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Trends in Parasitology

Opinion

Toxocara: time to let *cati* 'out of the bag'

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Zoonotic toxocariasis is increasingly prominent as knowledge of its insidious impact on human health accumulates. *Toxocara canis* dominates research attention, with *Toxocara cati* relegated to the periphery. We argue that there are few grounds to support this bias, and that differences in life history and epidemiology between *T. canis* and *T. cati* could have implications for disease impacts and control. Research on *T. cati* should be cognisant of its unique characteristics and not extrapolate uncritically from knowledge about *T. canis*. Key research gaps identified long ago remain largely unfilled. We set challenges for future research to better understand the biology of *T. cati* and its role in zoonotic disease – essential for guiding urgently needed actions in support of public health.

Highlights

Continued neglect of *Toxocara cati* relative to its better studied counterpart, *Toxocara canis*, is increasingly untenable and should be urgently reconsidered.

Traditional viewpoints, based on older studies, have a tendency to attribute most human toxocariasis to *T. canis* by default. The zoonotic potential of *T. cati* is poorly understood due to lack of available data caused by diagnostic limitations.

T. cati is an important parasite in its own right, with distinct biological differences from *T. canis* in its life cycle, epidemiology, pathogenesis, and host dynamics, leading to important implications for its control.

We aim to stimulate and influence the direction of research on this neglected parasite species. Progress in molecular biology and modelling approaches offers potential to address knowledge gaps and challenge assumptions.

Toxocariasis and the prevailing dogma

Zoonotic (see Glossary) infection with *Toxocara* spp. is increasingly recognised as an important cause of human disease [1]. The genus *Toxocara* (Ascaridoidea: Toxocaridae) contains as many as 26 species, but only two are recognised as zoonotic: *T. canis* and *T. cati* [2]. **Toxocariasis** is common worldwide, with global human seroprevalence estimated to be 19% [3]. Health impacts are extremely variable, ranging from asymptomatic infection through to severe tissue damage caused by larval migration [4,5]. The disease is subject to growing attention as a neglected parasitic disease, driven by epidemiological information on its widespread distribution, pervasive effects on human health, persistence despite long-term veterinary and public health efforts, and future projections [1,6].

Large numbers of eggs are produced by adult *T. canis* and *T. cati* worms in the intestine of their respective canine and feline **definitive hosts**, which then accumulate extensively in the environment via faeces, particularly in soil and sand [7]. Eggs are tolerant, surviving unlarvated for months even in freezing conditions, and once larvated remaining viable for at least 4 weeks [8,9]. Consumption of infective eggs results in new infections; in definitive hosts larvae mature as they migrate from the gastrointestinal tract through tissues, usually via the hepato pulmonary route, resulting in pathology and eventually returning back to the intestines [10,11].

Toxocara also infects a diverse range of **paratenic hosts** in which infective eggs that are consumed develop into migratory or dormant larvae residing in various tissues, commonly brain, muscle, and liver, and subsequently infect new definitive hosts through predation [11]. Small mammals, such as rats and mice, are highly susceptible, but also large mammals such as pigs and macaques, avian species, and invertebrates have been demonstrated to be capable of hosting the parasite [11,12]. Humans are accidentally infected by consuming larvated eggs from the environment [7] or larvae in food animals acting as paratenic hosts [13].

While *T. canis* and *T. cati* have both been implicated in zoonotic disease, clinical and research attention has focused asymmetrically on *T. canis*, or does not distinguish effectively between the two species, resulting in a shortfall of primary research on *T. cati* (Figure 1). Literature is

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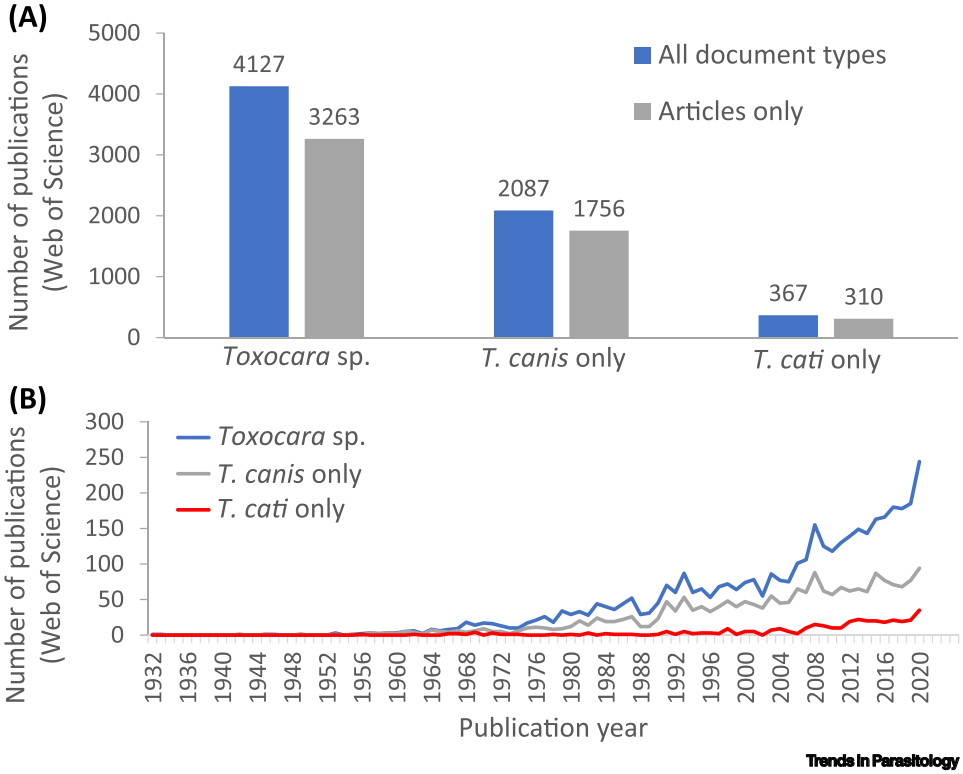

Figure 1. Graph to compare publication metrics for different *Toxocara* species. A literature search using key terms was performed in August 2021 using the Web of Science (v.5.35 Clarivate) Core Collection database, for years 1932–2020. No limits regarding language, document type, or access were applied. Document types included articles, reviews, meeting abstracts, letters, proceedings papers, notes, editorial material, book chapters, early access, corrections, discussions, reprints, book reviews, correction additions, data papers, and news items. (A) Total number of publications and (B) number of publications per year, considering *Toxocara* parasites collectively (search terms: "Toxocara" OR "Toxocara spp." OR "Toxocara sp." OR "Toxocara cati" OR "T. cati" OR "Toxocara canis" OR "T. canis" OR "Toxocar*"), only *T. canis* (search terms: "T. canis" OR "Toxocara canis" NOT "cati" AND "canis"), or only *T. cati* (search terms: "T. cati" OR "Toxocara cati" NOT "cati" AND "canis"). Figure created with BioRender.com.

scattered with superficial comments attributing the majority of human toxocariasis cases to be caused by *T. canis,* with *T. cati* commonly treated as an afterthought to *T. canis* in reviews [2,14,15]. Our opinion is that there is a lack of adequate supporting evidence to justify this broad viewpoint at present. The relative neglect of *T. cati* as a cause of zoonotic disease was argued by Fisher in 2003 [16], whereby in the face of diagnostic limitations the assumed dominance of *T. canis* as a cause of zoonotic disease was misplaced and self-fulfilling, and called for a renewed research focus on *T. cati* in order to properly evaluate its role in zoonotic disease. Despite the intervening years, major knowledge gaps remain, and the role of *T. cati* in zoonotic disease is still uncertain [16,17].

A further issue is a tendency in the literature for extrapolation, filling knowledge gaps on *T. cati* using the more extensive knowledge base that exists for *T. canis*. For example, the widely cited statement that *Toxocara* adult worms shed 200 000 eggs per day is based only on experimental work with *T. canis* adult worms [18], with no equivalent attempt to estimate *T. cati* fecundity. Studies from the 20th century examining the life history of both *T. cati* and *T. canis* indicated fundamental differences between the species, demonstrating that *T. cati* is an important and distinct parasite in its own right, yet such studies have not been revisited recently. The implications of

Glossary

Cross-reactivity: occurs when antibodies raised to other common parasitic infections (e.g., *Ascaris lumbricoides*) cross react with *Toxocara* antigens in diagnostic tests.
Definitive host: a host within which a parasite develops to an adult worm and is capable of producing offspring (eggs).
Enzyme-linked immunosorbent assay (ELISA): used as a diagnostic test to bind parasite antigen to a specific antibody coupled to an enzyme. It can be used to identify prior exposure to specific immunogenic infection.
ITS-1 and ITS-2: internal transcribed spacer is nuclear DNA located in between genes coding for ribosomal subunit rRNA, of which there are two in eukaryotic cells.
Loop-mediated isothermal amplification (LAMP): a relatively new nucleic acid amplification technique based on isothermal conditions where temperature cycling is not required. When compared with PCR it is considered to be lower-cost, more specific, and produces greater yields of DNA product.
Mitochondrial DNA (mtDNA): circular DNA, located in the matrix of mitochondria, coding for transfer RNA and enzyme subunits. Maternal inheritance and high mutation rates mean that genomic sequencing of mtDNA is useful for population genetics and phylogenetic studies.
Neuroaffinity: the affinity of a pathogen for the brain or other parts of the nervous system.
Paratenic hosts: hosts in which parasites are unable to complete development to adult stages but may serve to bridge an ecological or trophic gap in the parasite's life cycle by passing infection on to definitive hosts that ingest them.
Prevalence: the number of hosts infected with one or more individuals of a particular parasite species divided by the number of hosts examined for that parasite species.
***Toxocara* excretory–secretory (TES):** a secretory–excretory *Toxocara* larval antigen commonly used in diagnostic tests for detection of *Toxocara* antibodies. It can also be used for other purposes, such as inducing immune responses for study in model organisms.
Toxocariasis: the disease in humans caused by infection with *Toxocara* species. Clinical syndromes are caused by larval migration through body tissues

differences in the biology of the two *Toxocara* species for disease epidemiology and control are largely unexplored.

The present article revisits the dominance of *T. canis* in the scientific literature on toxocariasis, and questions its basis. It goes on to consider approaches and tools commonly used to study *T. cati* epidemiology, and discusses the implications of biological and contextual differences between *T. cati* and *T. canis* for the epidemiology and control of toxocariasis. The article concludes by highlighting important research gaps. The unique features of *T. cati* clearly demand that greater attention be given to this species in its own right, and not just as an understudy to *T. canis*.

causing damage to a wide variety of tissues, including the eyes, leading to blindness (ocular larva migrans, OLM), brain (neurotoxocariasis, NT) and other organs such as lungs, skin, liver, spleen, kidney, and heart (visceral larva migrans, VLM). Covert toxocariasis (CT) includes nonspecific symptoms, developmental delays, and asthma.

Transplacental: prenatal transmission of infective parasite stages across the placenta to offspring.

Transmammary: postnatal transmission of infective parasite stages through lactation to offspring.

Vertical transmission: transmission of a pathogen from mother to offspring either *in utero* (transplacental) or after birth in, for example, breast milk (transmammary).

Zoonotic: the ability of an infectious agent found in animals to infect humans, causing zoonotic disease.

Specificity might change perceptions

Assumptions about the relative roles of *T. canis* and *T. cati* in zoonotic disease are based on limited data. There are fewer reported cases of confirmed *T. cati* human infection than *T. canis* infection [2]; however, the study of toxocariasis has been inhibited by a lack of ability or requirement by health agencies to conduct species-specific serological analysis. A striking example of this is in the UK, where 94% of the 762 human toxocariasis cases reported over three decades were not diagnosed to species level [14]. Many immunodiagnostic tests utilise antigens from *T. canis*, and positive results are consequently assumed to be caused by that species, despite demonstrated **cross-reactivity** with *T. cati* (Box 1). As a result, there is generally no attempt to eliminate *T. cati* from the diagnosis, so the proportion of toxocariasis cases involving *T. cati* is unknown.

In faecal sample studies, the host of origin should not determine the *Toxocara* species by default, nor even indicate patent infection, since 'spurious' *T. cati* eggs can be shed by dogs. For example, 32% of eggs in dog faeces were identified to be *T. cati*, likely to be an outcome of coprophagia, leading to false-positive results [19,20]. As a consequence, assumptions about infection based on the host alone can lead to inaccurate estimates of **prevalence**.

The problem of limited specificity extends to environmental surveys of eggs, and larvae recovered from biological tissues, which usually do not distinguish between *T. canis* and *T. cati*, or at least not reliably. The validity problems associated with commonly used diagnostic techniques to determine aetiology raises concerns that *T. canis* can be misdiagnosed as *T. cati* and vice versa. In addition, risk factors are commonly inferred from nonspecific *Toxocara* spp. data, but then ascribed uncritically to *T. canis*, as the de facto accepted major cause.

As genetic diversity among *Toxocara* spp. is explored, including the recognition of new species of unknown zoonotic potential such as *T. malaysiensis* [21], test specificity will become increasingly relevant for targeted and successful public health interventions. Furthermore, standardisation of tests used across different laboratories for all forms of sample examination will enable better comparisons between future studies. Continued development of species-specific diagnostic tools that are affordable, reliable, and uniform is fundamental to help disentangle and better understand the relative significance of zoonotic species of *Toxocara*, to either challenge or substantiate assumptions about the relative importance of *T. cati* from an epidemiological standpoint.

Life history divergence affects transmission risk and pathogenesis

There are important differences in the biology of *T. canis* and *T. cati* that affect how the parasite cycles between hosts, and the effect of infection on the hosts, which require further investigation (Figure 2, Key figure).

Box 1. Test specificity limits knowledge of *T. cati* epidemiology

Egg morphology

When examining microscopic stages of the parasite, the use of morphology, such as egg size, is not reliable without molecular underpinning [64]. Smaller size and coarser surface pitting of *T. cati* eggs is a commonly applied descriptor to differentiate from *T. canis* eggs; however, the use of light microscopy, and even electron microscopy cannot reliably distinguish between the two species using eggs from environmental samples [64]. This should lead us to question the reliability of research publications that identify the species of *Toxocara* from environmental samples solely using egg morphology.

Larval morphology

Measuring the diameter of larvae within tissue biopsies to confirm infection, and also identify to species level [65], depends on a representative tissue section where larvae are present, intact, and orientated suitably [66]. Furthermore, the age of the larvae and the host immune response to the parasite will result in further size heterogeneity. Therefore, the use of larval morphology to distinguish between species is vulnerable to misinterpretation and should be treated with caution.

Imaging

Diagnostic imaging is a noninvasive alternative to biopsy for detection of *Toxocara*-related lesions. Ultrasound (US), computerised tomography (CT), positron emission tomography (PET), and magnetic resonance imaging (MRI) have been used to image symptomatic or subclinical human toxocariasis in various organs; however, the resolution is not great enough to differentiate between species of *Toxocara* and any results should be supplemented with species-specific molecular testing [67].

Serology

Immunodiagnostic tests are routinely used to diagnose human toxocariasis, such as **enzyme-linked immunosorbent assay (ELISA)** and Western blotting to detect anti-*Toxocara* IgG antibodies in host sera and ***Toxocara* excretory–secretory (TES)** molecules in definitive host faeces/sera. Serology is more sensitive than egg flotation when used to study definitive hosts [68]. However, immunoassays demonstrate cross-reactivity between *T. canis* and *T. cati*, and also potentially with other species of helminth due to homology between TES antigens [68–70]. Progress in improving test specificity is ongoing, for example, development of *T. cati* recombinant TES protein [71]. ELISAs and Western blots that use *T. cati* TES antigen instead of *T. canis* TES are found to work with greater sensitivity in some cases, suggesting that *T. cati* infections can be missed if only using *T. canis*-diagnostic reagents, leading to underestimation of seroprevalence in past data [72].

Molecular tests

Tools with potential for greater diagnostic specificity, for example, using nucleic acid amplification [such as polymerase chain reaction (PCR) and **loop-mediated isothermal amplification (LAMP)**] to enable testing of *Toxocara* samples to species level have emerged in the last two decades [73–76]. To date, *T. canis* is the only *Toxocara* species to have a draft genome sequenced [14], although the **mitochondrial DNA (mtDNA)** genome of *T. cati*, *T. canis*, and *T. malaysiensis* have been sequenced alongside nuclear ribosomal DNA (**ITS-1** and **ITS-2**) for *T. canis*, *T. cati*, and *T. vitulorum*, enabling clarification of phylogenetic relationships between *Toxocara* species and improved specificity of diagnostic tests [21,77]. These are not yet consistently applied in human toxocariasis research but they are being successfully used to identify the parasite to species level in animal studies [56,78]. However, there are reported discrepancies in identification when using some widely used 'validated' primers [79]; therefore, there remains a requirement for confirmatory sequencing. Continued exploration of genomic data is needed to identify more robust molecular markers for use in tests to ensure validity of results and therefore a more complete understanding of the parasite life cycle and distribution.

Infection intensity

Most studies of definitive host infections are based on faecal examination rather than adult worm counts, for example, 83% (n = 149) of cat prevalence studies examined only eggs in faecal samples [22]. Information on egg shedding must be combined with adult worm density to draw conclusions about infection intensity for each parasite; however, worm burden data are scarce and incomplete. Existing studies draw variable conclusions due to the fact that worm burden is heavily context-dependent. One survey of stray animals in Ireland found differences in burden depending on the *Toxocara* species, where on average dogs had a heavier worm burden (16.25 per animal) than cats (2.77) [23]. Other studies are restricted to either dogs or cats, preventing comparisons between the two *Toxocara* species; for example, in adult cats in Iran, an average of ten adult worms were recovered from the intestines [24], and in Australia an average of just two adult worms per adult dog were observed [25]. To our knowledge there are no data on kittens to

Key figure

Key comparisons in parasite biology for *Toxocara cati* and *Toxocara canis*

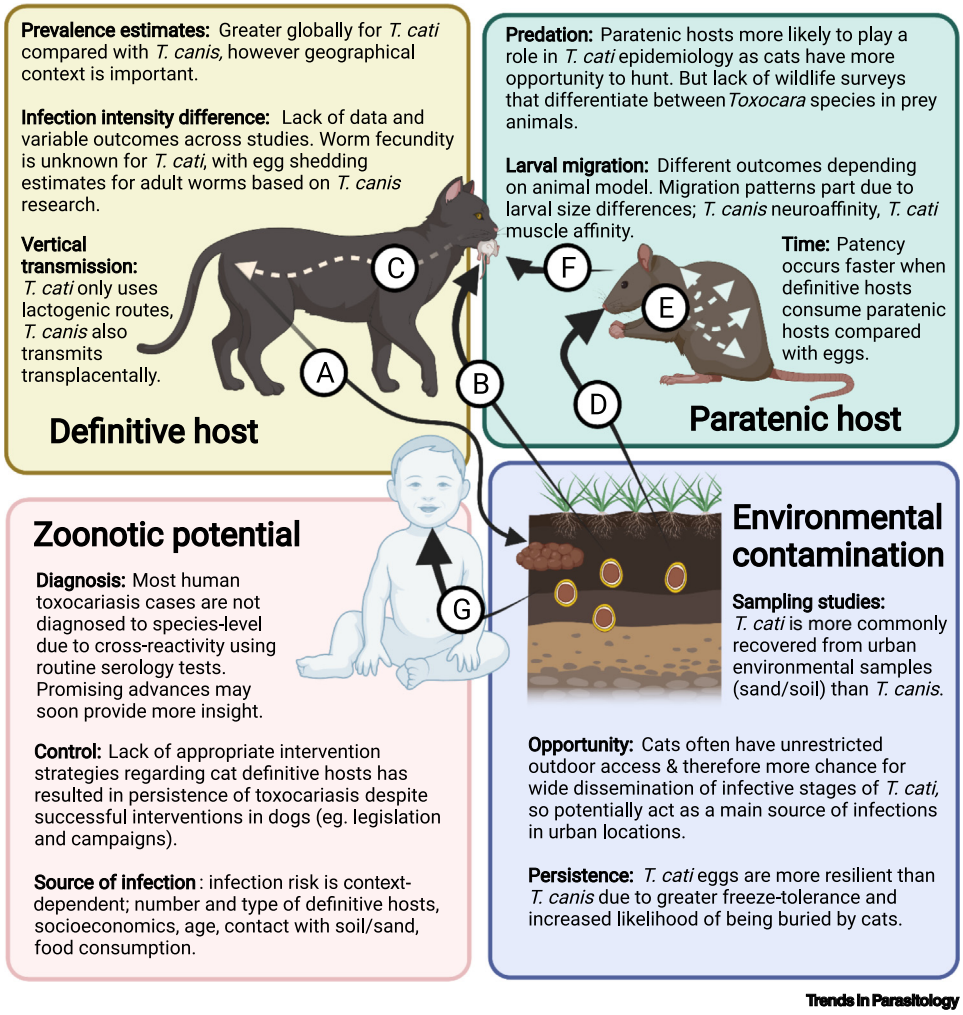

Figure 2. Differences and knowledge gaps between the two zoonotic species of *Toxocara* include prepatent period following different infection routes, importance of somatic larval arrest and vertical transmission, varying routes of migration depending on route of infection, egg shedding, contrasting larval behaviour of *Toxocara* species in paratenic hosts. Arrows denote a basic life cycle. (A) *Toxocara* eggs are produced by adult worms in the intestines of the definitive host and shed into the environment within faeces. (B) Under favourable conditions, eggs become larvated and can infect definitive hosts through oral contact with soil, for example, during grooming. (C) Eggs hatch in the gastrointestinal tract, and larvae typically migrate through the liver, heart, and lungs, eventually returning to the intestines as mature adults. (D) Eggs in the environment can also be consumed by other animals (paratenic hosts) such as wild rodents. (E) Larvae migrate from the intestines to various organs, including the brain and muscle, but do not mature into adults. (F) During a predation event, infective larvae may be consumed by the definitive host whilst within the tissues of the paratenic host. Once inside the definitive host development recommences to maturity. (G) If humans consume infective eggs from the environment, or larvae within food animals, larvae will migrate through body tissues causing damage leading to a range of toxocariasis syndromes. Figure created with BioRender.com.

compare with pups, in which worm burdens can be higher, averaging 100 [25]. There is a need for meta-analysis of existing worm burden data and collection of new data to better understand the differences in typical worm burden and fecundity between *T. cati* and *T. canis*, drivers of infection intensity, and implications of this for disease risk and control.

Larval migration

In contrast to canids, in which both **transplacental** and **transmammary** migration of larvae from infected bitches into pups has been observed, prenatal infection in kittens has not been demonstrated [26]. **Vertical transmission** from dam to kittens, however, can still occur lactogenically [26]. Different transmission routes in definitive hosts will influence the success of control strategies, and hence their optimal design, for example, the age of first deworming to eliminate egg output.

In paratenic host tissues, *T. cati* has been found to migrate more slowly than *T. canis*, perhaps due to spatial restrictions related to larger larval body diameter than *T. canis* [27]. Tissue predilection sites also vary; for example, *T. cati* has been shown to more commonly reside in muscle tissue in rats [28], with *T. canis* showing instead greater **neuroaffinity** in mice [29]. Differences in parasite distribution in paratenic hosts should provoke discussion about variable pathogenesis and challenge concepts of parasite-mediated manipulation of host behaviour [30]. For example, *T. canis*-infected mice exhibit more neurological and motor dysfunction, whereas *T. cati*-infected mice show delayed and less severe neurological alterations and instead exhibit reduced fear- and flight-associated behaviour and increased grooming behaviour [31].

Pathogenesis

A large number of *in vitro* studies have tested how *T. canis* infects different animal species [10]; however, there are fewer studies exploring *T. cati* infection [32–34]. Pathogenesis varies depending on the animal model selected, *Toxocara* species involved, and infection dosage. For example, Mongolian gerbils (*Meriones unguiculatus*) have been demonstrated to be more prone to ophthalmic pathology following experimental *Toxocara* spp. infection [35] than are macaques (*Macaca fascicularis*) [36]. Signs of ataxia in Mongolian gerbils, meanwhile, appeared less commonly but more quickly when infected with *T. canis* (50 days postinfection, 49% incidence) compared with *T. cati* (120 days postinfection, 71% incidence) [35], while ophthalmic haemorrhages caused by *T. cati* were less severe and less common (63%, $n = 8$) when compared to gerbils infected with *T. canis* (83%, $n = 57$) [34], implying that, in this rodent host, *T. cati* infection is more benign compared to infection by *T. canis*.

The strong influence of host species on observed disease should limit extrapolation. It is tempting to use differences in the pathological consequences in rodent models experimentally infected with *T. canis* or *T. cati* to surmise different health outcomes in people infected with each species. The fact that both species cause disease in animal models, and pathogenesis consistent with manifestations of human toxocariasis, suggests that an open mind should be kept on the ability of *T. cati* to cause significant disease in humans. However, in animal models, laboratory-derived infections tend to be high-dosage, sometimes of thousands of eggs [37], achieving infection challenge that is unrealistic under natural conditions. Extrapolation to consequences for paratenic and accidental hosts in nature, including humans, should consequently be cautious.

Contextual factors influence zoonotic transmission risk from cats

In definitive hosts, *T. cati* is estimated to have a greater global prevalence than *T. canis* (17% and 11.1% respectively) [22,38]. Comparisons between the epidemiology of *T. cati* and *T. canis* are interesting and can be useful; however, there is an unhelpful inclination to rush to conclusions

over which of the two zoonotic *Toxocara* species is the most important for public health. This is too complex a question to answer by merely comparing prevalence studies in different geographical areas or merging global data, and will not help to gain effective control of *T. cati* (or *T. canis*) in a zoonotic context.

Relative populations of stray, owned, and wild felids and canids vary geographically, limiting the generality of conclusions from local studies. For example, pet dogs are more popular than cats in South America [39] – with the reverse elsewhere, such as in Western Europe and the Middle East [40]. In areas where dogs are less common, human toxocariasis still exists [3], implicating *T. cati* at least in those locations. To improve this situation, greater consideration needs to be given to contextual epidemiology to better establish where infection risk is greater for each of the two parasites, in what way, and how control can be adapted for greater success.

Cat toileting behaviour and environmental contamination

Domestic cats behave very differently to dogs. Outdoor access is often unrestricted in pet cats, with an estimated 59% of cats worldwide having outdoor access [41]. Cats defecate widely and bury faeces, often in places used by humans such as vegetable patches, gardens, and sandpits. When an infected cat sheds *Toxocara* eggs in faeces these locations become foci of contamination, wherein accidental transmission can occur. Eggs of *T. cati* have been demonstrated to have a higher tolerance to freezing than those of *T. canis* [42], and the burying of faeces can further protect *T. cati* eggs from desiccation and adverse weather conditions; this prolongs longevity and therefore increases the timeframe for transmission when compared with *T. canis* eggs, as dog faeces are less likely to be buried and are usually collected by owners [43].

Mounting evidence from soil contamination studies indicates that cats may act as the main reservoir for dissemination of *Toxocara* eggs in urban locations, with spaces used by humans more likely to be contaminated with *T. cati* than *T. canis* eggs [44,45]. Modelling indicates that, in urban areas in The Netherlands, where there are few stray dogs, up to 81% of *Toxocara* egg output is contributed by cats [46], while a recent study in New York found 29.6% of playgrounds in New York City were contaminated with *T. cati* as the predominant parasite [47]. Given that *T. cati* eggs are actually less easily recovered from soil samples than those of *T. canis* [48], these results suggest widespread soil contamination with *T. cati*, in areas used intensively by people, presenting substantial zoonotic infection risk. Human cases of toxocariasis in the UK dipped following interventions focusing on dog fouling in public places, for example, campaign work and introduction of legislation, but these measures were not extended to cats, nor could they realistically be. Since then, cases of toxocariasis remain stubbornly constant [14]. High levels of infection in cats and limited interventions, particularly in urban areas with high numbers of stray cats, could be part of the reason, although the role of urban foxes also needs consideration in areas where they are found in high densities. Better shaping of epidemiological data to the specific context will help to develop targeted intervention to more effectively reduce the global disease burden.

Models have been proposed to calculate the contributions of different populations of hosts to *Toxocara* egg contamination, which vary by context, for example, with owned dogs implicated as numerically more important contributors of eggs to urban areas in the UK [49] and stray cats in The Netherlands [50]. This approach offers great potential as a tool for the development of effective control measures for *Toxocara,* including through intervention scenario analysis, as conclusions depend on contextual factors such as urbanisation, host density and type (owned, stray, wild), definitive host infection prevalence and intensity, management of dog fouling, and use of anthelmintics. However, data for many of these variables are more available for *T. canis*

than for *T. cati*, and the knowledge gaps relating to *T. cati* – such as prevalence in paratenic hosts, species-specific diagnostics, and parasite fecundity – currently limit the attainable complexity and power of these models.

Cat predation behaviour and paratenesis

The life cycle of *T. cati* is more likely to include paratenic hosts than that of *T. canis* as uncontrolled predatory activity supports reinfection of adults, and owned domestic cats are more likely to eat wild animals than are owned domestic dogs, and consequently to become infected by paratenesis. This might explain higher infection prevalence in cats [51]. Vertical transmission in mice infected with *T. cati* has been demonstrated to occur and would further support the persistence of the parasite in a rodent population [11,52]. Use of paratenic hosts by parasites infecting carnivorous definitive hosts carries an evolutionary advantage as it facilitates life cycle completion, including in hosts with functional age resistance, as larvae ingested within paratenic hosts bypass hepatotracheal migration [10]. This bypass also results in a quicker infection with reduced lung pathology in the cat definitive host compared to infection with infective eggs [10]. A shorter prepatent period suggests that worming frequency ought to be increased to eliminate egg shedding where infections are likely derived through predatory behaviour.

There is limited primary research into *Toxocara* paratenesis; general surveys of endoparasites of wild animals such as rodents often overlook *Toxocara* spp. infection, perhaps because adult stages are not present in body tissues and the parasite is not detectable in faeces. Some studies have attempted to assess prevalence in captured free-living animals in a variety of European countries [53–57]; however, the vast majority do not distinguish between *T. cati* and *T. canis*. Only one ecological study to date has used molecular techniques to report species-specific data in wild paratenic hosts; it found that 1.6% of rodents sampled were infected with *T. cati* and 3.1% with *T. canis* [56]. Further research is required to explore the likelihood that infected wildlife actually forms part of a natural food chain for felids or canids through predation, and in addition assess the theoretical risk that comes with owners feeding infected raw meat diets to dogs and cats [58]. Surveillance of wild paratenic hosts could be useful to evaluate the impact of definitive host interventions on infection reservoirs [59].

Cat management

Anthelmintics are used in cats, but often inadequately; one study found that only 24.5% of cats received treatment at the recommended frequency [60]. In Europe, most pet cats were reported to fall into the high-risk category for *Toxocara* infection by virtue of outdoor access but were treated on average only twice per year, a frequency grossly insufficient to eliminate egg shedding [61]. Being able to identify cats that are more likely to shed eggs, based on modelling of risk factors, will help to target *T. cati* control measures more effectively. The factors influencing pet owner decisions on deworming of cats have barely been investigated, in contrast to more involved studies on dogs [62]. It appears that most cat owners consider the health of their pets a stronger motivator of anthelmintic treatment than public health considerations. Owner decisions relating to outdoor access of cats are generally based on conservation efforts to curtail predatory behaviour, or in response to safety concerns, rather than considering parasite transmission risk [63]. Outdoor access of pet cats, alongside low treatment frequency and consequent high prevalence of egg shedding, is liable to fuel high zoonotic infection pressure with *T. cati*. Low awareness among pet owners of the potential public health risks from *Toxocara* infection in cats, and the poor applicability to cats of interventions targeted at dogs, such as antifouling measures, mean that zoonotic toxocariasis from cats has barely been addressed in practical terms. Greater efforts are appropriate in light of the current evidence base and could bring rapid benefits.

Concluding remarks

Scientific research into *T. cati* has been woefully neglected when compared to that into *T. canis*. Gaps in our knowledge about *T. cati* are often filled by extrapolation from *T. canis*, which is often inappropriate as there are large differences between the two parasites in terms of life history and epidemiological context. Recognition of toxocariasis as an important zoonotic disease continues to increase; therefore, it is important to ensure that research is conducted reliably, contextually, and without bias of effort towards one parasite or the other until a better understanding is developed. There are still many gaps in knowledge of the basic biology and epidemiology of *Toxocara* spp., some of which have been discussed in this paper (see Outstanding questions). It is hoped that many of these gaps can be addressed through future development of improved diagnostic techniques and modelling, with the aim of clarifying the zoonotic impact of *T. cati* and its unique epidemiological characteristics.

Outstanding questions

What life history differences exist for different *Toxocara* species – such as adult worm lifespan, egg production, patency, and infection intensity?

How specific is *Toxocara* to its definitive host taxonomic families, how does the presence of incorrectly diagnosed 'spurious' eggs influence prevalence data, and how do closely related parasites interact during concurrent or subsequent events in different hosts?

What is the relative contribution of different subgroups of definitive feline hosts (owned, feral, wild; and by age and sex) to environmental contamination?

To what extent does wildlife act as a disease reservoir for each *Toxocara* parasite, what is the infection risk associated with predation behaviour by domestic and wild definitive hosts, and does infection by *Toxocara* affect the behaviour of wild paratenic hosts in the same way as demonstrated in laboratory animal models?

What is the biological significance of differences in larval migration patterns depending on the *Toxocara* species, host species, and route of infection (eggs or infected tissue)?

How can we better apply diagnostic techniques to determine the species-specific aetiology of human toxocariasis across different human populations, and are there pathological differences in human toxocariasis depending on species of *Toxocara* infection?

What is the public health relevance of emerging cryptic species, such as *T. malaysiensis*, which is similar in terms of genetics and lifecycle – does it need consideration in geographical areas where it is detected? Will other zoonotic strains emerge with increased genome scrutiny?

Does epidemiology of these two parasite species vary depending on definitive host distribution and geographical context, and how can this be applied more productively using animal management, medicine, education, and policy instruments, to reduce infection reservoirs?

Declaration of interests

The authors declare no competing interests.

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