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Are urban areas hotspots for pollution from pet parasiticides?

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Headlines

- Substances that are banned for routine agricultural purposes are still being sold and used for other purposes, including parasiticide treatments for pets in the UK.
- These chemicals can enter the natural environment and their active ingredients are toxic to many freshwater species, even at environmental concentrations as low as 0.013 micrograms per litre for the exemplar chemical in this piece, imidacloprid.
- Currently, existing legislation only requires a very limited environmental risk assessment for pet parasiticide products before they are authorised for domestic use.
- Recent technological improvements allow us to detect parasiticides in the environment, though formal monitoring for many of these chemicals remains inconsistent in the UK.
- The active ingredients in parasiticides are frequently detected at concerningly high concentrations in UK waterways, predominantly in urban areas (e.g., imidacloprid detected above 1 microgram per litre). These concentrations have been shown to negatively affect aquatic life in controlled laboratory trials and field studies.
- Exposure to parasiticides may affect vulnerable (i.e., sensitive) species within our rivers, lakes, and ponds – potentially disrupting communities and ecosystem processes. The full extent of the environmental impacts on aquatic ecosystems is yet to be quantified.
- Increased monitoring, stewardship, and regulation of veterinary parasiticides is needed to minimise potential pollution impacts on freshwater ecosystems.

Contents

Introduction: The trajectory of pesticides in the UK 2
Pet parasiticides: A rising threat? 3
Potential routes into the environment for active ingredients ... 5
Evidence of parasiticide pollution in UK waterways 6
The ecological impacts of parasiticides: From individuals to ecosystems............................... 8
Implications for UK policy and regulation 9
Conclusions................................. 11
References 11
About the authors 15
Acknowledgements...................... 16

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Glossary

- **Active ingredient:** a component of a pharmaceutical drug or pesticide that produces a chemical or biological effect.
- **Biomagnification:** the process by which a chemical compound increases in concentration in the tissues of organisms at successively higher levels of a food chain.
- **DDT:** Dichlorodiphenyltrichloroethane (DDT) is a banned insecticide that was used extensively around the world between the 1940s and 1970s, with disastrous consequences for wildlife.
- **Ecosystem services:** benefits people obtain from ecosystems (e.g., clean water, leisure opportunity).
- **Food web:** a representation of feeding interactions among organisms, typically composed of multiple food chains.
- **Leaching:** the downward movement of contaminants (such as water-soluble pesticides), carried by water through permeable soils into groundwater.
- **Levels of biological organisation:** the hierarchical classification of living things arranged from the simplest to the most complex (i.e., genes to ecosystems).
- **Limits of detection (LOD) and quantification (LOQ):** the lowest concentration at which a chemical's presence can be detected (LOD) and the lowest value where the concentration of a chemical can be given with assurance (LOQ).
- **Metabolites:** products of chemical breakdown, degradation, or transformation by biologically induced processes.
- **Neonicotinoids:** a class of insecticides that work by affecting the nervous system of insects. These pesticides are widely used in agriculture, but they have also been used as pet parasiticides to control fleas, ticks, and other pests.
- **Non-target species/system:** a species (or system) that is not intentionally targeted for control by a pesticide or herbicide, but which may suffer damage because of exposure to it. For instance, insecticides designed to kill crop pests can also kill freshwater invertebrates.
- **One Health:** a collaborative approach that recognises the interconnection between the health of animals, humans, and the environment, and acknowledges that issues affecting one sector can have consequences in the other sectors.
- **Parasite:** an organism that lives on or in a host animal or plant and is metabolically dependent on its host. Parasites can cause disease directly and/or carry the causative agents of other diseases.
- **Parasiticide:** a type of pesticide that is used to kill parasites such as fleas, ticks, and helminth worms (e.g., tapeworm, roundworm, hookworm). In many cases, a given chemical may also be used as an agricultural pesticide – this definition is defined by its use.
- **Pesticide:** a substance used to kill or control pests that are considered harmful to crops, animals, or humans. Examples of pesticides include parasiticides, insecticides, herbicides, fungicides, and rodenticides.
- **Prophylactic use:** a situation where a medication or a treatment is used to guard against the development of a disease by acting ahead of time. For example, treating healthy animals to prevent the establishment of parasites.
- **Stressor:** a change in environmental conditions that negatively affects the health and/or functioning of an organism, population, or ecosystem.
- **Wastewater:** water generated from ground, surface, or municipal supply sources and after use for domestic, industrial, agricultural and commercial purposes, and public services.

Introduction: The trajectory of pesticides in the UK

Chemicals are used to control pest species in a wide variety of agricultural and domestic settings, with global pesticide use almost doubling between 1990 and 2018[1]. Over time, regulations and bans in the European Union (inherited by the UK, post-Brexit) have made it harder to manufacture and use chemicals that are unsafe or environmentally unfriendly[2,3].

Even so, the widespread and continued use of pesticides in their various forms has come at an environmental cost, as many have become common pollutants[4,5], with negative impacts on water quality[6], biodiversity[7], and human health[8].

The harmful environmental effects of pesticides first came to the general public's attention in the 1960s with the publication of Rachel Carson's 'Silent Spring'. At the time, dichlorodiphenyltrichloroethane (commonly known as "DDT") was used worldwide with little regard or understanding of the consequences. Pioneering research demonstrated that organochlorine insecticides like DDT and its transformation products were responsible for a range of impacts on species and ecosystems, reflecting their persistence and ability to "biomagnify" (see Glossary) up the food web[9,10].

Many decades later, an estimated 2.7 million tonnes of pesticides are released into the environment each year, globally[11]. Though they are often less persistent, the new generation of pesticides are thousands of times more toxic than those used in the 60s[12]. As such, pesticides can still have significant effects on vulnerable non-target species and ecosystems.

Pesticides are designed to be toxic, and often target a specific critical biochemical process. As these targeted pathways may be shared among species, serious impacts on non-target species can occur[13]. A variety of regulatory mechanisms can be used to control chemical use, from outright bans to voluntary moratoria and restricted usage. Regulations that target a chemical's primary use can leave loopholes through which it can be sold for other uses. For example, one common pesticide sold in the UK is imidacloprid[14], a neonicotinoid originally used on crops as an alternative to other overused or banned pesticides (e.g., organophosphates and DDT). Eventually, concern about the potential impacts of neonicotinoid exposure on insects, especially bees[13], led the European Commission to restrict their use. Initially, a moratorium was imposed preventing use on flowering crops in 2013[15], followed by an outright ban for all outdoor use in EU member states in 2018[16]. This was not a *complete* ban, however, and other commercial products containing imidacloprid and other neonicotinoids are still being sold in the UK today. The largest remaining source of imidacloprid appears to be veterinary parasiticides, a group of pesticide products used predominantly to control ticks and fleas on cats and dogs[17], with 138 imidacloprid-containing products currently authorised in the UK[18]. For the purposes of this briefing paper, we will refer to imidacloprid and parasiticide products as pesticides (see Glossary). Despite often using the same active ingredient, veterinary medicines and agricultural pesticides are authorised by different regulatory bodies; this can cause inconsistencies in management and barriers to the implementation of further regulation of potentially harmful chemicals, such as imidacloprid. At present, there is minimal environmental risk assessment of parasiticide products used on domestic cats and dogs, due to the assumption that these products are applied in relatively low doses to a small population of animals, 'limiting' any environmental impacts[19]. However, when taken in aggregate the total volume of these chemicals represents a potential major route of exposure in both the environment and to humans, given the estimated 25 million cats and dogs in the UK[20], many of which are treated with parasiticides multiple times through the year[21]. Unfortunately, there are still gaps in our understanding of how veterinary parasiticides such as imidacloprid might affect the UK's freshwater ecosystems, and how they might interact with other pollutants and environmental stressors such as climatic warming[22]. In this policy briefing, we review the current knowledge on the possible routes of veterinary parasiticides to the environment, describe where these chemicals are being detected geographically, and draw from the literature to suggest what the potential impacts might be for non-target species and ecosystems. Finally, in the context of the emerging 'One Health' paradigm (see Glossary), we make suggestions as to how research, policy and management might align more effectively to balance the needs of domestic pets, people, and the environment.

Pet parasiticides: A rising threat?

Over the last 30 years, parasiticides have become increasingly effective due to the development of active ingredients with greater toxicity to target species[17] and persistent action that can last from weeks to months[21,23]. This has the potential to benefit pets by reducing the harm caused by parasite infestations, as well as reducing human health risks by lowering the transmission of parasites and associated diseases from animals to humans. That said, any reduction of disease burden by regular prophylactic parasiticide use is yet to be quantified because we lack the requisite large-scale incidence data for pet-associated zoonotic diseases. In the UK, some pet parasiticides require a veterinary prescription, whereas others are available to purchase over the counter or from online retailers. Treatments come in a range of different forms, including 'spot-on' solutions, infused collars, and tablets (Fig. 1). These products contain a range of active ingredients, with properties that help facilitate their use, including lower toxicity for vertebrates (e.g., veterinary practitioners, owners, and treated animals) and high solubility in water, which allows the chemical to be applied to the pet's body easily[24].

Although a host of substances are used for this purpose, one of the most popular active ingredients in parasiticides is imidacloprid[25], which is also one of the most toxic chemicals regularly detected in UK waters[26]. This chemical is currently one of the best resolved in terms of toxicity and monitoring data available, so in this paper we use it as an exemplar and major focus; but it is important to note that this is not the only active ingredient contributing to the issue of parasiticide pollution[17,27]. Even though it is often found in relatively small amounts in the environment, imidacloprid is so potent that even low concentrations can harm aquatic life[28]. In theory, one monthly flea treatment for a large dog contains enough pesticide to kill 25 million bees, if applied directly[29]. In the wild, the levels of exposure will be far lower, as dilution effects will result in lower environmental concentrations; but how these pathways operate and the potential impacts they may have remain to be fully quantified in natural systems. By weight, imidacloprid is one of the best-selling veterinary parasiticides in the UK[14]. Immediately before the ban on crop use, a combined total of over 4000 kg was used for agriculture and sold for veterinary use in a single year in the UK. After the chemical was fully banned for all outdoor use in 2018 this dropped markedly, but over 2500 kg was still being sold in the following year, all of which was destined for the domestic pet market as a parasiticide[30] (Fig. 2).

This represents a vast number of non-agricultural doses in circulation, given the estimated 25 million cats and dogs across the UK[20]. Altogether, it is unsurprising that concerns have been raised regarding parasiticides as a potential source of seemingly 'hidden' water pollution in the UK[14,17,27,29].

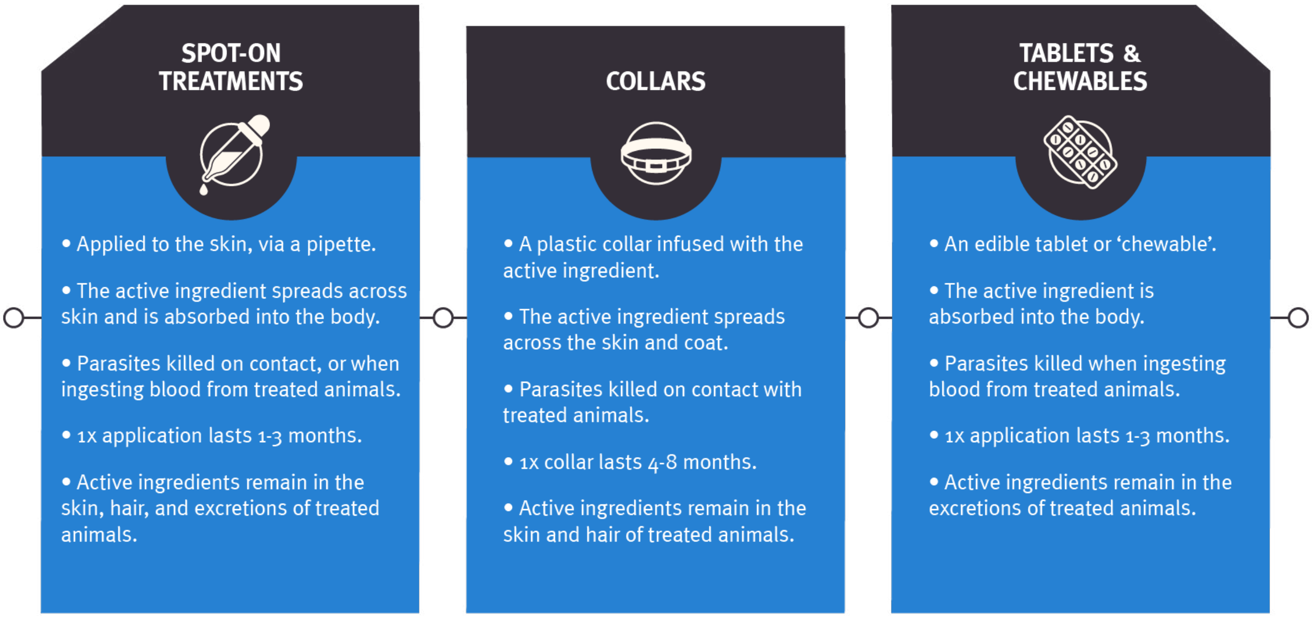

Figure 1: Three of the most common types of application for veterinary parasiticides used on pets (i.e., cats and dogs).

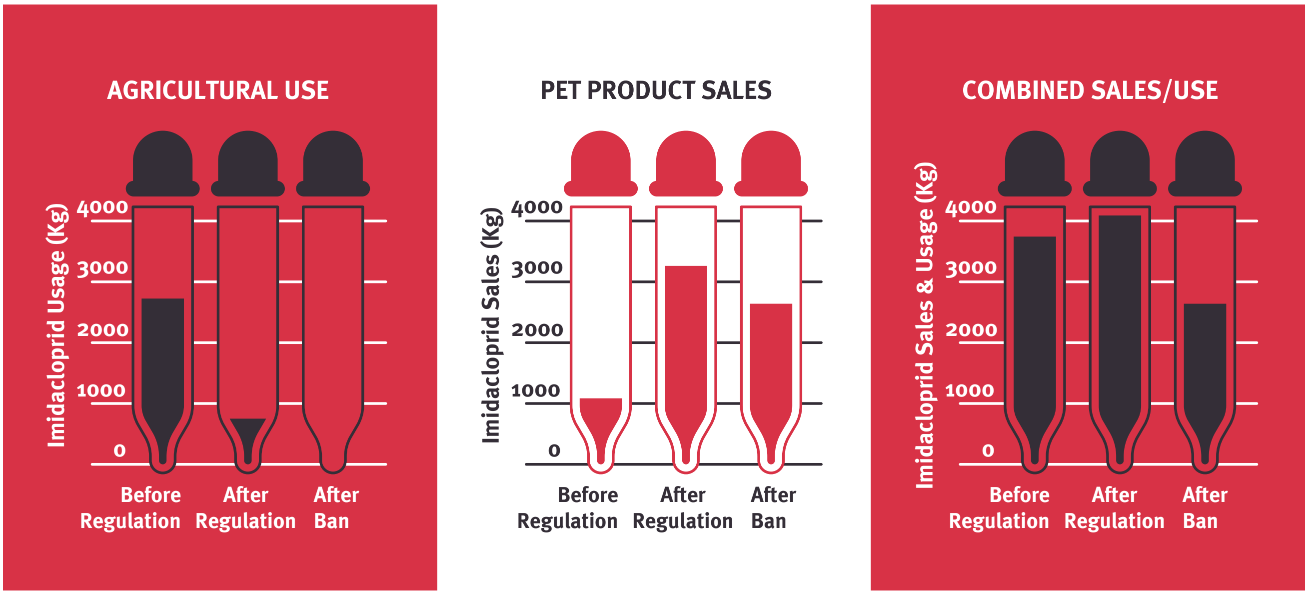

Figure 2: Patterns of the sales and usage of imidacloprid for agricultural and domestic pet parasiticide products in the UK. Imidacloprid was implicated in the global decline of bees and other terrestrial pollinators, and use was severely restricted in the EU in 2013[15], followed by a total ban on outdoor use in 2018[16]. Here we show the usage and sales of imidacloprid before (2009) and after the initial regulations (2014), as well as after the ban (2019). Agricultural use data were obtained from the Food and Environment Research Agency (FERA)[30]. Pet parasiticide sales data were obtained from the Veterinary Medicines Directorate (VMD) under the Freedom of Information Act.

The general restrictions on neonicotinoids in agriculture have been at least partially compensated for by increased use in other sectors in recent years, with an apparent shift from rural to more urban usage. For instance, while the agricultural use of imidacloprid disappeared across the 10 years from pre-regulations to post-ban, its sales as a veterinary parasiticide rose by 152% (Fig. 2). Increases in pet ownership have been well reported in recent years[31], with the number of cats and dogs in the UK estimated to have risen by over 35% in the last 5 years (2018-2022)[20], but we have also seen a change in the individual rate of treatment for ectoparasites such as fleas and ticks, with many cats and dogs now being routinely treated multiple times per year[17,32,33]. Not only are there now many more pets in the UK, but their dosing is more frequent.

To date, pet parasiticide usage has focused primarily on the consideration of animal and human health benefits, with seemingly little consideration of the possible risks – potentially resulting in their overuse. Many veterinary practices promote discounted health plans for cats and dogs which include year-round prophylactic parasiticide coverage, and sales of parasiticides represent a significant revenue stream for many veterinary clinics. This has led to widespread, continuous parasiticide use for much of the UK's pet population, even in circumstances where the benefit of prophylactic treatment to the animal and its owners might be minimal. Various factors are known to influence the risk of an animal becoming exposed to parasites (e.g., seasonality, lifestyle, and geography), so there might be little need for such preventative treatment if the real level of risk for a given pet is low[21]. If there were no risks associated with parasiticide use, the current level of use would not be a problem, but there are many to consider and a comprehensive evidence-based evaluation is still lacking[14]. Ideally, we should be able to weigh the animal welfare (and human health) benefits against potential environmental harm to gauge the optimum usage of parasiticides more objectively, based on sound and transparent science so that the actors involved can make better-informed decisions. Indeed, a host of veterinary bodies, including the British Veterinary Association (BVA), the British Small Animal Veterinary Association (BSAVA), and the British Veterinary Zoological Society (BVZS) have recognised this recently in joint policy statements[21].

Potential routes into the environment for active ingredients

Current national monitoring and focused studies to measure pesticide active ingredients in water have repeatedly noted the continued presence of insecticides, such as imidacloprid, ipronil, and others, despite severe restrictions on authorised outdoor use[17,26,34,35]. Veterinary parasiticides have been suggested as a potential primary source of these chemicals in the UK's waterways and there are several possible pathways through which their active ingredients may enter the environment (Fig. 3). One prominent route is believed to be through wastewater from people's homes, moving through treatment plants, combined sewer overflows or septic tanks into local rivers[14,36]. Currently, many of the UK's wastewater treatment plants fail to remove pesticides from water effectively because conventional treatment methods are not designed to remove some of the more persistent pesticides. However, investment in advanced tertiary treatments and infrastructure improvements to reduce overflows will improve wastewater treatment plants' ability to remove pesticides from water[37,38]. Exactly how parasiticides enter the wastewater system in the first place is not yet fully understood. It may be direct (e.g., owners washing their dogs after a walk) and/or indirect (e.g., flushing animal waste down the lavatory; handwashing after an application). Spot-on treatments are considered to be a likely source of parasiticide pollution[14], given that the active ingredient spreads externally across the treated animal and, once absorbed, is retained by the animal's body and released gradually via the hair follicles[39–42]. This means that the active ingredients in these products have the potential to disperse and accumulate in a treated animal's local environment via pet hair, shedding skin, and direct transfer after the initial application[40,43].

We now know that parasiticides are transferred from pets to the environment via several of these routes. In an experiment conducted at Wageningen University in the Netherlands[27], parasiticide active ingredients such as imidacloprid were detected in the hair shed from both treated and untreated animals – suggesting that contamination from secondary transfer is also common. The active ingredients were also detected in the urine of all tested animals, as well as in the water that the treated animals had bathed or swam in. 'Run-off' from treated pets in rainstorms or from wild swimming, as well as the gradual shedding of hair, are contamination routes into the natural environment that have the capacity to bypass wastewater treatments[17,46]. Surface runoff containing contaminated dust can flow into the sewage systems or directly into local water bodies. There is further evidence that parasiticides are shed gradually from pets, as significantly higher quantities of active ingredients have been found in the dust of households with treated animals[47]. Bathing treated pets has been suggested as a common pathway for active ingredients to enter wastewater[41], though the washing of pets' bedding could also be a contributing source.

In the UK, no agricultural use of imidacloprid has been recorded since 2016[30], and although we have focused on concerns about pet parasiticides here, there are other potential sources of contamination to consider and/or to rule out if appropriate. For instance, one potential non-veterinary pathway into the environment for imidacloprid is from plants grown in greenhouses. This was highlighted in 2017 when residues were found in 38% of potted plants sold in UK garden centres[48], but since then further regulations have been imposed and the only legal horticultural use is on plants that remain in greenhouses for their entire life cycle. Currently, there are no products approved for this use in the UK[45], this route is only recognised as a *potential* pathway and there is no hard evidence that it is in operation. Other possible sources of imidacloprid contamination include domestic pest control agents for ants, cockroaches, and flies, but the volumes are far lower, as well as being more geographically inconsistent and seasonal than the usage for domestic pet treatments.

Further research is required to characterise these potential sources, sinks, and pathways to enable effective mitigation in the future.

Evidence of parasiticide pollution in UK waterways

In recent years, there have been substantial improvements in the technology available for monitoring chemicals in the environment, meaning the detection of harmful chemicals such as pesticides has become increasingly common[4,26]. Even so, only a fraction of the UK's waters are routinely tested for these chemicals; and in many cases, only a small subset of potential pesticides are quantified, so much of this sampling is still relatively ad hoc and often done by non-regulatory bodies. An Environment Agency (EA) monitoring of 20 English rivers, sampled from 2016 to 2018, found that imidacloprid was present in two-thirds of samples, with seven of the sites exceeding chronic toxicity levels (35 ng/l)[17]. Another chemical regularly used in parasiticides – fipronil – which is even more toxic than imidacloprid per unit of concentration was detected in 98.6% of the samples examined. This pattern of detection is not confined to the UK, however: for instance, imidacloprid and fipronil were both found at all eight wastewater treatment plants sampled in San Francisco, USA[49]. This study suggested that the low level of daily variability in the amount of each chemical detected, indicated that many very small contributions of the chemical accounted for the contamination, rather than large individual pollution spills.

The Environment Agency monitoring datasets in the UK[35] currently represent some of the best-resolved sources available, and show clear evidence of imidacloprid in many urban areas where agricultural sources are extremely unlikely, though it is also found in rural systems where it has been investigated intensively, such as test catchments (Fig. 4). The EA monitoring data also shows that when detected, imidacloprid is at concentrations where risks to freshwater species are expected (i.e., moderate to high risk) in 52% of cases (Fig. 4). This may be a conservative estimate, as it does not consider risks from transformation products. If veterinary parasiticides are indeed the primary source of imidacloprid then we would expect to see an increasing divergence between rural and urban concentrations after the ban on outdoor use, with imidacloprid now most likely to be found in higher concentrations where most pets and people are living. Further analysis is required to test this hypothesis.

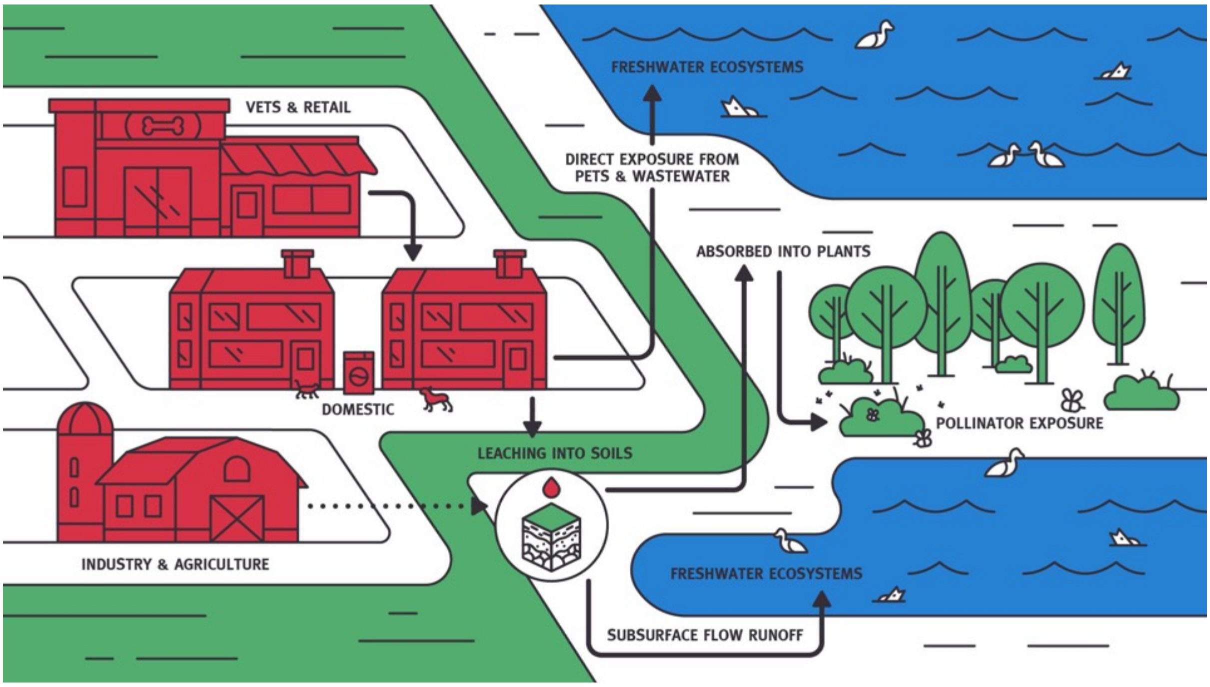

Figure 3: Possible pathways into the environment for the active ingredients used in pet parasiticides, such as imidacloprid. Veterinary parasiticides are implicated as a major source of imidacloprid waterway pollution[14,17,27,29], however, other potential sources exist, including ant and cockroach baits[17], and plant protection products used in greenhouses[44] (although no plant protection products containing imidacloprid are currently licensed for use in the UK[45]).

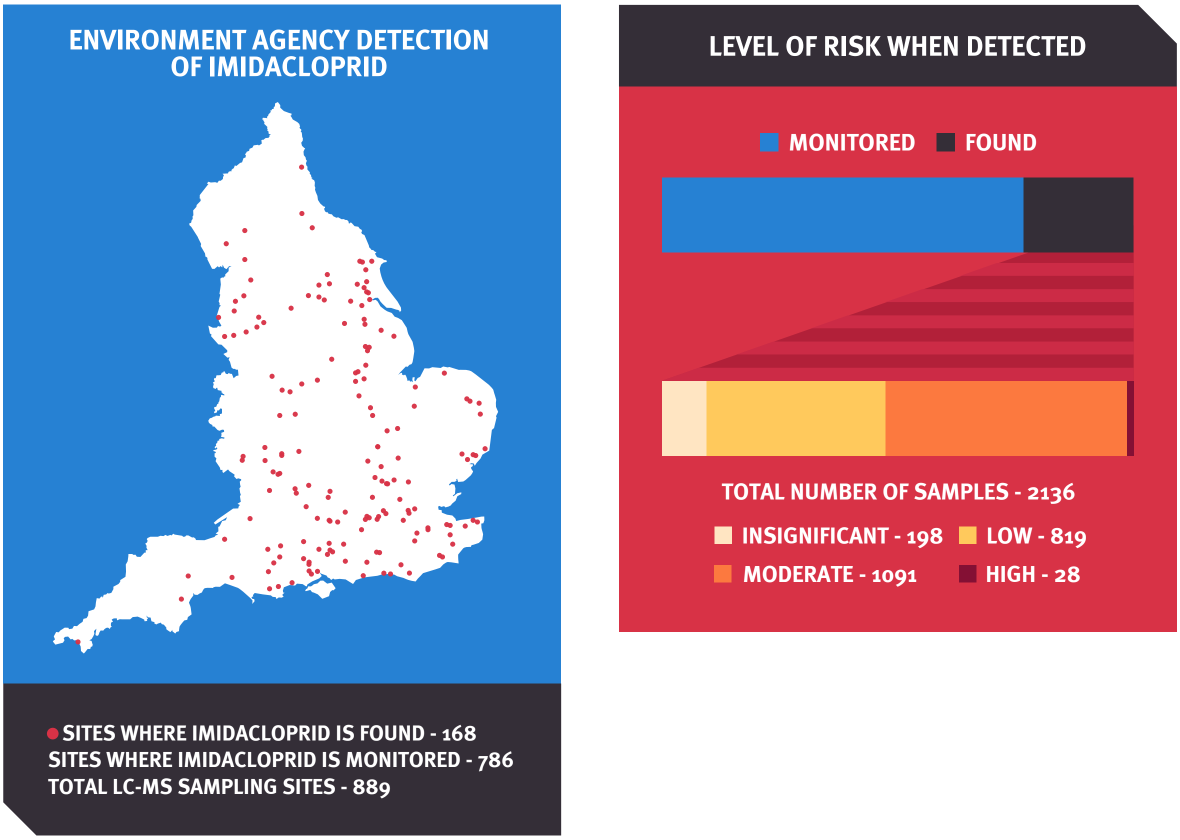

Figure 4: Detection, sampling, and level of risk to the environment associated with imidacloprid in England. Here, we show a map and stacked bar that depicts potential biases in the current detection and sampling of imidacloprid in an exemplary chemical monitoring dataset produced by the Environment Agency (EA)[35]. The map shows the sites within the dataset where imidacloprid has been detected since 2013. The upper stacked bar illustrates the proportion of monitored sampling sites where imidacloprid is detected, and the lower bar shows the risk category (i.e., insignificant, low, moderate, and high) assigned based on the detected concentrations of imidacloprid out of a total of 2136 samples tested across all sites. The lowest freshwater 'predicted no effect concentration' used to scale risk (0.013 µg/L) was obtained from the Swiss Centre for Applied Ecotoxicology, with only the active pure substance considered[50]. Only the data from the liquid chromatography mass spectroscopy (LC-MS) screening method was included in this analysis, as gas chromatography-mass spectrometry (GC-MS) has an operationally higher limit of detection (LOD), which is beyond the environmentally relevant concentration for monitoring imidacloprid. We included all sample types collected within England's land mass, including river water and groundwater.

Improvements in laboratory testing allow chemicals to be detected at ever-lower concentrations, yet there are still notable blind spots in the UK's formal monitoring programmes. The lack of coordinated spatiotemporal monitoring has resulted in patchy datasets that limit our ability to capture potential impacts on species. In the best available monitoring dataset for England, imidacloprid has been tested in 88% of the Environment Agency's liquid chromatography mass spectrometry (LC-MS) sampling sites (Fig. 4). However, if we only consider sites regularly tested for imidacloprid, this figure would be even lower, as testing is not consistently carried out across all sampling sites. Furthermore, the dataset's geographic coverage falls short of complete representation, as parasiticides such as imidacloprid are not tested in all river catchments in England. This is partly because there are no formal requirements for organisations such as the EA to monitor all these chemicals routinely under current regulations, although new methods and targeted programs (such as vulnerable catchment monitoring and pollution investigation studies) offer some promise for improving this situation in the near future. Also, the detection of a wide range of chemicals in tiny (but potentially harmful) quantities at scale is a major challenge and is particularly difficult for parasiticides, which often require lengthy and bespoke pre-treatment procedures before laboratory tests can be performed reliably[4]. Some of these undetected chemicals may still be having "hidden" ecological impacts because they are toxic at such low concentrations[12]. Similarly, since high-resolution chemical detection tools are relatively new, we lack data over a long enough period to fully understand how contamination changes over time and location. As the first neonicotinoid insecticide introduced in 1991, imidacloprid has been available long enough to be relatively well understood compared to many others, but even so, its detection remains challenging, as it degrades fairly rapidly in water and has a relatively high *limit of* *detection* (1 ng/l) in laboratory analysis[17]. For chemicals introduced as veterinary parasiticides more recently (e.g., afoxolaner, selamectin, and fluralaner), environmental data are even more scarce[17] – with most monitoring schemes ignoring them completely. Though parasiticides are used in small individual doses, they are now used so frequently on so many animals (i.e., in large aggregate volumes) that we consider it imperative to develop our understanding of their characteristics and effects.

The ecological impacts of parasiticides: From individuals to ecosystems

Pesticide pollution remains one of the biggest threats to freshwater ecosystems globally[51] and in the UK a multitude of ecosystem services linked to water quality – ranging from clean drinking water to water storage, recreation, and food production[52] – are potentially threatened. In natural ecosystems, invertebrates account for a large proportion of the biodiversity in food webs and serve as a crucial link for the transfer of nutrients and energy to the higher trophic levels, including fish, mammals and humans[53]. Many species depend on aquatic invertebrates as a food source and alterations to the abundance or behaviour of the latter could have negative consequences that ripple through the food web, and which could compromise important ecosystem services of value to humans[54]. Pesticides have already been implicated in pollinator collapses in agricultural systems in many parts of the world, including the UK. Even if the application of pesticides is substantially reduced in these areas, the concentrations seen in the environment remain of concern based on evidence from laboratory studies.

Although we often know the mode of action of an insecticide on its target invertebrate species, how this may affect non-target species or ecosystems is often not so clear. This is particularly true when scaling from individual physiology through to higher levels of biological organisation (i.e., populations, food webs, and ecosystems). Research that successfully spans these multiple levels is growing but is still relatively rare, especially in the field of ecotoxicology, where lab studies on single "model" species still predominate (Fig. 5). This is important because extrapolating from those few model species into the full span of biocomplexity we find in nature is challenging, and at present, there is little to no predictive power when shifting from the lab to the field, making so-called "ecological surprises"[55] relatively common. This is where effects are manifested that cannot be predicted from simple lab studies, because the model organisms and systems behave differently from those in the wild. Among the relatively small number of studies to date, we now know that the active ingredients in parasiticides can have both direct and indirect and lethal and sub-lethal effects on invertebrates and other animals in ponds and rivers – and that these can disrupt key ecosystem processes[56–60].

Freshwater invertebrates tend to be the most susceptible to direct effects of pesticides such as imidacloprid, though a range of toxic effects have been documented in fish, birds, and mammal species, as well as even in some microbes at the base of the food web[61]. Learning from our past mistakes, we know that pesticides can have powerful and often unanticipated consequences. Classic examples can be drawn from the first generation of pesticides like DDT, where biomagnification in apex predators such as otters and peregrine falcons triggered catastrophic population declines in many areas in the twentieth century[62]. Even now, we still find surprising and often counterintuitive impacts of pesticides in freshwaters – for example, a spill of the organophosphate chlorpyrifos in the River Kennet in 2013 triggered collapses in some keystone invertebrate species, but it also had direct and indirect effects across the wider food web, triggering algal blooms and suppressing decomposition rates at the base of the food web (due to the loss of the invertebrates that otherwise drove these processes)[63].

We know that concentrations of parasiticide active ingredients being detected in the UK's waterways overlap with those that can cause mortality and a host of sub-lethal effects in non-target species[17,64,65] (Fig. 4), so there is a possibility that this is already a potential threat that could be causing ecological damage right now – not in some distant future. The pressing challenge is to understand if, how, why, and to what extent negative impacts manifested on a few species in the lab translate to more complex natural systems, and to build a strong evidence base to help mitigate or avoid undesirable outcomes.

Another dimension of pet parasiticide pollution that needs attention is the strong urban signal – which is not surprising given that most humans and pets live in these areas. The challenge here is in sifting the signal from the noise because not only do these systems receive a high load and diversity of other pollutants, but our understanding of their ecology, relative to more pristine habitats, is also still rather limited. We need to be able to disentangle the effects of the individual chemicals, but we also need to understand how they interact with a variety of other stressors. In natural systems, the active ingredients in parasiticides are one part of a toxic cocktail of chemicals, rather than presenting in isolation. Although recent evidence suggests that multiple stressors often interact antagonistically (i.e., less than the sum of their parts), there are cases where combinations can be synergistic (greater than the sum of their parts)[66]. From laboratory studies, imidacloprid can have especially powerful synergistic (amplifying) effects when in combination with flumethrin[67]. Beyond this, we know very little about how most of the 30+ approved veterinary parasiticides affect each other's toxicity to wildlife, let alone with the other chemicals that are found in the UK's freshwaters.

This mix of pollutants in our freshwaters also needs to be considered against the backdrop of how changing temperatures might alter their toxicity. Temperature sets the pace of life, through the metabolic rate of individual organisms, and ultimately this shapes entire food webs and ecosystems. It can also shape the impacts of other stressors, including pesticides, and recent evidence suggests that warming may mask some of these local effects[56]. Not only are average annual global temperatures rising, but there are large spatial gradients to consider, including the "urban heat island effect"[68], as these could reshape how pesticides operate in the wild. Unfortunately, the role of temperature has been effectively ignored in lab studies, again making extrapolations to real ecosystems questionable. The vast majority of lab ecotoxicology trials are done at a single temperature (often 12°C as an "industry standard") so we cannot reliably predict the impact of these chemicals in real-world settings under different temperature regimes, especially if masking effects are prevalent. Ultimately, this means that realised levels of toxicity can be very different from those derived from classical ecotoxicology. Overall, this reflects the need for improved chemicals policy in the UK, and indeed, we are now seeing increased flexibility and consideration of new approaches[5,69,70]. The next big gap is not just to understand parasiticide impacts, but also how their impacts are shaped by temperature and other stressors and

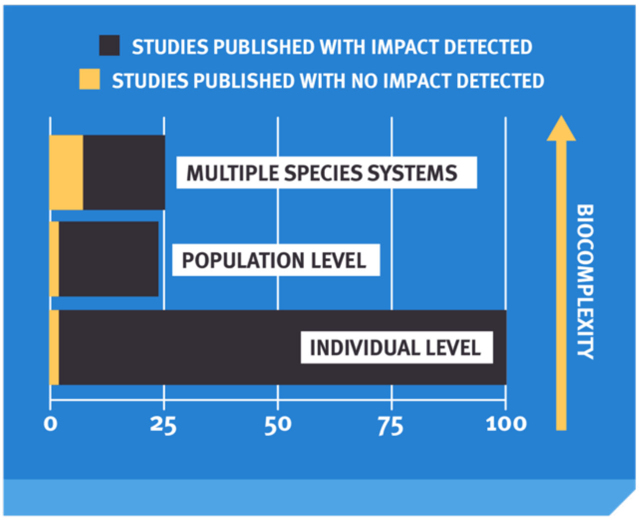

Figure 5: The number of published studies exploring the impacts of imidacloprid on freshwater systems at different biological organisation levels. To identify papers, we searched the Web of Knowledge database (www.webofscience.com/) for the key word combination ('imidacloprid*') and ('freshwater*' or 'river*' or 'stream*' or 'lake*') and ('impact*' or 'effect*' or 'response*' or 'threat*' or 'decline*'). In total, 420 papers were screened, and 160 papers were included in the analysis. We only considered papers that investigated quantifiable effects of imidacloprid in nature or under experimental conditions. Papers that reported monitoring or detection alone were excluded.

environmental gradients (e.g., pH, turbidity, nutrients) in the real world; especially in urban ecosystems, where most of the world's population now live.

Given that parasiticides are *designed to be highly toxic*, it is only logical to expect parasiticides to have strong negative impacts on freshwater ecosystems when released into the environment. At a time when the world is experiencing unprecedented declines in biodiversity[71], gauging the impact of these chemicals on ecosystems is critical; especially if societies are to manage their use (or misuse) in a rapidly changing world.

Implications for UK policy and regulation

As part of the authorisation process introduced by the European Medicines Agency (EMA), veterinary medicines undergo different levels of risk assessment[19]. Parasiticides intended for use in livestock generally undergo environmental safety testing that provides detailed information on their potential impacts on nature. Their use on pets is exempt from this level of scrutiny, so there is a serious lack of information on their impact and environmental fate[72]. At present, there is no requirement for a full environmental risk assessment because the current regulatory regimes inherited from EU legislation by regulatory bodies such as the UK Veterinary Medicines Directorate (VMD) assume that the use of veterinary parasiticides on pets leads to minimal environmental exposure.

This assumption is questionable given the vast quantities of parasiticides sold each year (Fig. 2), the extent to which active ingredients linked to these products are being detected in the environment (Fig. 4), and the high toxicity that is demonstrated in a wide range of non-target organisms to these chemicals (Fig. 5). In light of the evidence presented in this policy briefing and citations herein, we recommend that UK regulatory bodies review the legislation inherited from the EMA regarding the basis for the need for veterinary medicines used on pets to undergo full environmental risk assessments; this was a key recommendation made by the EMA in a recent 'reflection paper' in response to growing evidence on this issue[73]. Pet parasiticides are licenced based on the assumption that the benefits they provide outweigh the harm that they inflict. Until recently, it was common practice for the veterinary profession to use parasiticides on a targeted, reactive basis on individual animals with suspected infestations of parasites, minimising environmental exposure, rather than in a general prophylactic approach. The former instance is an example of a process where the benefits are likely to outweigh the harm of a single dose of the chemical, whereas the latter treatment of entire populations of healthy animals with parasiticides is substantially harder to justify. It is important to note that regulatory bodies (such as the VMD) are not the only organisation charged with the responsible management of these chemicals. This issue also requires buy-in and proactive collaboration from stakeholders within industry – manufacturers, distributors, and suppliers – to produce the necessary change.

Beyond the potential environmental risks, there are fears of longer-term resistance to these chemicals developing in target parasites[21]. This has happened countless times in the past due to the overuse of pesticides and could have serious consequences for animal welfare on a much larger scale: this mirrors growing concern in the medical profession about the analogous overuse of antibiotics to treat microbial pathogens selecting for the evolution of drug-resistant strains.
In agricultural settings, it is common practice to test animals before treatment with a parasiticide, in a bid to prevent resistance – but this is not the case for pets. One would assume that the cause must justify the means – that the rate of infestation, disease, and the extent that parasiticides reduce both, is well quantified. Unfortunately, there are few data available, effectively hindering an objective evidence-based risk analysis for this group of chemicals. These issues have been highlighted recently by industry bodies, such as the British Veterinary Association, and there are calls to switch to a more holistic risk- and evidence-based approach to parasiticide treatments in pets[21]. Even with this shift in thinking from veterinary practitioners, the need for some level of parasite control in pets will remain, but with a stronger evidence base, this can at least be managed more effectively, responsibly, and sustainably to deliver better all-around stewardship. Efforts to increase the public's awareness and education on the use and disposal and increasing regulatory limits on the purchase of the products will help decrease exposure and risk. Alongside this, there must be a drive to replace high-risk chemicals with lower-risk alternatives where possible.

The veterinary profession is becoming increasingly aware that there is a potential problem, but the legislative assessment of environmental risks is hampered by substantial gaps in our understanding[14,17]. Although the environmental impact of a single dose of parasiticide is tiny, many millions of doses are used repeatedly in the UK each year[14]: this warrants an in-depth scientific- and regulatory-driven investigation of the full spectrum of environmental risks and a potential reassessment of the existing marketing authorisation procedures.

Here, we propose a general framework of collaborative, evidence-based policy decision-making. The scientific community, regulatory bodies, and stakeholders must all work together to establish and resolve key problems and research gaps, while making the most of existing data. Furthermore, better governance of this issue will involve using this evidence to establish and communicate best practices for veterinary practitioners and consumers, minimising negative environmental consequences. Together, we must define opportunities for immediate change, whilst producing longer-term commitments to review key legislation, management, and infrastructure in the UK.

Hence, we recommend the implementation of several measures to reduce the level of risk potentially posed by pet parasiticides:

1. UK regulatory bodies should review the requirements for pet parasiticide products to undergo a rigorous environmental risk and impact assessments before approval.
2. A regulatory threshold should be applied to review parasiticide products that sell above a given quantity (e.g., million doses of an 'individual use' product) within a given timeframe (e.g., a year).
3. The authorisation of parasiticide products should be reviewed immediately by regulatory bodies when their active ingredients are banned for uses in other sectors (such as in agriculture).
4. Existing parasiticide active ingredients that fail to meet risk assessment standards should be phased out.
5. Reduce prescriptions to match the real, rather than perceived treatment needs: support the veterinary industry and pet owners to change from prophylactic use of parasiticides to risk-based or reactive treatment.
6. Regulate access to parasiticides: consider changing approved parasiticides to prescription-only classifications (POM-V or POM-VPS).
7. New safe disposal regulations: implementation of an incentivised return scheme for unused parasiticides to reduce improper waste disposal by pet owners.
8. Reduce the number of sewage overflow events (i.e., sewage spills) by increasing the capacity of Wastewater Treatment Plants to meet the influent flow at times of extreme rainfall.
9. Invest in new forms of tertiary treatment in Wastewater Treatment Plants to eliminate residual organic and inorganic compounds (i.e., pesticides such as imidacloprid).
10. Ultimately, mitigate the risks posed by stressors (such as chemical pollution) by improving ecosystem resilience through catchment-scale management strategies, such as habitat restoration, in locations defined by research.

Conclusions

The products used to prevent or treat parasites in pets require urgent attention in the interconnected spheres of research, industry, and policy. Contamination from the active ingredients used in pet parasiticides is extremely common in UK waters, and is regularly found at concentrations that exceed laboratory-defined safety thresholds. There is mounting evidence that these chemicals can be extremely toxic to a wide range of non-target species, and with largely unknown consequences for ecosystems.

The next steps require that stakeholders work together to address the sizable knowledge gaps (through research, evidence synthesis, and options appraisal), so that mistakes of the past are not repeated. Collectively, as a society, we need to move beyond relying on hindsight as pesticides are introduced, used intensively, and then banned; we need to be proactive and not reactive.

We recommend that future research should:

1. Quantify the extent of parasiticide usage on pets and assess the necessity for prophylactic treatment, including whether there is harm caused by low levels of parasite presence, and the potential for zoonotic disease(s) to occur in humans.
2. Stratify and increase the spatial extent of long-term monitoring of parasiticides in UK water bodies and coverage of the full spectrum of likely sources, entry points, and pathways of parasiticides entering the environment.
3. Assess the severity and geographic extent of contamination of freshwater ecosystems and impacts, especially at the higher community and ecosystem levels of biological organisation.
4. Assess how chemicals (including veterinary parasiticides) interact with other stressors and quantify the extent to which their impacts are temperature dependent.
5. Define geographic locations within the UK that have especially high levels of threat posed by pet parasiticides and identify possible management actions (e.g., restoration or water quality interventions).

Implementation of these recommendations would provide opportunities to mitigate current and future threats posed by environmental pollution from parasiticides and many other harmful chemicals.

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