

A meta-analysis on *Dirofilaria immitis* and *Dirofilaria repens* in countries of North Africa and the Middle East

Systematic Review

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Abstract

Dirofilaria immitis and *D. repens* are globally distributed mosquito-borne parasitic filarial nematodes. Data on the prevalence of *Dirofilaria* spp. is not aggregated or publicly available at the national level for countries in North Africa and the Middle East. A systematic review and meta-analysis of publications describing cases of *D. immitis* and *D. repens* in 21 countries in North Africa and the Middle East was performed following PRISMA guidelines to estimate the prevalence of *Dirofilaria* spp. where national and regional estimates don't exist. In total, 460 publications were reviewed, and 34 met all inclusion criteria for the meta-analysis model. This analysis found that the combined prevalence of *Dirofilaria* spp. in the included countries was 2.4% (95% CI: 1.6–3.6%; $I^2 = 81.7\%$, 95% CI: 78.6–84.3%). Moderator analysis showed a statistically significant difference in the prevalence estimate between diagnostic test methods used. The model detected a high degree of heterogeneity among studies and publication bias. Removal of model identified outliers reduced the estimated prevalence from 2.4% to 1.0%, whereas the trim-and-fill analysis suggested a higher adjusted prevalence (12%). Despite these findings, *Dirofilaria* spp. prevalence is likely dynamic due to seasonal variations in mosquito vector populations and differences in local mosquito control practices. Additional studies from the countries in and surrounding this region are needed to better identify key risk factors for *Dirofilaria* spp. in domestic canids and other species (including humans) to inform prevention and control decisions to limit further transmission.

Introduction

Dirofilaria immitis and *D. repens* are parasitic, filarial nematodes of epidemiological importance in both human and veterinary medicine (Genchi and Kramer, 2020). *D. immitis* causes canine heartworm disease in dogs; other species can be accidental hosts such as felids (Villanueva-Saz et al., 2021; Fagundes-Moreira et al., 2024), jackals and foxes (Otranto et al., 2019; Potkonjak et al., 2020). *Dirofilaria repens* causes subcutaneous dirofilariasis (Genchi and Kramer, 2017) in numerous mammalian species including canids such as red foxes, golden jackal and wolves (Rishniw et al., 2006; Capelli et al., 2018; Potkonjak et al., 2020). Nodules from *D. repens* can be located in the subcutaneous tissue, conjunctiva or thoracic wall (Choudhury et al., 2023) of an infected host.

Mosquitoes serve as the intermediate host for both *D. immitis* and *D. repens*. The overlapping presence of competent mosquito vectors and *Dirofilaria* spp. infected dogs in the right climactic conditions are required for transmission to occur. Both species are zoonotic, known to cause pulmonary (Simón et al., 2003; Kozlov et al., 2023; Tsai et al., 2024), subcutaneous (Popescu et al., 2012; Falidas et al., 2016) and ocular lesions (Aykur et al., 2021; Redón-Soriano et al., 2022) in humans (Simón et al., 2012); additional public health impact on humans remains unclear. There are several diagnostic methods that can be used depending on the host and presentation of symptoms. Across host species, identification of microfilaria in the peripheral blood (Ciucu et al., 2020) or recovery of adult worms from pleural fluid (Valčiukaitė-Žilinskienė et al., 2024), pulmonary artery (Gregory et al., 2023) or a skin lesion (Falidas et al., 2016) are the most common methods for diagnosis of both parasites.

It is expected that the distribution and prevalence of *D. immitis* and *D. repens* follow similar patterns to the distribution of dogs infected with *Dirofilaria* (McKay et al., 2013;

Alberigi et al., 2023) and competent mosquito vectors of *D. immitis* and *D. repens* belonging to the genera *Aedes*, *Anopheles* and *Culex* (Dyab et al., 2015). Therefore, prevalence of *D. immitis* and *D. repens* is expected in countries in North Africa and the Middle East. Specifically, competent mosquito vectors are known to be present, such as, *Culex* and *Aedes* in Türkiye (Biskin et al., 2010) and *Aedes*, *Anopheles* and *Culex* in Egypt (Dyab et al., 2015) as well as dogs infected with *Dirofilaria* spp. (Baneth et al., 2002; Selim et al., 2021); however, details of specific mosquito vectors are lacking. The climate of regions in North Africa and surrounding the Mediterranean (not to be confused with WHO MENA region), including Algeria, Bahrain, Egypt, Iraq, Israel, Jordan, Kuwait, Lebanon, Libya, Mauritania, Morocco, Oman, Occupied Palestinian Territory (State of Palestine), Qatar, Saudi Arabia, Sudan, Syria, Tunisia, Türkiye (Turkey), the United Arab Emirates and Yemen (Figure 1), are conducive to development and transmission of *Dirofilaria* spp. (Bowman and Atkins, 2009; Bowman and Wu, 2022; Atkinson et al., 2024). This is an area where pathogen transmission would be expected because of the overlap of host, vector and suitable climate. These 21 countries are significant and similar in the Mediterranean and North Africa because they have arid desert climates (Varela et al., 2020) and share social and cultural norms that may impact companion animal ownership (Mohr et al., 2017; Mohamed et al., 2019).

To date, there is no publicly available surveillance or reporting system for *Dirofilaria* spp. in any of the countries in North Africa, and the Middle East. Therefore, published reports are the only publicly accessible sources of information describing the location, host/vector species, diagnostic test used and prevalence of these 2 pathogens in the countries in this area. The data in these publications can be used to estimate pooled prevalence in a meta-analysis (Barendregt et al., 2013). The goal of this meta-analysis is to estimate the prevalence and geographic distribution of *Dirofilaria* spp., specifically *D. immitis* and/or *D. repens*, in the countries listed above where no national prevalence estimates are available. This analysis is the first to estimate the prevalence of *Dirofilaria* spp. in these countries and can be used by veterinarians and public health policy makers to guide animal owner education and outreach programmes and inform medical doctors about the zoonotic risk of these pathogens.

Additionally, this meta-analysis describes factors (moderators) that impact the prevalence of *D. immitis* and *D. repens* such as diagnostic approach and test used, *Dirofilaria* species detected, host species sampled and continent of origin. Publication bias is also examined. While other studies have described different aspects of the prevalence of *D. immitis* and *D. repens*, these authors are not aware of other meta-analyses estimating the prevalence of these parasites in the countries of interest (Table 1).

Methods

Literature search and data filtering

This literature review and meta-analysis follows the 2020 The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) checklist and flow diagram guidance (Page et al., 2021) (Figure 2). The literature search was conducted in April 2022 from the English language databases, PubMed (National Institute of Health. National Center for Biotechnology Information. U.S. National Library of Medicine, 2022) and Clarivate™ (Web of Science™ Core Collection) for publications reporting the identification and/or detection of '*D. immitis*', '*D.*

repens', '*Dirofilaria immitis*', '*Dirofilaria repens*' or 'heartworm' in any of the following countries or territories: 'Morocco', 'State of Palestine', 'Occupied Palestinian Territory', 'Tunisia', 'Algeria', 'Egypt', 'Libya', 'Mauritania', 'Sudan', 'Oman', 'Saudi Arabia', 'Yemen', 'Iraq', 'Jordan', 'Syria', 'Lebanon', 'Israel', 'Kuwait', 'Qatar', 'the United Arab Emirates', 'the United Arab Emirate', 'Bahrain', 'Türkiye' or 'Turkey' (Supplement 1). Results included all the relevant literature from 1986 to 2022. The search did not have limitations on host species, or diagnostic or detection method.

Covidence (Veritas Health Innovation, Melbourne, Australia) was used to manage the database of identified publications. First, author(s) name and publication title were assessed to identify and remove duplicate records. From the remaining publications, any that did not contain diagnostic information on *D. immitis* or *D. repens* in known and relevant hosts or locations of interest were removed. Other reasons for publication exclusion include reports of fish or plants, or reports of cases from countries not included in the search query list. Systematic reviews, review articles and other meta-analyses were removed because no new case data were contained in them. The remaining 591 publications proceeded to an in-depth assessment to identify those with the relevant pathogen detection data in the geographic range targeted by these analyses. At this stage, publications were excluded if they reported travel-related cases; only reported detection of other species of filaria, such as *Wuchereria bancrofti* (Moustafa et al., 2017; Dahesh and Ibrahim, 2018); those that experimentally infected animals; and publications about Rift Valley Fever (removed 460 publications). Finally, an additional intensive review of the remaining publications, focused on diagnostic methods and origin of infection. In this stage, publications with insufficient description of diagnostic method(s) and, the geographic origin of the patient or their infection was not clearly described were excluded.

The remaining 75 publications (Supplement 2) fully met all inclusion/exclusion criteria (referred to as 'Full dataset' from here on). From the 'Full dataset' of 75 publications, a subset of 34 publications (Supplement 3) was created for the meta-regression model (referred to as 'Meta-analysis dataset' from here on). This selection was based on satisfying inclusion criteria for the model to be properly powered and bias minimized; specifically, the publications included in the 'Meta-analysis dataset' have a sample size (denominator) greater than 3.

Data preparation

Data extracted from each of the 'Full dataset' publications to create the 'Meta-analysis dataset' included information about the source such as country of infection, city/region/province of infection, species sampled (i.e. dog, cat, human, and mosquito) and sample type (i.e. blood, serum, worms and mosquitoes). Other extracted data included total sample size, total number positive for *D. immitis* or *D. repens*, *Dirofilaria* species detected, and diagnostic test/technique used. Data from each publication were extracted by a single researcher into a Microsoft® Excel® (version 2408) spreadsheet as separate observations.

The meta-analysis dataset, model and analysis were structured and performed following the established methods and best practices (Harrer et al., 2022). Across the entire 'Meta-analysis dataset', an individual moderator (such as host species) must occur thrice for there to be enough weight in the analysis and satisfy data requirements for model performance. Observations from publications that otherwise met the inclusion criteria but occurred less than thrice had to be excluded from the model (Harrer et al., 2019).

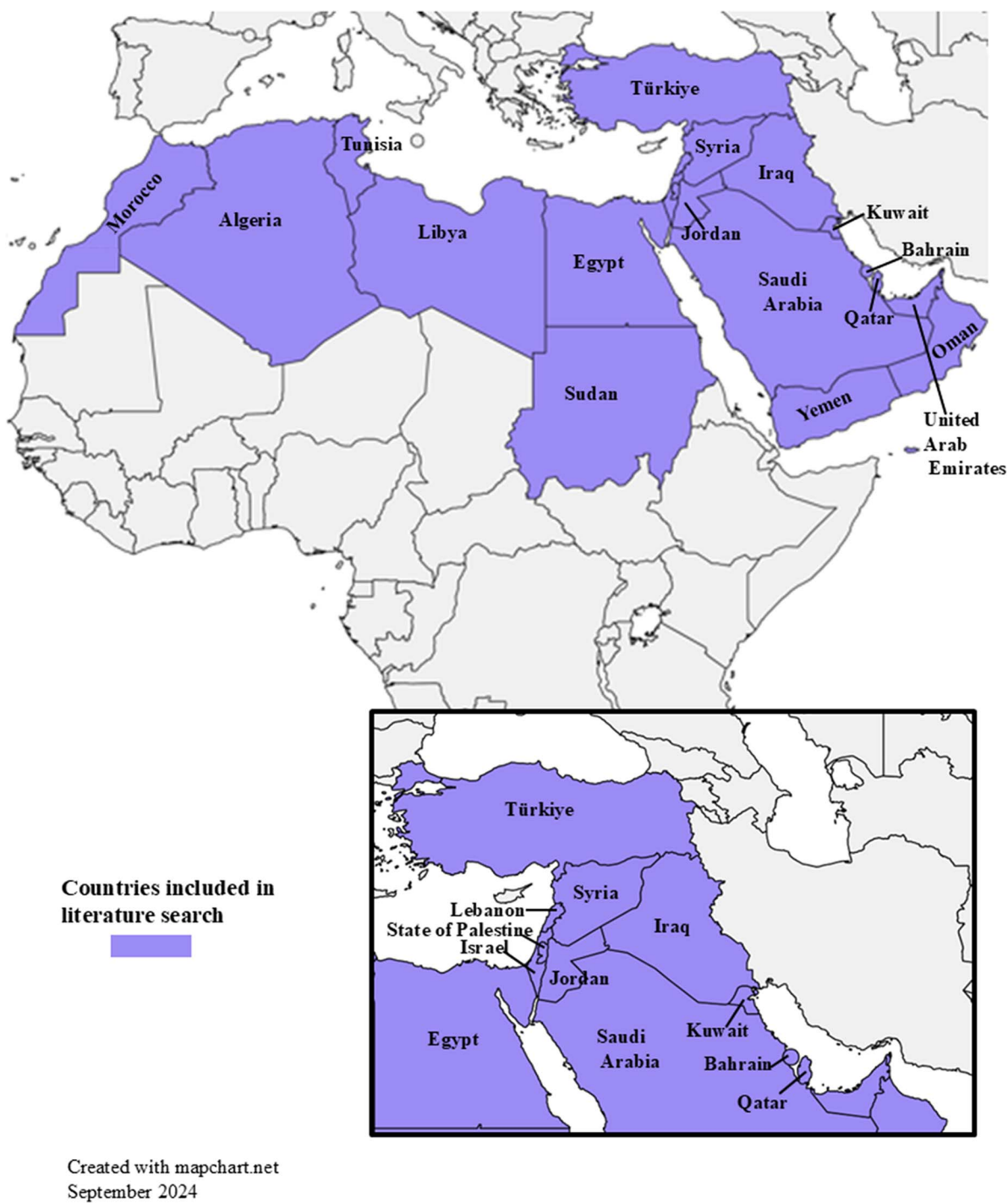


Figure 1. Map highlighting all 21 countries included in the literature search. The map inset is a zoomed in view of some of the countries in the Middle East along the Mediterranean Sea.

Table 1. Prior systematic reviews and meta-analyses of *D. immitis* and *D. repens* describing North Africa and the Middle East

Title and citation	Year
'Heartworm adulticide treatment: a tropical perspective' (Dantas-Torres et al., 2023)	2023
'Prevalence of <i>Dirofilaria immitis</i> in mosquitoes (Diptera) – systematic review and meta-analysis' (Riahi et al., 2021)	2021
'The global status of <i>Dirofilaria immitis</i> in dogs: a systematic review and meta-analysis based on published articles' (Anvari et al., 2020)	2020
'The prevalence of <i>Dirofilaria immitis</i> and <i>D. repens</i> in the Old World' (Genchi and Kramer, 2020)	2020
'What is happening outside North America regarding human dirofilariasis?' (Simon et al., 2005)	2005

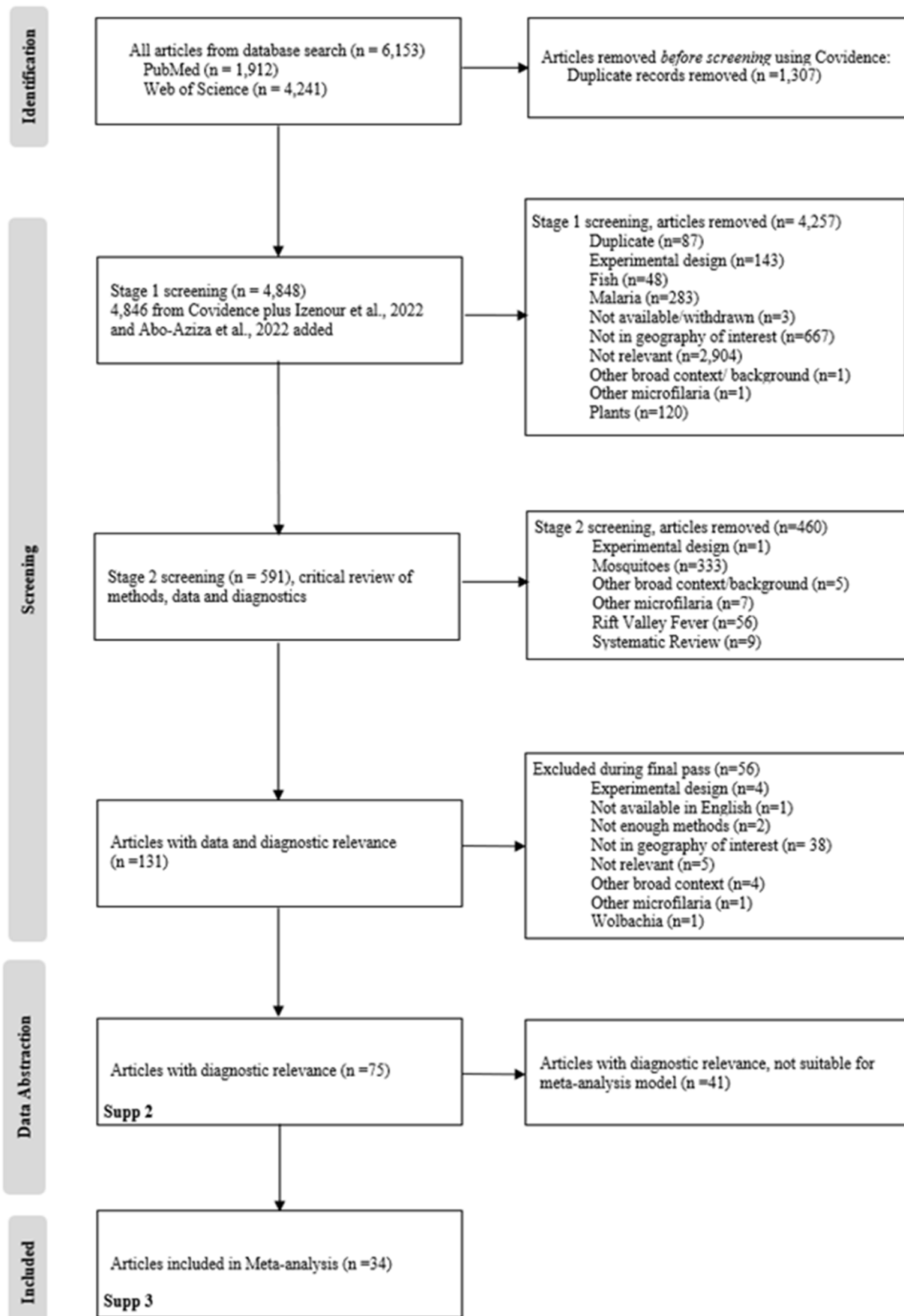


Figure 2. PRISMA flow diagram, depicting the publication identification, review and inclusion process for the systematic review and meta-analysis. It includes the number of publications excluded at each step and the reason for exclusion.

One example of this is in Otranto et al. (2019), in which the authors reported PCR results from fox and jackal host species. No other publications reported testing on these host species, so they could not be included in the 'Meta-analysis dataset', but these observations are retained in the 'Full dataset'. Other exceptions included publications from Tunisia and Jordan remained in the model even though they contribute 1 publication each with less than 3 rows of data because these locations were underrepresented in the dataset. Repeated testing on the same animal (e.g. a rapid test and PCR performed on blood from the same animal) was treated as independent tests and each sample/test combination was recorded as separate observations in the 'Meta-analysis dataset' because the results of one test did not influence administration of the other. A similar approach was used when a diagnostic test was performed on a subset of the original sample. The original sample and subset were treated as 2 separate samples, for example from the whole population, the ones that tested positive using the first diagnostic method then underwent a second diagnostic method.

Meta-analysis

Meta-analysis using R (R version 4.3.3, R Foundation for Statistical Computing, Vienna Austria, 2021) with the following statistical packages was performed: *readxl* version 1.4.3 (Wickham and Bryan, 2023), *metasens* version 1.5-2 (Schwarzer et al., 2023), *metafor* version 4.4-0 (Viechtbauer, 2010), *meta* version 7.0-0 (Balduzzi et al., 2019), *tidyverse* version 2.0.0 (Wickham et al., 2019), *devtools* version 2.4.5 (Wickham et al., 2022) and *dmatar* version 0.1.0 (Harrer et al., 2019) (R code in Supplement 4). A mixed-effects model, $k = 132$ events (also called observations), estimated overall prevalence was fit from 34 publications. Forest plots for the diagnostic test method aggregate moderator visualized the overlap of each observations' confidence interval. Outlier analysis was performed to identify observations with confidence intervals outside the 95% confidence limit of the pooled effect (Harrer et al., 2019). Influence analysis was performed using the 'Leave-One-Out' paradigm internally (Harrer et al., 2019) to produce a Baujat plot, which evaluates the relationship between heterogeneity and influence of each event.

Moderator analysis was guided by identification of common data themes in the included publications and consultations with *Dirofilaria* subject matter experts. The moderators are diagnostic method, diagnostic method type (aggregation of diagnostic method), *Dirofilaria* species, host species and continent of origin. Finally, to explore sources of publication bias, a contour-enhanced funnel plot of all observations in the dataset was created. Trim-and-fill analysis was conducted on both the complete 'Meta-analysis dataset' ($k = 132$ observations, where an observation is 1 independent prevalence data point extracted from each publication) and on the dataset with the identified outliers removed.

Results

Description of relevant publications

This literature search followed PRISMA (Page et al., 2021) (Figure 2) guidelines, for publication selection. The search in PubMed returned 1912 publications and Web of Science returned 4241, totaling 6153. Covidence (Veritas Health Innovation, Melbourne, Australia) was used to remove duplicates, leaving 4846 publications (1307 removed). The original literature search was conducted in 2022; in 2024, the search was conducted again to

identify any new publications, and this identified 2 additional publications (Izenour et al., 2022; Abo-Aziza et al., 2022), bringing the total number of records reviewed to 4848. The first stage of filtering identified publications that reported new data on *Dirofilaria* spp. in the targeted geographic region and resulted in the removal of 4257 publications. Of the 591 publications remaining, misalignment of topics in the publication with the stated research goals resulted in the removal of an additional 460 publications. Another 56 publications were removed because there was insufficient description of the diagnostic method. This left 75 publications (Supplement 2) with diagnostic data that fully met all inclusion/exclusion criteria ('Full dataset').

Description of 'Full dataset'

The 'Full dataset' (Supplement 2) includes publications from 11 countries: Algeria ($n = 2$), Egypt ($n = 7$), Iraq ($n = 2$), Israel ($n = 9$), Jordan ($n = 1$), Kuwait ($n = 3$), Morocco ($n = 2$), Saudi Arabia ($n = 4$), Tunisia ($n = 10$), Türkiye ($n = 33$) and the United Arab Emirates ($n = 2$). These publications reported sampling these host species: humans, dogs, cats, donkeys, horses, jackals, mosquitoes and foxes. *D. immitis* was reported in all host species except horses, donkeys and foxes (Table 2). *D. repens* was reported in all host species except jackals, horses and foxes. Publications from 7 countries: Egypt (Abdel-Rahman et al., 2008), Israel (Munichor et al., 2001; Raniel et al., 2006), Kuwait (Hira et al., 1994), Saudi Arabia (Chopra et al., 2004), Tunisia (Sassi et al., 2006; Fleck et al., 2009), Türkiye (Koltas et al., 2002; Beden et al., 2007) and the United Arab Emirates (Mittal et al., 2008) reported human cases of *D. repens*; 2 countries, Tunisia (Ziadi et al., 2005) and Türkiye (Aykur et al., 2021), reported human cases of *D. immitis* (Table 3). The 'Full dataset' did not meet model criteria, and the pooled prevalence was not calculated.

Description of publications for meta-analysis model

The 'Meta-analysis dataset' (Supplement 3), a subset of the 'Full dataset', was used to calculate the pooled prevalence. It contains data extracted from the final 34 publications that met all inclusion criteria and had sufficient data for the meta-analysis model (denominator > 3 and more than 3 occurrences of a variable across the entire dataset). These publications ranged in publication date from 1986 to 2022 from 10 countries: Algeria ($n = 2$), Egypt ($n = 4$), Iraq ($n = 1$), Israel ($n = 1$), Jordan ($n = 1$), Kuwait ($n = 1$), Morocco ($n = 2$), Saudi Arabia ($n = 1$), Tunisia ($n = 1$) and Türkiye ($n = 20$). The publications in the 'Meta-analysis dataset' reported 14 different diagnostic testing methods, all publications used blood or serum for the test sample and all sampled only dogs or cats as host species. *D. immitis* was the most frequently detected parasite, reported in 7 of 10 countries represented in the data and 29 of 34 publications included for meta-analysis. *D. repens* was reported in 6 of 10 countries and 6 of 34 publications.

Meta-analysis model

The mixed-effects model using the 34 publications ($k = 132$ observations, where an observation is 1 prevalence data point extracted from each publication) in the 'Meta-analysis dataset' estimated the combined prevalence of *D. immitis* and *D. repens* for all countries, diagnostic methods and species to be 2.4% (95% CI: 1.6–3.6%; $I^2 = 81.7\%$, 95% CI of $I^2 = 78.6$ –84.3%). Outlier analysis identified 39 observations as outliers. All of the outlier observations reported

Table 2. All reports of *D. immitis* or *D. repens* in any host or vector species by country

Country	Species of <i>Dirofilaria</i>	Host positive for <i>Dirofilaria</i> spp.	Vector positive for <i>Dirofilaria</i> spp.	Vector species by country
Algeria	<i>D. immitis</i>	Dog (Meriem-Hind and Mohamed, 2009; Tahir et al., 2017)		<i>Aedes albopictus</i>
				<i>Culex pipiens</i>
				<i>Culiseta longiareolata</i>
				<i>Culex quinquefasciatus</i> (Abdellahoum et al., 2022)
Bahrain	Not reported			<i>Anopheles</i> spp. (Ismaeel et al., 2004)
Egypt	<i>D. immitis</i>	Cat (Al-Kappany et al., 2011)	<i>Culex</i> spp. (Dyab et al., 2015)	<i>Anopheles</i> spp. (Dyab et al., 2015)
		Dog (Selim et al., 2021)		
	<i>D. repens</i>	Dog (Abdullah et al., 2021)	<i>Aedes</i> spp. (Dyab et al., 2015)	<i>Aedes aegypti</i> (Abozeid et al., 2018)
		Donkey (Abo-Aziza et al., 2022)	<i>Culex</i> spp. (Dyab et al., 2015)	
Iraq	<i>D. immitis</i>	Dog (Otranto et al., 2019; Tarish et al., 1986)		<i>Culex</i> spp. (Sharifi et al., 2022)
		Jackal (Otranto et al., 2019)		
	<i>D. repens</i>	Dog (Otranto et al., 2019)		
Israel	<i>D. repens</i>	Dog (Baneth et al., 2002; Harrus et al., 1999; Mazaki-Tovi et al., 2016)		<i>Aedes</i> spp. <i>Culex</i> spp. (Abbasi et al., 2022; Behar et al., 2021)
		Human (Chazan et al., 2001; Govrin-Yehudain et al., 2017; Gutierrez et al., 1995; Munichor et al., 2001; Raniel et al., 2006; Stayerman et al., 1999)		
Jordan	<i>D. immitis</i>	Dog (Obaidat and Alshehabat, 2018)		<i>Aedes</i> spp. (Kanani et al., 2017)
				<i>Culex</i> spp. (Al-Tammemi and Shtaiyat, 2024)
Kuwait	<i>D. repens</i>	Dog (Tarello, 2008)		<i>Culex</i> spp. (Colton et al., 2019)
		Human (Hira et al., 2008; Hira et al., 1994)		<i>Culiseta</i> spp. (Reeves et al., 2016)
Lebanon	Not reported			<i>Aedes</i> spp. (Haddad et al., 2022)
				<i>Culex</i> spp.
				<i>Culiseta</i> spp. (Zakhia et al., 2021)
Libya	Not reported			<i>Aedes</i> spp.
				<i>Anopheles</i> spp.
				<i>Culex</i> spp. (Nebbak et al., 2022)
Mauritania	Not reported			<i>Aedes vexans</i>
				<i>Culex poicilipes</i>
				<i>Culex antennatus</i> (Barry et al., 2022; El Ghassem et al., 2023)
				<i>Anopheles laranchae</i> (Faraj et al., 2008)
Morocco	<i>D. immitis</i>	Dog (Elhamiani Khatat et al., 2017; Pandey et al., 1987)		<i>Aedes</i> spp. (Abdelkrim et al., 2024)
				<i>Culex pipiens</i> (Arich et al., 2024; Arich et al., 2022)
				<i>Culiseta</i> spp. (Nebbak et al., 2022)

(Continued)

Table 2. (Continued.)

Country	Species of <i>Dirofilaria</i>	Host positive for <i>Dirofilaria</i> spp.	Vector positive for <i>Dirofilaria</i> spp.	Vector species by country
Oman	Not reported			<i>Aedes aegypti</i> (Al-Abri et al., 2020)
				<i>Anopheles</i> spp.
				<i>Culex</i> spp. (Ullah et al., 2020)
Occupied Palestinian Territory/State of Palestine	Not reported			<i>Aedes</i> spp. (Allah Adawi, 2012)
Qatar	Not reported			<i>Culex</i> spp.
				<i>Aedes</i> spp.
				<i>Anopheles</i> spp. (Tahir et al., 2022)
Saudi Arabia	<i>D. immitis</i>	Cat (Omar et al., 2018)		<i>Anopheles</i> spp. (Ahmed et al., 2011)
		Dog (Omar et al., 2018; Tarello, 2003)		<i>Aedes</i> spp. (Ahmed et al., 2011)
	<i>D. repens</i>	Dog (Tarello, 2003)		<i>Culex</i> spp. (Ahmed et al., 2011; Alahmed et al., 2019)
		Human (Chopra et al., 2004; Dababo et al., 2022)		
Sudan	Not reported			<i>Anopheles</i> spp. (Abdelwhab et al., 2021)
				<i>Aedes</i> spp. (Ali El Hadi Mohamed et al., 2020)
				<i>Culex</i> spp. (Ali El Hadi Mohamed et al., 2020)
Syria	Not reported			<i>Aedes</i> spp. (Haddad et al., 2007)
Tunisia	<i>D. immitis</i>	Dog (Chabchoub et al., 2003; Rjeibi et al., 2017)		<i>Aedes</i> spp. (Ben Ayed et al., 2019; Bohers et al., 2020)
		Human (Ziadi et al., 2005)		
	<i>D. repens</i>	Dog (Rjeibi et al., 2017)		<i>Anopheles</i> spp. (Tabbabi and Daaboub, 2017; Tabbabi and Daaboub, 2018; Tabbabi et al., 2018)
		Human (Fleck et al., 2009; Kaouech et al., 2010; Makni et al., 2007; Mrad et al., 1999; Saied et al., 2011; Soussi et al., 2004; Ziadi et al., 2005)		<i>Culex</i> spp. (Tabbabi and Daaboub, 2017; Tabbabi and Daaboub, 2018; Tabbabi et al., 2018)
Türkiye	<i>D. immitis</i>	Dog (Adanir et al., 2013; Atas et al., 2018; Ceribasi and Simsek, 2012; Cetinkaya et al., 2016; Ceylan et al., 2021; Colak et al., 2020; Guven et al., 2017; Icen et al., 2011; Köse and Erdogan, 2012; Oge et al., 2003; Oncel and Vural, 2005; Pasa et al., 2017; Sevimli et al., 2007; Simsek and Ciftci, 2016; Simsek et al., 2008; Tasci and Kilic, 2012; Ural et al., 2014; Voyvoda et al., 2004; Yaman et al., 2009; Yildirim et al., 2007; Yildiz et al., 2008)	<i>Aedes</i> spp. (Biskin et al., 2010; Demirci et al., 2021; Yildirim et al., 2011)	
			<i>Anopheles</i> spp. (Demirci et al., 2021)	
			<i>Culex</i> spp. (Demirci et al., 2021)	
		Human (Aykur et al., 2021)		
	<i>D. repens</i>	Dog (Simsek and Ciftci, 2016)	<i>Culex</i> spp.	
		Human (Beden et al., 2007; Koltas et al., 2002; Kutluturk et al., 2016; Latifoglu et al., 2002)	<i>Aedes</i> spp.	
			<i>Anopheles</i> spp. (Demirci et al., 2021)	

(Continued)

Table 2. (Continued.)

Country	Species of <i>Dirofilaria</i>	Host positive for <i>Dirofilaria</i> spp.	Vector positive for <i>Dirofilaria</i> spp.	Vector species by country
	<i>D. repens</i> and <i>D. immitis</i> co-infection	Dog (Simsek and Ciftci, 2016)	<i>Culex</i> spp. <i>Aedes</i> spp. <i>Anopheles</i> spp. (Demirci et al., 2021)	
United Arab Emirates	<i>D. repens</i>	Dog (Tarello, 2002), Human (Mittal et al., 2008)		<i>Aedes</i> spp. <i>Anopheles</i> spp. <i>Culex</i> spp. (Camp et al., 2019)
Yemen	Not reported			<i>Aedes</i> spp. (Tucker et al., 2020) <i>Anopheles</i> spp. (Assada et al., 2024)

Table 3. Human cases of *Dirofilaria* spp. by country

Country	<i>Dirofilaria</i> spp.	Sample source	Total sample	Total positive	Publication (author last name year)
Egypt	<i>D. repens</i>	Worm and blood	3	3	(Abdel-Rahman et al., 2008)
Israel	<i>D. repens</i>	Worms	1	1	(Chazan et al., 2001)
		Worms	1	1	(Munichor et al., 2001)
		Worms	1	1	(Raniel et al., 2006)
		Worms	1	1	(Govrin-Yehudain et al., 2017)
		Worms	1	1	(Gutierrez et al., 1995)
		Worms	1	1	(Stayerman et al., 1999)
Kuwait	<i>D. repens</i>	Worms	1	1	(Hira et al., 2008)
		Worms	1	1	(Hira et al., 1994)
Saudi Arabia	<i>D. repens</i>	Worms	1	1	(Chopra et al., 2004)
		Worms	1	1	(Dababo et al., 2022)
Tunisia	<i>D. immitis</i>	Worms	1	1	(Ziadi et al., 2005)
	<i>D. repens</i>	Worms	1	1	
		Worms	1	1	(Fleck et al., 2009)
		Worms	1	1	(Saied et al., 2011)
		Worms	1	1	(Mrad et al., 1999)
		Worms	1	1	(Sassi et al., 2006)
		Worms	1	1	(Soussi et al., 2004)
		Worms	1	1	(Makni et al., 2007)
		Worms	1	1	(Kaouech et al., 2010)
Turkey	<i>D. immitis</i>	Worms	1	1	(Aykur et al., 2021)
	<i>D. repens</i>	Worms	1	1	(Beden et al., 2007)
		Worms	1	1	(Koltas et al., 2002)
		Worms	3	2	(Kutluturk et al., 2016)
		Worms	1	1	(Latifoglu et al., 2002)
United Arab Emirates	<i>D. repens</i>	Worms	1	1	(Mittal et al., 2008)

positive detection of *Dirofilaria* spp. These outliers came from publications from Algeria ($n = 2$; 5%), Israel ($n = 1$; 3%), Morocco ($n = 3$; 7%), Saudi Arabia ($n = 2$; 5%), Tunisia ($n = 1$; 3%) and

Türkiye ($n = 30$; 77%). Most outlier observations reported a rapid test type (69%). Microscopy was the next most common (23%), followed by PCR (8%). The model removed these 39 observations,

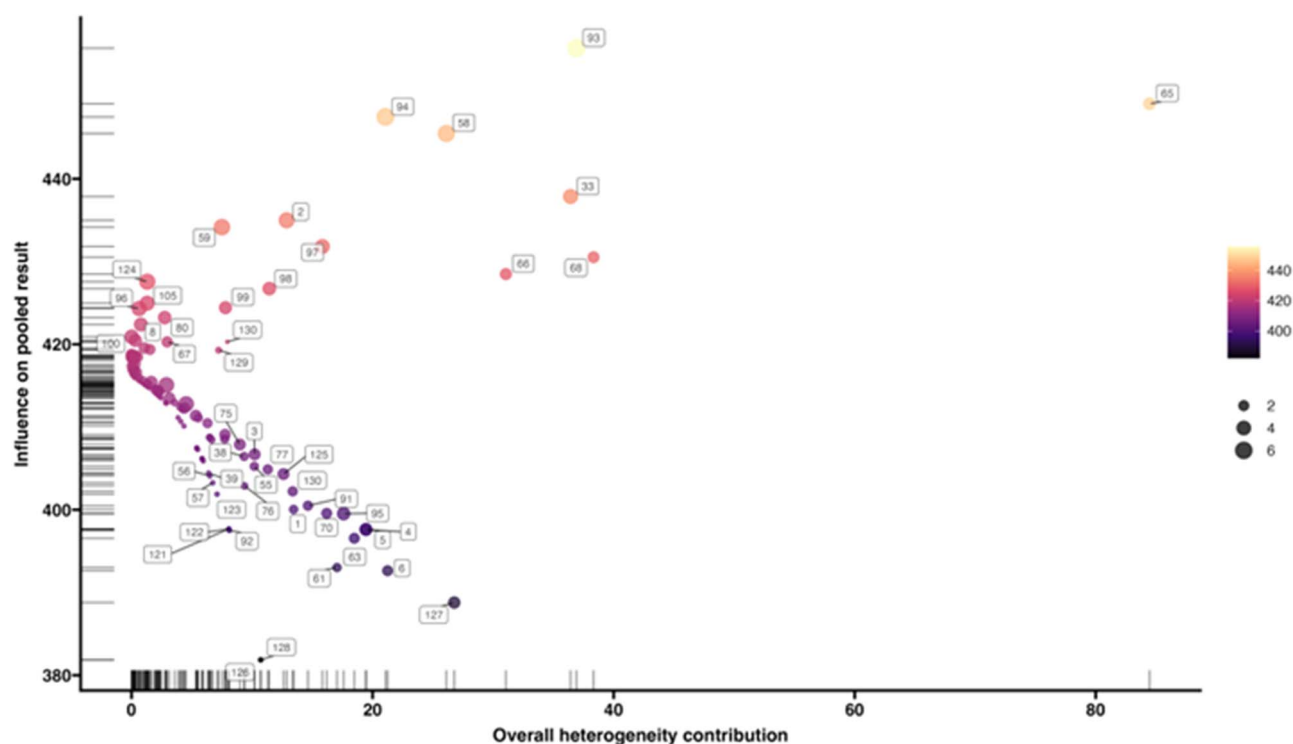


Figure 3. Baujat plot of the meta-analysis dataset. It displays each observation's contribution of heterogeneity along the horizontal axis and the influence of the pooled result along the vertical axis. Observations with more heterogeneity or influence can be visually detected with this plot.

leaving 93 observations. The estimated prevalence of *D. immitis* and *D. repens* with outliers removed was 1.0% (95% CI: 0.71–1.5%; $I^2 = 0.0\%$, 95% CI = 0.0–25.2%).

Exploration of heterogeneity

The Baujat plot (Figure 3) of the mixed-effects model for all observations in the 'Meta-analysis dataset' visualizes the relationship between heterogeneity and influence of each observation. Observations 65, 68, 33 and 93 have the highest heterogeneity. Observations 93, 94, 58 and 33 have the highest influence.

Effects of continent of origin on prevalence

Publications in the 'Meta-analysis dataset' came from countries in 2 continents – Asia ($n=108$ observations) and Africa ($n=24$ observations) (Supplement 5A). The estimated prevalence of *D. immitis* and *D. repens* in Asian countries in this dataset was 2.5% (95% CI: 1.6–3.9%; $I^2 = 81.0\%$) and in African countries in this dataset was 2.0% (95% CI: 0.7–5.2%; $I^2 = 84.4\%$). There was not a statistically significant difference in prevalence estimates between continents.

Effect of host species on prevalence

Diagnostic samples in the 'Meta-analysis dataset' were derived from 2 host species – dogs ($n=127$) and cats ($n=5$) (Supplement 5B). The estimated prevalence of *Dirofilaria* spp. among dogs was 2.6% (95% CI: 1.7–3.9%; $I^2 = 81.7\%$) and among cats was 0.48% (95% CI: 0.02–11.5%; $I^2 = 0.0\%$). There was not a statistically significant difference in prevalence between the 2 host species.

Effect of pathogen species on prevalence

D. immitis was tested in 121 observations in the 'Meta-analysis dataset', whereas *D. repens* was tested in 11 observations (Supplement 5C). The mixed-effects model estimated the prevalence of *D. immitis* to be 2.7% (95% CI: 1.8–4.0%; $I^2 = 81.0\%$), and the prevalence of *D. repens* to be 0.9% (95% CI: 0.05–14.3%; $I^2 = 55.1\%$). There was no statistically significant difference between species of parasite detected.

Effect of diagnostic tests on prevalence

The mixed-effects model of the diagnostic tests moderator was first conducted on the 14 individual diagnostic tests reported (Supplement 5D). The most commonly reported diagnostic test, *DiroCHECK*® Canine Heartworm Antigen Test Kit (Zoetis, Florham Park, NJ), $n=31$ publications, estimated the prevalence of *Dirofilaria* spp. to be 6.5% (95% CI: 4.0–10.5%; $I^2 = 88\%$) and contributed the most heterogeneity, $I^2 = 88\%$. The lowest prevalence was estimated from observations that used the Knotts method, 0.3% (95% CI: 0.0–100.0%; $I^2 = 0.0\%$). Prevalence was estimated to be <1% for observations that used each of the following 4 test methods: Knotts (0.3%), Microscopy (Giemsa stain) (0.5%), PCR (0.7%) and Microscopy blood smear (0.8%).

Some of the diagnostic tests were reported fewer than 3 times, such as the *FilarCHECK* Ag ELISA (Agrolabo, Scarmagno, Italy), *IDEXX SNAP*® 4Dx® Test (IDEXX, Westbrook, ME) and the *SNAP*® Feline Triple® (IDEXX, Westbrook, ME), so a second moderator analysis was performed with the diagnostic tests aggregated by test type to increase the number of observations. The 14 diagnostic tests could be classified into 3 groupings: (1) Rapid test to detect antigen (8 different antigen rapid tests reported), (2) 'Microscopy' to detect

microfilaria of *Dirofilaria* spp. or adults of *D. repens* (5 different microscopy methods reported) and (3) PCR to detect *Dirofilaria* spp. DNA (Supplement 5E). The estimated prevalence of both parasites varied based on diagnostic test group used: 3.9% (95% CI: 2.4–6.3%; $I^2 = 82.3\%$) for the grouped rapid antigen tests, 2.3% (95% CI: 0.98–5.2%; $I^2 = 79.5\%$) for the grouped microscopy techniques and 0.7% (95% CI: 0.2–2.4%; $I^2 = 81.1\%$) for PCR. There was a statistically significant difference in prevalence between at least 2 of the aggregated test types. However, this test does not indicate which ones, it only indicates that there is a difference between at least 2 of the tests. Diagnostic test type was the only moderator with a statistically significant influence on prevalence. Moderator analysis of continent of origin, host species and pathogen species did not produce statistically significant results.

Forest plots show the magnitude of difference between each observation in the moderator group. The boxes in the forest plot represent the point estimate of each observation and the horizontal lines represent the 95% confidence interval. The forest plot

for PCR (Figure 4), estimated the prevalence of *Dirofilaria* spp. between 0% and 2% when this test type is used. The prediction interval for a new study using PCR is between 0% and 55%. Most of the observations that reported results from a PCR test have a point estimate close to zero; however, the observation from Mazaki-Tovi et al. (2016) shows a point estimate equal to 1 with a large confidence interval. This is because this observation had a 100% positivity rate, all 4 samples tested positive. The forest plot for rapid test (antigen) (Figure 5) estimated the prevalence of *Dirofilaria* spp. between 2% and 6% when this test type is used. The prediction interval for a new study using rapid test (antigen) is between 0% and 58%. The studies with the highest rate of positivity (Yaman et al. 2009; Elhamiani Khatat et al. 2017; Sari et al. 2013; Pasa et al. 2017) also have the highest point estimates. The forest plot for microscopy (Figure 6) estimated the prevalence of *Dirofilaria* spp. between 1% and 5% when this test type is used. The prediction interval for a new study using microscopy is between 0% and 54%.

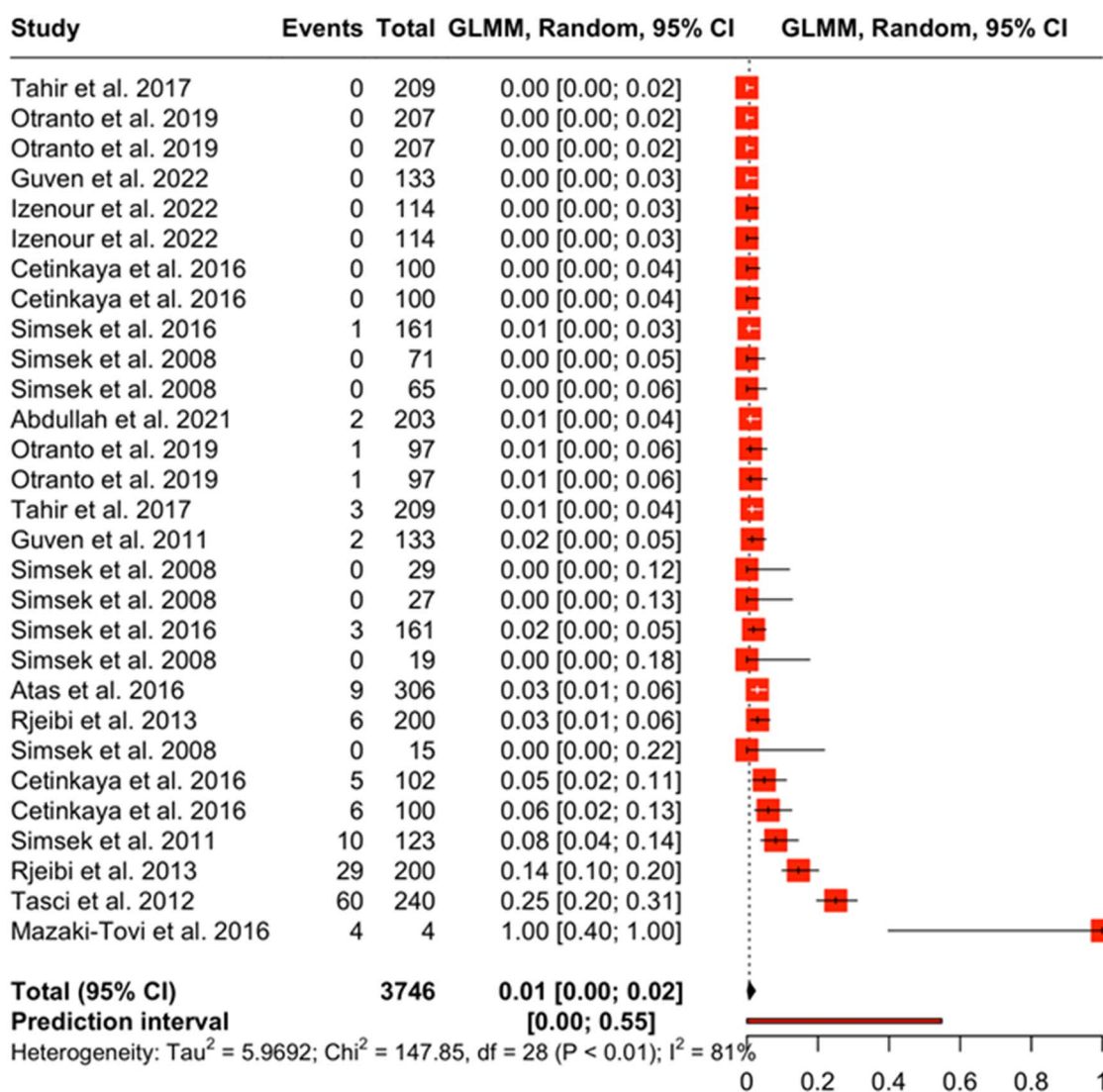


Figure 4. The forest plot shows the effect size of each observation against a predicted effect size (diamond symbol). This forest plot is from the PCR diagnostic method moderator analysis.

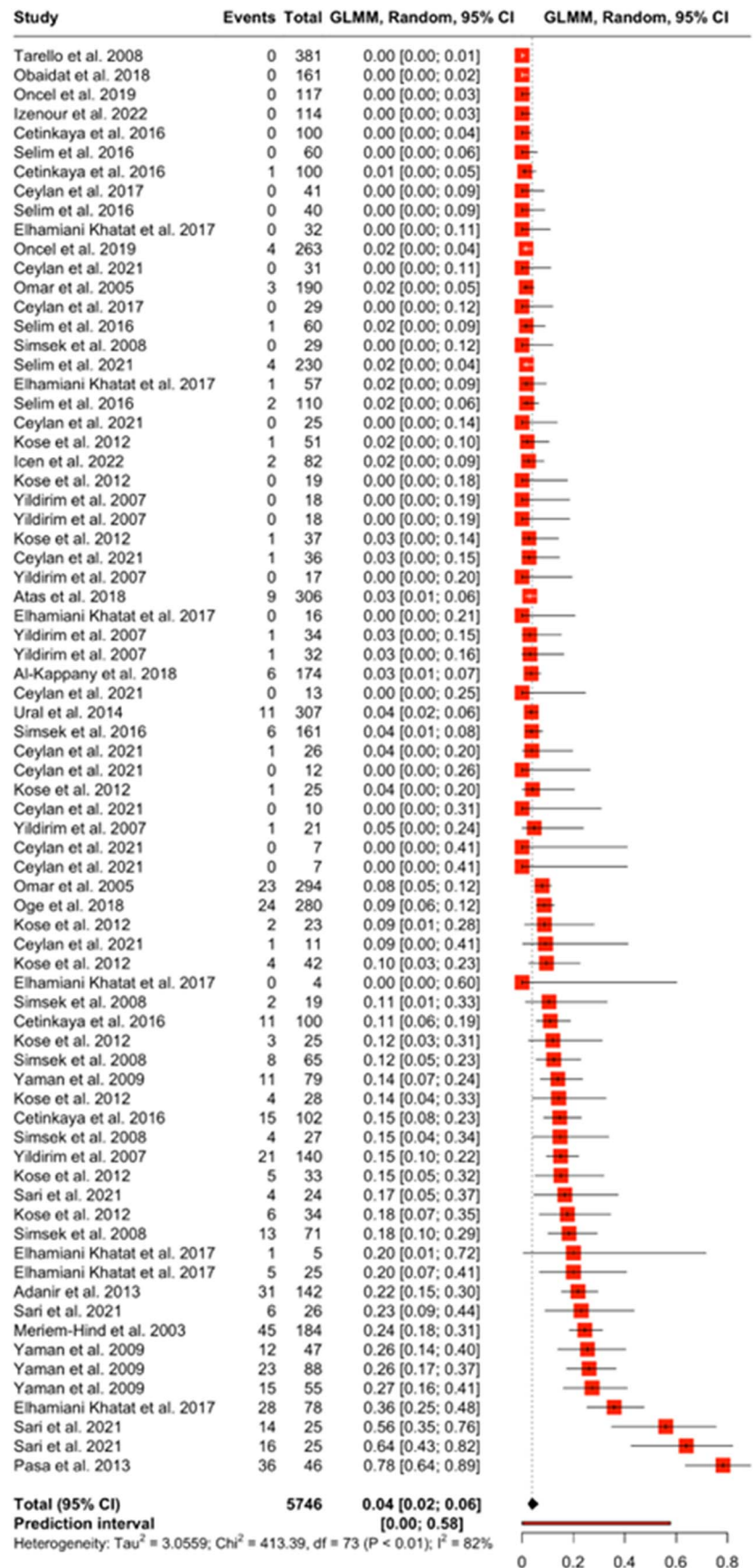


Figure 5. The forest plot shows the effect size of each observation against a predicted effect size (diamond symbol). This forest plot is from the rapid test diagnostic method moderator analysis.

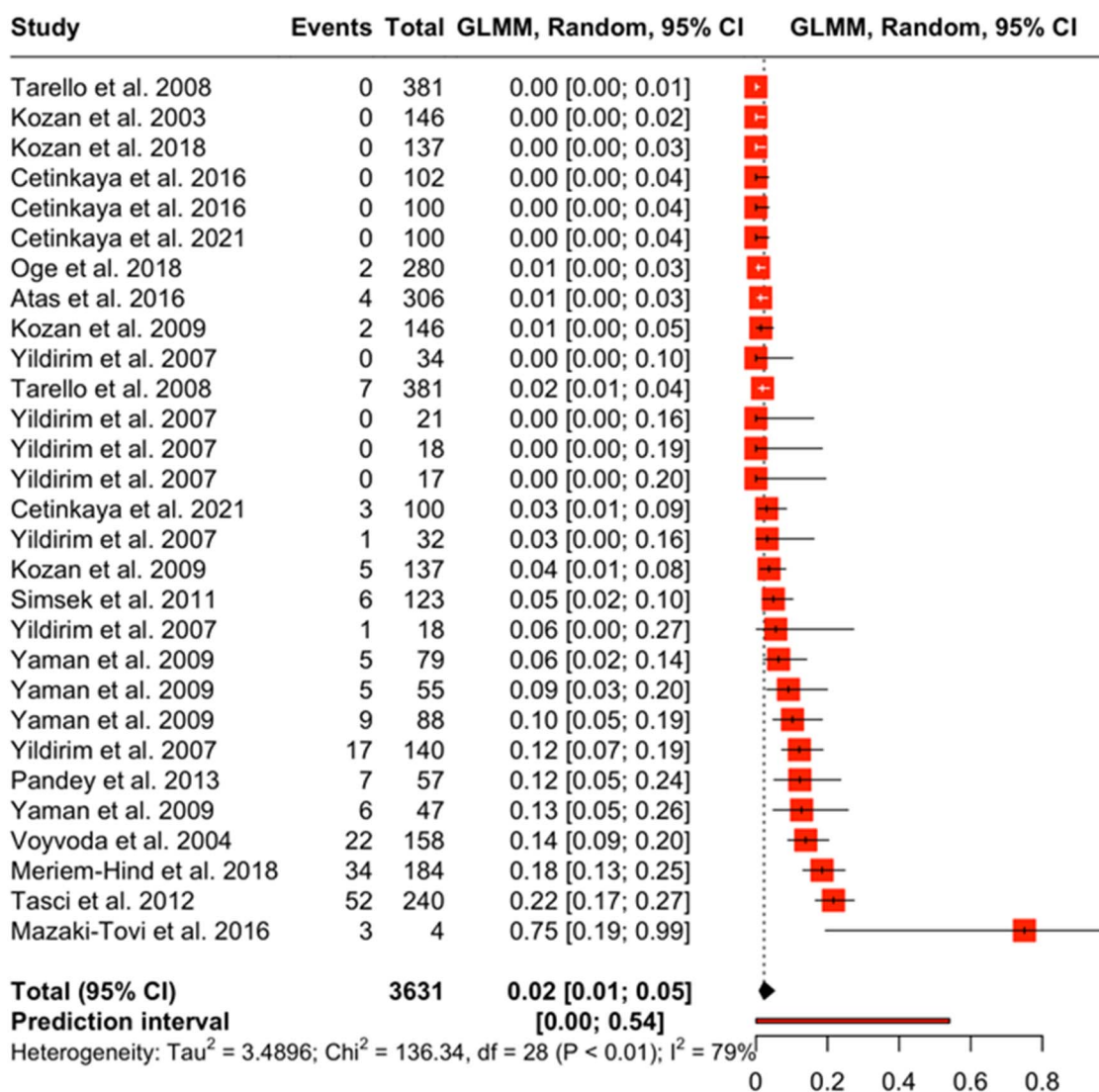


Figure 6. The forest plot shows the effect size of each observation against a predicted effect size (diamond symbol). This forest plot is from the microscopy diagnostic method moderator analysis.

Publication bias and outlier analysis

The contour-enhanced funnel plot (Figure 7) is a scatter plot of the effect estimate, prevalence, against the standard error (Sterne et al., 2011) for the entire meta-analysis dataset. Most observations fall beyond the $p < 0.1$ range of the plot with a wide distribution of observations across the x-axis.

The trim-and-fill method is a statistical method that serves 2 purposes; first, it indicates the significance of the publication bias and it provides bias-adjusted results (Shi and Lin, 2019). In the first trim-and-fill analysis, performed on the 'Meta-analysis dataset,' the model added 53 studies, total observations, $k = 185$ and the estimated prevalence was 12.45% (95% CI: 9.12–16.78%; $I^2 = 87.1\%$, 95% CI of I^2 : 85.5–88.5%), $p < 0.0001$ suggests a likelihood of publication bias. The second trim-and-fill analysis was on the data set with the 39 previously identified outlier observations removed. This model added 36 studies, total observations, $k = 131$ and the estimated prevalence of this dataset was 12.33% (95% CI: 8.80–17.02%; $I^2 = 85.7\%$, 95% CI of I^2 : 83.5–87.6%), $p < 0.0001$.

Discussion

There is a significant knowledge gap about *Dirofilaria* spp. in North Africa and the Middle East. This literature review and meta-analysis reviewed publications reporting cases of either *D. immitis* or *D. repens* in any host or vector species from 21 countries in Northern Africa and the Middle East. The data in the publications included in the model estimated a pooled prevalence of 2.4%. These findings show that there is transmission of *Dirofilaria* spp. in this geographic region, including to humans.

The meta-analysis model has a high degree of heterogeneity, $I^2 = 81.7\%$. Heterogeneity in meta-analysis is defined as variation in true effect size (prevalence) between publications (Higgins, 2008). Heterogeneity (I^2) is calculated as a percentage of the variation across publications, which is due to differences in the findings of the publication and not due to chance (Higgins and Thompson, 2002; Thorlund et al., 2012). It is considered high when it is greater than 50% (Deeks et al., 2023). The heterogeneity in this meta-analysis is likely due to several factors including the small number

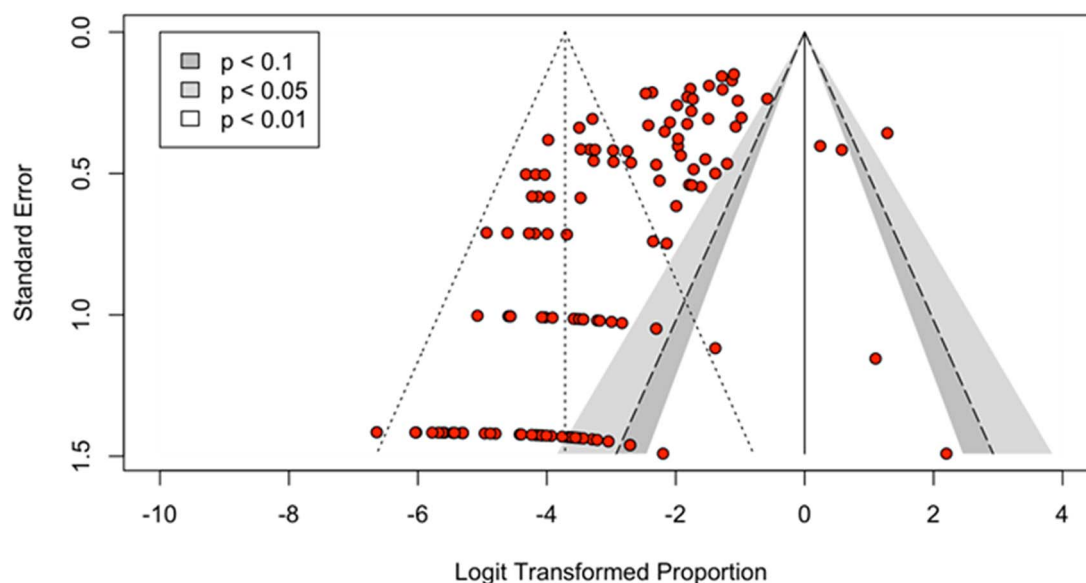


Figure 7. Funnel plot showing the relationship between the estimated effect size of each observation against the true effect size. When observations (red dots) are centred around 0 on the horizontal axis, the estimated effects are close to the true effect. This funnel, plot shows deviation in the estimated effect sizes from the true effect size.

of publications included in the analysis, and the small number of positive diagnoses for *D. immitis* or *D. repens* among included publications. The outlier analysis removed 39 observations and estimated the heterogeneity of the model equal to 0% as opposed to 81.7% when the outliers remained in the model. This provides strong evidence that the identified outliers are strong contributors to the heterogeneity of the dataset (Lin et al., 2017). The lower heterogeneity with outliers removed suggests that the studies being analysed are all estimating the same underlying population effect size, and any differences in effect sizes observed between studies are likely due to random sampling variability rather than true differences in the effects being studied. All observations identified as outliers did contain positive diagnostic events of *Dirofilaria* spp.; however, there was no pattern or trend based on country or diagnostic test type. More analysis is needed to understand how these observations influence the prevalence estimate.

The 2 trim-and-fill analysis investigated sources of the bias in the dataset by removing some of the extreme values and imputing new values to create a new estimate with less bias. The trimmed and filled datasets both estimated a prevalence of 12%, considerably higher than the 2.4% estimated in the original model. Trim-and-fill attempts to fill in missing observations due to publication bias by estimating the values of those missing values (Shi and Lin, 2019). The fivefold increase in estimated prevalence from the trim-and-fill analysis suggests the true prevalence of *Dirofilaria* spp. might be much higher. This also supports the need for additional studies and increased surveillance. Additional analysis exploring sources of bias and risk of bias assessments would be beneficial.

Specifically, observations 93 and 33 indicated high influence and heterogeneity when visualized on the Baujat plot. The asymmetry in the funnel plot also indicates the presence of bias in this study. *Dirofilaria* spp. is reported in many countries and hosts, but model constraints dictated the inclusion criteria for this study and resulted in the exclusion of small studies. The final dataset is heavily weighted with studies from Türkiye. Funnel plot asymmetry can be a symptom of a number of characteristics in the dataset including publication bias, presence of studies with small sample size, chance,

poor methodological design and true heterogeneity (Sterne et al., 2011).

Moderator analysis is an important component of meta-analysis because it allows exploration of drivers associated with the prevalence of *D. immitis* and *D. repens*. This analysis assessed 4 different moderators: continent of infection origin, host species, *Dirofilaria* spp. and diagnostic test method, and found a statistically significant difference in diagnostic test type as a moderator. Publications from Kuwait, Jordan, Israel, Iraq, Saudi Arabia and Tunisia occurred 1 time each in the dataset, less than the needed 3 occurrences of each variable value. The goal of this meta-analysis was to describe the prevalence of *Dirofilaria* spp. across the 21 countries of interest, so publications from these countries remained in the model to enhance geographic representation of publications. Inclusion of data from these countries might impact the heterogeneity and bias of the analysis. The decision to include publications from countries with fewer than 3 publications meant moderator analysis by country could not be performed; however, moderator analysis by continent was performed. This model did not detect a statistical difference in prevalence based on continent of infection origin, host species or *Dirofilaria* spp. in this dataset. However, there are important clinical and medical differences based on host and pathogen species. Differences in prevalence between continents are expected because of the difference in climate, but that was also not a statistically significant between group difference. The pooled prevalence in Asian countries was 2.5%, and 2.0% in African countries. Mosquito species competent for *Dirofilaria* spp. transmission are well documented in all of the countries included in this meta-analysis, but there are differences in humidity, population density, rainfall and pollution that might impact vector activity, how likely hosts are to come into contact with vectors and ultimately impact transmission.

With regard to host species, the meta-analysis dataset included more observations of sampled dogs ($n = 127$) than cats ($n = 5$). It is possible that a more balanced sample would produce different prevalence results. *D. immitis* and *D. repens* have different presentations in different hosts (Noack et al., 2021). *D. immitis* is of great

importance in veterinary medicine and can be diagnosed using a point-of-care test. Diagnosis of *D. repens* often requires excision and identification of adult worms from nodules. The model did not detect a statistical difference in prevalence between host species included in the 'Meta-analysis dataset'.

With regard to each species of *Dirofilaria* in the meta-analysis dataset, the model did not detect a statistical difference in the prevalence estimates of *D. immitis* or *D. repens*. *D. immitis* is often thought of as causing disease solely in dogs, but it causes clinical disease in cats and the effects can be devastating. *D. repens* is often thought of as a zoonotic disease, affecting both humans and animals. Preventatives for *D. repens* are available in some countries, but may not be available globally, especially in North Africa and the Middle East. Countries included in this analysis often experience ongoing conflict that jeopardizes stability and security, as well as health for both humans and animals. It is not surprising that countries with long-standing conflict like Libya, Syria and Yemen do not have publications on *Dirofilaria* spp. in the literature (Daw, 2021). Pathogens still circulate, and it is imperative that medical supplies and support reach areas in conflict to maintain the health of humans and animals.

Diagnostic test type was a key factor in estimating the prevalence of *Dirofilaria* spp. in this study – an expected finding due to inherent differences in test sensitivity, specificity and required operator skill. When multiple test methods were performed on the same animal, for example a rapid test and PCR, these were treated as independent tests because the results of one test did not impact the decision to provide a subsequent test. Differences in diagnostic tests are a key factor in understanding the findings of prevalence in the moderator analysis models, and their generalizability. The estimated prevalence using all diagnostic methods irrespective of the molecule/pathogen detected was 2.4%. The moderator analysis for the grouped diagnostic test types created models that account for each test's sensitivity, specificity and the underlying sample size. PCR (0.7%) detected parasite DNA, and the lateral flow ELISAs (rapid test antigen) (3.9%) detected antigen of adult female worms. Microscopy morphologically identified microfilaria/adult worms (2.3%). The differences in prevalence between diagnostic testing method are not surprising. Rapid antigen tests using whole blood or serum from the animal is currently the gold standard for point-of-care diagnostics. PCR is a high sensitivity testing method but will only detect an infection in a blood sample if microfilaria are circulating in the blood stream. An animal recently infected with *D. immitis* or an infection of *D. repens* that is in a subcutaneous nodule are likely to not have circulating microfilaria that can be detected by PCR. However, PCR used when adult worms are the sample source can detect *Dirofilaria* spp. with a high degree of sensitivity. Microscopy has similar considerations to PCR, with added dependence on the skill of the person looking through the microscope. The sample type used in each of these test types is critically important and that is not something that was assessed with this analysis.

Commercially manufactured rapid tests are the most commonly used among publications in this study, but there is variation in availability of test kits by geographic locations, not all tests are licensed in all countries. This limits the ability to standardize testing across countries and locations. Most of the case reports in humans determined infection based on microscopic analysis of the physical worm or microfilaria taken from the patient, but they omitted reference to the key or standard that was used to identify the species in the sample. Some authors used multiple tests on the same sample of animals, for example a rapid test and PCR but did

not indicate the degree of concordance between the two testing methods (Adanir et al., 2013; Omar et al., 2018). For this analysis, each test type was considered independently of any other test performed on the same sample of animals. There is a wide range of representation by each country included in the query. The literature search returned the most publications from Türkiye, but no publications from Mauritania, Libya or Sudan, for example.

This meta-analysis identified opportunities for improved reporting that would strengthen future meta-analytic approaches: (1) specify source/geographic location of definitive and intermediate host and vector samples, include coordinates if possible; (2) demographic details about where the host became infected if different from sampling location; (3) state what specimen was used in the diagnostic test (blood, serum, tissue); (4) the diagnostic tests used should include manufacturer name and full test name; (5) if performing microscopic or morphologic identification of *Dirofilaria* or mosquito vector species, include the citation or key that is used to determine specimen characteristics; (6) if multiple tests are performed on the same sample, indicate concordance/discordance.

The meta-analysis model did provide an estimate of *Dirofilaria* spp. prevalence for the 21 countries included in this study and also found variations in prevalence estimates. The overall prevalence was 2.4%, with outliers removed it was 1.0%, and with trim-and-fill analysis it was 12%. The drivers behind the variations in prevalence estimates warrant further investigation. Türkiye is heavily represented in the publications used in this analysis; a more balanced representation from countries in the region would provide an estimate that is more generalizable to the region. Additional studies with larger sample size are desirable to increase statistical power and representation across the region. The social and political landscape of North Africa and the Middle East might be a barrier to research and publication from some of these countries. The gaps and limitations identified in this study provide opportunities for future collaboration and research. This is the first estimate of *Dirofilaria* spp. for these countries; however, the true prevalence remains unknown. The model is limited by the data available in publications and inclusion criteria. This study highlighted gaps in research and opportunities for future research from this region on the topic of *Dirofilaria* spp. transmission. Foremost, adoption and adherence to recognized standards for testing, treatment and use of preventatives would enhance the welfare of dogs in this region by protecting them from canine heartworm disease. A standardized testing programme could also improve accuracy and timeliness of *Dirofilaria* spp. diagnosis because training and testing resources could be prepositioned within the country or jurisdiction.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S003118202500037X>.

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References

- Abbasi I, Akad F, Studentsky L, Avi IB, Orshan L and Warburg A (2022) A next-generation (DNA) sequencing (NGS)-based method for identifying the sources of sugar meals in mosquito vectors of West Nile virus in Israel. *Journal of Vector Ecology* 47(1), 109–116. <https://doi.org/10.52707/1081-1710-47.1.109>
- Abdelkrim O, Said Z and Souad L (2024) Anopheles mosquitoes in Morocco: Implication for public health and underlined challenges for malaria re-establishment prevention under current and future climate conditions. *Pest Management Science* 80(4), 2085–2095. <https://doi.org/10.1002/ps.7943>
- Abdellahoum Z, Nebbak A, Lafri I, Kaced A, Bouhenna MM, Bachari K, Boumegoura A, Agred R, Boudchicha RH, Smadi MA, Maurin M and Bitam I (2022) Identification of Algerian field-caught mosquito vectors by MALDI-TOF MS. *Veterinary Parasitology, Regional Studies and Reports* 31, 100735. <https://doi.org/10.1016/j.vprsr.2022.100735>
- Abdel-Rahman SM, Mahmoud AE, Galal LA, Gustinelli A and Pampiglione S (2008) Three new cases of human infection with *Dirofilaria repens*, one pulmonary and two subcutaneous, in the Egyptian governorate of Assiut. *Annals of Tropical Medicine and Parasitology* 102(6), 499–507. <https://doi.org/10.1179/136485908X300904>
- Abdelwhab OF, Elaagip A, Albsheer MM, Ahmed A, Paganotti GM and Abdel Hamid MM (2021) Molecular and morphological identification of suspected *Plasmodium vivax* vectors in Central and Eastern Sudan. *Malaria Journal* 20(1), 132. <https://doi.org/10.1186/s12936-021-03671-9>
- Abdullah HHAM, Amanzougaghene N, Dahmana H, Louni M, Raoult D and Mediannikov O (2021) Multiple vector-borne pathogens of domestic animals in Egypt. *PLoS Neglected Tropical Diseases* 15(9), e0009767. <https://doi.org/10.1371/journal.pntd.0009767>
- Abo-Aziza FAM, Hendawy SHM, Abdullah H, El Namaky A, Laidoudi Y and Mediannikov O (2022) Emergent and neglected equine filariosis in Egypt: Species diversity and host immune response. *Pathogens* 11(9). <https://doi.org/10.3390/pathogens11090979>
- Abozeid S, Elsayed AK, Schaffner F and Samy AM (2018) Re-emergence of *Aedes aegypti* in Egypt. *Lancet Infectious Diseases* 18(2), 142–143. [https://doi.org/10.1016/S1473-3099\(18\)30018-5](https://doi.org/10.1016/S1473-3099(18)30018-5)
- Adanir R, Sezer K and Kose O (2013) The prevalence of *Dirofilaria immitis* in dogs with different breed, ages and sex. *Ankara Universitesi Veteriner Fakültesi Dergisi* 60(4), 241–244. https://doi.org/10.1501/Vetfak_0000002586
- Ahmed AM, Shaalan EA, Aboul-Soud MA, Tripet F and Al-Khedhairi AA (2011) Mosquito vectors survey in the AL-Ahsaa district of eastern Saudi Arabia. *Journal of Insect Science* 11, 176. <https://doi.org/10.1673/031.011.17601>
- Al-Abri SS, Kurup PJ, Al Manji A, Al Kindi H, Al Wahaibi A, Al Jardani A, Mahmoud OA, Al Balushi L, Al Rawahi B, Al Fahdi F, Al Siyabi H, Al Balushi Z, Al Mahrooqi S, Al Manji A, Al Sharji A, Al Harthi K, Al Abri B, Al-Raidan A, Al Bahri Z, Al-Mukhaini S, Amin M, Prasanna AR, Petersen E and Al Ajmi F (2020) Control of the 2018–2019 dengue fever outbreak in Oman: A country previously without local transmission. *International Journal of Infectious Diseases* 90, 97–103. <https://doi.org/10.1016/j.ijid.2019.10.017>
- Alahmed AM, Munawar K, Khalil SMS and Harbach RE (2019) Assessment and an updated list of the mosquitoes of Saudi Arabia. *Parasites and Vectors* 12(1), 356. <https://doi.org/10.1186/s13071-019-3579-4>
- Alberigi B, Carvalho E, Mendes-de-almeida F, Labarthe N and Scott FB (2023) Dogs infected by *Dirofilaria immitis*: A threat to the health of human and non-human animals in Rio de Janeiro, Brazil. *Brazilian Journal of Veterinary Medicine* 45, e001723. <https://doi.org/10.29374/2527-2179.bjvm001723>
- Ali El Hadi Mohamed R, Abdelgadir DM, Bashab HM, Al-Shuraym LA, Sfour Aleanizy F, Alqahtani FY, Ahmed Al-Keridis L and Mohamed N (2020) First record of West Nile virus detection inside wild mosquitoes in Khartoum capital of Sudan using PCR. *Saudi Journal of Biological Sciences* 27(12), 3359–3364. <https://doi.org/10.1016/j.sjbs.2020.08.047>
- Al-Kappany YM, Lappin MR, Kwok OC, Abu-Elwafa SA, Hilali M and Dubey JP (2011) Seroprevalence of *Toxoplasma gondii* and concurrent *Bartonella* spp., feline immunodeficiency virus, feline leukemia virus, and *Dirofilaria immitis* infections in Egyptian cats. *Journal of Parasitology* 97(2), 256–258. <https://doi.org/10.1645/GE-2654.1>
- Allah Adawi SHA (2012) Presence of *Aedes albopictus* in Palestine – West Bank. *International Journal of Tropical Disease and Health* 2(4), 301–310. <https://doi.org/10.9734/IJTDH/2012/2660>
- Al-Tammemi AB and Shtaiyat B (2024) The unseen peril: Jordan's vulnerability amid the ongoing West Nile virus fatalities in Palestine. *New Microbes New Infections* 60–61, 101452. <https://doi.org/10.1016/j.nmni.2024.101452>
- Anvari D, Narouei E, Daryani A, Sarvi S, Moosazadeh M, Ziaei Hezarjaribi H, Narouei MR and Gholami S (2020) The global status of *Dirofilaria immitis* in dogs: A systematic review and meta-analysis based on published articles. *Research in Veterinary Science* 131, 104–116. <https://doi.org/10.1016/j.rvsc.2020.04.002>
- Arich S, Assaid N, Weill M, Tmimi FZ, Taki H, Sarih M and Labbé P (2024) Human activities and densities shape insecticide resistance distribution and dynamics in the virus-vector *Culex pipiens* mosquitoes from Morocco. *Parasites and Vectors* 17(1), 72. <https://doi.org/10.1186/s13071-024-06164-1>
- Arich S, Haba Y, Assaid N, Fritz ML, McBride CS, Weill M, Taki H, Sarih M and Labbé P (2022) No association between habitat, autogeny and genetics in Moroccan *Culex pipiens* populations. *Parasites and Vectors* 15(1), 405. <https://doi.org/10.1186/s13071-022-05469-3>
- Assada M, Al-Hadi M, Esmail MA, Al-Jurban J, Alkawri A, Shamsan A, Terreri P, Samake JN, Aljasari A, Awash AA, Al Eryani SM and Carter TE (2024) Molecular Confirmation of *Anopheles stephensi* mosquitoes in the Al Hudaydah Governorate, Yemen, 2021 and 2022. *Emerging Infectious Diseases* 30(7), 1467–1471. <https://doi.org/10.3201/eid3007.240331>
- Atas AD, Altay K, Alim A and Ozkan E (2018) Survey of *Dirofilaria immitis* in dogs from Sivas Province in the Central Anatolia Region of Turkey. *Turkish Journal of Veterinary & Animal Sciences* 42(2), 130–134. <https://doi.org/10.3906/vet-1707-93>
- Atkinson PJ, Stevenson M, O'Handley R, Nielsen T and Caraguel CGB (2024) Temperature-bounded development of *Dirofilaria immitis* larvae restricts the geographical distribution and seasonality of its transmission: Case study and decision support system for canine heartworm management in Australia. *International Journal for Parasitology* 54(6), 311–319. <https://doi.org/10.1016/j.ijpara.2024.02.001>
- Aykur M, Yağcı A, Simşek S, Palamar M, Yaman B, Korkmaz M and Dagci H (2021) First time identification of subconjunctival *Dirofilaria immitis* in Turkey: Giant episcleral granuloma mimicking scleritis. *Parasitology Research* 120(11), 3909–3914. <https://doi.org/10.1007/s00436-021-07317-2>
- Balduzzi S, Rücker G and Schwarzer G (2019) How to perform a meta-analysis with R: A practical tutorial. *Evidence-Based Mental Health* 22(4), 153–160. <https://doi.org/10.1136/ebmental-2019-300117>
- Baneth G, Volansky Z, Anug Y, Favia G, Bain O, Goldstein RE and Harrus S (2002) *Dirofilaria repens* infection in a dog: Diagnosis and treatment with melarsomine and doramectin. *Veterinary Parasitology* 105(2), 173–178. [https://doi.org/10.1016/s0304-4017\(02\)00006-7](https://doi.org/10.1016/s0304-4017(02)00006-7)
- Barendregt JJ, Doi SA, Lee YY, Norman RE and Vos T (2013) Meta-analysis of prevalence. *Journal of Epidemiology & Community Health* 67(11), 974. <https://doi.org/10.1136/jech-2013-203104>
- Barry Y, Elbara A, Bollahi MA, El Mamy AB O, Fall M, Beyit AD, Khayar MS, Demba BA, Haki ML, Faye O, Plee L, Bonbon E, Doumbia B, Arsevska E and Cêtre-Sossah C (2022) Rift Valley fever, Mauritania, 2020: Lessons from a one health approach. *One Health* 15, 100413. <https://doi.org/10.1016/j.onehlt.2022.100413>
- Beden U, Hokelek M, Acici M, Umur S, Gungor I and Sullu Y (2007) A case of orbital dirofilariasis in Northern Turkey. *Ophthalmic Plastic*

- and *Reconstructive Surgery* 23(4), 329–331. <https://doi.org/10.1097/IOP.0b013e318073cca3>
- Behar A, Rot A, Altory-Natour A and Davidson I (2021) A two-branched upgrade to demonstrate ITV transmission by blood-sucking insects. *Journal of Virological Methods* 296, 114229. <https://doi.org/10.1016/j.jviromet.2021.114229>
- Ben Ayed W, Amraoui F, M'ghirbi Y, Schaffner F, Rhaim A, Failloux A-B and Bouattour A (2019) A survey of *Aedes* (Diptera: Culicidae) mosquitoes in Tunisia and the potential role of *Aedes detritus* and *Aedes caspius* in the transmission of Zika virus. *Journal of Medical Entomology* 56(5), 1377–1383. <https://doi.org/10.1093/jme/tjz067>
- Biskin Z, Duzlu O, Yildirim A and Inci A (2010) The molecular diagnosis of *Dirofilaria immitis* in vector mosquitoes in Felahiye district of Kayseri. *Turkiye Parazitoloji Dergisi* 34(3), 200–205.
- Bohers C, Mousson L, Madec Y, Vazeille M, Rhim A, M'Ghirbi Y, Bouattour A and Failloux AB (2020) The recently introduced *Aedes albopictus* in Tunisia has the potential to transmit Chikungunya, Dengue and Zika viruses. *PLoS Neglected Tropical Diseases* 14(10), e0008475. <https://doi.org/10.1371/journal.pntd.0008475>
- Bowman DD and Atkins CE (2009) Heartworm biology, treatment, and control. *Veterinary Clinics of North America: Small Animal Practice* 39(6), 1127–1158. <https://doi.org/10.1016/j.cvsm.2009.06.003>
- Bowman DD and Wu TK (2022) Canine Filariasis (Heartworm) – Disease and Current Gaps. In Kaminsky, R and Geary, TG (eds), *Human and Animal Filariases*. Wiley-VCH GmbH, pp. 75–96. <https://doi.org/10.1002/9783527823413.ch4>
- Camp JV, Karuvantevida N, Chouhna H, Safi E, Shah JN and Nowotny N (2019) Mosquito biodiversity and mosquito-borne viruses in the United Arab Emirates. *Parasites and Vectors* 12(1), 153. <https://doi.org/10.1186/s13071-019-3417-8>
- Capelli G, Genchi C, Baneth G, Bourdeau P, Brianti E, Cardoso L, Danesi P, Fuehrer HP, Giannelli A, Ionica AM, Maia C, Modry D, Montarsi F, Krucken J, Papadopoulos E, Petric D, Pfeffer M, Savic S, Otranto D, Poppert S and Silaghi C (2018) Recent advances on *Dirofilaria repens* in dogs and humans in Europe. *Parasites and Vectors* 11(1), 663. <https://doi.org/10.1186/s13071-018-3205-x>
- Ceribasi A and Simsek S (2012) Histopathologic effects of *Dirofilaria immitis* microfilariasis on internal organs of dog confirming by PCR technique. *Iranian Journal of Parasitology* 7(2), 103–107.
- Cetinkaya H, Akyazi I, Ozkurt M and Matur E (2016) The serologic and molecular prevalence of Heartworm Disease in shelter dogs in the Thrace Region of Turkey. *Kafkas Universitesi Veteriner Fakultesi Dergisi* 22(5), 751–755. <https://doi.org/10.9775/kvfd.2016.15330>
- Ceylan O, Uslu A, Ozturk O and Sevinc F (2021) Serological investigation of some vector-borne parasitic and rickettsial agents in dogs in the western part of Turkey. *Pakistan Veterinary Journal* 41(3), 386–392. <https://doi.org/10.29261/pakvetj/2021.052>
- Chabchoub A, Landolsi F and Selmi C (2003) Serological survey and clinical study of dirofilariosis with *Dirofilaria immitis* carried out in working dogs in Tunis region (Tunisia). *Revue de Medecine Veterinaire* 154(11), 673–678.
- Chazan B, Scherbakov A, Kerner H and Raz R (2001) Autochthonous subcutaneous dirofilariasis in Israel. *Harefuah* 140(12), 1125–1126. 1232
- Chopra R, Panhotra BR, Al-Marzooq Y and Al-Mulhim AR (2004) Subcutaneous dirofilariasis caused by *Dirofilaria repens*. *Saudi Medical Journal* 25(11), 1694–1696.
- Choudhury PD, Raja D and Sarma V (2023) Human subcutaneous dirofilariasis: A diagnostic dilemma. *Tropical Parasitology* 13(2), 118–121. https://doi.org/10.4103/tp.TP_117_20
- Ciua L, Vismarra A, Lebon W, Beugnet F, Morchon R, Rinaldi L, Cringoli G, Kramer L and Genchi M (2020) New insights into the biology, diagnosis and immune response to *Dirofilaria repens* in the canine host. *Veterinary Parasitology* 4, 100029. <https://doi.org/10.1016/j.vpoa.2020.100029>
- Colak ZN, Kulluk E and Pekmezci D (2020) A rare microfilariuria case in a dog caused by *Dirofilaria immitis*. *Kafkas Universitesi Veteriner Fakultesi Dergisi* 26(4), 579–580. <https://doi.org/10.9775/kvfd.2020.24321>
- Colton L, Miller MM and Reeves WK (2019) New national record for *Culex perexiguus* from Kuwait. *Journal of the American Mosquito Control Association* 35(1), 65–66. <https://doi.org/10.2987/18-6783.1>
- Dababo N, Jain A, Joshi P and Alatoom A (2022) Subconjunctival dirofilariasis: A case report from the United Arab Emirates and review of literature from the Arabian Gulf region. *IJID Regions* 3, 126–128. <https://doi.org/10.1016/j.ijregi.2022.03.014>
- Daheesh S and Ibrahim B (2018) Update on Filariasis in villages of Menshiat Al Qanater District, Giza Governorate, Egypt. *Parasitologists United Journal* 11(1), 32–43. <https://doi.org/10.21608/puj.2017.1714.1003>
- Dantas-Torres F, Ketzis J, Pérez Tort G, Mihalca AD, Baneth G, Otranto D, Watanabe M, Linh BK, Inpankaew T, Borrás P, Arumugam S, Penzhorn BL, Ybañez AP, Irwin P and Traub RJ (2023) Heartworm adulticide treatment: A tropical perspective. *Parasites and Vectors* 16(1), 148. <https://doi.org/10.1186/s13071-023-05690-8>
- Daw MA (2021) The impact of armed conflict on the epidemiological situation of COVID-19 in Libya, Syria and Yemen. *Frontiers in Public Health* 9, 667364. <https://doi.org/10.3389/fpubh.2021.667364>
- Deeks J, Higgins J and Altman DG (2023) Chapter 10: Analysing data and undertaking meta-analyses. Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M and Welch V. (eds.). *Cochrane Handbook for Systematic Reviews of Interventions Version 6.4 (Updated August 2023)*. Cochrane.6.4ed.
- Demirci B, Bedir H, Taskin Tasci G and Vatansever Z (2021) Potential mosquito vectors of *Dirofilaria immitis* and *Dirofilaria repens* (Spirurida: Onchocercidae) in Aras Valley, Turkey. *Journal of Medical Entomology* 58(2), 906–912. <https://doi.org/10.1093/jme/tjaa233>
- Dyab AK, Galal LA, Mahmoud Ael S and Mokhtar Y (2015) Xenomonitoring of different filarial nematodes using single and multiplex PCR in mosquitoes from Assiut Governorate, Egypt. *Korean Journal of Parasitology* 53(1), 77–83. <https://doi.org/10.3347/kjp.2015.53.1.77>
- El Ghassem A, Abdoullah B, Deida J, Ould Lemrabott MA, Ouldabdallahi Moukham M, Ould Ahmedou Salem MS, Briolant S, Basco LK, Ould Ibrahim K and Ould Mohamed Salem Boukhary A (2023) Arthropod-borne viruses in Mauritania: A literature review. *Pathogens* 12(11). <https://doi.org/10.3390/pathogens12111370>
- Elhamiani Khatat S, Khallaayoune K, Errafyk N, Van Gool F, Duchateau L, Daminet S, Kachani M, El Amri H, Azrib R and Sahibi H (2017) Detection of *Anaplasma* spp. and *Ehrlichia* spp. antibodies, and *Dirofilaria immitis* antigens in dogs from seven locations of Morocco. *Veterinary Parasitology* 239, 86–89. <https://doi.org/10.1016/j.vetpar.2017.04.004>
- Fagundes-Moreira R, Bezerra-Santos MA, May-Junior JA, Berger L, Baggio-Souza V, Souza UA, Bilhalva LC, Reis AO, Wagner PGC, Peters FB, Favarini MO, Albano APN, Sartorello L, Rampim LE, Tirelli FP, Otranto D and Soares JF (2024) *Dirofilaria immitis* and *Onchocercidae* spp. in wild felids from Brazil. *Parasitology Research* 123(4), 195. <https://doi.org/10.1007/s00436-024-08209-x>
- Falidas E, Gourgiotis S, Ivopoulou O, Koutsogiannis I, Oikonomou C, Vlachos K and Villias C (2016) Human subcutaneous dirofilariasis caused by *Dirofilaria immitis* in a Greek adult. *Journal of Infection and Public Health* 9(1), 102–104. <https://doi.org/10.1016/j.jiph.2015.06.005>
- Faraj C, Adlaoui E, Brengues C, Fontenille D and Lyagoubi M (2008) Resistance of *Anopheles labranchiae* to DDT in Morocco: Identification of the mechanisms and choice of replacement insecticide. *Eastern Mediterranean Health Journal* 14(4), 776–783.
- Fleck R, Kurz W, Quade B, Geginat G and Hof H (2009) Human dirofilariasis due to *Dirofilaria repens* mimicking a scrotal tumor. *Urology* 73(1), 209e201–203. <https://doi.org/10.1016/j.urology.2008.02.015>
- Genchi C and Kramer L (2017) Subcutaneous dirofilariosis (*Dirofilaria repens*): An infection spreading throughout the old world. *Parasites and Vectors* 10(Suppl 2), 517. <https://doi.org/10.1186/s13071-017-2434-8>
- Genchi C and Kramer LH (2020) The prevalence of *Dirofilaria immitis* and *D. repens* in the Old World. *Veterinary Parasitology* 280, 108995. <https://doi.org/10.1016/j.vetpar.2019.108995>
- Govrin-Yehudain O, Francis N and Bar-Meir E (2017) Dirofilariasis in a female adult patient in Israel. *Israel Medical Association Journal* 19(9), 581–582.
- Gregory TM, Livingston I, Hawkins EC, Loyola A, Cave A, Vaden SL, Deresienski D, Breen M, Riofrio-Lazo M, Lewbart GA and Páez-Rosas D (2023) *Dirofilaria immitis* identified in Galapagos Sea Lions (*Zalophus wollebaeki*): A wildlife health and conservation concern. *Journal of Wildlife Diseases* 59(3), 487–494. <https://doi.org/10.7589/jwd-d-22-00119>

- Gutierrez Y, Misselevich I, Fradis M, Podoshin L and Boss JH (1995) *Dirofilaria repens* infection in northern Israel. *The American Journal of Surgical Pathology* **19**(9), 1088–1091. <https://doi.org/10.1097/00000478-199509000-00014>
- Güven E, Avcioglu H, Cengiz S and Hayirli A (2017) Vector-borne pathogens in stray dogs in northeastern Turkey. *Vector Borne and Zoonotic Diseases* **17**(8), 610–617. <https://doi.org/10.1089/vbz.2017.2128>
- Haddad N, Harbach RE, Chamat S and Bouharoun-Tayoun H (2007) Presence of *Aedes albopictus* in Lebanon and Syria. *Journal of the American Mosquito Control Association* **23**(2), 226–228. [https://doi.org/10.2987/8756-971x\(2007\)23\[226:Poaaill\]2.0.Co;2](https://doi.org/10.2987/8756-971x(2007)23[226:Poaaill]2.0.Co;2)
- Haddad N, Omran H, Amraoui F, Zakhia R, Mousson L and Failloux AB (2022) The tiger mosquito in Lebanon two decades after its introduction: A growing health concern. *PLoS Neglected Tropical Diseases* **16**(2), e0010206. <https://doi.org/10.1371/journal.pntd.0010206>
- Harrer M, Cuijpers P, Furukawa TA and Ebert DD (2022) *Doing Meta-Analysis with R: A Hands on Guide*. CRC Press.
- Harrer M, Cuijpers P, Furukawa T and Ebert DD (2019) dmetar: Companion R Package for the Guide 'Doing Meta-Analysis in R'. <http://dmetar.proctortab.org/> (accessed 3 September 2022).
- Harrus S, Harmelin A, Rodrig S and Favia G (1999) *Dirofilaria repens* infection in a dog in Israel. *The American Journal of Tropical Medicine and Hygiene* **61**(4), 639–641. <https://doi.org/10.4269/ajtmh.1999.61.639>
- Higgins JPT (2008) Commentary: Heterogeneity in meta-analysis should be expected and appropriately quantified. *International Journal of Epidemiology* **37**(5), 1158–1160. <https://doi.org/10.1093/ije/dyn204>
- Higgins JPT and Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* **21**(11), 1539–1558. <https://doi.org/10.1002/sim.1186>
- Hira PR, Al-Buloushi A, Khalid N, Iqbal J, Bain O and Eberhard ML (2008) Case Report: Zoonotic filariasis in the Arabian Peninsula: Autochthonous Onchocerciasis and Dirofilariasis. *American Journal of Tropical Medicine and Hygiene* **79**(5), 739–741. <https://doi.org/10.4269/ajtmh.2008.79.739>
- Hira PR, Madda JP, Alshamali MA and Eberhard ML (1994) Dirofilariasis in Kuwait - First report of human infection due to *Dirofilaria repens* in the Arabian Gulf. *American Journal of Tropical Medicine and Hygiene* **51**(5), 590–592. <https://doi.org/10.4269/ajtmh.1994.51.590>
- Icen H, Sekin S, Simsek A, Kochan A, Celik OY and Altas MG (2011) Prevalence of *Dirofilaria immitis*, *Ehrlichia canis*, *Borrelia burgdorferi* infection in dogs from Diyarbakir in Turkey. *Asian Journal of Animal and Veterinary Advances* **6**(4), 371–378. <https://doi.org/10.3923/ajava.2011.371.378>
- Ismael A, Senok A, Al Khaja K and Botta G (2004) Status of malaria in the Kingdom of Bahrain: A 10-year review. *Journal of Travel Medicine* **11**, 97–101. <https://doi.org/10.2310/7060.2004.17059>
- Izenour K, Zohdy S, Kalalah A, Starkey L, Blagburn B, Sundermann C and Salib F (2022) Detection of zoonotic vector-borne pathogens in domestic dogs in Giza, Egypt. *Veterinary Parasitology: Regional Studies and Reports* **32**, 100744. <https://doi.org/10.1016/j.vprsr.2022.100744>
- Kanani K, Amr Z, Katbeh-Bader A and Arbaji M (2017) First record of *Aedes albopictus* in Jordan. *Journal of the American Mosquito Control Association* **33**(2), 134–135. <https://doi.org/10.2987/17-6641.1>
- Kaouech E, Becheur M, Cheikh M, Belhadj S, Kallel K and Chaker E (2010) Subcutaneous dirofilariasis of the upper lip in Tunisia. *Sante* **20**(1), 47–48. <https://doi.org/10.1684/san.2009.0172>
- Koltas IS, Ozcan K and Duran N (2002) Subconjunctival infection with *Dirofilaria repens*. *Annals of Saudi Medicine* **22**(1–2), 75–76. <https://doi.org/10.5144/0256-4947.2002.75>
- Köse M and Erdogan M (2012) Serological screening of canine heartworm (*Dirofilaria immitis*) infections in Turkey. *Berliner und Münchener Tierärztliche Wochenschrift* **125**(11–12), 503–508.
- Kozlov SS, Ermakova LA, Lobzin YV, Nagorny SA, Kornienko IV, Telicheva VO, Kaliuzhina MA and Pshenichnaya NY (2023) A case of pleuropulmonary dirofilariasis caused by *Dirofilaria repens*. *Case Report. Terapevticheskii Arkhiv* **95**(11), 970–975. <https://doi.org/10.26442/00403660.2023.11.202477>
- Kutluturk I, Tamer GZ, Karabas L, Erbesler AN and Yazar S (2016) A rapidly emerging ocular zoonosis; *Dirofilaria repens*. *Eye* **30**(4), 639–641. <https://doi.org/10.1038/eye.2016.1>
- Latifoglu O, Ozmen S, Sezer C, Yavuzer R, Altintas K and Uluoglu O (2002) *Dirofilaria repens* presenting as a premasseteric nodule. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* **94**(2), 217–220. <https://doi.org/10.1067/moe.2002.125275>
- Lin L, Chu H and Hodges JS (2017) Alternative measures of between-study heterogeneity in meta-analysis: Reducing the impact of outlying studies. *Biometrics* **73**(1), 156–166. <https://doi.org/10.1111/biom.12543>
- Makni F, Hachicha L, Abdelkafi N, Guiaa N, Sellami H, Sellami T and Ayadi A (2007) Subcutaneous *Dirofilaria repens* dirofilariasis in the Sfax region (Tunisia). *Annales de Dermatologie et de Venerologie* **134**(1), 53–54. [https://doi.org/10.1016/s0151-9638\(07\)88990-3](https://doi.org/10.1016/s0151-9638(07)88990-3)
- Mazaki-Tovi M, Reich M, Karnieli A, Kuzi S and Aroch I (2016) Marked subcutaneous mast cell and eosinophilic infiltration associated with the presence of multiple *Dirofilaria repens* microfilariae in 4 dogs. *Veterinary Clinical Pathology* **45**(4), 703–709. <https://doi.org/10.1111/vcp.12410>
- McKay T, Bianco T, Rhodes L and Barnett S (2013) Prevalence of *Dirofilaria immitis* (Nematoda: Filarioidea) in mosquitoes from northeast Arkansas, the United States. *Journal of Medical Entomology* **50**(4), 871–878. <https://doi.org/10.1603/me12197>
- Meriem-Hind BM and Mohamed M (2009) Prevalence of canine *Dirofilaria immitis* infection in the city of Algiers, Algeria. *African Journal of Agricultural Research* **4**(10), 1097–1100.
- Mittal M, Sathish KR, Bhatia PG and Chidamber BS (2008) Ocular dirofilariasis in Dubai, UAE. *Indian Journal of Ophthalmology* **56**(4), 325–326.
- Mohamed A, Hawy A, Sawalhah M and Squires V (2019) Middle East and North Africa Livestock Systems. *Livestock: Production, Management Strategies and Challenges*. Hauppauge, NY, USA: Nova Science Publishers.
- Mohr BJ, Fakoya FA, Hau J, Souilem O and Anestidou L (2017) The Governance of Animal Care and Use for Scientific Purposes in Africa and the Middle East. *ILAR Journal* **57**(3), 333–346. <https://doi.org/10.1093/ilar/ilw035>
- Moustafa MA, Salamah MMI, Thabet HS, Tawfik RA, Mehrez MM and Hamdy DM (2017) Molecular xenomonitoring (MX) and transmission assessment survey (Tas) of lymphatic filariasis elimination in two villages, Menoufyia Governorate, Egypt. *European Journal of Clinical Microbiology & Infectious Diseases* **36**(7), 1143–1150. <https://doi.org/10.1007/s10096-017-2901-3>
- Mrad K, Romani-Ramah S, Driss M, Bougrine F, Hechiche M, Maalej M and Ben Romdhane K (1999) Mammary dirofilariasis - A case report. *International Journal of Surgical Pathology* **7**(3), 175–178. <https://doi.org/10.1177/106689699900700308>
- Munichor M, Gold D, Lengy J, Linn R and Merzbach D (2001) An unusual case of *Dirofilaria conjunctivae* infection suspected to be malignancy of the spermatocord. *Israel Medical Association Journal* **3**(11), 860–861.
- National Institute of Health. National Center for Biotechnology Information. U.S. National Library of Medicine (2022) PubMed. Available at <https://www.ncbi.nlm.nih.gov/pubmed/> (accessed 3 January 2022).
- Nebbak A, Almeras L, Parola P and Bitam I (2022) Mosquito vectors (Diptera: Culicidae) and mosquito-borne diseases in North Africa. *Insects* **13**(10), 962. <https://doi.org/10.3390/insects13100962>
- Noack S, Harrington J, Carithers DS, Kaminsky R and Selzer PM (2021) Heartworm disease – Overview, intervention, and industry perspective. *International Journal for Parasitology: Drugs and Drug Resistance* **16**, 65–89. <https://doi.org/10.1016/j.ijpddr.2021.03.004>
- Obaidat MM and Alshehabat MA (2018) Zoonotic *Anaplasma phagocytophilum*, *Ehrlichia canis*, *Dirofilaria immitis*, *Borrelia burgdorferi*, and spotted fever group rickettsiae (SFGR) in different types of dogs. *Parasitology Research* **117**(11), 3407–3412. <https://doi.org/10.1007/s00436-018-6033-1>
- Oge H, Doganay A, Oge S and Yildirim A (2003) Prevalence and distribution of *Dirofilaria immitis* in domestic dogs from Ankara and vicinity in Turkey. *Deutsche Tierärztliche Wochenschrift* **110**(2), 69–72.
- Omar IO, Elgailani AE, Sawsaana AO, Abdulaziz NA and Osama BM (2018) Seroprevalence of *Dirofilaria immitis* in dogs and cats in Riyadh City, Saudi Arabia. *Tropical Biomedicine* **35**(2), 531–540.

- Oncel T and Vural G (2005) Seroprevalence of *Dirofilaria immitis* in stray dogs in Istanbul and Izmir. *Turkish Journal of Veterinary & Animal Sciences* 29(3), 785–789.
- Otranto D, Iatta R, Baneth G, Cavalera MA, Bianco A, Parisi A, Dantas-Torres F, Colella V, McMillan-Cole AC and Chomel B (2019) High prevalence of vector-borne pathogens in domestic and wild carnivores in Iraq. *Acta Tropica* 197, 105058. <https://doi.org/10.1016/j.actatropica.2019.105058>
- Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P and McKenzie JE (2021) PRISMA 2020 explanation and elaboration: Updated guidance and exemplars for reporting systematic reviews. *The British Medical Journal* 372, n160. <https://doi.org/10.1136/bmj.n160>
- Pandey VS, Dakkak A and Elmamoune M (1987) Parasites of stray dogs in the Rabat region, Morocco. *Annals of Tropical Medicine and Parasitology* 81(1), 53–55. <https://doi.org/10.1080/00034983.1987.11812090>
- Pasa S, Ural K and Gultekin M (2017) Interpretation of coagulation tendency contributing to thrombosis in vector-borne diseases (Ehrlichiosis, Anaplasmosis, Leishmaniosis, and Dirofilariasis) among dogs. *Acta Scientiae Veterinariae* 45. <https://doi.org/10.22456/1679-9216.80033>
- Popescu I, Tudose I, Racu P, Muntau B, Giurcaneanu C and Poppert S (2012) Human *Dirofilaria repens* infection in Romania: A case report. *Case Reports in Infectious Diseases* 2012, 472976. <https://doi.org/10.1155/2012/472976>
- Potkonjak A, Rojas A, Gutierrez R, Nachum-Biala Y, Kleinerman G, Savic S, Polacek V, Pusic I, Harrus S and Baneth G (2020) Molecular survey of *Dirofilaria* species in stray dogs, red foxes and golden jackals from Vojvodina, Serbia. *Comparative Immunology, Microbiology & Infectious Diseases* 68, 101409. <https://doi.org/10.1016/j.cimid.2019.101409>
- Raniel Y, Machamudov Z and Garzozzi HJ (2006) Subconjunctival infection with *Dirofilaria repens*. *Israel Medical Association Journal* 8(2), 139.
- Redón-Soriano M, Blasco A, Gomila B, González-Sánchez M, Simón F and Esteban JG (2022) Subconjunctival human dirofilariasis by *Dirofilaria repens* in the Mediterranean Basin. *American Journal of Ophthalmology Case Reports* 26, 101570. <https://doi.org/10.1016/j.ajoc.2022.101570>
- Reeves WK, Connors B, Miller MM, Berry D, White S, Morey RR and Brooks C (2016) *Culiseta annulata*: A new mosquito for Kuwait. *Journal of the American Mosquito Control Association* 32(4), 323–325. <https://doi.org/10.2987/16-6616.1>
- Riahi N, Yusuf MA, Azari-Hamidian S and Solgi R (2021) Prevalence of *Dirofilaria immitis* in mosquitoes (Diptera) - systematic review and meta-analysis. *Journal of Nematology*, 53. <https://doi.org/10.21307/jofnem-2021-012>
- Rishniw M, Barr SC, Simpson KW, Frongillo ME, Franz M and Dominguez Alpizar JL (2006) Discrimination between six species of canine microfilariae by a single polymerase chain reaction. *Veterinary Parasitology* 135(3–4), 303–314. <https://doi.org/10.1016/j.vetpar.2005.10.013>
- Rjeibi MR, Rouatbi M, Mabrouk M, Tabib I, Rekik M and Gharbi M (2017) Molecular study of *Dirofilaria immitis* and *Dirofilaria repens* in dogs from Tunisia. *Transboundary and Emerging Diseases* 64(5), 1505–1509. <https://doi.org/10.1111/tbed.12541>
- Saied W, Amara K, Bouchoucha S, Khaled S, Mrad K, Nessib MN, Smida M and Ben Ghachem M (2011) An unusual cause of hand nodule: Peri-tendon dirofilariasis. *Chirurgie de la Main* 30(1), 66–68. <https://doi.org/10.1016/j.main.2010.10.012>
- Sari B, Tasci GT and Kilic Y (2013) Seroprevalence of *Dirofilaria immitis*, *Ehrlichia canis* and *Borrelia burgdorferi* in dogs in Igdir Province, Turkey. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi* 19(5), 735–739. <https://doi.org/10.9775/kvfd.2012.8466>
- Sassi SH, Abid L, Dhouib R, Mrad K, Bouguila H, Abbes I, Driss M, Ben Ghorbel R and Ben Romdhane K (2006) Conjunctival dirofilariasis due to *Dirofilaria repens*. A new Tunisian case. *Journal Français d'Ophthalmologie* 29(2), e5.
- Schwarzer G, Carpenter J and Rucker G (2023) *metasens*: Statistical Methods for Sensitivity Analysis in Meta-Analysis ver 1.5-2. <https://CRAN.R-project.org/package=metasens> (accessed 3 September 2022).
- Selim A, Alanazi AD, Sazmand A and Otranto D (2021) Seroprevalence and associated risk factors for vector-borne pathogens in dogs from Egypt. *Parasites and Vectors* 14(1), 175. <https://doi.org/10.1186/s13071-021-04670-0>
- Sevimli FK, Kozan E, Bulbul A, Birdane FM, Kose M and Sevimli A (2007) *Dirofilaria immitis* infection in dogs: Unusually located and unusual findings. *Parasitology Research* 101(6), 1487–1494. <https://doi.org/10.1007/s00436-007-0665-x>
- Sharifi F, Banafshi O, Rasouli A, Ghoreishi S, Saeedi S, Khalesi M, Rezai A, Moradi Asl E, Zareie B, Veisi Khodlan N and Veyssi A (2022) Biodiversity and spatial distribution of mosquitoes (Diptera: Culicidae) in Kurdistan Province, western Iran. *Journal of Arthropod-borne Diseases* 16(4), 350–363. <https://doi.org/10.18502/jad.v16i4.12194>
- Shi L and Lin L (2019) The trim-and-fill method for publication bias: Practical guidelines and recommendations based on a large database of meta-analyses. *Medicine (Baltimore)* 98(23), e15987. <https://doi.org/10.1097/md.00000000000015987>
- Simon F, Lopez-Belmonte J, Marcos-Atxutegi C, Morchon R and Martin-Pacho JR (2005) What is happening outside North America regarding human dirofilariasis? *Veterinary Parasitology* 133(2–3), 181–189. <https://doi.org/10.1016/j.vetpar.2005.03.033>
- Simón F, Prieto G, Morchón R, Bazzocchi C, Bandi C and Genchi C (2003) Immunoglobulin G antibodies against the endosymbionts of filarial nematodes (Wolbachia) in patients with pulmonary dirofilariasis. *Clinical and Diagnostic Laboratory Immunology* 10(1), 180–181. <https://doi.org/10.1128/cdli.10.1.180-181.2003>
- Simón F, Siles-Lucas M, Morchón R, González-Miguel J, Mellado I, Carretón E and Montoya-Alonso JA (2012) Human and animal dirofilariasis: The emergence of a zoonotic mosaic. *Clinical Microbiology Reviews* 25(3), 507–544. <https://doi.org/10.1128/cmr.00012-12>
- Simsek S and Ciftci AT (2016) Serological and molecular detection of *Dirofilaria* species in stray dogs and investigation of Wolbachia DNA by PCR in Turkey. *Journal of Arthropod-borne Diseases* 10(4), 445–453.
- Simsek S, Utuk AE, Koroglu E and Rishniw M (2008) Serological and molecular studies on *Dirofilaria immitis* in dogs from Turkey. *Journal of Helminthology* 82(2), 181–186. <https://doi.org/10.1017/S0022149X0896079X>
- Soussi A, Farah Klibi F, Zermani R, Rammeh S, Ismail O, Zakraoui A, Atallah K and Ben Jilani S (2004) Subcutaneous dirofilariasis due to *Dirofilaria repens* in Tunisia: A case involving the scrotum. *Médecine Tropicale* 64(4), 375–378.
- Stayerman C, Szvalb S and Sazbon A (1999) *Dirofilaria repens* presenting as a subcutaneous nodule in the penis. *BJU International* 84(6), 746–747. <https://doi.org/10.1046/j.1464-410x.1999.00301.x>
- Sterne JAC, Sutton AJ, Ioannidis JPA, Terrin N, Jones DR, Lau J, Carpenter J, Rücker G, Harbord RM, Schmid CH, Tetzlaff J, Deeks JJ, Peters J, Macaskill P, Schwarzer G, Duval S, Altman DG, Moher D and Higgins JPT (2011) Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *The British Medical Journal* 343, d4002. <https://doi.org/10.1136/bmj.d4002>
- Tabbabi A and Daaboub J (2017) Mosquitoes (Diptera: Culicidae) in Tunisia, with Particular Attention to proven and potential vectors: A review. *Journal of Tropical Diseases*, 05. <https://doi.org/10.4172/2329-891X.1000249>
- Tabbabi A and Daaboub J (2018) First studies showing high temephos resistance in *Anopheles labranchiae* (Diptera: Culicidae) from Tunisia. *African Health Sciences* 18(1), 41–47. <https://doi.org/10.4314/ahs.v18i1.7>
- Tabbabi A, Daaboub J, Cheikh RB, Laamari A, Feriani M, Boubaker C, Jha IB and Cheikh HB (2018) Resistance status to deltamethrin pyrethroid of *Culex pipiens pipiens* (Diptera: Culicidae) collected from three districts of Tunisia. *African Health Sciences* 18(4), 1182–1188. <https://doi.org/10.4314/ahs.v18i4.39>
- Tahir D, Damene H, Davoust B and Parola P (2017) First molecular detection of *Dirofilaria immitis* (Spirurida: Onchocercidae) infection in dogs from Northern Algeria. *Comparative Immunology, Microbiology & Infectious Diseases* 51, 66–68. <https://doi.org/10.1016/j.cimid.2017.04.001>
- Tahir F, Bansal D, Rehman AU, Ajur SB, Skariah S, Belhaouari SB, Al-Romaihi H, Al-Thani MHJ, Farag E, Sultan AA and Al-Ghamdi SG (2022) Assessing the impact of climate conditions on the distribution of mosquito

- species in Qatar. *Frontiers in Public Health* **10**, 970694. <https://doi.org/10.3389/fpubh.2022.970694>
- Tarello W (2002) Dermatitis associated with *Dirofilaria repens* microfilariae in a dog in Dubai. *The Veterinary Record* **151**(24), 738–739. <https://doi.org/10.1136/vr.151.24.738>
- Tarello W (2003) Dermatitis associated with *Dirofilaria repens* microfilariae in three dogs in Saudi Arabia. *Journal of Small Animal Practice* **44**(3), 132–134. <https://doi.org/10.1111/j.1748-5827.2003.tb00134.x>
- Tarello W (2008) Autochthonous *Dirofilaria* (Nochtiella) *repens* infection in dogs in Kuwait. *Zoonoses and Public Health* **55**(6), 328–330. <https://doi.org/10.1111/j.1863-2378.2008.01140.x>
- Tarish JH, Al-Saqur IM, Al-Abbassy SN and Kadhim FS (1986) The prevalence of parasitic helminths in stray dogs in the Baghdad area, Iraq. *Annals of Tropical Medicine and Parasitology* **80**(3), 329–331. <https://doi.org/10.1080/00034983.1986.11812024>
- Tasci GT and Kilic Y (2012) The prevalence of *Dirofilaria immitis* (Leidy, 1856) in dogs and investigations on potential vector mosquito species in Kars and Igdir. *Kafkas Universitesi Veteriner Fakultesi Dergisi* **18**, A29–A34.
- Thorlund K, Imberger G, Johnston BC, Walsh M, Awad T, Thabane L, Gluud C, Devereaux PJ and Wetterslev J (2012) Evolution of heterogeneity (I²) estimates and their 95% confidence intervals in large meta-analyses. *PloS One* **7**(7), e39471. <https://doi.org/10.1371/journal.pone.0039471>
- Tsai -C-C, Chang Y-C and Chang IW (2024) Human pulmonary dirofilariasis mimicking a metastatic disease in a cancer patient. *Asian Journal of Surgery* **47**(1), 538–539. <https://doi.org/10.1016/j.asjsur.2023.09.096>
- Tucker CJ, Melocik KA, Anyamba A, Linthicum KJ, Fagbo SF and Small JL (2020) Reanalysis of the 2000 Rift Valley fever outbreak in Southwestern Arabia. *PloS One* **15**(12), e0233279. <https://doi.org/10.1371/journal.pone.0233279>
- Ullah MM, Al Balushi A, Al Aliyani NRS, Kalarikkal B, Miranda RIC, Sherif SM, Al Habsi ASM, Al Saidi EK, Anver A and Qassem NH (2020) Imported bancroftian filariasis discovered in a patient infected with *Plasmodium falciparum*: First case of concomitant parasitism in the Al-Buraimi Governorate, Oman. *Infectious Disease Reports* **12**(1), 8304. <https://doi.org/10.4081/idr.2020.8304>
- Ural K, Gultekin M, Atasoy A and Ulutas B (2014) Spatial distribution of vector borne disease agents in dogs in Aegean region, Turkey. *Revista Mvz Cordoba* **19**(2), 4086–4098. <https://doi.org/10.21897/rmvz.102>
- Valčiukaitė-Žilinskienė R, Zablockienė B and Zablockis R (2024) Dirofilariasis presenting as pleural effusion: A rare case report with unusual manifestations and treatment modalities. *BMC Pulmonary Medicine* **24**(1), 340. <https://doi.org/10.1186/s12890-024-03154-y>
- Varela R, Rodríguez-Díaz L and deCastro M (2020) Persistent heat waves projected for Middle East and North Africa by the end of the 21st century. *PloS One* **15**(11), e0242477. <https://doi.org/10.1371/journal.pone.0242477>
- Viechtbauer W (2010) Conducting Meta-Analyses in R with the metafor Package. *Journal of Statistical Software* **36**(3), 1–48. <https://doi.org/10.18637/jss.v036.i03>
- Villanueva-Saz S, Giner J, Verde M, Yzuel A, Gonzalez A, Lacasta D, Marteles D and Fernandez A (2021) Prevalence of microfilariae, antigen and antibodies of feline dirofilariasis infection (*Dirofilaria immitis*) in the Zaragoza metropolitan area, Spain. *Veterinary Parasitology, Regional Studies and Reports* **23**, 100541. <https://doi.org/10.1016/j.vprsr.2021.100541>
- Voyvoda H, Pasa S, Toz SO, Ozbel Y and Ertabaklar H (2004) Prevalence of *Leishmania infantum* and *Dirofilaria immitis* infection in dogs in Aydin province and the town of Selcuk, Izmir, Turkey. *Turkish Journal of Veterinary & Animal Sciences* **28**(6), 1105–1111.
- Wickham H, Averick M, Bryan J, Chang W, McGowan L D and Francois R (2019) Welcome to the Tidyverse. *Journal of Open Source Software* **4**(43). <https://doi.org/10.21105/joss.01686>
- Wickham H and Bryan J (2023) Readxl: Read Excel Files ver 1.4.3. <https://github.com/tidyverse/readxl> (accessed 17 June 2024).
- Wickham H, Hester J, Chang W and Bryan J (2022) Devtools: Tools to Make Developing R Packages Easier. <https://github.com/r-lib/devtools> (accessed 17 June 2024).
- Yaman M, Guzel M, Koltas IS, Demirkazik M and Aktas H (2009) Prevalence of *Dirofilaria immitis* in dogs from Hatay province, Turkey. *Journal of Helminthology* **83**(3), 255–260. <https://doi.org/10.1017/S0022149X08198832>
- Yildirim A, Ica A, Atalay O, Duzlu O and Inci A (2007) Prevalence and epidemiological aspects of *Dirofilaria immitis* in dogs from Kayseri Province, Turkey. *Research in Veterinary Science* **82**(3), 358–363. <https://doi.org/10.1016/j.rvsc.2006.08.006>
- Yildirim A, Inci A, Duzlu O, Biskin Z, Ica A and Sahin I (2011) *Aedes vexans* and *Culex pipiens* as the potential vectors of *Dirofilaria immitis* in Central Turkey. *Veterinary Parasitology* **178**(1–2), 143–147. <https://doi.org/10.1016/j.vetpar.2010.12.023>
- Yildiz K, Duru SY, Yagci BB, Ocal N and Gazyagci AN (2008) The prevalence of *Dirofilaria immitis* in dogs in Kirikkale. *Turkiye Parazitoloji Dergisi* **32**(3), 225–228.
- Zakhia R, Dupuis AP, 2nd, Khodr F, Fadel M, Kramer LD and Haddad N (2021) Evidence of West Nile virus circulation in Lebanon. *Viruses* **13**(6). <https://doi.org/10.3390/v13060994>
- Ziadi S, Trimeche M, Mestiri S, Mokni M, Trabelsi A, Ben Abdelkader A, Ben Said M, Ben Hadj Hamida F and Korbi S (2005) Human subconjunctival dirofilariasis: Two Tunisian case studies. *Journal Français d'Ophtalmologie* **28**(7), 773. [https://doi.org/10.1016/s0181-5512\(05\)80993-3](https://doi.org/10.1016/s0181-5512(05)80993-3)