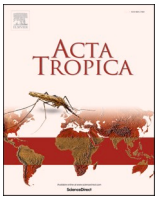
Acta Tropica 249 (2024) 107049

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica



Prevalence of zoonotic (brugian) filariasis in Asia: A proportional meta-analysis

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ARTICLE INFO

Keywords:
Zoonotic filariasis
Brugian filariasis
Prevalence
Meta-analysis

ABSTRACT

Lymphatic filariasis is a public health problem and targeted for global elimination. WHO recommends mass drug administration to interrupt transmission of the parasites involved. There are concerns that transmission interruption may be difficult in areas of zoonotic filarial infections. This study aimed to estimate the pooled prevalence of zoonotic brugian filariasis, and to compare the pooled prevalence of brugian filariasis in human and animal populations in the same area based on available studies. A comprehensive literature search was conducted in health-related electronic databases (PubMed, Ovid MEDLINE, Index Medicus, google scholar). A random-effect meta-analysis of the pooled overall prevalence of filariasis in animal populations was conducted. Sixteen studies from four different Asian countries were identified. Studies were conducted most frequently in Thailand ($n = 7$), followed by Malaysia ($n = 5$), India ($n = 3$), and Sri Lanka ($n = 1$). Regardless of animal group, the pooled overall prevalence of animal *Brugia* infections was 13% (95%CI: 7–21%, I^2:98%, 16 studies). On stratification, the pooled overall prevalence in the animal population was 19% (95%CI: 1–50%, I^2: 99%, 3 studies) in India, 8% (95%CI: 2–7%, I^2: 97%, 5 studies) in Malaysia, and 13% (95%CI: 7–20%, I^2: 94%, 7 studies) in Thailand. The prevalence in the animal population was 17% (95%CI: 13–21%, 1 study) in Sri Lanka. The pooled overall prevalence of *Brugia malayi* was 13% (95%CI: 7–21%, I^2:98%, 12 studies), while for *Brugia pahangi* this was 12% (95%CI: 7–19%, I^2:86%, 7 studies). Regardless of animal group, geographic area, or diagnostic test, the prevalence of *B. malayi* was consistently high. On stratification by animal category, the pooled overall prevalence was 10% (95%CI: 6–14%, I^2:92%, 13 studies) in cats, 12% (95%CI: 2–28%, I^2: 99%, 6 studies) in dogs, and 55% (95%CI: 47–63%, 1 study) in leaf-eating monkeys. The findings show the extent of zoonotic *Brugia*infections in domestic cats and dogs, suggesting that these animals are potential reservoirs for human brugian filariasis in the study countries. To substantiate this with more accuracy, future well designed whole genomic sequencing of individual mf collected from humans and *B. malayi* infected animals in the same area are needed.

1. Introduction

Neglected tropical diseases (NTD) in humans can be a threat that arises in domestic and wild animals, often called neglected zoonotic tropical diseases (NZTD), which can then serve as reservoirs for certain zoonotic parasitic infections, including lymphatic filariasis (LF) (WHO, 2015; Laing et al., 2021). LF is a neglected tropical disease in humans caused by the infection with three species of nematode parasites, *Wuchereria bancrofti, Brugia malayi and Brugia timori,* (Nutman and Kazura, 2011). Globally, 51.4 million people are estimated to be infected with LF (WHO, 2021).

Epidemiological studies had reported that B. malayi and other closely related species are found in several species of animals. *B. malayi* is the most prevalent form with interhuman transmission (WHO, 1984) and this filaria parasite can also infect felid animals (Areekit et al., 2009). Canine filariasis is caused by several filarial parasites including *B. pahangi, B. malayi*, amongst others (Irwin, 2002). Subperiodic *B. malayi* and *B. pahangi* have been found in leaf monkeys, slow loris, domestic dogs, cats and some wild carnivores (Dissanaike, 1979). In contrast to the periodic brugian filariasis, in previously endemic areas,

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https://doi.org/10.1016/j.actatropica.2023.107049
Received 28 August 2023; Received in revised form 18 October 2023; Accepted 19 October 2023
Available online 20 October 2023

the re-emergent strain is subperiodic, thus suggesting a zoonotic origin (Mallawarachchi et al., 2018a). Dogs and cats are usually asymptomatic but can demonstrate clinical symptoms of infection similar to human manifestations including lymphadenopathy and limb oedema but rarely and often undetected and of minimum veterinary clinical concern (Snowden and Hammerberg, 1989). Similarly in laboratory studies *Presbytis entellus* (Indian leaf monkeys) were found to be either asymptomatic or cold exhibit limb oedema and occasionally scrotal hydrocoele (Murthy et al., al.,1999).

B. pahangi, a closely related species of *B. malayi*, is a filarial worm of mammals, but essentially of domestic cats and dogs (Denham and McGreevy., 1977; Muslim et al., 2013). Species such as the sub-periodic strain of *B. malayi* and perhaps also *B. pahangi* that are primarily parasites of other vertebrates can also infect humans. These two species are found in wild and domestic animals and monkeys (Dissanaike, 1979).

In 2000, the Global Programme to Eliminate Lymphatic Filariasis (GPELF) was launched to eliminate the disease as a public health problem by 2020 (Laing et al., 2021; Nutman and Kazura, 2011). To assess the impact of GPELF, it is necessary to measure the reduction in the burden of LF and the risk of acquiring infection amongst people residing in endemic areas (Ramaiah and Ottesen, 2014). In addition to *B. malayi* in human hosts, zoonotic *Brugia* filariae involving cats and/or dogs have been reported in India (Ambily et al., 2011), Malaysia (Mak et al., 1984), Sri Lanka (Mallawarachchi et al., 2018a), and Thailand (Nuchprayoon et al., 2006). WHO has reported that in subperiodic *B. malayi* endemic areas, an increase in microfilaria (mf) rate in humans was accompanied by corresponding increase rate in cats (WHO, 1992). In 1962, Edeson warned that existence of an animal reservoir of infection might have important implications for filariasis control (Edeson, 1962). Within the NTD community, there has been a growing recognition of the importance of animal and environmental controls in the epidemiology and control of many NTDs (WHO, 2021). As such, NZTDs such as LF should be addressed in an integrated "One Health" approach to control since they all have potential animal reservoirs (Molia et al., 2021).

There are individual studies on the prevalence of *Brugia* infection in animal species. These individual studies vary in study areas, confirmation methods and sample sizes. As individual studies are subject to bias, pooling of studies that follow specified pre-set criteria regarding content and quality may result in more reliable conclusions (Ioannidis and Lau, 1998). Several systematic reviews have addressed the prevalence of human LF in a particular region (Dickson et al., 2017). However, systematic reviews that address the prevalence of *Brugia* infection in animal species in LF endemic countries are limited. Understanding the prevalence of filariasis in the animal population is important to determine their potential reservoir status. Moreover, it can provide information useful for the formulation of better control strategies. Taken together, a research question was *"What are the prevalence of zoonotic filariasis in the Asian countries*". To answer this question. a meta-analysis was performed with two objectives; to estimate the pooled prevalence of zoonotic filariasis, and to compare the prevalence of filariasis in both human and animal populations in the same study region based on available studies. This review is intended to inform public health authorities and health policy-makers of the importance of this neglected zoonotic filariasis as they seek to reach the elimination of LF.

2. Materials and methods

In conducting this review, we followed the PRISMA 2020 statement (Page et al., 2021) (Supplementary Table 1). The protocol is available on reasonable request from the corresponding author. This study solely used published data, and therefore the need for consent from participants was waived by the Institutional Ethics Review Committee.

2.1. Search strategy

Relevant studies were searched in the health-related electronic databases of PubMed, Ovid MEDLINE, Ovid Embase, Index Medicus, Google Scholar and African online journals. The search terms included brugian, *Brugia malayi, Brugia timori, Brugia pahangi*, and microfilariae. The search was limited to English language publications between 1 January 1975 and 27 June 2023. The search strategy used in PubMed is provided in Supplementary Table 2.

2.2. Eligibility criteria

Studies were included, if they

(a) were conducted in the Asia region;
(b) assessed filariasis in animal population, regardless of category (e.g., dogs, cats, monkeys, domestic, wild, stray), and method of diagnosis (e.g., thick blood film, TBF, PCR);
(c) reported prevalence (proportion) of filariasis in animal populations;
(d) provided data for both numerator and denominator populations of the tested group. and
(e) conducted studies with naturally infected animals.

Additionally, studies were considered, if they simultaneously examined the prevalence of filariasis in humans and in animal populations in the study area.

Studies that did not meet the inclusion criteria were excluded. Hence, studies with experimentally infected animals, diagnostic test accuracy studies, drug efficacy studies, or reviews were excluded.

2.3. Selection process and data collection

Two investigators (CN, WST) independently employed title and abstract screening of articles retrieved from the databases. Full-text articles deemed potentially relevant were checked to make final decision regarding eligibility. Any differences between the two investigators were settled by reaching a consensus. One investigator (CN) collected data using a pre-tested data extraction sheet from the eligible studies. This was cross-checked by another investigator (HHA). The following data were collected: study author, study country, study design, prevalence (numerator and denominator), study population (animals, humans), type of animals, and diagnostic methods.

The quality of the eligible studies was not rated due to a shortage of recommended tool for animal studies. The existing tool, the Systematic Review Centre for Laboratory Animal Experimentation (SYRCLE), only provides a risk of bias tool for animal intervention studies (Hooijmans et al., 2014), and it is not relevant for animal prevalence studies.

2.4. Data analysis

A proportion meta-analysis was performed as describe elsewhere (Barker et al., 2021). This analysis provides a single summary estimate along with its variance of the prevalence of a condition across the included studies. The prevalence of *Brugia* infections was expressed as the proportion/percentage of study participants with *Brugia* infections. For each study, the prevalence of *Brugia* infection in animal species was computed as the number of *Brugia* positive cases divided by the total number tested. On stratification, species-specific prevalence (e.g., *B.* malayi, *B. pahangi*), animal-specific prevalence, and diagnostic-specific prevalence were calculated. For pooled prevalence, we used the random effects model of DerSimonian and Laird method (DerSimonian and Laird, 1986), after Freeman-Tukey double arcsine transformation for normalization of variance (Nyaga et al., 2014). Since there are no specific tests to assess heterogeneity in proportional meta-analysis (Barker et al., 2021), the commonly applied I^2 value for heterogeneity

across studies was used, and the value of >75% indicates substantial heterogeneity (Higgins and Green, 2011). The pooled overall prevalence of *Brugia* infection and the subgroup-specific pooled prevalence were estimated, as described elsewhere (Nyaga et al., 2014; Barker et al., 2021), publication bias was not investigated. There is a shortcoming with Egger's tests and conventional funnel plots for assessing publication bias for proportional meta-analysis (Barker et al., 2021).

Data analysis was done with the *metaprop* command in STATA software (version 15) (Txt, USA).

3. Results

The search in the electronic databases yielded 398 citations. Additionally, two studies were obtained through a manual search of the reference lists of eligible studies. After the screening of the titles and abstracts and removal of 37 duplicates, 48 full-text papers were reviewed. Of them, a final of 16 studies that contained relevant data were identified for this review (Fig. 1). A summary of 32 excluded studies is provided in Supplementary Table 3.

3.1. Characteristics of the studies identified

In the 16 studies included, 14 were exclusively animal studies (Al-Abd et al., 2015; Ambily et al., 2011; Nuchprayoon et al., 2006; Chirayath et al., 2017; Mak et al., 1980, 1982; Mallawarachchi et al., 2018b; Phuakrod et al., 2019; Ravindran et al., 2014; Rawangchue et al., 2022; Tan et al., 2011; Yotmek et al., 2015; Wongkamchai et al., 2013. Wongkamchai et al., 2014), and two studies included both human and animal populations (Chansiri et al., 2002; Mak et al., al.,1977). Table 1 presents characteristics of the included studies. Twelve, five and one studies were carried out with cats, dogs and monkeys, respectively. In the case of monkeys, the meta-analysis could not be performed because there was only one study assessing this population. The studies identified were published between 1977 and 2022 across four countries in the Asian region. The most frequent studies were done in Thailand (7/16, 44%), followed by Malaysia (5/16, 31%), India (3/16, 19%), and Sri Lanka (1/16, 6%). Diagnostic methods used in these 16 studies were thick blood film (TBF) and/or PCR.

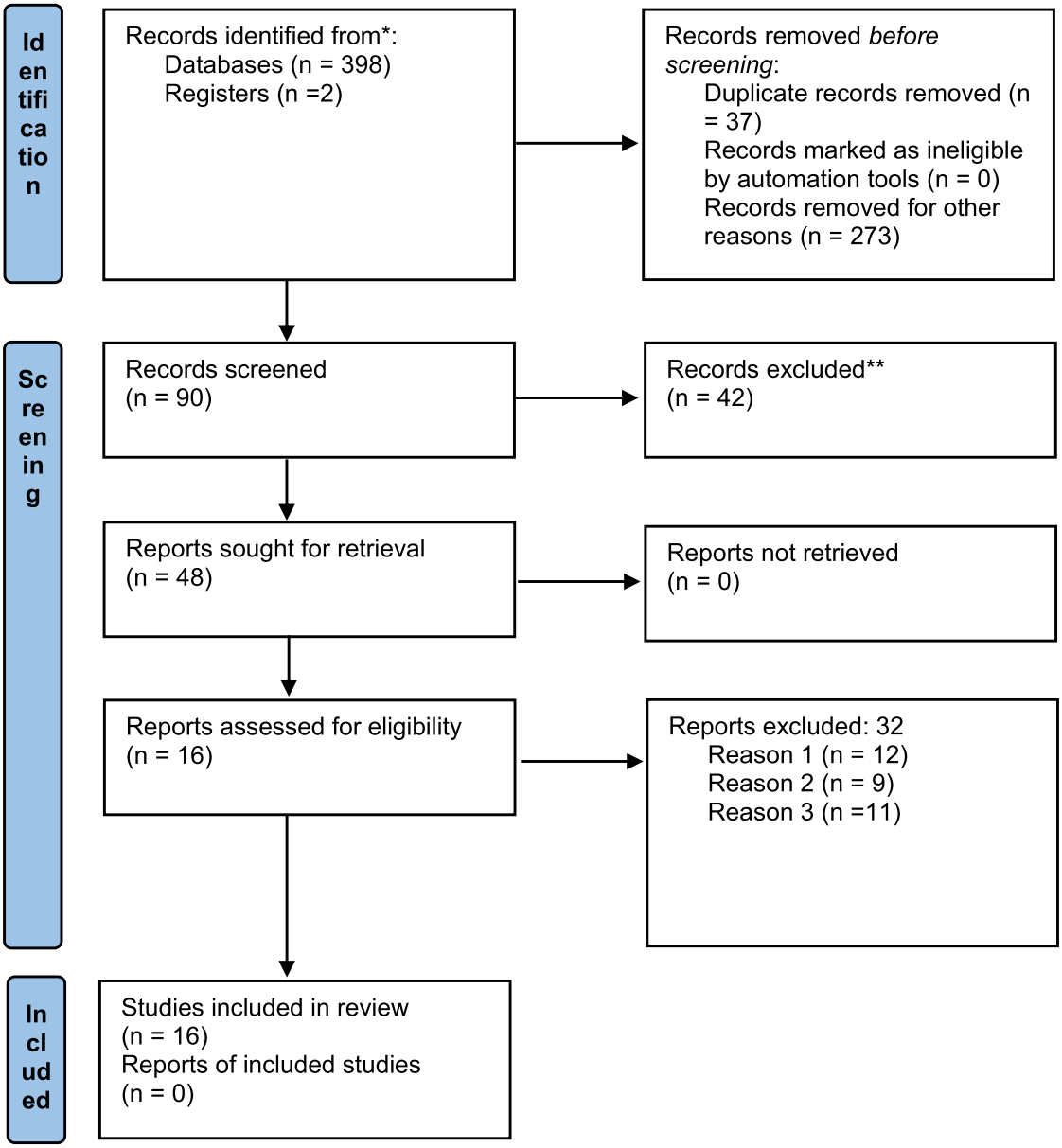

Fig. 1. Study selection process.

Table 1
Characteristics of the studies included.

No.	Study, yr	Ref no.	Country	Participants	Study type	Samples	Age (range)	Outcome measure	Species	Method
1	Al-Abd et al. (2015)	29	Malaysia	cats	survey	170	NA	mf	BM; BP	TBS
2	Ambily et al. (2011)	15	India	dogs	survey	100	>6m	mf	BM	TBS
3	Chansiri et al. (2002)	30	Thailand	Humans & cats	survey	316 (H) 53(cats)	NA	mf	BM	PCR
4	Chirayath et al. (2017)	31	India	dogs	survey	1600	>6m	mf	BM	PCR
5	Mak et al. (1977)	32	Malaysia	Humans & cats	survey	850 (H); 61(cats)	17–40	mf; MBD	BM	NBS
6	Mak et al. (1980)	33	Malaysia	cats & dogs	survey	447(cats); 68 (dogs)	NA	mf	BM, BP	TBS
7	Mak et al. (1982)	34	Malaysia	monkeys, cats, dogs	survey	160(mok);30 (cats); 14 (dogs)	NA	mf	BM	TBS
8	Mallawarachchi et al. (2018)	35	Sri Lanka	dogs & cats	survey	dogs: 250; cats:134	NA	mf	BM	TBS; PCR
9	Nuchprayoon et al. (2006)	17	Thailand	cats	survey	52	NA	mf	BP	TBS
10	Phuakrod et al. (2019)	36	Thailand	cats	survey	383	NA	mf	BM	PCR
11	Ravindran et al. (2014)	37	India	dogs	survey	164	>2 (66.7%)	mf	BM, BP	histo/ PCR
12	Rawangchue et al. (2022)	38	Thailand	cats	survey	196	6m-10yr	mf	BP	PCR
13	Tan et al. (2011)	39	Malaysia	cats	survey	12	NA	mf	BP	NBS
14	Yotmek et al. (2015)	40	Thailand	cats	survey	816	1–4	mf	BM	TBS
15	Wongkamchai et al. (2013)	41	Thailand	Cats & dogs	survey	34 (cats) & 14 (dogs)	NA	mf	BM, BP	PCR
16	Wongkamchai et al. (2014)	42	Thailand	cats	survey	2039		mf	BM,& other mf	PCR

Note. BM: *Brugia malayi*; BP: *Brugia pahangi*; BT: *Brugia* timori; BRT: *Brugia* rapid test; CS: cross-sectional study; d: day; H: humans; grp: group; histo: histology; hosp: hospital- based study; IgG4: antifilarial IgG4 antibodies; MBD: morbidity; mf: prevalence of microfilariamia; m: month; md (r): median & range; mean density: mean mf density; RCT: randomized controlled trial; TBS: thick blood smears; yr.: years.

3.2. Prevalence of brugia infections in animal population (Fig. 2)

The overall pooled prevalence of animals *Brugia* infections was 13% (95% CI: 8–18%, I^2: 97%, 16 studies), regardless of animal category, geographic location, diagnostic test and species. On stratification by animal category, the pooled prevalence in cats was 10% (95% CI: 6–14%, I^2:92%, 13 studies), while it was 12% (95% CI: 2–28%, I^2: 98%, 6 studies) in dogs. The pooled prevalence was 55% (95% CI: 47–63%, 1 study) in leaf-eating monkeys. Of note, *Brugia* infections in the dog population were significantly higher than that in the cat population ($p = 0.001$).

3.3. Prevalence of animal brugia infections stratified by country (Fig. 3)

Regardless of species, the pooled prevalence in the animal population was 8% (95% CI: 2–17%, I^2: 97%, 5 studies) in Malaysia, 13% (95% CI: 7–20%, I^2: 94%, 7 studies) in Thailand, 19% (95% CI: 1–50%, I^2: 99%, 3 studies) in India, and 17% (95% CI: 13–21%, 1 study) in Sri Lanka. It should be noted that between-study heterogeneities were substantial.

3.4. Prevalence of animal brugia infections stratified by species (Fig. 4)

Across all 16 studies, the pooled prevalence with *B. malayi* was 13% (95% CI: 7–21%, I^2: 98%, 12 studies), with *B. pahangi* it was 12% (95% CI: 7–19%, I^2: 86%, 7 studies), and with a mixed *B. malayi* and *B. pahangi* it was 3% (95% CI: 2–5%, 1 study). It should be noted that substantial between-study heterogeneities also appeared in these subgroup analyses.

3.5. Prevalence of animal brugia infections stratified by confirmatory tests

On stratification by confirmatory test, PCR detected the pooled prevalence of 23% (95% CI: 8–42%, I^2:92%, 5 studies), while TBF detected 10% (95% CI: 6–16%, I^2:97%, 11 studies) (Supplementary Fig. 1). Of note, between-study heterogeneities were substantial in these analyses.

3.6. Prevalence of brugia infections in cats and dogs stratified by species

For cat populations, the pooled prevalence was 10% (95% CI:6–14%) (Fig. 5). *B. pahangi* monoinfection was 14% (95% CI: 6–24%, I^2: 90%, 6 studies), *B. malayi* monoinfection was 9% (95% CI: 5–14%, I^2: 93%, 9 studies), and mixed infection was 3%, 95% CI: 2–5%, 1 study).

Dog populations had a pooled prevalence of 12% (95% CI: 2–28%), with *B. pahangi* monoinfection of 10% (95% CI: 6–14%, I^2:0%, 2 studies) and *B. malayi* monoinfection of 14% (95% CI: 1–37%, I^2:0%, 5 studies) (Supplementary Fig. 2). *B. pahangi* monoinfections predominated in the cat population in general, whereas *B. malayi* predominated in the dog population. It should be noted that substantial between-study heterogeneities also appeared in these subgroup analyses.

3.7. Prevalence in humans and animals located in the same areas

Two studies assessed filarial infections in both humans and animals (cats) residing in the same areas (Chansiri et al., 2002; Mak et al., 1977). In cats, pooled prevalence of filarial infections 2% (95% CI: 0.0–4.0%, I^2: 0%, 2 studies), while this was 1.0% (95% CI: 0.00–2.0%, I^2:0%, 2 studies) in humans (Supplementary Fig. 3). However, there was no statistically significant difference between the prevalence of the two groups ($p = 0.092$).

4. Discussion

Based on the available data from 16 individual observational studies across four LF endemic countries of the Asian region, this review provides information on the prevalence of zoonotic *Brugia* infections.

The current findings provided information on the distribution of zoonotic *Brugia* infection. It appeared that the overall prevalence of *Brugia* infections was significantly higher in dog population than that in cat population. The semi-domestic lifestyle of cats, who spent more time indoors than outside compared to dogs might explain this difference in transmission potential. *Brugia* infections in animal population were varied between animal category, species, and confirmation methods. For instance, infections were relatively more prevalent by PCR compared to TBF. Hence, differences in prevalence of zoonotic filariasis infection

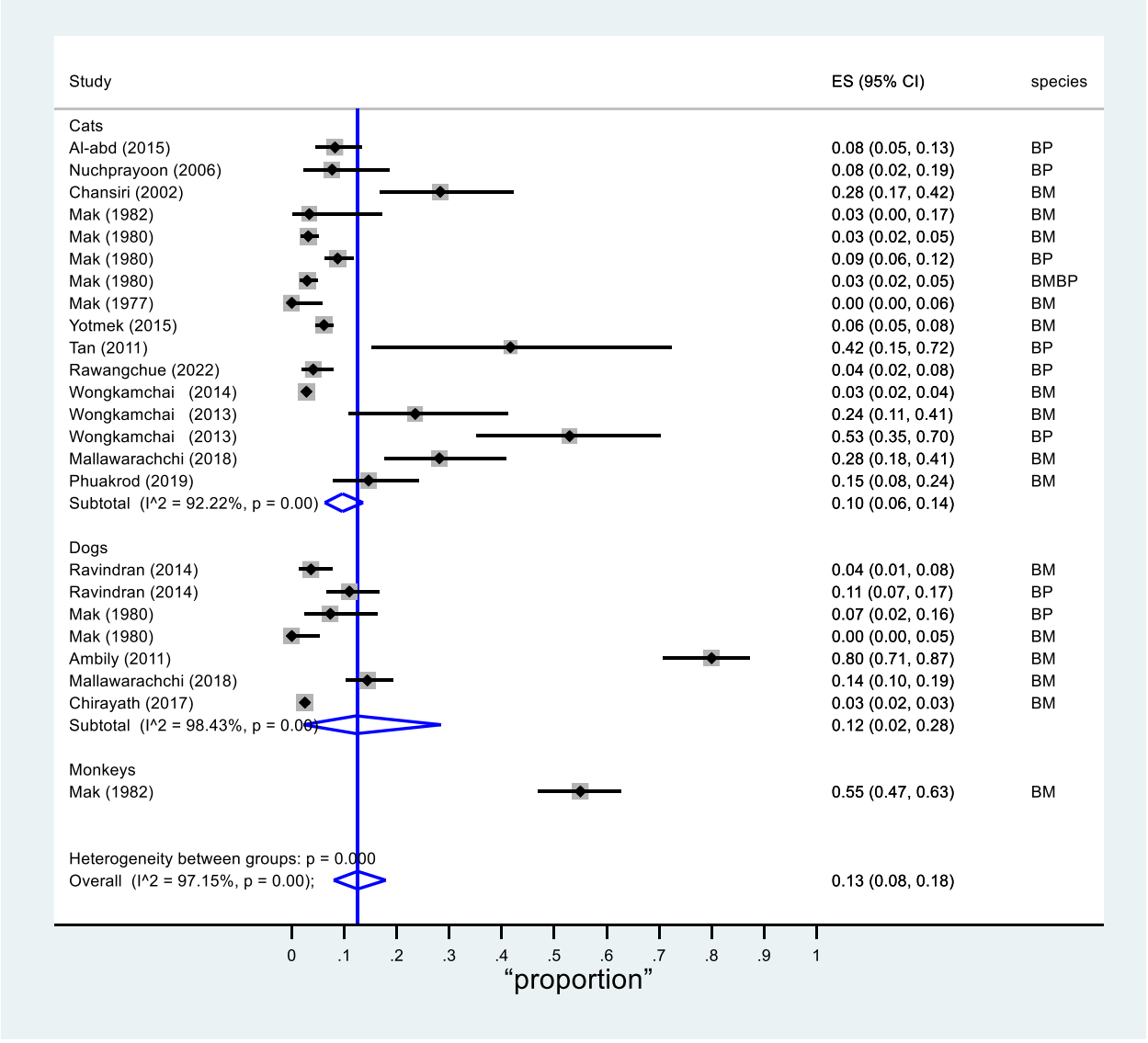

Fig. 2. Forest plot showing study-specific and pooled prevalence of animal Brugia infections stratified by animal types.
Note. A vertical line in the centre. This is the line of 1.0 proportion. A horizontal line represents each study. The width of the line represents the 95% interval. The diamond/point/square in the centre of the line is a point estimate of the true value. The bigger the shape, the larger the sample size. A diamond at the base of the graph represents a weighted average of prevalence for all studies. ES = Estimated prevalence in proportion. For example, Mallawarachchi et al., 2018 reported higher prevalence (14%, 95% CI: 10–19%) than Chirayath et al. (2017) (3%, 95% CI: 2–28%) in dogs. I^2 value in% represents magnitude of between-study heterogeneity.

within-countries and between-countries might also be related to variation in diagnostic methods. If all studies employed high accurate methods such as PCR, a higher prevalence was to be expected than what we had estimated in this review. Additionally, there were reports of *Brugia* infection in humans as well as of zoonotic filariasis in the same study area. This calls for a need to formulate the control strategies for these infections from both veterinary and human public health perspectives.

The findings of considerable mf-positive rates in animals including domestic cats and dogs suggested that these animals were potential reservoirs for human *Brugia* filariasis in the study countries such as India, Malaysia, Sri Lanka and Thailand. However, *B. malayi* infection in animals transmitted to humans in the same areas still need confirmation with genomic sequencing of individual mf collected from humans and *B. malayi* infected in the same area. The detection of the re-emergent sub-periodic strain in the endemic countries that were previously associated with periodic *Brugia* infection is suggestive of a zoonotic origin of the sub-periodic version of the disease (Muslim et al., 2013; Mak et al., 1982; Mallawarachchi et al., 2018b). Of note is that the vectors of brugian filariasis in dogs and cats (Irwin and Jefferies, 2004) (no studies found for wild monkeys or other species) are ones that also will bite humans including *Aedes, Anopheles* and *Culex*, and have been implicated in human LF transmission (Barendregt et al., 2013). Mf infections in cats can be transmitted to humans or directly transmitted to cats by infected mosquito vectors. Regardless of the mode of transmission, it is important to be aware of filarial infection in domestic cats and their close association with humans. It was reported that an increase in mf rate in humans corresponded to an increased infection in cats in the same study area in Malaysia (Mak et al., 1977), albeit with a limited number of samples. Similar studies were not found for dogs nor monkeys, or other potential animal reservoir species to be able to hypothesise on such linkages.

Fundamentally, the GPELF employs an MDA as the main elimination strategy to eliminate human infections, but not the non-human reservoirs (Mak et al., 1984; Yotmek et al., 2015). To achieve effective suppression, a repeated dose of antifilarial drugs every 8–12 months is required for the prevention of disease transmission in animals (Chansiri

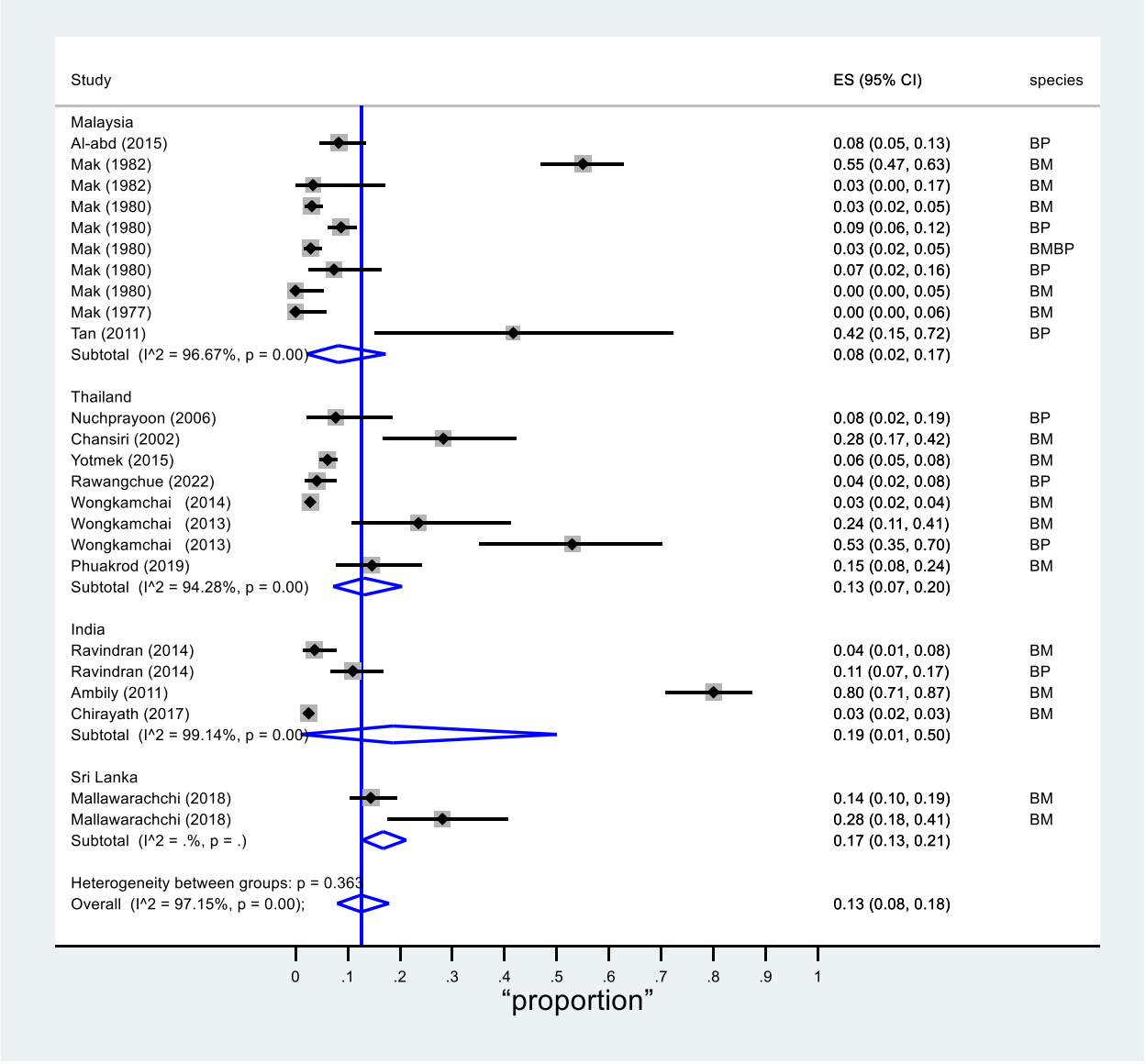

Fig. 3. Forest plot showing study-specific and pooled prevalence of animal Brugia infections stratified by country.
Note. A vertical line in the centre; this is the line of 1.0 proportion. A horizontal line represents each study. The width of the line represents the 95% interval. The diamond/point/square in the centre of the line is a point estimate of the true value. The bigger the shape, the larger the sample size. A diamond at the base of the graph represents a weighted average of prevalence for all studies. ES = Estimated prevalence in proportion. For example, Chansiri et al. (2002) reported higher prevalence (28%, 95% CI: 17–47%) than Phukarod (2019) (15%, 95% CI: 8–24%). I^2 value in% represents magnitude of between-study heterogeneity.

et al., 2002; Mak et al., 1982). Logistical issues may be a potential barrier to such an approach being feasible and practical. Cats are probably infected with sub-periodic *B. malayi* from humans and their mf positivity status is a reflection of the endemicity of the area (Mak et al., 1982). Moreover, *B. pahangi* is commonly found in cats and dogs; although only proven to infect humans under experimental conditions to date (Edeson et al., 1960). Overall, it is likely that zoonotic filarial transmission to humans occurs from these animal species, and needs to be considered in designing LF control and elimination strategies. The use of a ‘One Health’ approach for disease surveillance, programme planning, education and behaviour change, and the potential of improving animal health services for NZTD (LF in this case) control is required (Laing et al., 2021).

4.1. Study limitation

There are several limitations. Due to limited availability of data, this review could assess filariasis only in cats, dogs and monkeys. There remains a concern about the prevalence of filariasis in other animals such as rodents that could be also a reservoir that can be in contact with humans, especially in domestic settings. There was an underpowering issue because only two studies concurrently investigated the prevalence of filariasis in both humans and animals. This study included only published studies in English language. Information bias is a concern as we may have missed unpublished studies or non-English publications. Proof of the actual transmission of *B. malayi* infection in animals to humans residing in the same areas still needs substantiation with whole genomic sequencing of individual mf collected from *B. malayi* infected human and animals in the same area.

Due to an inherent limitation of cross-sectional/survey studies included in this review, the estimates in the primary studies in this review could change from time to time. On the other hand, the merit of observational studies is that they can assess the health problems in a real setting, reflecting real life situations.

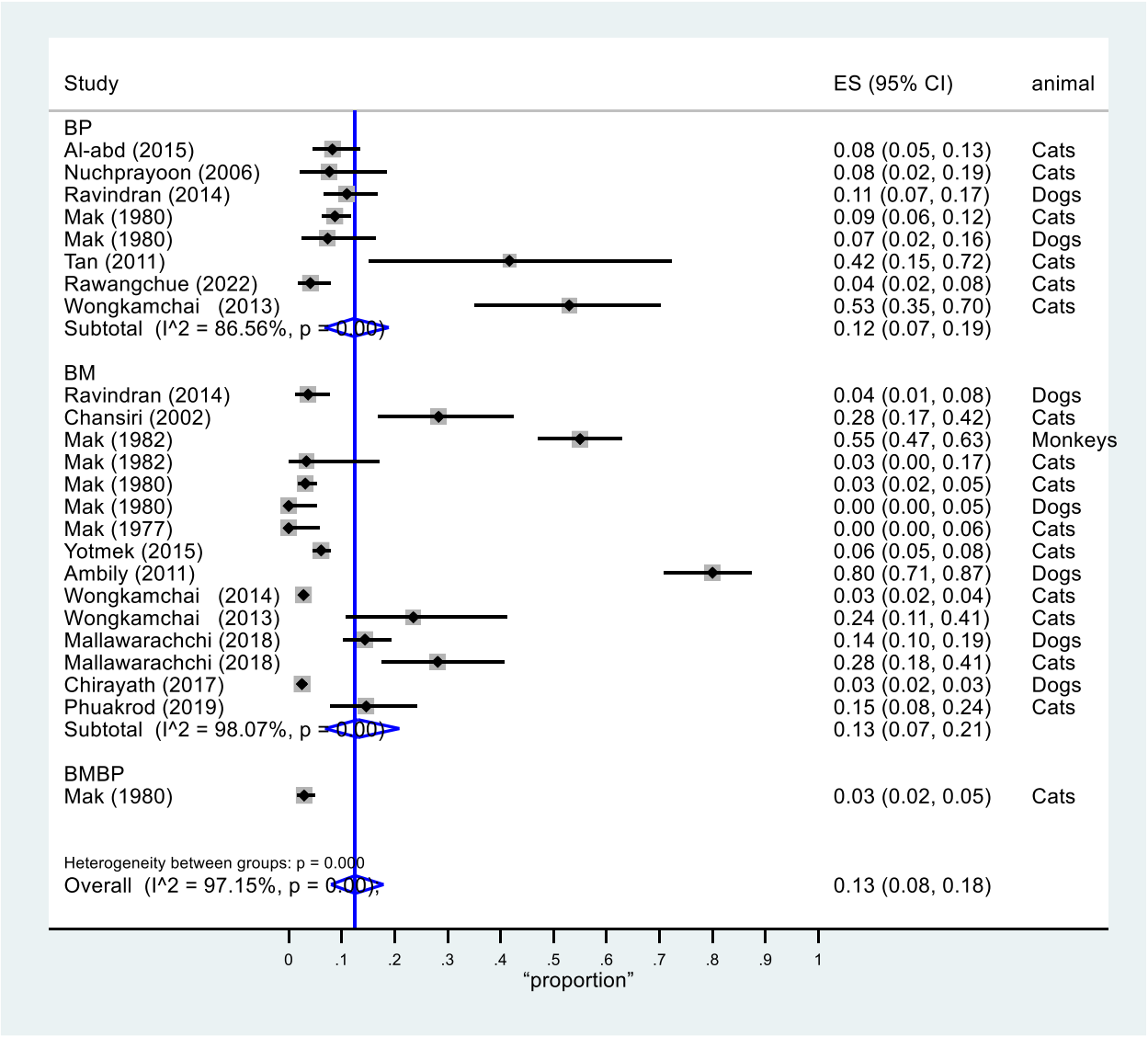

Fig. 4. Forest plot showing study-specific and pooled prevalence of animal Brugia infections stratified by species.
Note: A vertical line in the centre. This is the line of 1.0 proportion. A horizontal line represents each study. The width of the line represents the 95% interval. The diamond/point/square in the centre of the line is a point estimate of the true value. The bigger the shape, the larger the sample size. A diamond at the base of the graph represents a weighted average of prevalence for all studies. ES = Estimated prevalence in proportion. For example, Phukarod (2019) reported higher prevalence of BM (15%, 95% CI: 8–24%) than hirayth 2017 (3%, 95% CI: 2–3%). I^2 value in% represents magnitude of between-study heterogeneity. BM: B. malayi; BP: B. pahangi; BMBP: mixed B. malayi/B. pahangi.

4.2. The issue of heterogeneity

Prevalence and heterogeneity are the main issue with the current meta-analysis. When study results are heterogeneous (in the present study), it cannot be assumed that the same phenomenon has been measured in a sufficiently equivalent way and that differences in results are due to sampling error only (Barendregt et al., 2013). Substantial heterogeneity exists even with several stratifications of analysis of studies with more homogenous subgroups (e.g. by species, diagnostic methods, or animal categories). True heterogeneity is to be expected in prevalence estimates due to variations in the time and place where included studies were conducted. Therefore, high I^2 does not necessarily mean that data is inconsistent (Barker et al., 2021). Hence, interpretation of the findings should be undertaken with caution.

4.3. Public health implications

Humans are the only known definitive hosts of the nocturnally periodic form of *B. malayi*, but the nocturnally sub-periodic form shows little host specificity with zoonotic reservoirs described in primates and feline species (palm civet cats, wild cats and domestic cats) and reportedly causing infections in humans (Mallawarachchi et al., 2018b). *B. pahangi* is now found in both humans and animal reservoirs. In addition, increasing urbanisation in the region intensifies the chance of interactions between companion and wild animals, increasing the risk of zoonotic transmission (Irwin and Jefferies, 2004).

Thus far, studies showed that MDA targeted to the humans in the community are, in general, effective with evidence of a reduction in the prevalence of LFs and mf density in humans (Terhell et al., 2003; Oqueka et al., 2005). Treatment of individual animals detected with infection is usual and MDA is not practiced for animal reservoirs but may be a strategy for domestic reservoirs such as cats and dogs. The approach for MDA in domestic cats and dogs could be various combinations of albendazole, ivermectin and doxycycline and other effective treatment combinations, noting that cats react badly to DEC (thus triggering possible community resistance to the programme) (Mak et al., 1977).

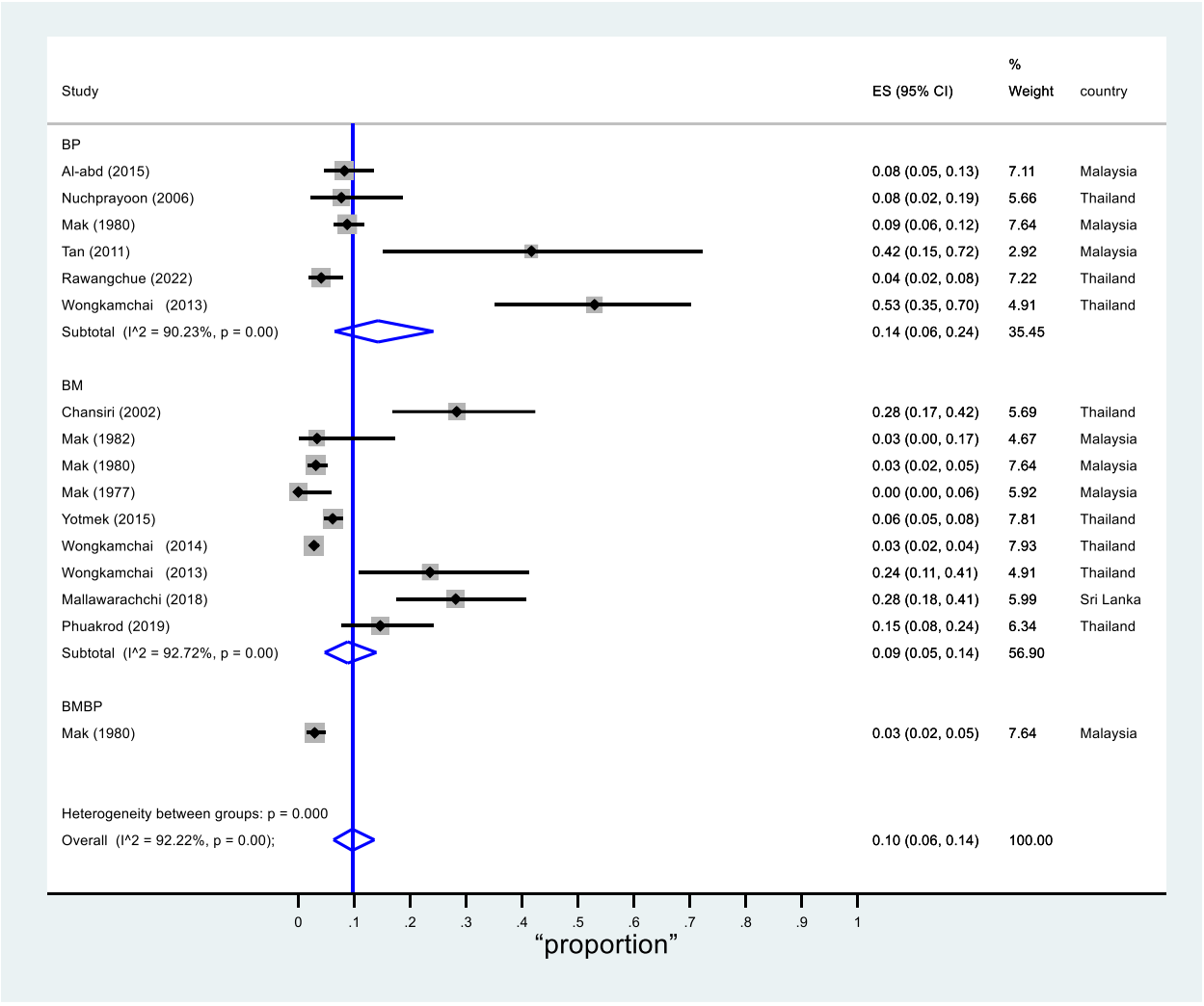

Fig. 5. Forest plot showing study-specific and pooled prevalence of Brugia infection in cats stratified by species.
Note. A vertical line in the centre. This is the line of 1.0 proportion. A horizontal line represents each study. The width of the line represents the 95% interval. The diamond/point/square in the centre of the line is a point estimate of the true value. The bigger the shape, the larger the sample size. A diamond at the base of the graph represents a weighted average of prevalence for all studies. ES = Estimated prevalence in proportion. For example, Mallawarachchi et al. (2018) reported higher prevalence (28%, 95% CI: 18–41%) than Mak et al. (1980) (3%, 95% CI: 2–5%) in cats. I^2 value in% represents magnitude of between-study heterogeneity.

Barriers to the practical issue of implementation of drug provision to domestic animals such as community's acceptance/rejection, and the logistics of ensuring all cats and dogs receive the dose in the situation, where ownership cannot be established e.g., strays. The usual asymptomatic presentation of the infection in these common companion animals as well as limited veterinary services in many parts of the Asian region especially in rural settings, means clinic-based reporting of infections from animals is unlikely and unreliable and affects the measurement of the true prevalence of this infection.

The success of such a more integrated LF control programme, will depend on strong inter-sectoral collaboration (including, the Veterinary Department, Rural Development Department, Health department, etc.,) to ensure the control of animal (domestic) reservoir. If more robust evidence is developed on the zoonotic transmission between wildlife reservoirs and humans (either in wildlife or domestic settings e.g., markets) then the sectors engaged will need to be broadened and strategies to prevent transmission expanded. The need for strengthened advocacy for the NZTDs with relevant Ministries responsible for domestic, wild and production animal is critical to secure their collaboration in control and elimination a disease that affects humans but is of limited health (and therefore economic or conservation) concern for an animal species (Molia et al., 2021).

5. Conclusion

The findings identify the magnitude and transmission potential of zoonotic *Brugia* infections. To substantiate these findings, future well-designed, large-scale, prospective studies on animal species that assess transmission of *Brugia* infections in endemic areas are recommended as well as reviewing the situation when land use and climate change affect vulnerable areas. Further research on the potential of filariasis transmit from animals to humans is also required. A number of studies from other regions, and studies with monkeys and other potential reservoir animals may be added in the future, when they are available.

Consent for publication

Not applicable.

Funding

No funding received.

CRediT authorship contribution statement

Cho Naing: Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Maxine A Whittaker:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Wong Siew Tung:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Htar Aung:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Joon Wah Mak:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We thank the participants and researchers of the primary studies, and our institutions for allowing us to conduct this study. In an effort to enhance the quality of our manuscript, we also appreciate the input and comments provided by the editors and anonymous reviewers.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.actatropica.2023.107049.

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