CPD article

UK parasite risk factors and control challenges

Endemic and emerging parasites pose a risk to companion animals and their owners. Emerging parasites can also impose a significant public health burden. The discovery of new parasites, the insurgence of endemic ones, and the emergence of new information has made managing parasitic diseases a topical subject for veterinarians, who are now starting to see more patients with these diseases. Better understanding of the extent and burden of parasites on animals and humans is essential for control interventions. This article discusses the known risk factors of UK parasites in the current literature, use of parasiticides in small animal medicine, known challenges to effective parasite control, risks of parasiticides and current guidelines surrounding their use.

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uman-animal interaction from dog and cat ownership elicits many positive benefits to human health (Beetz et al, 2012). However, infestations and potential infections, including zoonoses caused by endo- and ectoparasites, interfere with these effects and cause animal health and welfare concerns (European Scientific Council for Companion Animal Parasites (ESCCAP), 2018). Immunocompromised individuals and children are at an even greater risk of zoonoses, especially given the often-close proximity in which pets and owners live and the increasingly important role they play in our lives. There are many parasites of current and growing veterinary importance in the UK; understanding their epidemiology allows the development of appropriate prophylaxis guidelines based on individual risk, as well as the risk posed to the families they live with (ESCCAP, 2018, 2021).

Parasites: spectrum, significance and risk factors Endoparasites

Many endoparasites affect cats and dogs in the UK with some helminth infections causing severe clinical disease with zoonotic potential risking the health of livestock and threatening human health.

Intestinal roundworms

Roundworms of *Toxocara* spp. (*Figure 1*) infect most puppies and kittens at or shortly after birth, causing severe clinical disease through transmammary (puppies and kittens) and transplacental (puppies) transmission. Arrested stages can remain after host

immunity eliminates most infection, leading to intermittent infection in older cats and dogs and egg shedding. Eggs become infective after several weeks and can survive in the environment for years. Infection can also occur from ingestion of eggs from the environment or paratenic host consumption (Overgaauw and van Knapen, 2013). *Toxocara* spp. is prevalent in all areas of the UK, with variations between 3.5 and 34% of adult domestic dogs and 8–76% of adult domestic cats potentially shedding eggs, posing a zoonotic risk to humans and causing ocular and visceral toxocariasis, particularly in children and immunocompromised individuals (Overgaauw and van Knapen, 2013).

Many risk factors for companion animal roundworm infection are known in current literature. Puppies and kittens under 6 months have the highest worm burdens and patent infection prevalence (Overgaauw and Nederland, 1997). Animals that have access to outdoors and ability to free-roam, consume paratenic hosts (have hunting and scavenging propensities) and are in contact with other animals, such as those used in competitions or shows, kept in kennels or working dogs, all have an increased risk (Overgaauw and van Knapen, 2013; ESCCAP, 2021). Studies in the Netherlands found that for young cats living in rural areas and spending a greater time free roaming outdoors pose the most significant risk (Nijsse et al, 2016). Dogs aged up to 12 months are still at a significantly greater risk of infection, as well as those who spend greater time off-leash, have been recently kennelled or exhibit coprophagy (Nijsse et al, 2015). It has also been found that where elevated levels of wildlife reservoirs may exist, such as in areas with a high density of voles, rodents or foxes, as well as high stray cat populations, the risk of roundworm infection in



Figure 1. Roundworms of Toxocara spp.

companion animals also increased (Reperant et al, 2009; Wright, 2019a). A Bristol-based study found the main contributors to contamination were privately owned dogs (Morgan et al, 2013).

Intestinal tapeworms

Tapeworms of importance in the UK include Dipylidium caninum, Taenia spp., and Echinococcus granulosus. Infection is generally subclinical but may cause sickness or diarrhoea in dogs. There is little risk in cats unless other disease is present. Fleas act as an intermediate host for the zoonotic D. caninum where humans can be accidental hosts. Where there is infestation, segments can be seen passed out in faeces, or actively crawl out of the anus which can be itchy. Pets can become infected with Taenia spp. through ingestion of tissue cysts in sheep, rabbits and rodents. Both are ubiquitous in the UK. Dogs can be infected by E. granulosus from tissue cysts in sheep and cattle offal, and accidental ingestion of eggs from dogs causes hydatid disease in humans (Wright, 2013). Distribution is changing in the UK and is potentially spreading through abattoirs (Bonner, 2017), but certain geographical foci have historically existed in Herefordshire, mid-Wales and the Western Isles of Scotland (Wright, 2013; Collins, 2019).

Risk factors for tapeworm infection include a history of flea infestations, outdoor access with an increased ability to free roam, particularly those with hunting, scavenging or predation propensities, contact with farmland and access to potentially infected offal or carcasses, as well as living in or visiting known Echinococcus endemic areas (Wright, 2013; ESCCAP, 2021). Contaminated agricultural land from disposal of dog faeces in muck heaps or farmland pose an under-researched risk of infection (Collins, 2019). Exposure to these parasites may increase seasonally with increased flea exposure and hunting behaviour of cats during the summer, and during hunting and shooting seasons for working and gun dogs (Wright, 2013). A systematic review of Echinococcus also found that younger and/or male dogs are at increased risk of infection (Otero-Abad and Torgerson, 2013). Age- and sex-related trends in D. caninum infection risk have also been found. The highest prevalence of infection of cats in Pennsylvania was found to occur in the age group of 1-5 years (Gates and Nolan, 2009) and higher prevalence rates have been reported in adult and male dogs in Ethiopia (Gutema et al, 2021).

Lungworms

Angiostrongylus vasorum is highly pathogenic to dogs and fatal if untreated. It is transmitted through ingestion of the intermediate



Figure 2. Adult cat flea and eggs.

snail and slug hosts, as well as through slime trails. Infection mainly causes pulmonary clinical signs, but coagulopathies, neuropathies and cardiac diseases can also occur (Helm et al, 2010). It is now thought to be endemic throughout the UK with non-uniform distribution following continued spread north beyond established endemic foci in Wales, the southwest and southeast of England, possibly from climate change and increased movement of dogs (Kirk et al, 2014).

At-risk dogs include those living in or visiting known endemic areas, or areas where cases have been reported, as well as those that deliberately eat slugs, have grass-eating or coprophagic propensities, and drink from puddles and other outdoor stillwater sources (Wright, 2020a). Access to woodland and moorland increases risk of exposure to slugs and snails and therefore infection risk (Tolhurst et al, 2021). A small retrospective study in the southeast of England by Holmes et al (2020) found a significant relationship between *A. vasorum* infection and dogs less than 1 year of age, as well as the Cocker Spaniel breed. Purebred dogs were also found as more likely to be infected. An earlier larger study by Morgan et al (2010) found similar age-related risk factors, as well as a seasonal risk factor, with more cases earlier in the calendar year. However, they did not find sex, neuter-status or breed to be significant risk factors.

Ectoparasites

Ectoparasites can cause cutaneous lesions which may lead to secondary infections, induce an immune response leading to allergic reactions, transmit disease-causing pathogens, cause infestations resulting in itching and scratching, cause anaemia where there are intense burdens and on rare occasions, can lead to death of an animal (ESCCAP, 2018).

Fleas

Fleas (*Ctenocephalides* spp.) are common throughout Europe, with the cat flea (*Ctenocephalides felis*; *Figure 2*) being the most common flea affecting dogs and cats in the UK. Rates have been reported as part of 'The Big Flea Project' by Abdullah et al (2019) as 28.1% of cats and 14.4% of dogs being infested, this is likely to be higher in the wider population. Milder climates and central heating have allowed for more favourable breeding conditions and year-round persistence of environmental life-cycle stages (Wright, 2018). Fleas can cause flea allergic dermatitis and anaemia if infestations are heavy. They are also vectors for multiple zoonotic infections such as *Bartonella* spp. (cause of cat scratch disease) and *Rickettsia felis*



Figure 3. Ixodes spp. ticks (a, b) are endemic to the UK and most of Europe. If they are visible, ticks may be manually removed with a tick hook (b) to reduce the risk of zoonotic disease transmission.

(cause of spotted fever) (ESCCAP, 2018). Fleas also serve as an intermediate host for the zoonotic tapeworm *D. caninum* (Dobler and Pfeffer, 2011).

Flea prevalence in the UK varies from year to year, with consistent increases from spring to autumn (McGarry, 2019). This implies that access to wild reservoirs (therefore pets in contact with farms, forests or moorlands) remains a significant risk factor for flea infestation (Clark et al, 2018). Geography is also important as a risk factor, with Cooper et al (2020) demonstrating infestation within the UK increases from north to south. Multi-pet households increase rates of infestation, a study in Hungary showed that dogs living outdoors with cats and outdoor cats are at especially high risk (Farkas et al, 2009). However, the extent of this risk may vary in the UK because of potential differences in parasite control trends. It may also be that age, breed and coat-type differences alter the risk of flea infestation. Behaviour differences also predispose certain age groups and breeds to an increased risk of flea exposure, for example by being more energetic or inquisitive (Figure 3). Animals with longer and/or denser fur might harbour fleas more readily, or at least make their detection difficult, so owners are less likely to monitor and treat. This has been demonstrated in cats in Malaysia, where statistically significant associations were found with flea infestations, age and hair-length, along with weight and body condition (Azrizal-Wahid et al, 2019). Again, the extent of these risks may vary in the UK.

Ticks

Ticks (generally *Ixodes* spp. in the UK; *Figures 3a* and *3b*) are endemic throughout most of Europe and risk of exposure in the UK has increased with milder climate, but the prevalence of tick attachment varies across the UK as recently reported by studies



Figure 4. Energetic and inquisitive dogs with access to woodland and long grass are at an increased risk of exposure to ectoparasites such as fleas and ticks.

involved in 'The Big Tick Project' (Abdullah et al, 2016; Wright, 2018). Ticks can cause infestations but more significantly, they are vectors for multiple zoonotic pathogens including Borrelia burgdorferi (cause of Lyme disease). A UK study found that 2.37% of ticks on dogs and 1.8% on cats were carrying Borrelia spp. (Abdullah et al, 2016; Davies et al, 2017). Babesia canis (cause of babesiosis) has also been identified where there has been endemic foci in West Wales, Devon, Essex and London (Phipps et al, 2016), as well as tick-borne encephalitis with established focus in Thetford Forest and possibly the New Forest (Holding et al, 2020). Other tick-borne pathogens seem to be on the rise as a result of increases in other tick species attaching onto travelled dogs and their ability to establish indoor infestations; including Ehrlichia canis which is pathogenic to dogs, and zoonotic pathogens such as Rickettsia conorii and Crimean Congo haemorrhagic fever-causing virus. Risk factors for these tick-borne pathogens include animals living in or visiting endemic foci areas, as well as pets who travel outside of the UK (Wright, 2020b).

Risk factors for tick attachment include seasonal changes, with UK peaks seen in March to June and August to November, a preexisting exposure history, contact with woodland and moorland including areas with long grass, bracken and undergrowth (*Figure 4*) and land shared with ruminants and deer, as well as urban recreational spaces (Nelson et al, 2015; Tulloch et al, 2017; ESCCAP, 2018; Wright, 2020b). Pastoral and gundog breeds, unneutered males and females and dogs older than 1 year were also found to be at higher risk (Smith et al, 2011; Abdullah et al, 2016). It may be more difficult to identify ticks on larger and long-coated breeds, as well as in individuals who are reluctant to be examined, potentially resulting in increased risk of infection.

Emerging parasite threats

A variety of exotic parasites and their vectors have been diagnosed in travelled UK cats and dogs recently. Of note are the aforementioned ticks and tick-borne diseases, the protozoa *Leishmania infantum* (Silvestrini et al, 2016; McKenna et al, 2019) and the endoparasite *Dirofilaria immitis* (heartworm) (Stokes and Wright, 2021). All three can have long incubation periods and carrier states, infection can be lifelong and prognosis can be poor (Wright, 2020b). Additionally, there have been reported cases of the zoonotic endoparasites *Thellazia callipaeda* (eyeworm), *Linguatula serrata* (tongue worm), *Dirofilaria repens* (Wright, 2018), and *Echinococcus multilocularis* can also be acquired abroad (Otero-Abad and Torgerson, 2013).

Travelling abroad to endemic foci increases the risk of both contracting and spreading these parasites and their vectors.

Parasiticides and routine use

Parasiticides are pharmaceutical agents used to treat endo- and ectoparasites (Rock, 2010). There are a variety of parasiticide agents used in veterinary medicine for prophylactic control and therapeutic treatment, which can be split into three broad categories:

- Anthelmintics, which kill helminths
- Ectoparasiticides, which kill arthropods and include insecticides (used to treat insects such as fleas) and acaricides (used to treat acarids, such as ticks)
- Endectocides, which kill both (Wright and Elsheikha, 2018).

With such a wide-ranging and extensive threat of parasitism, particularly when infection signs are subtle or unnoticeable, preventative control is prudent to avoid clinical disease and minimise zoonotic threat to ultimately safeguard the health and welfare of companion animals and owners. The development of spot-on products made product application much simpler and there has since been a surge in use and development of parasiticide products (Rust, 2020).

Licenced parasiticide products are widely commercially available with 324 anthelmintic, 781 ectoparasiticide, and 200 endectocide products for dogs and/or cats currently authorised by the Veterinary Medicines Directorate (VMD, 2021). Tablets and spot-on solutions make up 20.89% and 60.58% of all parasiticide products respectively (VMD, 2021).

A total of 25.31% of anthelmintic products and 37.77% of ectoparasiticide products are currently classified as 'AVM-GSL' (Authorised Veterinary Medicine-General Sales List) for cats and dogs. This means they are readily available for purchase in shops or online, without the mandatory condition of discussing the product and its use with a veterinary professional before purchasing (VMD, 2014).

The development of combination products has further fuelled product use, with 42.28% of anthelmintic, 40.85% of ectoparasiticide and 59.0% of endectocide products containing combinations of active ingredients often used to target different parasites or parasite life-cycle stages (VMD, 2021). Routine prophylactic parasite control is now a widespread practice in the veterinary profession, with comprehensive healthcare packages based on routine and regular parasite control being commonplace.

Challenges to parasite control Epidemiological changes

With a rise in pet travel, importation of relocated animals and climatic changes, the epidemiological situation is in flux; conditions are more favourable for increased spread of certain parasites and their vectors, enabling the introduction of exotic diseases to the UK (Wright, 2019b). Veterinary professionals need to ensure they remain up to date with the latest distributions across the UK and globally to help inform accurate diagnosis, treatment and travel advice (Wright, 2019b). This is difficult with fluid distributions and risk factors. For example, although lungworm is thought to be endemic throughout the UK, its distribution is still patchy, with some areas being infection-free (Kirk et al, 2014). An infection-free area is not technically riskfree, and The ESCCAP UK and Ireland recommends that for dogs in local areas of high endemicity, dogs used for hunting, or dogs that eat grass, slugs or snails, prevention can be achieved with the monthly administration of macrocyclic lactones (ESCCAP, 2021). Lungworm is not notifiable and so distribution mapping relies on veterinary professionals reporting cases. Although it is not difficult to stay up to date with changing distributions, it is difficult to know how up to date these distributions are and therefore what the risk to the individual animal actually is. It is sensible to assume that any dog can be exposed to infection and the decision to treat should always be made in discussion with the pet owner based on a risk assessment.

Owner compliance

Owner compliance is a well-recognised problem and poor compliance can result from poor communication, language barriers, insufficient understanding of parasites and their control, cost of treatment and the client simply forgetting (Elsheikha, 2016a, 2017). Owner compliance is the cornerstone of effective parasite control and decreasing infection risk. Compliance ensures correct administration of any treatment, such as spot-on application or tableting, as well as following of recommendations, for example avoiding swimming or shampooing after topical treatment administration, monitoring for fleas and ticks, responsible disposal of faeces or practicing good hygiene.

Parasiticide concerns

Companion animal veterinary medicines do not require an environmental fate and toxicity report as it is assumed they will have limited effects (EMA, 2000). However, concerns have recently been raised about spot-on ectoparasiticides contaminating the natural environment (Perkins et al, 2021). Since ectoparasiticides are harmful to a wide range of invertebrates, this has implications on wildlife, ecosystems and in turn, public health. Parasiticide resistance is not currently a widely evidenced threat in companion animal medicine (ESCCAP, 2018, 2021), but is highly reported in farming and equine industries (Silva et al, 2019; Hennessey et al, 2020) and evidence has suggested that cat fleas have the potential to develop resistance to insecticides (Rust et al, 2018).

With dogs and cats being the most popular companion animals in the UK, where numbers are estimated to be 9.6 and 10.7 million dogs and cats, respectively (PDSA, 2021), the unknown magnitude of environmental fate and toxicity levels of the parasiticide products is called into question (Domingo-Echaburu et al, 2021). Parasiticide resistance could potentially become an increasing concern. That said, it is important to point out that resistance is not limited by not treating uninfected animals. For resistance to be limited by reducing treatment, infected animals must be left untreated, deliberately allowing zoonotic worm egg shedding and flea infestations to occur. While this strategy has worked for parasites of livestock and horses, the zoonotic nature of cat and dog parasites makes this approach risky.

Pathways for a topical treatment contamination may include pets directly entering bodies of water, bathing, washing of pet bedding, hands or other surfaces that come into contact with treated pets, as well as runoff from closed surfaces (Perkins et al, 2021); similar pathways could also be considered for collars. Pathways of oral formulations include excretion via urine and faeces, manufacturing and storage. The disposal of unused medicines, containers and faeces must also be considered (Boxall, 2004).

In response to these concerns, Wright (2021) reports that owner education is key to reducing contamination, while ensuring parasites are still being controlled. The author asserts that advice should be given in relation to correct application of product, responsible disposal of packaging and avoiding swimming and shampooing after topical applications. However, this proves difficult given the wide availability of AVM-GSL products, the popularity of products on mail order schemes or repeat prescriptions, and current owner compliance challenges. Many pet owners will not seek veterinary advice, or indeed read the label insert on the method of application or frequency of use when purchasing AVM-GSL products. Increasing education of cross–counter sales staff will therefore also play a role in reducing environmental contamination.

Another concern is that the prevalence of combination and broad-spectrum treatments, that are designed to treat multiple parasites at once, could be leading to overtreatment and unnecessary treatment. The risk of adverse reactions from drug side-effects or drug-drug interactions can be increased when combination products are used (Wright and Elsheikha, 2018). For example combinations of macrocytic lactones, with the exception of selamectin and milbemycin/pyrantel, can lead to neurological side effects (Elsheikha, 2018).

Risk-based parasite control

Risk-based parasite control involves prescribing prophylactic treatment and offering of bespoke advice that is individualised based on assessment of demographic, geographical and lifestyle factors (Wright, 2020b). Given that *Toxocara* spp. and cat fleas are ubiquitous across the UK, it is recommended that regular treatment for these parasites forms the basis of all parasite control programmes and other parasite prevention should be risk-assessed based on lifestyle and geographical distribution (Wright, 2021).

Current guidelines

Appropriate control guidelines based on individual risk have been developed by The ESCCAP, which offers evidence-based independent advice regarding risk factors and recommended

deworming frequency. Educational material summarising the
ESCCAP UK and Ireland recommendations are freely accessible
and available to download from the ESCCAP website.
ESCCAP's endoparasite guidelines on worm control in

ESCCAP's endoparasite guidelines on worm control in cats and dogs (2021) categorise four risk groups based upon individual lifestyle and geography. Consideration of factors including outdoor status, freedom to roam, in-contact animals, eating offal, carcasses or an unprocessed raw diet, or actively hunting, form the basis of recommendations as to appropriate treatment frequency for roundworms and/or tapeworms. Additional recommendations are also given based on risk factors such as pregnancy or lactation status, the animal's age, eating slugs or snails, travel to endemic areas, flea infestation, other parasite infection history, and contact with children or immunocompromised individuals, to treat for additional worms and/or treatment intervals (ESCCAP, 2021).

Additionally, guidelines on the control of ectoparasites in dogs and cats (ESCCAP, 2018) categorise five and six different risk scenarios for fleas and ticks respectively and give recommendations on control, including both treatment and/or practical measures. Groups consider the main risk factors to be outdoor access, history of infestation, multi-pet households or shelters, history of flea allergic dermatitis and risk of tick-borne disease transmission. Recommendations range from regular examination for ticks and fleas (where found, attempt manual removal in the case of ticks and administer treatment for both), to sustained integrated tick and flea control generally administered monthly, alongside environmental cleaning and treatment (ESCCAP, 2018).

Preventative drug treatment should be used in combination with giving practical advice to clients about environmental control and reducing zoonotic risk. General recommendations to give include daily picking up and responsible disposal of dog faeces, covering sandpits and fencing off play areas, daily monitoring for ticks and removal using a tick hook, regular washing of pets' bedding and vacuuming of areas frequented by pets, as well as good hand hygiene and thorough washing of fruit and vegetables before raw consumption (Wright, 2017).

Stokes and Wright (2018) summarised best practice for creating tailored parasite control plans for clients. This includes performing a risk assessment to allocate pets into a risk group on which to base a tailored parasite control plan, with an annual review. Demographics should be taken into account, and questions should be asked regarding general health, lifestyle, parasitic infection/ infestation history, previous treatment, adverse reactions and geography. Wright (2020a) gave an update on UK parasite trends and emerging threats, alongside some simple risk assessment questions to ask. Owner involvement and discussion was recommended as essential to compliance, as understanding why and how best to give treatment increases the likelihood of following instructions (Richmond, 2017). It was also recommended that consideration of owner preferences and circumstances should be integrated into this approach to maximise compliance. Elsheikha (2016a, 2016b) discusses strategies to promote compliance including client education, improving and maintaining good communication, nurturing trusting relationships, and realistically assessing owners' knowledge and understanding.

KEY POINTS

- Not only do known parasitic diseases change, but new diseases are also emerging.
- Washing hands frequently, especially after touching animals, and avoiding contact with animal faeces can help prevent infections.
- People with compromised immune systems should avoid direct contact with animals that could transmit zoonotic parasitic infections.
- Emergence and re-emergence of parasitic diseases of pets and humans can be directly or indirectly influenced by environmental and climatic factors.
- Surveillance of emerging parasitic diseases is needed to inform the development of evidence-based approaches to prevention and control of these diseases.
- Comprehensive risk assessment is needed to identify the interfaces where transmission of emerging parasites occurs and the feasibility of risk reduction interventions.

The entire veterinary team should be involved in consistent risk-based parasite control. With an average vet consult time of 10 minutes (Gray and Cripps, 2005), there is limited time to comprehensively discuss risk-based parasite control and formulate an individualised protocol, on top of the other duties involved. Thus, it is well reported that veterinary nurses are best placed to carry out parasite control plans and can play a vital role by leading parasite prevention clinics (Richmond, 2017; Richmond et al, 2017; Wright, 2017, 2020b; Stokes and Wright, 2018).

Responsible use of parasiticides

The British Veterinary Association (2021) and British Small Animal Veterinary Association policy position on the responsible use of parasiticides for cats and dogs was published recently, stating that 'Veterinary professionals must always follow a risk-based approach to parasite control'. Their position outlined the concerns of current parasite control practices involving 'blanket-treatment' and called for more responsible use of parasiticides to limit the risk of resistance developing and minimise environmental contamination.

Recommendations for veterinary professionals included education on and use of risk-based control, including consideration of integrating frequent testing, alternative methods of parasite control, using targeted treatment rather than combination or broad-spectrum products where appropriate, and promoting owner education to improve parasite control and product usage compliance. Extensive recommendations for areas of further research were also outlined (British Veterinary Association, 2021).

Conclusions and future direction

Effective parasite control is critically important for the health and welfare of companion animals and their owners. A pet owner survey (McNamara et al, 2018) found that dosing frequencies used for endoparasites in the UK are lower than recommended, highlighting the need for improved education around cat and dog patient risk assessments and greater adherence to ESCCAP guidelines. Owner education and therefore compliance in many cases will come secondary to that of the veterinary professionals advising on and administering parasite control, although the current understanding of and attitudes towards risk-based parasite control among UK veterinary professionals remains unknown. Future studies are needed to ascertain the overall understanding, observance and attitude towards using a risk-assessment based approach to canine and feline preventative parasite control by current veterinary professionals.

Events in the last few years have taught us that pets are now, more than ever, vulnerable to emerging parasitic diseases, some of which are zoonotic. Individual risk of parasitism is altered based upon demographic, lifestyle and geographical host-related factors. The climate is also having an immense effect on the dynamics of the life cycle and epidemiology of many parasites. Mitigating risks should be the primary aim of parasite control, with a combination of practical advice and an individually tailored parasiticide programme to strike a balance between appropriate parasite control and minimising of adverse effects. Maximising effective control also requires pet owner involvement with the veterinary team. An up-to-date veterinary curriculum is crucial to engage future graduates in disease surveillance, veterinary public health, animal welfare and good quality client communication. Future research activities should focus on solving the problems arising at the interface between animals and humans.

Conflicts of interest

The authors have no conflicts of interest to declare.

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