the importance of considering the range of chemical properties (e.g., lipid and water solubility, protein sorption) and their propensity for tissue accumulation in exposure assessments.

Assimilation efficiency is a convenient multiplier, often used for metals and some organic compounds, to adjust contaminant concentrations based on their relative availability to an organism reflecting chemical hydrophobicity and physicochemical properties. For example, assimilation efficiency of chlorinated organic chemicals in many organisms often declines with increasing chemical hydrophobicity. However, many vertebrates, such as birds and mammals, express similar degrees of assimilation efficiency of neutral hydrophobic chemicals as they both possess cytochrome P450 monooxygenases (Drouillard & Norstrom, 2000). Uptake may also vary with the exposure route and its duration or in combination with the physicochemical properties of the contaminant. For instance, absorption of highly volatile chemicals like decamethylcyclopentasiloxane (D5) in rats was approximately 10% after oral exposure but less than 3% after inhalation exposure (Dekant & Klaunig, 2016).

Complex mechanistic models are available that account for organic contaminant uptake in plants (Hyland et al., 2015), fish (Arnot & Gobas, 2004), and small mammals (Armitage & Gobas, 2007) or for entire terrestrial food webs (Gobas et al., 2015). They can be used subsequently to estimate bioavailability and internal organic contaminant concentrations in wildlife. These complex models are often taxon- and location-specific and may not be widely applicable to contaminants other than commercial organic chemicals. Thus, variations in food intake and absorption efficiency via diverse routes of exposure are key parameters in uptake assessment.

ENVIRONMENTAL COMPLEXITY

Spatial heterogeneity

By design, screening-level exposure assessments focus on representative or generic wildlife receptors, address only worst-case exposure scenarios, and are limited in accounting for environmental variation and habitat suitability for the selected receptors. The resulting wildlife exposure assessment is not designed to provide outputs that can be used to design appropriate remediation or mitigation strategies. Historically, assessors have tried to improve exposure assessments using simplistic exposure adjustment factors or probabilistic approaches to account for variability in contaminant concentrations and time spent by receptors on or off contaminated areas. Such improvements require more intensive characterization of wildlife habitats, their use by each species, and measures of chemical concentrations across the site. There are readily available tools that can improve the realism of wildlife exposure assessment by incorporating both habitat use and environmental variation in exposure calculations. There has been resistance to the use of spatial models due to regulatory inertia, lack of data and resources, and a limited history of application (Hope et al., 2011; Topping et al., 2020). The fact that the models are only partially validated also hampers regulatory acceptance. The use of spatially explicit sampling or modeling designs, biomonitoring, and habitat assessments can greatly improve the realism of and specificity to the receptors of interest. Geostatistical tools allow the characterization and prediction of spatial patterns of environmental contamination to assess exposure at the site investigation scale and over broader landscapes (Rate, 2021). Predictions about contaminant fate and spatial distribution over small and large scales are increasingly becoming a reality (Gassmann, 2021), even where detailed biomonitoring data are limited, such as pesticide use in developing countries (Tang et al., 2021).

The traditional single sampling event method has been improved using systematic and longer-term monitoring approaches, often over broad areas and incorporating sampling of multimedia and biota. Monitoring allows the identification of contaminant spatial spread such as drift and leaching. Further, field monitoring data are essential to developing and validating modeling tools. Monitoring of environmental contamination, such as sources and sinks of terrestrial or aquatic contamination and presence in wildlife tissues, further provides data essential to assessing spatial and temporal variation in wildlife exposure and to identifying areas or habitats of primary concern (Fritsch et al., 2011, 2012; Marcot et al., 2015). In a recent review of monitoring of current-use pesticides in agricultural soils worldwide over the past five decades (Sabzevari & Hofman, 2022), the resulting integrated data set emphasizes the value of establishing long-term monitoring programs that can better predict fate and accumulation of contaminants in realistic contexts and at various scales.

Species differ in the way they exploit their local resources in space and time driven in part by habitat suitability. Areas

that do not have habitat or where species distributions do not overlap can be mapped and excluded. The accessibility to numerical and digital spatial data has greatly improved due to open-source databases, software, and numerical tools. Land cover and land use spatial data that use satellite, aerial drone, and LiDAR remote sensing imagery are now widely available and at high resolution (e.g., integrative initiatives such as CORINE land cover monitoring; https://land.copernicus.eu/pan-european/corine-land-cover). Spatial databases already exist that can map the degree of overlap between species ranges and areas where contaminants can occur (e.g., Environmental Conservation Online System for threatened and endangered species; https://ecos.fws.gov/ecp/). Habitat surveys and species range maps are now widely available to apply habitat suitability indexing tools (e.g., ArcHSI by Rumble, 2006). At smaller scales, habitat surveys can also provide time-series site use by wildlife. These databases can be used to develop more scientifically defensible area use factors including probabilistic exposure adjustment factors, which account for interindividual variability in time spent foraging in different areas. Although such simple adjustments may improve exposure estimates in some cases, they may also misrepresent important species–habitat–diet interactions or over- or underrepresent actual exposures caused by individual variation in movement patterns as well as patchy local contaminant distributions. Differences in habitat selection and spatial habitat use may significantly affect exposure magnitude. Schipper et al. (2012) modeled exposure of little owls to cadmium and found that habitat-specific occurrences of prey items strongly influenced exposure patterns. Although the presence or absence of available habitat is an important first consideration in determining whether a site confers a risk, a more refined habitat survey will more efficiently and effectively assess which vulnerable wildlife use a site, the suitability for different species, and where exposures are most likely to occur. Geographic information systems (GIS) provide the framework for compiling and analyzing habitat and contaminant distribution data.

Spatially explicit exposure models integrate higher resolution habitat data with species behaviors (e.g., foraging area, habitat preferences, ingestion rates, diet). By using probabilistic methods, such models can apply decision-based "movements" to determine exposure at different time steps as each individual moves around a complex environment. Ultimately, there is a higher probability of exposure where the habitat is most suitable and these areas may overlap with the highest chemical concentrations (Schipper et al., 2012). Moore et al. (2018) used a spatially explicit, probabilistic random walk model to estimate exposure of individual Kirtland's warblers whose foraging habitats may be contaminated by downwind spray drift deposition of malathion and chlorpyrifos (see case study below). Agent-based risk assessment modeling tools such as the Animal, Landscape and Man Simulation System (ALMaSS; https://projects.au.dk/almass) can better predict multiple exposures and the spatiotemporal heterogeneity of landscape use by animals and their interactions with pesticide applications (Mayer et al., 2020; Topping et al., 2020). Several retrospective risk assessments have demonstrated the benefits of using detailed habitat data and spatially explicit chemical data for wide-ranging wildlife species (Fritsch et al., 2013; Johnson et al., 2021). Simple to more complex spatial exposure models can incorporate multiple scenarios based on the species-specific and individual variation in diet, trophic position, and foraging ecology. Whether full, spatially explicit models are applied in exposure assessments or smaller, incremental improvements are included through habitat-use assumptions, diet, or foraging scenarios, there is strong evidence exposure estimates can be improved by incorporating spatial variability.

Climate change

Climate change is increasingly influencing both the distribution of environmental contaminants and the distribution of wildlife populations. Direct and indirect impacts of climate change are altering phenotypic and ecological attributes that influence contaminant exposure in wildlife, particularly in Arctic ecosystems (Borgå et al., 2022; McKinney et al., 2022). Noyes et al. (2009) identified changes in exposure and risks from increased levels and redistribution of persistent organic pollutants (POPs) caused by alterations in temperature and precipitation patterns, ice and snow melt, stream runoff, and organic carbon cycling. In the Arctic, where climate change is occurring faster and with greater amplitude than elsewhere, there is increased long-range transport of contaminants, resulting in elevated exposure at the base of the food web, and increased levels of biomagnifying contaminants in both resident and migrant fish and wildlife (Borgå et al., 2022). Ecological shifts in species distributions, food webs, lipid dynamics, and biotransformation rates are also expected under a warming climate, with unknown cumulative effects on wildlife exposure and accumulation. Range shifts (northward shift of southern species) can also lead to elevated contaminant exposure to wildlife, for example, migrating prey fish such as capelin had higher levels than the Arctic resident polar cod of both legacy PCBs, DDTs, and emerging contaminants (Pedro et al., 2017).

Recent development of climate models and access to high resolution satellite imagery (e.g., Sentinel and Landsat imagery) and freely available data processing cloud-based analytics (e.g., Google Earth Engine; https://earthengine.google.com/) mean risk assessors can more accurately identify land use and climate stressors, predict species occurrences or distributions, and model the probability of contaminant release (Beketov & Liess, 2012). For example, macroscale GIS-based models have been applied to predict pesticide use, runoff potential, and fate in Canada's prairie wetlands that are important wildlife habitats (Malaj et al., 2020; Malaj & Morrissey, 2022). Macroecotoxicological approaches suggest promise for predicting the effects of climate change and for addressing the issues of multiple stressors from processes that occur at local and large scales.

 DOI: 10.1002/ieam.4743

Causal analysis frameworks can also identify which combinations of stressors may be driving risk observed in climate and other stressors (Salatas et al., 2013; Wickwire & Menzie, 2010). Similarly, object-oriented models or food-chain models have been developed to assess the risk of multiple environmental stressors (e.g., flooding, starvation, predation, contamination) on terrestrial vertebrate populations (Baudrot et al., 2018; Loos et al., 2010).

ORGANISMAL COMPLEXITY

External versus internal exposure

Extrapolating between internal concentrations in organisms and external concentrations in environmental media (i.e., diet, water, soil, or air) requires a mechanistic understanding of the relationships between these (Scholz et al., 2022). When this relationship is understood, simple proxies, such as chemical or biological measurements, can be developed to infer internal exposure concentrations when it is difficult to measure or obtain data directly from wildlife sampling. Chemicals that disrupt cellular or endocrine functions only do so once they are absorbed, emphasizing the importance of internal exposure for interpreting toxicity (Escher & Hermens, 2004).

Nonlethal or minimally invasive collection methods may be used as proxies for internal tissue residues in wildlife matrices such as blood, hair, feathers, feces, muscle or fat biopsies, and eggs. Contaminant concentrations measured in these matrices are extrapolated to whole body concentrations or doses to match the units of available toxicity data to enable risk predictions. However, because species differ in physiology, dietary ecology, and reproductive strategies, conclusions regarding exposure risks vary depending on the matrix sampled and physicochemical properties of the contaminant (Thorstensen et al., 2021). Therefore, it is important to consider multiple proxies of contaminant exposure.

Beyond collecting samples or proxies from wildlife to deduce internal concentrations, toxicokinetic (TK) and toxicodynamic (TD) models can provide a link between realistic exposure scenarios and relevant patterns of toxicity effects for vertebrates and are a promising tool to refine wildlife risk assessment. Reverse-dosimetry based on physiologically based kinetic (PBK) models describe internal kinetics by integrating various internal processes, such as absorption, distribution, metabolism, and excretion, also known as ADME processes (Louisse et al., 2017). This approach is often chemical- and species-specific and may be data-demanding, but meta-analyses and reviews can help support PBK model development (Scanes et al., 2022), and user-friendly interfaces have been made available (Charles et al., 2022; see https://mosaic.univ-lyon1.fr/guts). For example, modeled risk scenarios of pesticides in birds (e.g., skylark) and mammals (e.g., wood mouse) demonstrated the advantage of TK–TD modeling as it not only incorporates information about internal exposure but also accounts for the biological processes that influence those internal exposures, such as feeding patterns and seasonality (Ducrot et al., 2016). Model-based approaches also have the advantage of incorporating probabilistic methods to assess uncertainty, variation, and probability to meet protection goals.

Multiple exposure routes

Beyond dietary exposure, wildlife are exposed to contaminants through dermal uptake, drinking water, preening, and inhalation as well as maternal transfer. These pathways have been largely overlooked or ignored because of a lack of data or for the sake of simplicity (Mineau, 2011). Oral exposure may occur through ingestion of contaminants deposited on fur or feathers during grooming behaviors. Eggs and chicks in nests or small mammals that rely on camouflage may be exposed from pesticide overspray. The risk of dermal exposure from pesticides has been identified as an important route to consider for bats, reptiles, and amphibians, as their biology and ecology make them susceptible to this exposure route, particularly for amphibians, which have highly permeable skin (EFSA, 2008; EFSA et al., 2020). Maternal transfer is also an important source of exposure for offspring as well as an elimination pathway for the mother with placental transfer of protein-associated chemicals and lactational or egg transfer of lipid soluble chemicals.

Several practical solutions have been developed to evaluate potential wildlife risk from alternative routes of exposure. For example, Mayer et al. (2020) used an agent-based model to demonstrate that uptake via oral grooming after overspray of hares could be sevenfold higher than uptake via foraging. Maternal transfer has been estimated with mechanistic physiologically based toxicokinetic (PBTK) models (Hickie et al., 1999; Norstrom et al., 2007). Such scenario-based simulations are a promising tool to address exposure pathways beyond a diet-only approach. In addition, experimental approaches that allow multimedia exposure or exposure via spraying (e.g., indoor trial or in situ caging) represent another way to assess exposure pathways beyond the diet (Mineau, 2011). The use of passive sampling devices and methods can predict and compare the risk of exposure to wildlife from nondietary routes. Chemical concentrations collected via passive sampling can be evaluated with environmental fate modeling for chemical flux or the mass transport rate of the chemical into wildlife (Fremlin et al., 2021).

Uptake and bioavailability

Given the vast numbers of synthetic chemicals, metals, and transformation products in the environment, their differential availability is key to understanding uptake. Contaminant bioavailability is a concept that is defined as "the fraction of the total concentration that is, or can be made, available for uptake, accumulation, and induce an effect in the organism" (Peijnenburg & Jager, 2003). The assessment of bioavailability depends on the physicochemical characteristics of the contaminant, which are usually referred to as environmental availability and the biological characteristics

of the organisms (sometimes referred to as host factors; Peakall & Burger, 2003).

Several methods have been developed to assess bioavailability, such as chemical extractions that enable measuring the available fraction of a contaminant in a given medium; approaches based on equilibrium partitioning, speciation, or assessment in pore waters; and considering water, soil, or sediment physicochemical characteristics such as pH and organic matter content (Baker et al., 2003; Harmsen, 2007; Peijnenburg & Jager, 2003; V. W. van den Brink et al., 2010). However, the relevance of such methods for estimating bioavailability and uptake may be limited for some wildlife taxa occupying complex environments that often do not reflect local physicochemical conditions of a single medium (e.g., diversified diet and trophic food web accumulation, high mobility and home-range size, and patchy spatial distribution of contamination; Fritsch et al., 2011; P. J. van den Brink, Alexander, et al., 2011; van Gestel, 2008). Further, the default assumption for WERA is that the dose ingested by wildlife in natural environments has the same bioavailability as that in laboratory studies conducted on laboratory species, although this simplifying assumption is likely incorrect.

Assessment of contaminant bioavailability in different environmental matrices and across different species and food webs is therefore needed to improve the reliability of exposure predictions (Baker et al., 2003; Peakall & Burger, 2003; Peijnenburg & Jager, 2003; van Gestel, 2008). The bioaccessible fraction should estimate the maximal proportion of a chemical present in ingested food, water, soil, or sediment that can be released or made available after digestion (Peijnenburg & Jager, 2003). Given that the bioaccessible fraction is related to estimates of uptake, biotransformation, compartmentalization, and excretion within the organisms and is the fraction that interacts with internal biological targets, it is highly relevant to both exposure and toxicity assessments.

A promising method involves physiologically based extraction tests (PBET). A physiologically based extraction test is an in vitro chemical extraction method first designed to measure the bioavailability of lead-contaminated mine wastes in a simulated human gastrointestinal tract (Ruby et al., 1993). A standard test method to measure the bioaccessibility of lead and arsenic from soils was developed (USEPA, 2017c) and is routinely used to provide a site-specific adjustment for lead and arsenic for the soil ingestion pathway in human health risk assessment. Physiologically based extraction test data are equally valuable in ecological risk assessments for wildlife. Although a standard method has not yet been recognized internationally, the basic PBET methods have been modified to reflect differences in the gastrointestinal tracts of mammals (Kaufman et al., 2007), or birds (Beyer et al., 2016; Furman et al., 2006; Kaufman et al., 2007). PBET data have successfully been used to measure the bioaccessibility in soil and dietary items to improve the dose calculations in food-chain models for several species including shrews (Bennett et al., 2007; Moriarty et al., 2012), rabbits (Bennett et al., 2007), mice (Ollson et al., 2009), quail (Beyer et al., 2016), and bats (Hernout et al., 2015). The PBET approach better characterize bioavailability and improve food-chain models, as demonstrated for metals and organics (Armstrong et al., 2007; Dean & Ma, 2007), and have even been effective for estimating bioaccessibility of plants exposed to mine waste (Brumbaugh et al., 2011). Further development may be required to adapt the current available methods to other wildlife exhibiting physiological differences such as ruminants and hindgut fermenters.

Biotransformation and elimination

In screening-level risk assessments, chemicals are often considered recalcitrant to metabolism, thus, elimination through biotransformation is assumed negligible. This assumption may result in an overestimated accumulation of chemicals in organisms particularly for rapidly metabolized chemicals. However, biotransformation may concurrently produce recalcitrant products that accumulate in the organism and are more toxic than the parent compound, such as *p,p*′-DDE, which is a transformation product of DDT. Furthermore, some pesticides require biotransformation to become active. Differences in available enzyme systems in species often result in different toxicity profiles. To avoid an overly conservative estimation of bioaccumulation, biotransformation can be included as an elimination pathway in accumulation assessments through mechanistic models such as the Bioaccumulation Assessment Tool (BAT; Arnot et al., 2022) or PBK models. The ability of a species to biotransform a chemical can be determined with in vitro biotransformation assays based on methods using hepatocytes or liver subcellular fractions, which have recently been standardized for fish (OECD, 2018a, 2018b) and adapted to wildlife risk assessments (Lee et al., 2012).

Biomagnification and trophic magnification

Bioaccumulation of a chemical is typically assessed using water-based metrics, specifically the laboratory-based BCFs, which is a ratio between the chemical concentration in an organism and the ambient water (e.g., OECD, 2012). However, BCFs do not account for dietary exposure and only reflect branchial exposure from water and thus are not applicable to air-breathing organisms. Likewise, the BAF, which is the ratio between the chemical concentration in an organism and the surrounding media, such as water, sediment, or soil, can consider both respiratory and dietary exposure, but is only appropriate to aquatic organisms or soil- and sediment-dwelling invertebrates (e.g., OECD, 2008, 2010). Bioaccumulation metrics that consider dietary exposure and are appropriate to both water- and air-breathing organisms include the biomagnification factor (BMF) and trophic magnification factor (TMF). BMFs represent a species- or organism-specific ratio between the chemical concentration in the organism and its diet, whereas TMFs represent a BMF averaged across an entire food web (Borgå et al., 2012). When determining BMFs and TMFs of organic chemicals, it is

 DOI: 10.1002/ieam.4743

often important to lipid normalize the chemical concentrations in the organisms to remove the effect of differences in lipid content across species and to allow a direct comparison of concentrations on a common basis (Borgå et al., 2012; Burkhard et al., 2012; Fremlin et al., 2020).

ECOLOGICAL COMPLEXITY

Species selection versus trait selection

Exposure assessment has long been dominated by the selection of single model species and phylogenetic and allometric extrapolation. Several approaches have been used for species selection including selecting sentinels for a specific ecosystem, compartment, or trophic level; studying taxonomic groups related to different trophic levels of the food web; or using multiple indicator species with contrasting biological traits of interest (Badry et al., 2020; Fremlin et al., 2020; Gómez-Ramírez et al., 2014). The major criticism of the model species approach is that it lacks standardization and fails to account for the observed variability in exposure and toxicity risk within and among individuals and species. For example, in birds, there is at least a 1000-fold difference in sensitivity to dioxin-like compounds, although the aryl hydrocarbon (AhR) signaling pathway is highly conserved among evolutionary lineages (Farmahin et al., 2013). Extrapolation and generalization of exposure between phylogenetically related or ecologically similar species may still lead to oversimplification and overlooking of important biotic variation in exposure, sensitivity, and interpretation of toxicity risk (Moore et al., 2020).

Receptor species selection should still be based on ecological, morphological, and physiological traits, along with chemical-related exposure concerns (Gómez-Ramírez et al., 2014). Intraspecies variation should not be ignored and can be bracketed by estimating upper and lower quartiles within the population and identifying which traits contribute disproportionately to exposure variance under different scenarios. Although community responses have been embraced in the regulatory world using Species Sensitivity Distribution approaches to extrapolation of toxicity endpoints (Maltby et al., 2005), there has been little effort to incorporate the same community approaches to multispecies assessments when characterizing species vulnerability to contaminant exposure.

Systematic understanding of the role of biological traits, that is, morphometric, ecological, and physiological characters of an individual or species, on intra- and interspecies variability in exposure is critical to better reconstruct and predict exposure patterns across species and their life histories. There is evidence that much of the variation in species sensitivity can be explained more by ecological and physiological trait characteristics than by phylogenetic relatedness (Bianchini & Morrissey, 2020; Hwang et al., 2016). Similarly, trait-based ecological risk assessment (TERA) is a promising avenue to advance wildlife exposure risk assessment as it provides mechanistic and diagnostic understanding of causal linkages between intra- and interspecific biotic variation and chemical stress (Spurgeon et al., 2020; P. J. van den Brink, Rubach, et al., 2011). Variability in species and individual exposure are influenced by life-history traits such as longevity, reproductive strategy and investment, developmental rates, and maturity; ecological traits such as dietary, spatial foraging, and movement ecology; and ecophysiological traits such as thermoregulatory strategy, body condition, lipid content, and metabolic capacity. Accounting for such biological traits will allow for better species read-across of external exposure, intrinsic risk, and population vulnerability (P. J. van den Brink, Alexander, et al., 2011).

Adoption of TERA to advance ecological risk assessment requires published trait data for a wide range of taxonomies (P. J. van den Brink, Alexander, et al., 2011). There has been a rapid increase in the development and publication of open-access trait databases that cover both ecological and toxicological traits for a wide range of species (e.g., http://animaltraits.org; Herberstein et al., 2022). Many distributed trait data sets have been aggregated and harmonized into greater collections with a taxonomic or regional focus. Progress is underway to increase our understanding of trait-based responses for wildlife to determine which traits respond to chemical stress, and compare TERA with current ERA approaches (P. J. van den Brink, Rubach, et al., 2011).

Ecological traits: Trophic position, diet and foraging ecology

Trophic position, foraging guild, diet composition, and foraging strategy are major drivers of dietary exposure. These are neither static nor uniform across species or populations—reflecting different needs based on the individual and life stage (growth, breeding, and migration; Peakall & Burger, 2003). There is large variation in trophic status among individuals of a population and thus generalizations by foraging guild may be inaccurate. Previously, researchers assumed that killer whales (*Orcinus orca*) in the North Atlantic only fed on herring and thus occupied a midtrophic level. However, recent studies demonstrated that some individuals feed higher in the food web, including on seabirds and other marine mammals, leading to elevated exposure to bioaccumulative chemicals (Andvik et al., 2020; Jourdain et al., 2020; Remili et al., 2021).

Modern analytical approaches are now widely used in wildlife ecotoxicology studies and risk assessments to characterize diet and link it to contaminant exposure. For example, stable isotope analysis (SIA; e.g., $\delta^{13}C$, $\delta^{15}N$, $\delta^{34}S$, $\delta^{2}H$) is a powerful technique, and stable isotopes are routinely analyzed with tissue contaminant residues to link individual diet composition to contaminant sources. The use of SIA has identified exposure sources in food web biomagnification studies across a wide range of wildlife species in diverse habitats from Arctic seabirds (Renedo et al., 2020) to Canadian grizzly bears (Christensen et al., 2007) to urban raccoons (Gaines et al., 2002). Stable isotopes in tissues reflect diet during the period when the tissue is produced providing useful quantitative data on trophic level,

food-chain length, biomagnification potential, and major exposure pathways particularly for contaminants that readily bioaccumulate (Borgå et al., 2012; Jardine et al., 2006). Stable isotope analysis data can be incorporated into food web models as a powerful tool to estimate trophic linkages, daily ingested dose for birds, and other wildlife receptors. They can also account for unexpected exposure patterns resulting from indirect effects on species at the top (predators) or bottom of the food web (primary producers and primary consumers). Other complementary emerging techniques such as environmental DNA (eDNA; ter Schure et al., 2021) and quantitative fatty acid analysis (Remili et al., 2022) also show promise in understanding the frequency of specific items or lipid sources and their relative contribution to the diet (Ozaki et al., 2019).

Ecological traits: Migration and movement ecology

Many wildlife species undergo short- and long-distance migration or seasonal movement, most prominently between breeding and nonbreeding habitats, which complicates exposure assessments. Resident wildlife species are frequently selected in risk assessment as they are assumed to be a simplified worst-case scenario of local site-level exposure. However, migratory species may be differentially exposed to chemicals and experience high concentrations particularly for hyperphagic migrants when rapidly refueling at stopping points during migration (Bianchini & Morrissey, 2018; Colabuono et al., 2016) or on the breeding and nonbreeding grounds (Elliott et al., 2007; Lavoie et al., 2014; Pratte et al., 2020). For example, exposure during bird migration was implicated as the source of elevated contaminant levels in species breeding in the Arctic (Baert et al., 2013; Leat et al., 2013) and the Antarctic regions (Corsolini et al., 2011). Comparisons between migratory and nonmigratory species (Knutsen & Varian-Ramos, 2020; Roscales et al., 2019; Wild et al., 2022) or partial migrant populations (Morrissey et al., 2004) has further revealed distinct exposure profiles suggesting that migratory movements can predict exposure source and intensity.

Open-source data on migration routes and migration timing are now widely available for birds (e.g., eBird; https://ebird.org) that can inform exposure models. Moore et al. (2018) developed a comprehensive migration model that simulates exposure of Kirtland's warblers to chlorpyrifos and malathion during the 12- to 23-day migration between their breeding area in Michigan and Wisconsin and the Bahamas using over a century of observations of when, where, and for how long Kirtland's warblers forage in different habitats during their migration. The data revealed that most Kirtland's warblers are not exposed to chlorpyrifos or malathion during migration, primarily because of the infrequency of stopping over in treated orchards.

From traditional radio beeper tags to Motus nanotags, light level loggers, GPS, cellular, solar-powered satellite tags, and remote sensing radar data, researchers can now accurately track wildlife to gather detailed information on local movements and larger scale migrations (Katzner & Arlettaz, 2020; Kays et al., 2015). Tags have become smaller and lighter allowing for detailed information on the movement ecology of small animals that can provide more accurate estimates of habitat use, home-range size, contaminant sources, foraging range, migration timing, and connectivity between breeding and wintering areas with high levels of precision (Wilson et al., 2015). GPS sensors or accelerometry functions enable characterization of complex animal behaviors that can then be modeled as a function of energy expenditure or response to exposure or other disturbances (Elliott et al., 2007). Monitoring wildlife movements and spatial behavior using receiver "fence trapping" or telemetry can indicate when animals move in and out of a contaminated area and permit a more accurate area use factor adjustment to exposure estimates. Some recent studies of amphibians, mammals, and birds (Bro et al., 2015; Leeb et al., 2020; Lenhardt et al., 2015; Mayer et al., 2020) have successfully characterized habitat use and its variation between seasons, providing useful information on both individual and population-level exposure to pesticides across multiple seasons, and identify critical periods of vulnerability.

Life-history traits: Demography, longevity, life stage, and reproductive strategies

Windows of differential exposure can occur during key life stages—such as during incubation, fasting, migration, and hibernation when remobilization of chemicals stored in tissues to the bloodstream occurs (Bustnes et al., 2012; Christensen et al., 2007). For reproductive females, energetic and nutritional demands can result in a necessary shift in diet to produce eggs or young which can enhance female exposure to contaminants as revealed for mercury, PCBs, and organochlorines in populations of American and Eurasian dippers (Morrissey et al., 2010). Both age and longevity will affect exposure in periods of potentially elevated levels of contaminants (Mauritsson et al., 2022), with chronic exposure and bioaccumulation resulting in elevated levels with age. The alteration of body condition of wildlife caused by migration, breeding, or aging renders necessary consideration of dynamic lipid or protein use and metabolism associated with life stage when addressing exposure to circulating toxicants. Although there are demographic patterns that have been observed across many species, differences between sexes or life stages caused by depuration or foraging patterns may not always be predictable as demonstrated in a review of mercury body burden in birds (Robinson et al., 2012).

Several solutions exist to tackle the issue of differential exposure over time or during life stage or critical time windows of sensitivity. Surveying individuals over their life span or by cohort can be done using nonlethal sampling. Transsectional monitoring studies involving subsampling of several life stages within populations are relatively easy to perform (Scholz et al., 2022; Zemanova, 2020). Longitudinal time-trend studies can be achieved using tissues from growth layers, such as teeth of mammals (Dietz et al., 2021) or ear plugs for baleen whales (Trumble et al., 2013). Targeted sampling of tissues that have distinct turnover times can pinpoint timing and location-specific exposure. For

 DOI: 10.1002/ieam.4743

example, by knowing the molting and regrowth pattern of inert feathers or claws of birds, strategic sampling can be used to represent mercury or other metal exposures at a specific time in history, for example, after breeding or in the wintering area (Leat et al., 2013). The application of the DEBtox modeling approach holds promise to address the complexity of time-varying exposure caused by varying energetic demands (Jager et al., 2010, 2014). Currently, guidance by OECD and ISO includes this method (OECD, 2006) as a tool to address ecotoxicity data, but opportunities are available for broader application and model developments (see https://github.com/add-my-pet).

Morphometric and physiological traits: Body size, lipid content, and metabolic capacity

Several organismal traits affect exposure and bioaccumulation through differences in uptake, biotransformation, and elimination, for example, body size, lipid content, body temperature, and metabolism. For example, metabolism during fasting may result in lowering burdens of chemicals in organisms; however, this depends on the metabolic capacity of organisms and chemical properties (Polischuk et al., 2002). Allometric scaling based on body size is often used to predict food intake rates, metabolism, and elimination (Nagy, 2001), although this may be overly simplistic.

Recently, powerful new global databases have started to emerge that provide data on relevant organismal traits (Tobias et al., 2022). AVONET has individual bird measurements for bill, wing, and leg, and mass from 11 000 species compiled from 90 000 records. Such data provide much more detailed information on species trophic position, metabolic capacity, how they move, and how far they travel. Similarly, the new AnimalTraits database (https://animaltraits.org/) demonstrates that body mass is a strong predictor of metabolic rate and brain size based on records from almost 2000 species (Herberstein et al., 2022). Combinations of these morphological traits and inclusion of key species traits such as temperature, body mass, and lipid content can predict functional characteristics of species, such as their diet, food intake, metabolism, foraging behavior, and internal body burdens with much greater accuracy than body mass alone.

CROSS-CUTTING SOLUTIONS

Although solutions to specific challenges in wildlife exposure assessment have been described above, there are also cross-cutting solutions that can address multiple challenges. We highlight some promising integrative solutions below.

Spatially explicit modeling and explicit scenario-based simulations

We have already described above several readily available GIS tools and models that integrate contaminant and environmental variation using spatially explicit exposure assessment (Topping et al., 2020). Agent-based models are a powerful tool to simulate exposure and assess risk related to pesticides at the landscape level, with examples of use on various taxa such as birds (Johnson et al., 2007; Topping et al., 2020) and mammals (Dalkvist et al., 2013; Topping et al., 2016; Topping & Weyman, 2018). Spatially based models have the capability to not only aid in the assessment of exposure and risk but also help in designing sampling plans, evaluation of management alternatives, and scenario building through the simulation of landscape patterns and contamination maps (Fritsch et al., 2013; Topping et al., 2020). Figure 2 presents a comparison of two evaluation approaches—one a screening approach and the other an example of integrating contamination heterogeneity with habitat variation using the Breaking Ecotoxicological Restraints in Spatial Planning (BERISP) model (N. W. van den Brink et al., 2007). The screening approach uses generic food-chain models with a single diet item and area use factor of 1. BERISP modeling captures spatial variability (e.g., spatial foraging model, distribution of soil parameters that determine contaminant availability such as organic matter and pH), land use considering habitat-specific preferences for foraging and habitat-specific relative abundance, and availability of prey and functional responses (multiple prey functional response equation).

Biomonitoring and environmental monitoring

Biomonitoring and environmental monitoring range from surveys of environmental releases and site-level contamination to tissue biomonitoring and monitoring of behavior and population dynamics. In addition to characterizing real-world exposure and spatiotemporal patterns and dynamics, monitoring data are critical to validating modeling tools and identifying unexpected events (Gómez-Ramírez et al., 2014). Monitoring data are also used to investigate the effects of regulation and mitigation actions and are considered indispensable in postregistration procedures (Ankley et al., 2021; Vijver et al., 2017).

Long-term monitoring of contaminants in the environment or biota has been proven a valuable tool to track temporal and spatial trends in exposure that are crucial to evaluate the recovery or resilience of ecosystems (Eeva & Lehikoinen, 2000), changes in bioavailability (Ozaki et al., 2022), or the effectiveness of regulatory amendments (Bustnes et al., 2013). Large-scale monitoring has been applied successfully even at a global scale (N. W. van den Brink, Bervoets, et al., 2011) and in identifying threats to wildlife (Hallmann et al., 2014; Millot et al., 2017). Environmental specimen banks with standardized sampling and storage of tissue provide valuable repositories allowing for retrospective analysis of temporal trends of known and unknown chemicals. Other biological archives have included nanoparticles in growth layers of trees (Ballikaya et al., 2022) and mercury in marine mammal teeth (Dietz et al., 2021).

Careful consideration of the design and planning of sample collections regarding timing, season, and frequency of sampling can inform a spatially and temporally integrated assessment of exposure to single contaminants or mixtures (Espín et al., 2016; Scholz et al., 2022). For example, under the Arctic Monitoring and Assessment Programme (AMAP) for

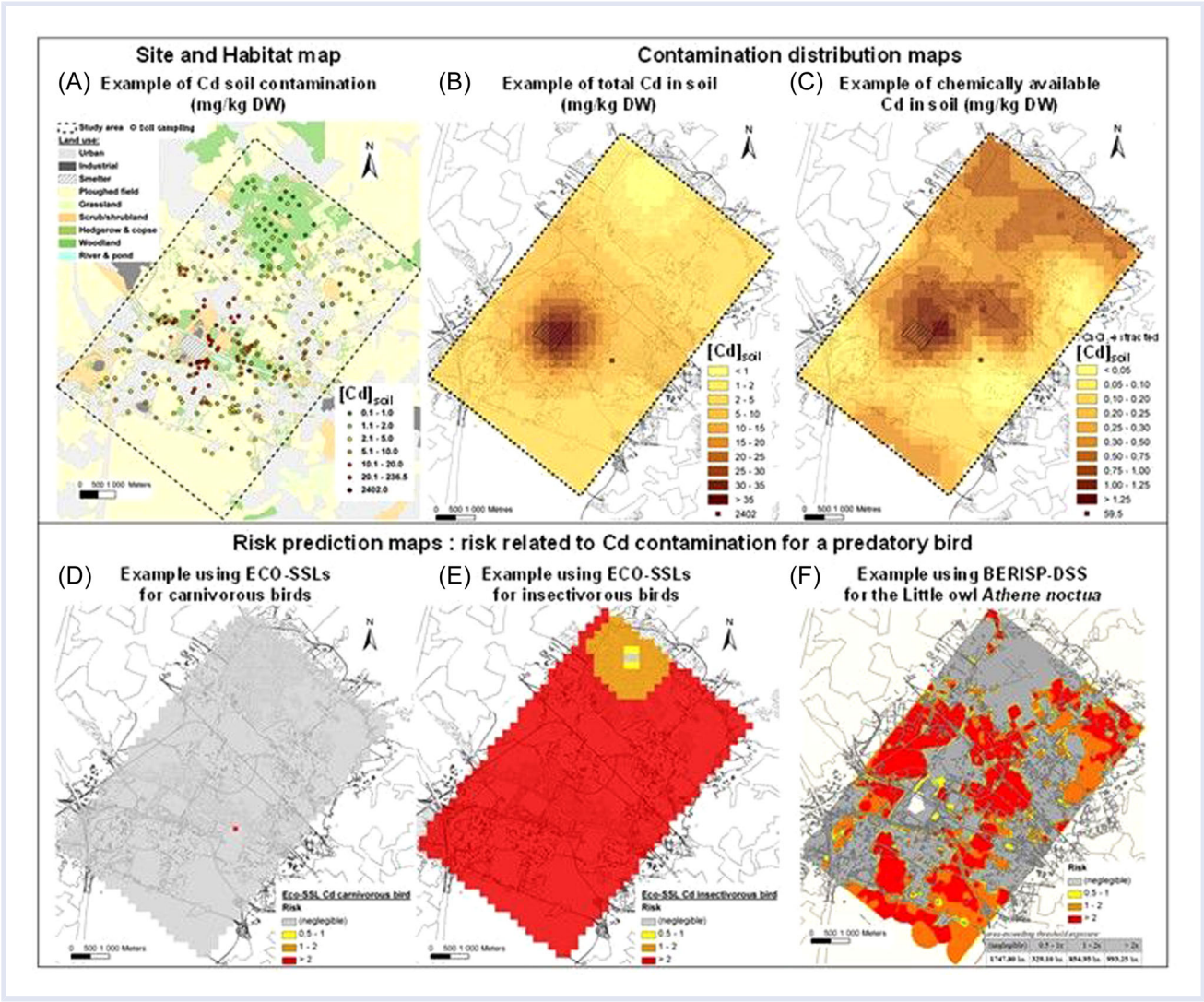

FIGURE 2 Maps of contaminant distributions, habitats, and risk in a smelter-affected area. The first map (A) shows the study area (9 × 6 km), soil sampling locations, and concentrations of cadmium (Cd). The contamination distribution maps were obtained by spatial interpolation statistics using kriging, with total Cd concentrations in soil on (B) and available Cd concentrations in soil assessed through chemical extraction ($CaCl_2$) on (C). The maps of risk related to Cd contamination for a predatory bird were estimated using Ecological Soil Screening Levels (ECO-SSL; USEPA, 2005) for carnivorous birds in (D) and for insectivorous birds in (E) or using the spatially explicit tool BERISP Decision Support System (BERISP-DSS; N. W. van den Brink et al., 2007) for the little owl *Athene noctua* in (F)

POPs and metals (see https://www.amap.no/), biomonitoring surveys have been conducted regularly to understand the importance of long-range transport for exposure in wildlife. The program has demonstrated that dozens of POPs are present in environmental matrices and biota, even far from their site of production, use, and emission. Legacy and current-use compounds as well as their metabolites are detectable in wildlife sentinels (Brodeur et al., 2022; Kuzukiran et al., 2021; Rial-Berriel et al., 2021).

Long-term and large-scale biomonitoring data hold tremendous value and are needed to detect changes in exposure conditions. Investments such as the Long-Term Ecological Research network (LTER Network) are an excellent example of this. Created by the National Science Foundation in 1980, the LTER aims to understand ecological processes at individual sites, coupled with integrative studies to reveal broader patterns that operate at a global scale. The LTER benefits from interdisciplinary and multidisciplinary research that "could help unravel the principles and processes of ecological science, which frequently involves long-lived species, legacy influences, and rare events." By providing reliable and accessible scientific information, scientists, risk assessors, resource managers, and policymakers can more readily detect environmental contamination and the effects on wildlife over longer timescales. Other similar initiatives are still emergent in ecotoxicological sciences, such as AMAP or surveillance schemes that monitor diseases and contaminants in vertebrate wildlife (e.g., WILDCOMS in the UK or the SAGIR network in France).

Optimization and improvement of experimental designs in applied research

By assessing TKs and TDs simultaneously during experiments, controlled designs allow making direct links

 DOI: 10.1002/ieam.4743

between external exposure, internal exposure, potential for bioaccumulation and biomagnification, and toxicological responses of organisms (Glinski et al., 2019; Peakall & Burger, 2003; Scholz et al., 2022). Moreover, the measurement of bioaccumulation during toxicological experiments would allow the establishment of critical body residues or toxicological reference values usable in the field for wildlife surveys. Tritrophic experimental designs in laboratory testing would allow assessing exposure, bioaccumulation, and transfer in food webs under more realistic contexts without involving the multiplication of several dedicated experiments. Running experiments with only one single batch of test animals to assess different endpoints on accumulation and toxicity is a way to use a reduced number of individuals promoting the 3R principles.

There is a need for more mixture and multimedia experiments in wildlife ecotoxicology (Glinski et al., 2019). Semifield experiments using enclosures have been used to quantify multimedia exposure under controlled but realistic conditions (Cusaac et al., 2015, 2017; Vyas et al., 2007). Use of complex effluents or contaminated soils in laboratory and field testing provides an opportunity to assess both bioavailability and uptake of weathered mixtures (Panico et al., 2022). Multimedia tests using tritrophic designs allow simultaneous assessment of direct alternative exposure routes via respiratory uptake, dermal contact, and dietary exposure (Z. Wang et al., 2021). Developments of tests conducted following the recommendation of good practices, as listed in ARRIVE guidelines, will ensure both quality and reproducibility of data collection and reporting as well as accessibility and usability (Ankley et al., 2021).

Use of available and open-source data

Large amounts of data are being incorporated in unified databases. For example, the European Food Safety Authority (EFSA) has sponsored open access ecological and residue databases (Lahr et al., 2018). The databases include data on diets and foraging behavior of approximately 150 bird and 70 mammal species and residues of approximately 190 pesticides and metabolites in Europe. A parallel database is available in the USA, the Wildlife Scenario Builder (USEPA, 2013), which contains data on life history (e.g., distribution, habitat, diet), physiology (e.g., body weight, intake requirements for air, water, and food/energy) for 49 North American species of wildlife. The application has been developed with the aim of "making wildlife exposure estimates more consistent, transparent and efficient." Similarly, in Canada, ecological risk assessment guidance has been released by the Federal Contaminated Sites Action Plan (FCSAP) to enhance the standardization of wildlife receptor characteristics with detailed information about life history and diet features for 27 common wildlife receptor species used in Canadian ERAs (https://www.canada.ca/en/environment-climate-change/services/federal-contaminated-sites/publications.html). Other promising initiatives involve the public release of open-source ecotoxicological databases such as the Ecotoxicology Database (ECOTOX Knowledgebase; USEPA, 2022).

Current open science policies are now routinely promoted by granting agencies, journals, universities, research institutions, and governments to increase data accessibility. Tools to harvest data on the internet have been diversified and improved in recent decades, with the development of existing and new platforms. These advances have removed the common barrier to risk assessors to search and access repositories containing vast scientific data and metadata.

Chemical activity and fugacity-based approaches to exposure and risk assessment

A common issue in exposure and effects risk assessment is that exposure and toxicity information is expressed in different quantities with different units. This means that, although there is often a considerable amount of information, only a small fraction of the available information is in the right form. Given the current trend toward in vitro toxicity testing and passive sampling of exposure media, the disconnect between the metrics used for exposure and toxicity characterization will likely further increase.

A practical solution includes the application of the fugacity or chemical activity approach (Gobas et al., 2018). First developed by Lewis (1901) and applied to environmental problems (Mackay, 2001; Mackay & Arnot, 2011; Mackay et al., 2011), the concept is to express exposure and toxicity measures in a common metric with a common unit, so that they can be compared (Gobas et al., 2018). For example, D5 risk assessment required expressing a wide range of observed concentrations and reported no-observed-effect-concentrations (NOECs) in various environmental media and wildlife species in their corresponding fugacities and chemical activities (Gobas et al., 2015). This resulted in probability distributions of the chemical activities, which corresponded to the concentrations of D5 in environmental media and NOECs for D5 in wildlife species. The extent of risk could be subsequently estimated by the overlap between the probability distributions for exposure and NOEC. A key finding was that chemical activities corresponding to the NOECs from toxicity tests were typically greater than 1, indicating that concentrations of the substance in toxicity test media (i.e., water, sediments, and soil) were above the solubilities, which cannot normally occur in the environment. Therefore, chemical activities of D5 in a range of wildlife species were orders of magnitude lower than the corresponding NOECs.

There are also several examples of the application of a chemical activity and fugacity-based analysis for determining whether chemical substances can biomagnify in food chains (Connolly & Pedersen, 1988; Fremlin et al., 2021; Kelly & Gobas, 2001; Mackintosh et al., 2004). A statistically positive relationship between the chemical activity or fugacity of the substance within organisms and their relative trophic positions indicates biomagnification occurs. Burkhard et al. (2012) confirmed the fugacity approach successfully predicted bioaccumulation or biodilution of 15 nonionic organic chemicals

using 2393 measured data points from 171 reports and is therefore useful for predicting bioaccumulation.

This thermodynamic-based fugacity relationship is preferred over an increase in the wet weight concentrations of the substance in organisms because organisms often differ in their biochemical composition (e.g., lipid content and body temperature) making it difficult to compare concentrations between organisms. Fremlin et al. (2021) found that TMFs in a terrestrial food web based on total lipid-normalized concentrations were lower than fugacity-based TMFs primarily because of differences in body temperature between endothermic and poikilothermic organisms in the food web. Although lipid-normalized concentrations are often used to overcome some of these challenges, both lipid content and temperature are better captured in the chemical activity or fugacity-based analysis approach.

Uncertainty estimation

Uncertainty analyses are infrequently conducted in regulatory wildlife exposure assessments despite the known uncertainty and the readily available quantitative methods. Deterministic estimates of exposure and risk require a comprehensive description of sources of uncertainty and, in higher tier assessments, quantifying the uncertainty to the extent possible. Presented with a risk quotient of 2.37, which clearly exceeds 1, a risk manager might make a different decision if the quotient was biased by numerous conservative assumptions requiring further data collection and analysis than if the quotient was estimated to be the 50th percentile of the risk quotient distribution that may be justification for implementing risk mitigation measures.

There are two fundamental types of uncertainty that should be communicated, epistemic and linguistic (Regan, Colyvan, et al., 2002; Regan, Hope, et al., 2002; Sahlin et al., 2021). Epistemic uncertainty is most widely understood and addresses variation from experimental or model simulation and includes measurement error, systemic error, natural variation, inherent stochasticity, model error, and subjective judgment. In contrast, linguistic uncertainty is less often explicitly described and evaluated in wildlife risk assessment but includes numeric vagueness, context dependence, and ambiguity (Regan, Colyvan, et al., 2002; Regan, Hope, et al., 2002).

Quantification of uncertainty can range from a simple cataloging of uncertainty sources in an exposure assessment to semiquantitative or fully quantitative methods. A properly conducted exposure and risk analysis results in both a quantitative and qualitative set of information from which the severity, validity, robustness, and usefulness of the exposure and risk estimates can be judged (National Research Council, 2009). There are many approaches to quantitative uncertainty analysis, and the choice of which method to use depends on a variety of factors including data availability, intended use, and preferences of the analyst, risk manager, and stakeholders. In data-rich situations, first-order Monte Carlo analysis is typically the method of choice (e.g., Luo et al., 2011; Moore et al., 2016; B. Wang et al., 2009). Where incertitude is prevalent because of limited data, second-order methods that separate variability and incertitude (e.g., second-order Monte Carlo analysis, probability bounds analysis) can be used to determine the potential influence that the incertitude may have on estimated risks (Ferson et al., 2004; Moore et al., 2010, 2016). Bayesian methods may be used for a wide variety of data-rich and data-poor situations. Such methods encompass a wide variety of uncertainty analysis techniques (Warren-Hicks & Hart, 2010). In recent years, Bayesian networks have been used in wildlife risk assessments, particularly those involving multiple stressors (Moe et al., 2021). One important advancement in addressing uncertainties in ecology and ecotoxicology in recent years has been multimodel inference and model averaging. The use of Akaike's Information Criterion allows one to compare and rank competing models to better estimate the true relationship between two or more variables without needing to nullify any single hypothesis (Burnham & Anderson, 2002).

To achieve the routine use of uncertainty analysis in wildlife risk assessment in the future, particularly in regulatory settings, the limitations of point estimates and a movement away from simple hazard quotients must be emphasized. This requires a shift in regulatory practices, training and professional development programs, and development of appropriate guidance for standardization of practice. Agencies need to develop decision criteria and specific guidelines to help risk managers and stakeholders know how to proceed given the outputs of an uncertainty analysis. With deterministic risk estimates, agencies are given clear decision criteria (e.g., no action when risk quotients are less than 1). Such decision criteria are also needed for probabilistic outputs for both the exposure and effects components to mainstream implementation of risk curves (Moore et al., 2014).

Reducing animal use

Many of the methods applied in wildlife risk assessment today rely on invasive or destructive methods on live animals. At the same time, animal use in research is becoming less and less accepted because of ethical considerations. Thus, various jurisdictions that mandate chemical safety assessments, such as the US Toxic Substance Control Act (with amendments) and the European Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) regulation, have encouraged the use of alternatives to animal experiments (Taylor, 2018).

The concept of New Approach Methodologies (NAMs) has emerged as a catch-all for any nonlive-animal-based approaches that can provide information in support of chemical hazard and risk assessment. Emerging NAMs include in silico, in chemico, and in vitro methods to fill existing information gaps (e.g., Arck, 2019). Several approaches falling into these categories have been outlined and recommended above, such as improved prediction and read-across tools, passive sampling, and other minimally invasive approaches, as well as in vitro biotransformation assays in combination with in silico extrapolation models. Recent attention to and improvements in analytical chemistry allow for exposure characterization

 DOI: 10.1002/ieam.4743

through non- (or less) invasive or nondestructive sampling through analysis of body fluids, fat biopsies, feces, and hair or feathers, and through the best use of toxicovigilance networks (Espín et al., 2016; Zemanova, 2020). Environmental passive sampling techniques have emerged and largely developed within the past decade, providing useful tools that are applicable to risk assessment based on contamination in air, soil, or water (Lévy et al., 2020; Li et al., 2019; Taylor et al., 2021). Coupled with multiresidue target and nontarget screenings of contaminants, integrated passive samplers represent an option to address multimedia and multicompound external exposures for wildlife, even without sampling any animals and can be more easily deployed and retrieved at sites of interest.

MATRIX EXPOSURE MODEL: FRAMEWORK FOR IMPROVING WILDLIFE EXPOSURE ASSESSMENT

To advance exposure assessment for wildlife, we recommend that risk assessors move away from reliance on screening-level assessments that are overly simplistic, conservatively biased, and lack ecological relevance and more transparently adopt a system that documents what factors were included at each stage. Key to understanding true exposure means inclusion of the many chemical, environmental, organismal, and ecological factors (Table 2). With the advent of new tools in recent decades such as those discussed in the preceding sections, many of the factors listed in Table 2 can be readily incorporated into screening exposure assessments for wildlife from the outset and iteratively populated throughout the risk assessment life cycle as data become available. In general, the more factors from each of the four categories from Table 2 that are included in a wildlife exposure assessment, the more realistic the resulting wildlife exposure assessments will be and the greater confidence in the conclusions. In some cases, it may not be necessary or relevant to incorporate all factors (e.g., bioaccumulation potential need not be considered for lipophobic chemicals that are rapidly metabolized), but the inclusion or exclusion and provision of a rationale can greatly increase transparency.

TABLE 2 A matrix checklist for improving wildlife exposure assessment

1. Chemical □ Sources (past, present, and future) □ Parent compounds □ Metabolites □ Mixtures □ Persistence □ Environmental partitioning and transport □ Dissipation and degradation pathways □ Bioaccumulation potential	2. Environmental □ Types of habitats □ Spatial extent of habitats □ Connectivity of habitats □ Temporal variation in chemical concentrations □ Spatial variation in chemical concentrations □ Environmental conditions □ Climate change □ Other stressors
4. Ecological □ Diet □ Foraging behavior and range □ Habitat and area use □ Prey availability □ Seasonal phenology □ Migration and movement □ Demography and reproductive strategy □ Trophic position □ Species interactions □ Environmental interactions	3. Organismal □ Exposure routes □ Uptake and bioavailability □ Biotransformation □ Internal distribution □ Whole body and tissue concentrations □ Elimination □ Internal interactions with other chemicals □ Life stage

Note: As wildlife exposure assessments proceed from screening level to more refined tiers, additional factors from each of the four categories of complexity (chemical, environmental, organismal, ecological) should be considered and described.

Application of the exposure assessment matrix: Three case studies

To illustrate how to use the matrix in Table 2, we present three diverse risk assessment case studies that have been comprehensively completed for wildlife involving a pesticide, PCB mixture, and a metal across varying scales of contamination from local (wetlands) to continental (migration range in the USA) to transboundary (Arctic). Each case study provides an example of how to apply the matrix approach and demonstrates the value of including and transparently communicating the multiple components of complexity and realism in an exposure assessment. Although these completed multiyear cases exhibit a high level of detail, the matrix approach can be adopted from the outset for even small and data-deficient exposure assessments to encourage, where possible, inclusion of factors in each of the four categories and provide greater visibility on the degree of confidence in the assessment's depth and weight of evidence when forming conclusions.

Case Study 1: Insecticides and Kirtland's warblers. The first case study involved an assessment of exposure of Kirtland's warbler (*Setophaga kirtlandii*) to the organophosphate insecticides chlorpyrifos and malathion. Until recently delisted because of recovery and development of a long-term management plan, the Kirtland's warbler was an endangered migratory species in the USA. Kirtland's warblers nest exclusively in young jack pine stands in the Upper Peninsula of Michigan and nearby Wisconsin, and winter in the Bahamas in similar habitats. The USEPA (2017a, 2017b) conducted probabilistic risk analyses for 13 listed bird species exposed to flowable chlorpyrifos and malathion, including the Kirtland's warbler. The USEPA analyses, however, did not incorporate chemical-specific monitoring data for these pesticides, species-specific foraging behavior, and proximity of warbler territories to pesticide use sites. The USEPA (2017a, 2017b) estimated exposure during the breeding season but not during migration. Therefore, Moore et al. (2018) developed probabilistic, species-specific exposure and risk models to assess risks of the organophosphates to Kirtland's warblers during

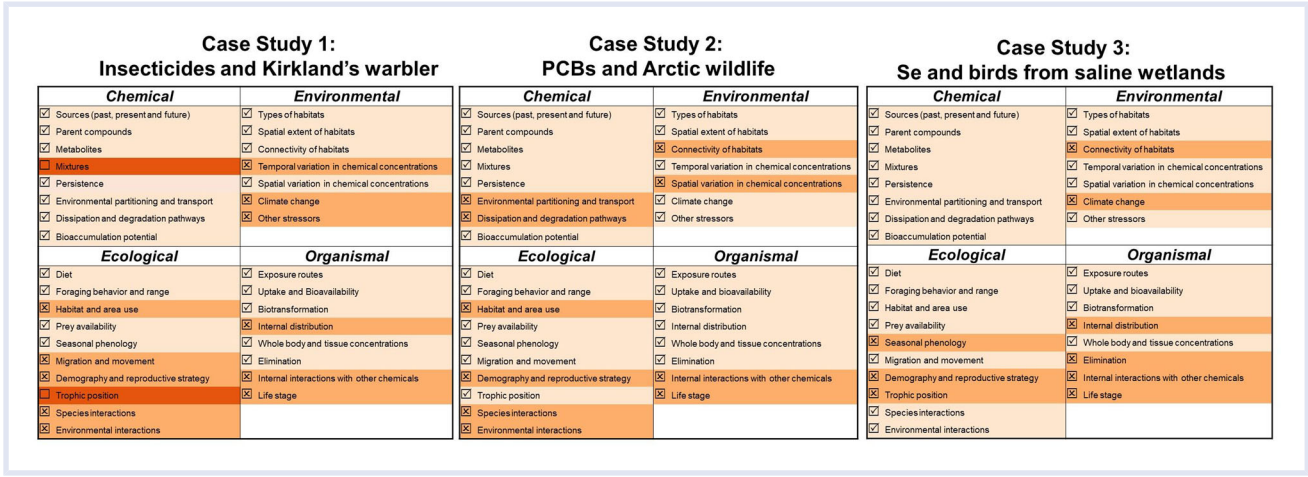

FIGURE 3 Three case studies illustrating application of the matrix approach to assessing and communicating exposure risk factors for different wildlife: (A) chlorpyrifos and malathion to the Kirtland's warbler (Moore et al., 2018), (B) PCBs in the Arctic glaucous gulls and polar bears (AMAP, 2009; Letcher et al., 2010), and (C) selenium in waterbird species nesting in Great Salt Lake wetlands (Parametrix, 2000). The matrix shows which exposure factors were included (light), partially included (orange), or missing (red) in the wildlife exposure assessment case

the full life cycle (breeding and migration). The breeding area model quantitatively incorporated species-specific foraging behavior, proximity of breeding territories to treated areas, and pesticide-specific data on prey concentrations. Similarly, the migration model took advantage of over a century of observations of when, where, and for how long Kirtland's warblers forage in different habitats during migration. The models found that chlorpyrifos and malathion pose negligible risk to Kirtland's warblers because of limited exposure. Figure 3A summarizes the exposure factors in the four assessment categories that were incorporated in the Kirtland's warbler assessment, either qualitatively or quantitatively, and those that were not. Although the Moore et al. (2018) assessment did not ultimately affect decision-making with regard to chlorpyrifos and malathion use in the species range, this was because the Kirtland's warbler was delisted before completion of the national endangered species assessments for these pesticides and not from an inherent flaw in design or implementation.

Case Study 2: PCBs in Arctic wildlife. In the second case study, a 2010 assessment investigated exposure of Arctic marine wildlife to PCBs. Although regulated for more than 40 years regionally and on the Stockholm Convention list since 2004, Arctic wildlife are still exposed to PCBs, predominantly through their diet because of their high K_{OW} and lipid solubility. Wildlife occupy high trophic levels and are at risk of accumulating high levels of recalcitrant lipid soluble PCBs. The risk assessment of Arctic wildlife is a moving target and has been through several phases, from the mere assessment of the presence of PCBs and comparison with wildlife threshold values for effects (AMAP, 1998, 2004), to more detailed studies of biomarker endpoints of exposure and effects correlating with tissue residue levels of PCBs (AMAP, 2009, 2018; Dietz et al., 2019; Letcher et al., 2010). These assessments reviewed ongoing Arctic monitoring campaigns across species, regions, habitats, and chemicals within the POPs and chemicals of emerging concern (AMAP, 2018).

The assessment concluded that the glaucous gull (*Larus hyperboreus*) and polar bear (*Ursus maritimus*) were at risk due to high accumulation of PCBs combined with rapid climate change effects, especially in the East Greenland and Svalbard region (Letcher et al., 2010). This is a region of elevated PCB levels in the wildlife populations that is also under the pressure of other stressors, such as climate change, increased human activity, shipping, and petroleum activity. The true effects of POPs such as PCBs in Arctic wildlife must be interpreted in the context of other stressors (both anthropogenic and natural, environmental, ecological, and physiological). Of the species at highest risk, little is known of the Svalbard glaucous gull population, but the local colonies at the islands Hopen and Bjørnøya have been declining since 1986 (www.npolar.no). The polar bear population on Svalbard has recovered since hunting was banned in 1973; however, the overall population development under the current challenges with pollution, climate change, and increased activity is not known. Figure 3B summarizes the factors that were addressed fully or partially that contributed to the Arctic wildlife POPs (PCB) exposure assessment.

Case Study 3: Selenium in waterbirds from the Great Salt Lake wetlands. Releases of metals from mining operations in the Great Salt Lake (GSL) Valley in Utah over the past 150 years have resulted in metal accumulation in a wetland complex along the south shore of the GSL. The GSL is a major flyway and stopover for millions of birds including waterfowl and especially shorebirds (American avocets, black-necked stilts, snowy plovers, grebes, etc.). The potential for metals to affect birds along the south shore of the GSL was investigated as part of a remedial investigation and feasibility study for the Kennecott Mining Corporation. A preliminary investigation was performed across the entire mining area and the results identified arsenic, lead, zinc, and

 DOI: 10.1002/ieam.4743

especially selenium (Se) as a key focus for further study in the wetlands. Interactions with stakeholders identified charismatic shorebirds as the receptor of interest for additional assessment.

The detailed assessment focused on monitoring of water, macroinvertebrates, and bird eggs for selenium, and less for other metals (Parametrix, 2000). For birds, fish, and amphibians, the target receptor is the avian embryo as selenium is incorporated in amino acids with sulfur (e.g., selenomethionine, selenocysteine) within eggs. Surveys of macroinvertebrates (bird diet) and bird populations were conducted, and selenium concentrations were measured. A diet-to-bird-egg trophic transfer model built from the regional study data was applied to these site-specific macroinvertebrate Se concentrations to predict spatially variable egg Se concentrations at the site. Probability distribution functions for shorebird exposures were then derived based on nest location data and limited site-specific egg Se data to calibrate the predicted distribution of egg Se concentrations. Concentration–response relationships for both embryo teratogenesis and cumulative mortality (i.e., egg fertilization through posthatch) were developed and integrated with the spatially explicit exposure estimates to provide population risk estimates. Se-induced teratogenic risks to stilt embryos ranged from approximately 3% to 11% depending on the concentration–response relationship used and was 0.3% for avocet embryos. In addition, the assessment concluded that 13% and 3% of stilt and avocet eggs, respectively, would either fail to hatch or result in hatchling mortality in an area of 1100 acres where maximum exposure occurred. Figure 3C summarizes the factors used in the exposure assessment that contributed to the decision to require remediation.

CONCLUSIONS AND RECOMMENDATIONS

There is a long-standing disconnect between the disciplines of ecological risk assessment and wildlife ecotoxicology that has severely hindered progress in the field and led to oversimplification of exposure assessments for wildlife. This paradox of simplification, despite known chemical, environmental, organismal, and ecological complexity, has led to a common criticism of over- or underestimating wildlife risk. Greater standardization of exposure assessment methods and integration of the best available science and approaches described above can address this complexity more accurately and capture variability and realism associated with wildlife exposure—the goal for wildlife conservation and environmental protection. Although this article cannot fully review the ever-growing literature on wildlife exposure for various taxa and contaminants, we identified the major challenges in wildlife exposure assessment and provided available solutions to improve, rather than overhaul, wildlife risk assessments, which are largely under restrictive jurisdictional control. By introducing a new framework using the exposure assessment matrix, our aim is to encourage risk assessors to consider four discrete elements of complexity—the chemical, environmental, organismal, and ecological realities—and more explicitly, incorporate and communicate these in wildlife exposure assessments.

There are four general recommendations that our team believes need to be prioritized to further modernize and transform the field.

1. *Improve data acquisition, accessibility, and collaboration among scientists and risk assessors*. Scientists working with wildlife and environmental contaminants of concern need to make their field-collected data more accessible to risk assessors through open-source data repositories and public databases, particularly raw contaminant field data and trait data that capture region- and species-specific variation in individual morphological traits, diets, foraging patterns, body masses, population demographics, and movement patterns. There must also be greater consideration and cross-institutional collaboration to flag both the common and specific data gaps in exposure assessments (e.g., improve and validate food intake rates across species using equation-based allometric scaling).
2. *Move from a tier-based to standardized scenario-based assessment framework*. Given the challenges of capturing all possible real-world variation in exposure and the well-identified problems of reliance on conservative screening-level assessments, the tier-based system has proven limited. An upfront system that better characterizes a standardized set of commonly accepted real-world scenarios may offer a better balance between realism and practicality. The screening-level WERA is, by design, built as a nonstandardized conservative worst-case scenario. We propose to move toward establishing a series of increasingly ecologically relevant scenarios that include the four matrix categories of complexity—chemical, environmental, organismal, and ecological. Through development and adoption of standard exposure assessment scenarios, risk assessors can parameterize and characterize a set of real-word exposures based on standardized receptor species at key life stages, habitats, and environmental conditions. Using such an approach, wildlife exposure and risk could be identified earlier, and each scenario could be further used to both identify what information is missing and provide clear lines of evidence of mitigation and research needs along the way. The benefit of such a design also lies in the possibility to implement more consistent, reliable, transparent, and less resource-demanding risk communication to stakeholders.
3. *Quantify variation, provide transparency in assumptions, and communicate the uncertainty*. Throughout this review, we have identified that many exposure estimates are inappropriately communicated as absolute, fixed, and certain. Equally, there is inconsistency in the treatment of identified risk based on overly conservative worst-case scenarios. We recommend inclusion of details about how specific exposure parameters affect the risk

outcomes by explicitly measuring and disclosing uncertainty estimates (both epistemic and linguistic). This will demonstrate the effect of assumptions on the overall exposure estimates more transparently. It also opens the door to embracing conditional probability statistics (e.g., Bayesian approaches) that better reveal the confidence and likelihood of calculated exposure estimates.

4. *Track postregulatory signals for unexpected exposure events and population trends*. After screening-level or higher tier assessments, there is still a need to monitor environmental conditions and wildlife populations for temporal and spatial trends that may signal that contaminant exposure duration, magnitude, and/or sources were missed. An established process for postregulatory surveys and biomonitoring programs may aid in determining the effectiveness and accuracy of the overall risk assessment, while also informing management practices and mitigation strategies to conserve wildlife. This will promote an adaptive learning loop to improve future exposure assessments and species conservation.

ACKNOWLEDGMENT

The authors acknowledge the discussions, ideas, and contributions of members of the SETAC Wildlife Toxicology Interest Group Wildlife Risk Assessment Steering Committee including Mark Johnson, John Elliott, Beth Power, and Barnett Rattner as well as former Exposure working group members Christine Custer and Ken Drouillard and two anonymous reviewers who provided constructive comments on the manuscript drafts. Funding for the workshop was provided by United States Geological Survey, Teck Resources Ltd, and SETAC.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTION

Christy Morrissey: Conceptualization; investigation; project administration; supervision; visualization; writing—original draft preparation; writing—review and editing. **Clémentine Fritsch**: Conceptualization; investigation; project administration; supervision; writing—original draft preparation; writing—review and editing. **Katharine Fremlin**: Project administration; data curation; visualization; writing—original draft preparation; writing—review and editing. **William Adams**: Investigation; writing—original draft preparation. **Katrine Borgå**: Conceptualization; investigation; writing—original draft preparation; writing—review and editing. **Markus Brinkmann**: Conceptualization; investigation; writing—original draft preparation; writing—review and editing. **Igor Eulaers**: Conceptualization; investigation; writing—original draft preparation. **Frank Gobas**: Conceptualization; investigation; writing—original draft preparation. **Dwayne R. J. Moore**: Conceptualization; investigation; writing—original draft preparation; writing—review and editing. **Nico van den Brink**: Conceptualization; investigation; writing—original draft preparation. **Ted Wickwire**: Conceptualization; investigation; visualization; writing—original draft preparation; writing—review and editing.

DISCLAIMER

The peer review for this article was managed by the Editorial Board without the involvement of Dwayne R. J. Moore.

DATA AVAILABILITY STATEMENT

This review article contains no new data.

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